ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 75 mg solution for injection in pre-filled syringe

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pre-filled syringe contains 75 mg secukinumab in 0.5 ml.

Secukinumab is a recombinant fully human monoclonal antibody produced in Chinese Hamster Ovary (CHO) cells.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection)

The solution is clear and colourless to slightly yellow.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Paediatric plaque psoriasis

Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years who are candidates for systemic therapy.

Juvenile idiopathic arthritis (JIA)

Enthesitis-related arthritis (ERA)
Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active enthesitis-related arthritis in patients 6 years and older whose disease has responded inadequately to, or who cannot tolerate, conventional therapy (see section 5.1).

Juvenile psoriatic arthritis (JPsA)
Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active juvenile psoriatic arthritis in patients 6 years and older whose disease has responded inadequately to, or who cannot tolerate, conventional therapy (see section 5.1).

4.2 Posology and method of administration

Cosentyx is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of conditions for which Cosentyx is indicated.

Posology

Paediatric plaque psoriasis (adolescents and children from the age of 6 years)
The recommended dose is based on body weight (Table 1) and administered by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 75 mg dose is given as one subcutaneous injection of 75 mg. Each 150 mg dose is given as one subcutaneous injection of 150 mg. Each 300 mg dose is given as one subcutaneous injection of 300 mg or as two subcutaneous injections of 150 mg.

Table 1 Recommended dose for paediatric plaque psoriasis

Body weight at time of dosing	Recommended dose
<25 kg	75 mg
25 to <50 kg	75 mg
≥50 kg	150 mg (*may be increased to 300 mg)

*Some patients may derive additional benefit from the higher dose.

Juvenile idiopathic arthritis (JIA)

Enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA)
The recommended dose is based on body weight (Table 2) and administered by subcutaneous injection at weeks 0, 1, 2, 3, and 4, followed by monthly maintenance dosing. Each 75 mg dose is given as one subcutaneous injection of 75 mg. Each 150 mg dose is given as one subcutaneous injection of 150 mg.

Table 2 Recommended dose for juvenile idiopathic arthritis

Body weight at time of dosing	Recommended dose
<50 kg	75 mg
≥50 kg	150 mg

Cosentyx may be available in other strengths and/or presentations depending on the individual treatment needs.

For all of the above indications, available data suggest that a clinical response is usually achieved within 16 weeks of treatment. Consideration should be given to discontinuing treatment in patients who have shown no response by 16 weeks of treatment. Some patients with an initial partial response may subsequently improve with continued treatment beyond 16 weeks.

The safety and efficacy of Cosentyx in children with plaque psoriasis and in the juvenile idiopathic arthritis (JIA) categories of ERA and JPsA below the age of 6 years have not been established.

The safety and efficacy of Cosentyx in children below the age of 18 years in other indications have not yet been established. No data are available.

Special populations

Renal impairment / hepatic impairment
Cosentyx has not been studied in these patient populations. No dose recommendations can be made.

Method of administration

Cosentyx is to be administered by subcutaneous injection. If possible, areas of the skin that show psoriasis should be avoided as injection sites. The syringe must not be shaken.

After proper training in subcutaneous injection technique, patients may self-inject Cosentyx or be injected by a caregiver if a physician determines that this is appropriate. However, the physician should ensure appropriate follow-up of patients. Patients or caregivers should be instructed to inject the full amount of Cosentyx according to the instructions provided in the package leaflet. Comprehensive instructions for administration are given in the package leaflet.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Clinically important, active infection, e.g. active tuberculosis (see section 4.4).

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Infections

Secukinumab has the potential to increase the risk of infections. Serious infections have been observed in patients receiving secukinumab in the post-marketing setting. Caution should be exercised when considering the use of secukinumab in patients with a chronic infection or a history of recurrent infection.

Patients should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, the patient should be closely monitored and secukinumab should not be administered until the infection resolves.

In clinical studies, infections have been observed in patients receiving secukinumab (see section 4.8). Most of these were mild or moderate upper respiratory tract infections such as nasopharyngitis and did not require treatment discontinuation.

Related to the mechanism of action of secukinumab, non-serious mucocutaneous candida infections were more frequently reported for secukinumab than placebo in the psoriasis clinical studies (3.55 per 100 patient years for secukinumab 300 mg versus 1.00 per 100 patient years for placebo) (see section 4.8).

No increased susceptibility to tuberculosis was reported from clinical studies. However, secukinumab should not be given to patients with active tuberculosis. Anti-tuberculosis therapy should be considered prior to initiation of secukinumab in patients with latent tuberculosis.

Inflammatory bowel disease (including Crohn's disease and ulcerative colitis)

Cases of new or exacerbations of inflammatory bowel disease have been reported with secukinumab (see section 4.8). Secukinumab is not recommended in patients with inflammatory bowel disease. If a patient develops signs and symptoms of inflammatory bowel disease or experiences an exacerbation of pre-existing inflammatory bowel disease, secukinumab should be discontinued and appropriate medical management should be initiated.

Hypersensitivity reactions

In clinical studies, rare cases of anaphylactic reactions have been observed in patients receiving secukinumab. If an anaphylactic or other serious allergic reactions occur, administration of secukinumab should be discontinued immediately and appropriate therapy initiated.

Latex-sensitive individuals

The removable needle cap of Cosentyx 75 mg solution for injection in pre-filled syringe contains a derivative of natural rubber latex. No natural rubber latex has to date been detected in the removable needle cap. Nevertheless, the use of Cosentyx 75 mg solution for injection in pre-filled syringe in latex-sensitive individuals has not been studied and there is therefore a potential risk of hypersensitivity reactions which cannot be completely ruled out.

Vaccinations

Live vaccines should not be given concurrently with secukinumab.

Patients receiving secukinumab may receive concurrent inactivated or non-live vaccinations. In a study, after *meningococcal* and inactivated *influenza* vaccinations, a similar proportion of healthy volunteers treated with 150 mg of secukinumab and those treated with placebo were able to mount an adequate immune response of at least a 4-fold increase in antibody titres to *meningococcal* and *influenza* vaccines. The data suggest that secukinumab does not suppress the humoral immune response to the *meningococcal* or *influenza* vaccines.

Prior to initiating therapy with Cosentyx, it is recommended that paediatric patients receive all age-appropriate immunisations as per current immunisation guidelines.

Concomitant immunosuppressive therapy

In psoriasis studies, the safety and efficacy of secukinumab in combination with immunosuppressants, including biologics, or phototherapy have not been evaluated. Secukinumab was administered concomitantly with methotrexate (MTX), sulfasalazine and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and ankylosing spondylitis). Caution should be exercised when considering concomitant use of other immunosuppressants and secukinumab (see also section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

Live vaccines should not be given concurrently with secukinumab (see also section 4.4).

In a study in adult subjects with plaque psoriasis, no interaction was observed between secukinumab and midazolam (CYP3A4 substrate).

No interaction was seen when secukinumab was administered concomitantly with methotrexate (MTX) and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and axial spondyloarthritis).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 20 weeks after treatment.

Pregnancy

There are no adequate data from the use of secukinumab in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Cosentyx during pregnancy.

Breast-feeding

It is not known whether secukinumab is excreted in human milk. Immunoglobulins are excreted in human milk and it is not known if secukinumab is absorbed systemically after ingestion. Because of the potential for adverse reactions in nursing infants from secukinumab, a decision on whether to discontinue breast-feeding during treatment and up to 20 weeks after treatment or to discontinue therapy with Cosentyx must be made taking into account the benefit of breast-feeding to the child and the benefit of therapy to the woman.

Fertility

The effect of secukinumab on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility.

4.7 Effects on ability to drive and use machines

Cosentyx has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse reactions are upper respiratory tract infections (17.1%) (most frequently nasopharyngitis, rhinitis).

Tabulated list of adverse reactions

Adverse reactions from clinical studies and post-marketing reports (Table 3) are listed by MedDRA system organ class. Within each system organ class, the adverse reactions are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse reaction is based on the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1 000 to <1/100); rare (≥1/10 000 to <1/1 000); very rare (<1/10 000); and not known (cannot be estimated from the available data).

Over 20 000 patients have been treated with secukinumab in blinded and open-label clinical studies in various indications (plaque psoriasis, psoriatic arthritis, axial spondyloarthritis, hidradenitis suppurativa [HS] and other autoimmune conditions), representing 34 908 patient years of exposure. Of these, over 14 000 patients were exposed to secukinumab for at least one year. The safety profile of secukinumab is consistent across all indications.

Table 3 List of adverse reactions in clinical studies[1)] and post-marketing experience

System organ class	Frequency	Adverse reaction
Infections and infestations	Very common	Upper respiratory tract infections
	Common	Oral herpes
	Uncommon	Oral candidiasis
		Otitis externa
		Lower respiratory tract infections
		Tinea pedis
	Not known	Mucosal and cutaneous candidiasis (including oesophageal candidiasis)
Blood and lymphatic system disorders	Uncommon	Neutropenia
Immune system disorders	Rare	Anaphylactic reactions
Nervous system disorders	Common	Headache
Eye disorders	Uncommon	Conjunctivitis
Respiratory, thoracic and mediastinal disorders	Common	Rhinorrhoea
Gastrointestinal disorders	Common	Diarrhoea
	Common	Nausea
	Uncommon	Inflammatory bowel disease
Skin and subcutaneous tissue disorders	Uncommon	Urticaria
		Dyshidrotic eczema
	Rare	Exfoliative dermatitis[2)]
		Hypersensitivity vasculitis
	Not known	Pyoderma gangrenosum
General disorders and administration site conditions	Common	Fatigue

[1)] Placebo-controlled clinical studies (phase III) in plaque psoriasis, PsA, AS, nr-axSpA and HS patients exposed to 300 mg, 150 mg, 75 mg or placebo up to 12 weeks (psoriasis) or 16 weeks (PsA, AS, nr-axSpA and HS) treatment duration
[2)] Cases were reported in patients with psoriasis diagnosis

Description of selected adverse reactions

Infections
In the placebo-controlled period of clinical studies in plaque psoriasis (a total of 1 382 patients treated with secukinumab and 694 patients treated with placebo for up to 12 weeks), infections were reported in 28.7% of patients treated with secukinumab compared with 18.9% of patients treated with placebo. The majority of infections consisted of non-serious and mild to moderate upper respiratory tract infections, such as nasopharyngitis, which did not necessitate treatment discontinuation. There was an increase in mucosal or cutaneous candidiasis, consistent with the mechanism of action, but the cases were mild or moderate in severity, non-serious, responsive to standard treatment and did not necessitate treatment discontinuation. Serious infections occurred in 0.14% of patients treated with secukinumab and in 0.3% of patients treated with placebo (see section 4.4).

Over the entire treatment period (a total of 3 430 patients treated with secukinumab for up to 52 weeks for the majority of patients), infections were reported in 47.5% of patients treated with secukinumab (0.9 per patient-year of follow-up). Serious infections were reported in 1.2% of patients treated with secukinumab (0.015 per patient-year of follow-up).

Infection rates observed in psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) clinical studies were similar to those observed in the psoriasis studies.

Patients with hidradenitis suppurativa are more susceptible to infections. In the placebo-controlled period of clinical studies in hidradenitis suppurativa (a total of 721 patients treated with secukinumab and 363 patients treated with placebo for up to 16 weeks), infections were numerically higher compared to those observed in the psoriasis studies (30.7% of patients treated with secukinumab compared with 31.7% in patients treated with placebo). Most of these were non-serious, mild or moderate in severity and did not require treatment discontinuation or interruption.

Neutropenia
In psoriasis phase III clinical studies, neutropenia was more frequently observed with secukinumab than with placebo, but most cases were mild, transient and reversible. Neutropenia <1.0-0.5x10^9/l (CTCAE grade 3) was reported in 18 out of 3 430 (0.5%) patients on secukinumab, with no dose dependence and no temporal relationship to infections in 15 out of 18 cases. There were no reported cases of more severe neutropenia. Non-serious infections with usual response to standard care and not requiring discontinuation of secukinumab were reported in the remaining 3 cases.

The frequency of neutropenia in psoriatic arthritis, axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) and hidradenitis suppurativa was similar to psoriasis.

Rare cases of neutropenia <0.5x10^9/l (CTCAE grade 4) were reported.

Hypersensitivity reactions
In clinical studies, urticaria and rare cases of anaphylactic reaction to secukinumab were observed (see also section 4.4).

Immunogenicity
In psoriasis, psoriatic arthritis, axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) and hidradenitis suppurativa clinical studies, less than 1% of patients treated with secukinumab developed antibodies to secukinumab up to 52 weeks of treatment. About half of the treatment-emergent anti-drug antibodies were neutralising, but this was not associated with loss of efficacy or pharmacokinetic abnormalities.

Paediatric population

Undesirable effects in paediatric patients from the age of 6 years with plaque psoriasis
The safety of secukinumab was assessed in two phase III studies in paediatric patients with plaque psoriasis. The first study (paediatric study 1) was a double-blind, placebo-controlled study of 162 patients from 6 to less than 18 years of age with severe plaque psoriasis. The second study (paediatric study 2) is an open-label study of 84 patients from 6 to less than 18 years of age with moderate to severe plaque psoriasis. The safety profile reported in these two studies was consistent with the safety profile reported in adult plaque psoriasis patients.

Undesirable effects in paediatric patients with JIA
The safety of secukinumab was also assessed in a phase III study in 86 juvenile idiopathic arthritis patients with ERA and JPsA from 2 to less than 18 years of age. The safety profile reported in this study was consistent with the safety profile reported in adult patients.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Doses up to 30 mg/kg (approximately 2000 to 3000 mg) have been administered intravenously in clinical studies without dose-limiting toxicity. In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC10

Mechanism of action

Secukinumab is a fully human IgG1/κ monoclonal antibody that selectively binds to and neutralises the proinflammatory cytokine interleukin-17A (IL-17A). Secukinumab works by targeting IL-17A and inhibiting its interaction with the IL-17 receptor, which is expressed on various cell types including keratinocytes. As a result, secukinumab inhibits the release of proinflammatory cytokines, chemokines and mediators of tissue damage and reduces IL-17A-mediated contributions to autoimmune and inflammatory diseases. Clinically relevant levels of secukinumab reach the skin and reduce local inflammatory markers. As a direct consequence treatment with secukinumab reduces erythema, induration and desquamation present in plaque psoriasis lesions.

IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. IL-17A plays a key role in the pathogenesis of plaque psoriasis, psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) and is up-regulated in lesional skin in contrast to non-lesional skin of plaque psoriasis patients and in synovial tissue of psoriatic arthritis patients. The frequency of IL-17-producing cells was also significantly higher in the subchondral bone marrow of facet joints from patients with ankylosing spondylitis. Increased numbers of IL-17A producing lymphocytes have also been found in patients with non-radiographic axial spondyloarthritis. Inhibition of IL-17A was shown to be effective in the treatment of ankylosing spondylitis, thus establishing the key role of this cytokine in axial spondyloarthritis.

Pharmacodynamic effects

Serum levels of total IL-17A (free and secukinumab-bound IL-17A) are initially increased in patients receiving secukinumab. This is followed by a slow decrease due to reduced clearance of secukinumab-bound IL-17A, indicating that secukinumab selectively captures free IL-17A, which plays a key role in the pathogenesis of plaque psoriasis.

In a study with secukinumab, infiltrating epidermal neutrophils and various neutrophil-associated markers that are increased in lesional skin of plaque psoriasis patients were significantly reduced after one to two weeks of treatment.

Secukinumab has been shown to lower (within 1 to 2 weeks of treatment) levels of C-reactive protein, which is a marker of inflammation.

Clinical efficacy and safety

Adult plaque psoriasis
The safety and efficacy of secukinumab were assessed in four randomised, double-blind, placebo-controlled phase III studies in patients with moderate to severe plaque psoriasis who were candidates for phototherapy or systemic therapy [ERASURE, FIXTURE, FEATURE, JUNCTURE]. The efficacy and safety of secukinumab 150 mg and 300 mg were evaluated versus either placebo or etanercept. In addition, one study assessed a chronic treatment regimen versus a "retreatment as needed" regimen [SCULPTURE].

Of the 2 403 patients who were included in the placebo-controlled studies, 79% were biologic-naive, 45% were non-biologic failures and 8% were biologic failures (6% were anti-TNF failures, and 2% were anti-p40 failures). Approximately 15 to 25% of patients in phase III studies had psoriatic arthritis (PsA) at baseline.

Psoriasis study 1 (ERASURE) evaluated 738 patients. Patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Psoriasis study 2 (FIXTURE) evaluated 1 306 patients. Patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients randomised to etanercept received 50 mg doses twice per week for 12 weeks followed by 50 mg every week. In both study 1 and study 2, patients randomised to receive placebo who were non-responders at week 12 then crossed over to receive secukinumab (either 150 mg or 300 mg) at weeks 12, 13, 14, and 15, followed by the same dose every month starting at week 16. All patients were followed for up to 52 weeks following first administration of study treatment.

Psoriasis study 3 (FEATURE) evaluated 177 patients using a pre-filled syringe compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of secukinumab self-administration via the pre-filled syringe. Psoriasis study 4 (JUNCTURE) evaluated 182 patients using a pre-filled pen compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of secukinumab self-administration via the pre-filled pen. In both study 3 and study 4, patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients were also randomised to receive placebo at weeks 0, 1, 2, 3 and 4, followed by the same dose every month.

Psoriasis study 5 (SCULPTURE) evaluated 966 patients. All patients received secukinumab 150 mg or 300 mg doses at weeks 0, 1, 2, 3, 4, 8 and 12 and then were randomised to receive either a maintenance regimen of the same dose every month starting at week 12 or a "retreatment as needed" regimen of the same dose. Patients randomised to "retreatment as needed" did not achieve adequate maintenance of response and therefore a fixed monthly maintenance regimen is recommended.

The co-primary endpoints in the placebo and active-controlled studies were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 "clear" or "almost clear" response versus placebo at week 12 (see Tables 4 and 5). The 300 mg dose provided improved skin clearance particularly for "clear" or "almost clear" skin across the efficacy endpoints of PASI 90, PASI 100, and IGA mod 2011 0 or 1 response across all studies with peak effects seen at week 16, therefore this dose is recommended.

Table 4 Summary of PASI 50/75/90/100 & IGA* mod 2011 "clear" or "almost clear" clinical response in psoriasis studies 1, 3 and 4 (ERASURE, FEATURE and JUNCTURE)

		Week 12		Week 16		Week 52	
	Placebo	**150 mg**	**300 mg**	**150 mg**	**300 mg**	**150 mg**	**300 mg**
Study 1							
Number of patients	246	244	245	244	245	244	245
PASI 50 response n (%)	22 (8.9%)	203 (83.5%)	222 (90.6%)	212 (87.2%)	224 (91.4%)	187 (77%)	207 (84.5%)
PASI 75 response n (%)	11 (4.5%)	174 (71.6%)**	200 (81.6%)**	188 (77.4%)	211 (86.1%)	146 (60.1%)	182 (74.3%)
PASI 90 response n (%)	3 (1.2%)	95 (39.1%)**	145 (59.2%)**	130 (53.5%)	171 (69.8%)	88 (36.2%)	147 (60.0%)
PASI 100 response n (%)	2 (0.8%)	31 (12.8%)	70 (28.6%)	51 (21.0%)	102 (41.6%)	49 (20.2%)	96 (39.2%)
IGA mod 2011 "clear" or "almost clear" response n (%)	6 (2.40%)	125 (51.2%)**	160 (65.3%)**	142 (58.2%)	180 (73.5%)	101 (41.4%)	148 (60.4%)
Study 3							
Number of patients	59	59	58	-	-	-	-
PASI 50 response n (%)	3 (5.1%)	51 (86.4%)	51 (87.9%)	-	-	-	-
PASI 75 response n (%)	0 (0.0%)	41 (69.5%)**	44 (75.9%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	27 (45.8%)	35 (60.3%)	-	-	-	-
PASI 100 response n (%)	0 (0.0%)	5 (8.5%)	25 (43.1%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	31 (52.5%)**	40 (69.0%)**	-	-	-	-
Study 4							
Number of patients	61	60	60	-	-	-	-
PASI 50 response n (%)	5 (8.2%)	48 (80.0%)	58 (96.7%)	-	-	-	-
PASI 75 response n (%)	2 (3.3%)	43 (71.7%)**	52 (86.7%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	24 (40.0%)	33 (55.0%)	-	-	-	-
PASI 100 response n(%)	0 (0.0%)	10 (16.7%)	16 (26.7%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	32 (53.3%)**	44 (73.3%)**	-	-	-	-

* The IGA mod 2011 is a 5-category scale including "0 = clear", "1 = almost clear", "2 = mild", "3 = moderate" or "4 = severe", indicating the physician's overall assessment of the psoriasis severity focusing on induration, erythema and scaling. Treatment success of "clear" or "almost clear" consisted of no signs of psoriasis or normal to pink colouration of lesions, no thickening of the plaque and none to minimal focal scaling.

** p-values versus placebo and adjusted for multiplicity: $p<0.0001$.

Table 5 Summary of clinical response on psoriasis study 2 (FIXTURE)

	Week 12				Week 16			Week 52		
	Placebo	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**
Number of patients	324	327	323	323	327	323	323	327	323	323
PASI 50 response n (%)	49 (15.1%)	266 (81.3%)	296 (91.6%)	226 (70.0%)	290 (88.7%)	302 (93.5%)	257 (79.6%)	249 (76.1%)	274 (84.8%)	234 (72.4%)
PASI 75 response n (%)	16 (4.9%)	219 (67.0%) **	249 (77.1%) **	142 (44.0%)	247 (75.5%)	280 (86.7%)	189 (58.5%)	215 (65.7%)	254 (78.6%)	179 (55.4%)
PASI 90 response n (%)	5 (1.5%)	137 (41.9%)	175 (54.2%)	67 (20.7%)	176 (53.8%)	234 (72.4%)	101 (31.3%)	147 (45.0%)	210 (65.0%)	108 (33.4%)
PASI 100 response n (%)	0 (0%)	47 (14.4%)	78 (24.1%)	14 (4.3%)	84 (25.7%)	119 (36.8%)	24 (7.4%)	65 (19.9%)	117 (36.2%)	32 (9.9%)
IGA mod 2011 “clear” or “almost clear” response n (%)	9 (2.8%)	167 (51.1%) **	202 (62.5%) **	88 (27.2%)	200 (61.2%)	244 (75.5%)	127 (39.3%)	168 (51.4%)	219 (67.8%)	120 (37.2%)

** p-values versus etanercept: p=0.0250

In an additional psoriasis study (CLEAR) 676 patients were evaluated. Secukinumab 300 mg met the primary and secondary endpoints by showing superiority to ustekinumab based on PASI 90 response at week 16 (primary endpoint), speed of onset of PASI 75 response at week 4, and long-term PASI 90 response at week 52. Greater efficacy of secukinumab compared to ustekinumab for the endpoints PASI 75/90/100 and IGA mod 2011 0 or 1 response (“clear” or “almost clear”) was observed early and continued through to week 52 (Table 6).

Table 6 Summary of clinical response on CLEAR study

	Week 4		Week 16		Week 52	
	Secukinumab 300 mg	**Ustekinumab***	**Secukinumab 300 mg**	**Ustekinumab***	**Secukinumab 300 mg**	**Ustekinumab***
Number of patients	334	335	334	335	334	335
PASI 75 response n (%)	166 (49.7%)**	69 (20.6%)	311 (93.1%)	276 (82.4%)	306 (91.6%)	262 (78.2%)
PASI 90 response n (%)	70 (21.0%)	18 (5.4%)	264 (79.0%)**	192 (57.3%)	250 (74.9%)***	203 (60.6%)
PASI 100 response n (%)	14 (4.2%)	3 (0.9%)	148 (44.3%)	95 (28.4%)	150 (44.9%)	123 (36.7%)
IGA mod 2011 “clear” or “almost clear” response n (%)	128 (38.3%)	41 (12.2%)	278 (83.2%)	226 (67.5%)	261 (78.1%)	213 (63.6%)

* Patients treated with secukinumab received 300 mg doses at weeks 0, 1, 2 3 and 4, followed by the same dose every 4 weeks until week 52. Patients treated with ustekinumab received 45 mg or 90 mg at weeks 0 and 4, then every 12 weeks until week 52 (dosed by weight as per approved posology)

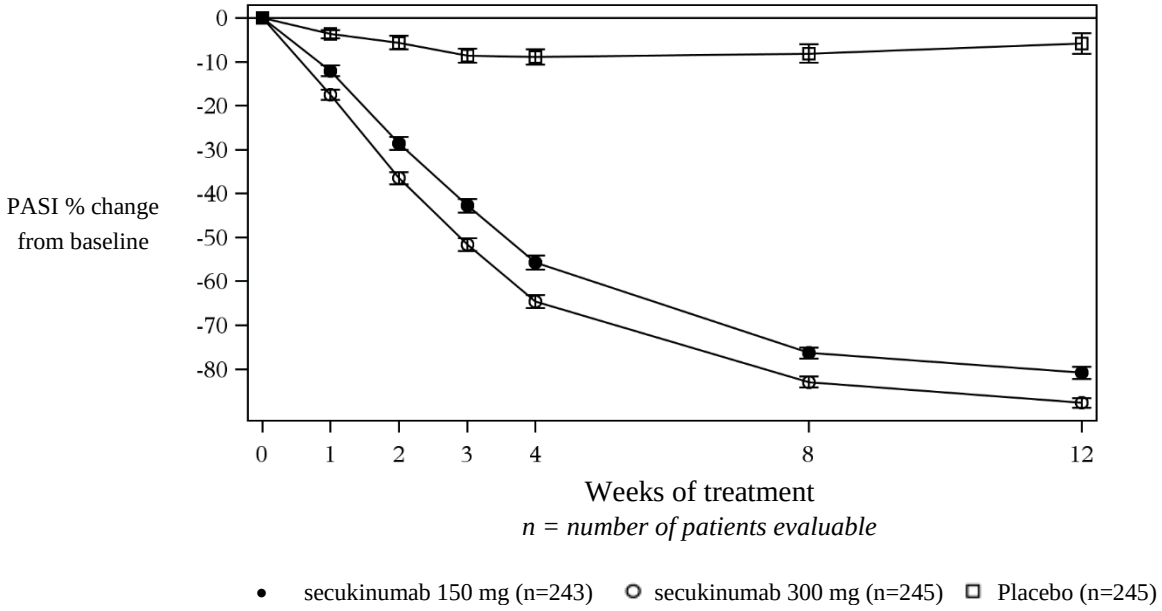
** p-values versus ustekinumab: p<0.0001 for primary endpoint of PASI 90 at week 16 and secondary endpoint of PASI 75 at week 4

*** p-values versus ustekinumab: p=0.0001 for secondary endpoint of PASI 90 at week 52

Secukinumab was efficacious in systemic treatment-naive, biologic-naive, biologic/anti-TNF-exposed and biologic/anti-TNF-failure patients. Improvements in PASI 75 in patients with concurrent psoriatic arthritis at baseline were similar to those in the overall plaque psoriasis population.

Secukinumab was associated with a fast onset of efficacy with a 50% reduction in mean PASI by week 3 for the 300 mg dose.

Figure 1 Time course of percentage change from baseline of mean PASI score in study 1 (ERASURE)



Specific locations/forms of plaque psoriasis
In two additional placebo-controlled studies, improvement was seen in both nail psoriasis (TRANSFIGURE, 198 patients) and palmoplantar plaque psoriasis (GESTURE, 205 patients). In the TRANSFIGURE study, secukinumab was superior to placebo at week 16 (46.1% for 300 mg, 38.4% for 150 mg and 11.7% for placebo) as assessed by significant improvement from baseline in the Nail Psoriasis Severity Index (NAPSI %) for patients with moderate to severe plaque psoriasis with nail involvement. In the GESTURE study, secukinumab was superior to placebo at week 16 (33.3% for 300 mg, 22.1% for 150 mg, and 1.5% for placebo) as assessed by significant improvement of ppIGA 0 or 1 response ("clear" or "almost clear") for patients with moderate to severe palmoplantar plaque psoriasis.

A placebo-controlled study evaluated 102 patients with moderate to severe scalp psoriasis, defined as having a Psoriasis Scalp Severity Index (PSSI) score of ≥12, an IGA mod 2011 scalp only score of 3 or greater and at least 30% of the scalp surface area affected. Secukinumab 300 mg was superior to placebo at week 12 as assessed by significant improvement from baseline in both the PSSI 90 response (52.9% versus 2.0%) and IGA mod 2011 0 or 1 scalp only response (56.9% versus 5.9%). Improvement in both endpoints was sustained for secukinumab patients who continued treatment through to week 24.

Quality of life/patient-reported outcomes
Statistically significant improvements at week 12 (studies 1-4) from baseline compared to placebo were demonstrated in the DLQI (Dermatology Life Quality Index). Mean decreases (improvements) in DLQI from baseline ranged from -10.4 to -11.6 with secukinumab 300 mg, from -7.7 to -10.1 with secukinumab 150 mg, versus -1.1 to -1.9 for placebo at week 12. These improvements were maintained for 52 weeks (studies 1 and 2).

Forty percent of the participants in studies 1 and 2 completed the Psoriasis Symptom Diary©. For the participants completing the diary in each of these studies, statistically significant improvements at week 12 from baseline compared to placebo in patient-reported signs and symptoms of itching, pain and scaling were demonstrated.

Statistically significant improvements at week 4 from baseline in patients treated with secukinumab compared to patients treated with ustekinumab (CLEAR) were demonstrated in the DLQI and these improvements were maintained for up to 52 weeks.

Statistically significant improvements in patient-reported signs and symptoms of itching, pain and scaling at week 16 and week 52 (CLEAR) were demonstrated in the Psoriasis Symptom Diary© in patients treated with secukinumab compared to patients treated with ustekinumab.

Statistically significant improvements (decreases) at week 12 from baseline in the scalp psoriasis study were demonstrated in patient reported signs and symptoms of scalp itching, pain and scaling compared to placebo.

Paediatric population

Paediatric plaque psoriasis
Secukinumab has been shown to improve signs and symptoms, and health-related quality of life in paediatric patients 6 years and older with plaque psoriasis (see Tables 8 and 10).

Severe plaque psoriasis
The safety and efficacy of secukinumab were assessed in a randomised, double-blind, placebo and etanercept-controlled phase III study in paediatric patients from 6 to <18 years of age with severe plaque psoriasis, as defined by a PASI score ≥20, an IGA mod 2011 score of 4, and BSA involvement of ≥10%, who were candidates for systemic therapy. Approximately 43% of the patients had prior exposure to phototherapy, 53% to conventional systemic therapy, 3% to biologics, and 9% had concomitant psoriatic arthritis.

The paediatric psoriasis study 1 evaluated 162 patients who were randomised to receive low dose secukinumab (75 mg for body weight <50 kg or 150 mg for body weight ≥50 kg), high dose secukinumab (75 mg for body weight <25 kg, 150 mg for body weight between ≥25 kg and <50 kg, or 300 mg for body weight ≥50 kg), or placebo at weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks, or etanercept. Patients randomised to etanercept received 0.8 mg/kg weekly (up to a maximum of 50 mg). Patient distribution by weight and age at randomisation is described in Table 7.

Table 7 Patient distribution by weight and age for paediatric psoriasis study 1

Randomisation strata	**Description**	**Secukinumab low dose n=40**	**Secukinumab high dose n=40**	**Placebo n=41**	**Etanercept n=41**	**Total N=162**
Age	6-<12 years	8	9	10	10	37
	≥12-<18 years	32	31	31	31	125
Weight	<25 kg	2	3	3	4	12
	≥25-<50 kg	17	15	17	16	65
	≥50 kg	21	22	21	21	85

Patients randomised to receive placebo who were non-responders at week 12 were switched to either the secukinumab low or high dose group (dose based on body weight group) and received study drug at weeks 12, 13, 14, and 15, followed by the same dose every 4 weeks starting at week 16. The co-primary endpoints were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 'clear' or 'almost clear' (0 or 1) response at week 12.

During the 12 week placebo-controlled period, the efficacy of both the low and the high dose of secukinumab was comparable for the co-primary endpoints. The odds ratio estimates in favour of both secukinumab doses were statistically significant for both the PASI 75 and IGA mod 2011 0 or 1 responses.

All patients were followed for efficacy and safety during the 52 weeks following the first dose. The proportion of patients achieving PASI 75 and IGA mod 2011 'clear' or 'almost clear' (0 or 1) responses showed separation between secukinumab treatment groups and placebo at the first post-baseline visit at week 4, the difference becoming more prominent at week 12. The response was maintained throughout the 52 week time period (see Table 8). Improvement in PASI 50, 90, 100 responder rates and Children's Dermatology Life Quality Index (CDLQI) scores of 0 or 1 were also maintained throughout the 52 week time period.

In addition, PASI 75, IGA 0 or 1, PASI 90 response rates at weeks 12 and 52 for both secukinumab low and high dose groups were higher than the rates for patients treated with etanercept (see Table 8).

Beyond week 12, efficacy of both the low and the high dose of secukinumab was comparable although the efficacy of the high dose was higher for patients ≥50 kg. The safety profiles of the low dose and the high dose were comparable and consistent with the safety profile in adults.

Table 8 Summary of clinical response in severe paediatric psoriasis at weeks 12 and 52 (paediatric psoriasis study 1)*

Response criterion	Treatment comparison 'test' vs. 'control'	'test' n**/m (%)	'control' n**/m (%)	odds ratio estimate (95% CI)	p-value
At week 12* **					
PASI 75	secukinumab low dose vs. placebo	32/40 (80.0)	6/41 (14.6)	25.78 (7.08, 114.66)	<0.0001
	secukinumab high dose vs. placebo	31/40 (77.5)	6/41 (14.6)	22.65 (6.31, 98.93)	<0.0001
	secukinumab low dose vs. etanercept	32/40 (80.0)	26/41 (63.4)	2.25 (0.73, 7.38)	
	secukinumab high dose vs. etanercept	31/40 (77.5)	26/41 (63.4)	1.92 (0.64, 6.07)	
IGA 0/1	secukinumab low dose vs. placebo	28/40 (70.0)	2/41 (4.9)	51.77 (10.02, 538.64)	<0.0001
	secukinumab high dose vs. placebo	24/40 (60.0)	2/41 (4.9)	32.52 (6.48, 329.52)	<0.0001
	secukinumab low dose vs. etanercept	28/40 (70.0)	14/41 (34.1)	4.49 (1.60, 13.42)	
	secukinumab high dose vs. etanercept	24/40 (60.0)	14/41 (34.1)	2.86 (1.05, 8.13)	
PASI 90	secukinumab low dose vs. placebo	29/40 (72.5)	1/41 (2.4)	133.67 (16.83, 6395.22)	<0.0001
	secukinumab high dose vs. placebo	27/40 (67.5)	1/41 (2.4)	102.86 (13.22, 4850.13)	<0.0001
	secukinumab low dose vs. etanercept	29/40 (72.5)	12/41 (29.3)	7.03 (2.34, 23.19)	
	secukinumab high dose vs. etanercept	27/40 (67.5)	12/41 (29.3)	5.32 (1.82, 16.75)	
At week 52					
PASI 75	secukinumab low dose vs. etanercept	35/40 (87.5)	28/41 (68.3)	3.12 (0.91, 12.52)	
	secukinumab high dose vs. etanercept	35/40 (87.5)	28/41 (68.3)	3.09 (0.90, 12.39)	
IGA 0/1	secukinumab low dose vs. etanercept	29/40 (72.5)	23/41 (56.1)	2.02 (0.73, 5.77)	
	secukinumab high dose vs. etanercept	30/40 (75.0)	23/41 (56.1)	2.26 (0.81, 6.62)	
PASI 90	secukinumab low dose vs. etanercept	30/40 (75.0)	21/41 (51.2)	2.85 (1.02, 8.38)	
	secukinumab high dose vs. etanercept	32/40 (80.0)	21/41 (51.2)	3.69 (1.27, 11.61)	

* non-responder imputation was used to handle missing values
** n is the number of responders, m = number of patients evaluable
*** extended visit window at week 12
Odds ratio, 95% confidence interval, and p-value are from an exact logistic regression model with treatment group, baseline body-weight category and age category as factors

A higher proportion of paediatric patients treated with secukinumab reported improvement in health-related quality of life as measured by a CDLQI score of 0 or 1 compared to placebo at week 12 (low dose 44.7%, high dose 50%, placebo 15%). Over time up to and including week 52 both secukinumab dose groups were numerically higher than the etanercept group (low dose 60.6%, high dose 66.7%, etanercept 44.4%).

Moderate to severe plaque psoriasis
Secukinumab was predicted to be effective for the treatment of paediatric patients with moderate plaque psoriasis based on the demonstrated efficacy and exposure response relationship in adult patients with moderate to severe plaque psoriasis, and the similarity of the disease course, pathophysiology, and drug effect in adult and paediatric patients at the same exposure levels.

Moreover, the safety and efficacy of secukinumab was assessed in an open-label, two-arm, parallel-group, multicentre phase III study in paediatric patients from 6 to <18 years of age with moderate to severe plaque psoriasis, as defined by a PASI score ≥12, an IGA mod 2011 score of ≥3, and BSA involvement of ≥10%, who were candidates for systemic therapy.

The paediatric psoriasis study 2 evaluated 84 patients who were randomised to receive low dose secukinumab (75 mg for body weight <50 kg or 150 mg for body weight ≥50 kg) or high dose secukinumab (75 mg for body weight <25 kg, 150 mg for body weight between ≥25 kg and <50 kg, or 300 mg for body weight ≥50 kg) at weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks. Patient distribution by weight and age at randomisation is described in Table 9.

Table 9 Patient distribution by weight and age for paediatric psoriasis study 2

Sub-groups	**Description**	**Secukinumab low dose n=42**	**Secukinumab high dose n=42**	**Total N=84**
Age	6-<12 years	17	16	33
	≥12-<18 years	25	26	51
Weight	<25 kg	4	4	8
	≥25-<50 kg	13	12	25
	≥50 kg	25	26	51

The co-primary endpoints were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 'clear' or 'almost clear' (0 or 1) response at week 12.

The efficacy of both the low and the high dose of secukinumab was comparable and showed statistically significant improvement compared to historical placebo for the co-primary endpoints. The estimated posterior probability of a positive treatment effect was 100%.

Patients were followed for efficacy over a 52 week period after first administration. Efficacy (defined as PASI 75 response and IGA mod 2011 'clear' or 'almost clear' [0 or 1]) was observed as early as the first post-baseline visit at week 2, and the proportion of patients who achieved a PASI 75 response and IGA mod 2011 'clear' or 'almost clear' (0 or 1) increased up to week 24 and were sustained until week 52. Improvement in PASI 90 and PASI 100 were also observed at week 12, increased up to week 24, and were sustained until week 52 (see Table 10).

The safety profiles of the low dose and the high dose were comparable and consistent with the safety profile in adults.

Table 10 Summary of clinical response in moderate to severe paediatric psoriasis at weeks 12 and 52 (paediatric psoriasis study 2)*

	Week 12		**Week 52**	
	Secukinumab low dose	**Secukinumab high dose**	**Secukinumab low dose**	**Secukinumab high dose**
Number of patients	42	42	42	42
PASI 75 response n (%)	39 (92.9%)	39 (92.9%)	37 (88.1%)	38 (90.5%)
IGA mod 2011 'clear' or 'almost clear' response n (%)	33 (78.6%)	35 (83.3%)	36 (85.7%)	35 (83.3%)
PASI 90 response n (%)	29 (69%)	32 (76.2%)	32 (76.2%)	35 (83.3%)
PASI 100 response n (%)	25 (59.5%)	23 (54.8%)	22 (52.4%)	29 (69.0%)
* non-responder imputation was used to handle missing values				

These outcomes in the paediatric moderate to severe plaque psoriasis population confirmed the predictive assumptions based on the efficacy and exposure response relationship in adult patients, mentioned above.

In the low dose group, 50% and 70.7% of patients achieved a CDLQI 0 or 1 score at weeks 12 and 52, respectively. In the high dose group, 61.9% and 70.3% achieved a CDLQI 0 or 1 score at weeks 12 and 52, respectively.

Juvenile idiopathic arthritis (JIA)

Enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA)
The efficacy and safety of secukinumab were assessed in 86 patients in a 3-part, double-blind, placebo-controlled, event-driven, randomised, phase III study in patients 2 to <18 years of age with active ERA or JPsA as diagnosed based on a modified International League of Associations for Rheumatology (ILAR) JIA classification criteria. The study consisted of an open-label portion (Part 1) where all patients received secukinumab until week 12. Patients demonstrating a JIA ACR 30 response at week 12 entered into the Part 2 double-blind phase and were randomised 1:1 to continue treatment with secukinumab or to begin treatment with placebo (randomised withdrawal) until week 104 or until a flare occured. Patients who flared then entered open-label secukinumab treatment until week 104 (Part 3).

The JIA patient subtypes at study entry were: 60.5% ERA and 39.5% JPsA, who either had inadequate response or were intolerant to ≥1 disease-modifying antirheumatic drugs (DMARDs) and ≥1 non-steroidal anti-inflammatory drugs (NSAIDs). At baseline, MTX use was reported for 65.1% of patients; (63.5% [33/52] of ERA patients and 67.6% [23/34] of JPsA patients). There were 12 out of 52 ERA patients concomitantly treated with sulfasalazine (23.1%). Patients with a body weight at baseline <50 kg (n=30) were given a dose of 75 mg and patients with a body weight ≥50 kg (n=56) were given a dose of 150 mg. Age at baseline ranged from 2 to 17 years, with 3 patients between 2 to <6 years, 22 patients 6 to <12 years and 61 patients 12 to <18 years. At baseline the Juvenile Arthritis Disease Activity Score (JADAS)-27 was 15.1 (SD:7.1).

The primary endpoint was time to flare in the randomised withdrawal period (Part 2). Disease flare was defined as a ≥30% worsening in at least three of the six JIA ACR response criteria and ≥30% improvement in not more than one of the six JIA ACR response criteria and a minimum of two active joints.

At the end of Part 1, 75 out of 86 (87.2%) patients demonstrated a JIA ACR 30 response and entered into Part 2.

The study met its primary endpoint by demonstrating a statistically significant prolongation in the time to disease flare in patients treated with secukinumab compared to placebo in Part 2. The risk of flare was reduced by 72% for patients on secukinumab compared with patients on placebo in Part 2 (Hazard ratio=0.28, 95% CI: 0.13 to 0.63, p<0.001) (Figure 2 and Table 11). During Part 2, a total of 21 patients in the placebo group experienced a flare event (11 JPsA and 10 ERA) compared with 10 patients in the secukinumab group (4 JPsA and 6 ERA).

Figure 2 Kaplan-Meier estimates of the time to disease flare in Part 2

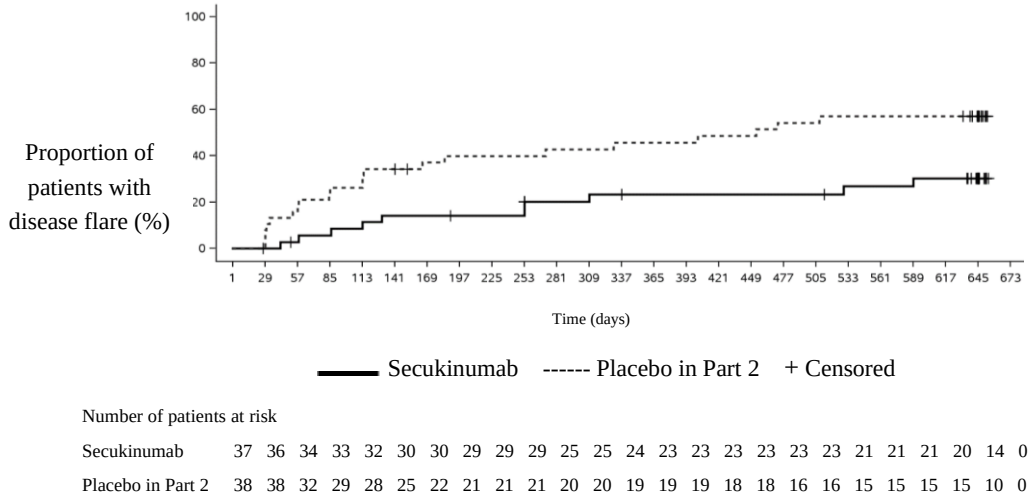
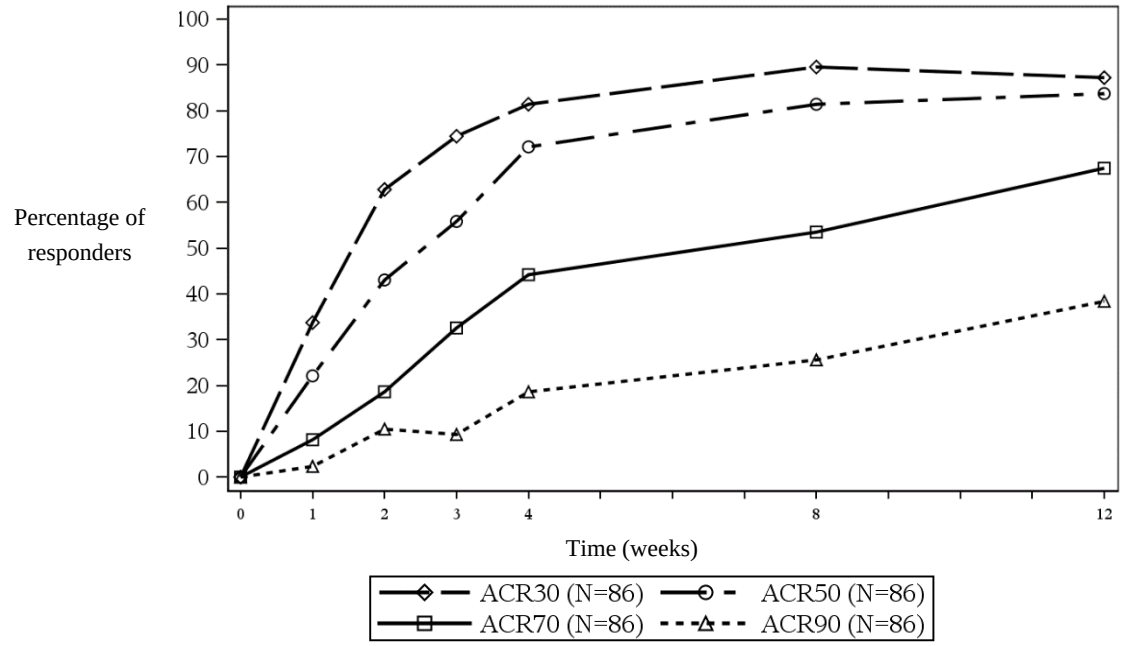


Table 11 Survival analysis of time to disease flare – Part 2

	Secukinumab (N=37)	**Placebo in Part 2** (N=38)
Number of flare events at the end of Part 2, n (%)	10 (27.0)	21 (55.3)
Kaplan-Meier estimates:		
Median, in days (95% CI)	NC (NC, NC)	453.0 (114.0, NC)
Flare-free rate at 6 months (95% CI)	85.8 (69.2, 93.8)	60.1 (42.7, 73.7)
Flare-free rate at 12 months (95% CI)	76.7 (58.7, 87.6)	54.3 (37.1, 68.7)
Flare-free rate at 18 months (95% CI)	73.2 (54.6, 85.1)	42.9 (26.7, 58.1)
Hazard ratio to placebo: Estimate (95% CI)	0.28 (0.13, 0.63)	
Stratified log-rank test p-value	<0.001**	
Analysis was conducted on all randomised patients who received at least one dose of study drug in Part 2. Secukinumab: all patients who did not take any placebo. Placebo in Part 2: all patients who took placebo in Part 2 and secukinumab in other period/s. NC = Not calculable. ** = Statistically significant on one-sided significance level 0.025.		

In open-label Part 1, all patients received secukinumab until week 12. At week 12, 83.7%, 67.4%, and 38.4% of children were JIA ACR 50, 70 and 90 responders, respectively (Figure 3). The onset of action of secukinumab occurred as early as week 1. At week 12 the JADAS-27 score was 4.64 (SD:4.73) and the mean decrease from baseline in JADAS-27 was -10.487 (SD:7.23).

Figure 3 JIA ACR 30/50/70/90 response for subjects up to week 12 in Part 1*



*non-responder imputation was used to handle missing values

The data in the 2 to <6 age group were inconclusive due to the low number of patients below 6 years of age enrolled in the study.

The European Medicines Agency has waived the obligation to submit the results of studies with Cosentyx in plaque psoriasis in paediatric patients aged from birth to less than 6 years and in chronic idiopathic arthritis for paediatric patients aged from birth to less than 2 years (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Most pharmacokinetics properties observed in patients with plaque psoriasis, psoriatic arthritis and ankylosing spondylitis were similar.

Paediatric population

Plaque psoriasis
In a pool of the two paediatric studies, patients with moderate to severe plaque psoriasis (6 to less than 18 years of age) were administered secukinumab at the recommended paediatric dosing regimen. At week 24, patients weighing ≥25 and <50 kg had a mean ± SD steady-state trough concentration of 19.8±6.96 µg/ml (n=24) after 75 mg of secukinumab and patients weighing ≥50 kg had mean ±SD trough concentration of 27.3±10.1 µg/ml (n=36) after 150 mg of secukinumab. The mean ± SD steady-state trough concentration in patients weighing <25 kg (n=8) was 32.6±10.8 µg/ml at week 24 after 75 mg dose.

Juvenile idiopathic arthritis
In a paediatric study, ERA and JPsA patients (2 to less than 18 years of age) were administered secukinumab at the recommended paediatric dosing regimen. At week 24, patients weighing <50 kg, and weighing ≥50 kg had a mean ± SD steady-state trough concentration of 25.2±5.45 µg/ml (n=10) and 27.9±9.57 µg/ml (n=19), respectively.

Adult population

Absorption
Following a single subcutaneous dose of 300 mg as a liquid formulation in healthy volunteers, secukinumab reached peak serum concentrations of 43.2±10.4 µg/ml between 2 and 14 days post dose.

Based on population pharmacokinetic analysis, following a single subcutaneous dose of either 150 mg or 300 mg in plaque psoriasis patients, secukinumab reached peak serum concentrations of 13.7±4.8 µg/ml or 27.3±9.5 µg/ml, respectively, between 5 and 6 days post dose.

After initial weekly dosing during the first month, time to reach the maximum concentration was between 31 and 34 days based on population pharmacokinetic analysis.

On the basis of simulated data, peak concentrations at steady-state ($C_{max,ss}$) following subcutaneous administration of 150 mg or 300 mg were 27.6 µg/ml and 55.2 µg/ml, respectively. Population pharmacokinetic analysis suggests that steady-state is reached after 20 weeks with monthly dosing regimens.

Compared with exposure after a single dose, the population pharmacokinetic analysis showed that patients exhibited a 2-fold increase in peak serum concentrations and area under the curve (AUC) following repeated monthly dosing during maintenance.

Population pharmacokinetic analysis showed that secukinumab was absorbed with an average absolute bioavailability of 73% in patients with plaque psoriasis. Across studies, absolute bioavailabilities in the range between 60 and 77% were calculated.

The bioavailability of secukinumab in PsA patients was 85% on the basis of the population pharmacokinetic model.

Following a single subcutaneous injection of 300 mg solution for injection in pre-filled syringe in plaque psoriasis patients, secukinumab systemic exposure was similar to what was observed previously with two injections of 150 mg.

Distribution
The mean volume of distribution during the terminal phase (V_z) following single intravenous administration ranged from 7.10 to 8.60 litres in plaque psoriasis patients, suggesting that secukinumab undergoes limited distribution to peripheral compartments.

Biotransformation
The majority of IgG elimination occurs via intracellular catabolism, following fluid-phase or receptor mediated endocytosis.

Elimination
Mean systemic clearance (CL) following a single intravenous administration to patients with plaque psoriasis ranged from 0.13 to 0.36 l/day. In a population pharmacokinetic analysis, the mean systemic clearance (CL) was 0.19 l/day in plaque psoriasis patients. The CL was not impacted by gender. Clearance was dose- and time-independent.

The mean elimination half-life, as estimated from population pharmacokinetic analysis, was 27 days in plaque psoriasis patients, ranging from 18 to 46 days across psoriasis studies with intravenous administration.

Linearity/non-linearity
The single and multiple dose pharmacokinetics of secukinumab in plaque psoriasis patients were determined in several studies with intravenous doses ranging from 1x 0.3 mg/kg to 3x 10 mg/kg and with subcutaneous doses ranging from 1x 25 mg to multiple doses of 300 mg. Exposure was dose proportional across all dosing regimens.

Special populations

Patients with renal or hepatic impairment
No pharmacokinetic data are available in patients with renal or hepatic impairment. The renal elimination of intact secukinumab, an IgG monoclonal antibody, is expected to be low and of minor importance. IgGs are mainly eliminated via catabolism and hepatic impairment is not expected to influence clearance of secukinumab.

Effect of weight on pharmacokinetics
Secukinumab clearance and volume of distribution increase as body weight increases.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans (adult or paediatric) based on conventional studies of safety pharmacology, repeated dose and reproductive toxicity, or tissue cross-reactivity.

Animal studies have not been conducted to evaluate the carcinogenic potential of secukinumab.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Trehalose dihydrate
Histidine
Histidine hydrochloride monohydrate
Methionine
Polysorbate 80
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years
If necessary, Cosentyx may be stored unrefrigerated for a single period of up to 4 days at room temperature, not above 30°C.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). Do not freeze.
Store in the original package in order to protect from light.

6.5 Nature and contents of container

Cosentyx 75 mg solution for injection in pre-filled syringe is supplied in a pre-filled 0.5 ml glass syringe with a silicone-coated bromobutyl rubber plunger stopper, staked 27G x ½″ needle and rigid needle shield of styrene butadiene rubber assembled in an automatic needle guard of polycarbonate.

Cosentyx 75 mg solution for injection in pre-filled syringe is available in unit packs containing 1 pre-filled syringe and in multipacks containing 3 (3 packs of 1) pre-filled syringes.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Cosentyx 75 mg solution for injection is supplied in a single-use pre-filled syringe for individual use. The syringe should be taken out of the refrigerator 20 minutes before injecting to allow it to reach room temperature.

Prior to use, a visual inspection of the pre-filled syringe is recommended. The liquid should be clear. Its colour may vary from colourless to slightly yellow. You may see a small air bubble, which is normal. Do not use if the liquid contains easily visible particles, is cloudy or is distinctly brown. Detailed instructions for use are provided in the package leaflet.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/012-013

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15 January 2015
Date of latest renewal: 03 September 2019

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled syringe
Cosentyx 300 mg solution for injection in pre-filled syringe
Cosentyx 150 mg solution for injection in pre-filled pen
Cosentyx 300 mg solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Cosentyx 150 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 150 mg secukinumab in 1 ml.

Cosentyx 300 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 300 mg secukinumab in 2 ml.

Cosentyx 150 mg solution for injection in pre-filled pen

Each pre-filled pen contains 150 mg secukinumab in 1 ml.

Cosentyx 300 mg solution for injection in pre-filled pen

Each pre-filled pen contains 300 mg secukinumab in 2 ml.

Secukinumab is a recombinant fully human monoclonal antibody produced in Chinese Hamster Ovary (CHO) cells.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection)

The solution is clear and colourless to slightly yellow.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Adult plaque psoriasis

Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

Paediatric plaque psoriasis

Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years who are candidates for systemic therapy.

Hidradenitis suppurativa (HS)

Cosentyx is indicated for the treatment of active moderate to severe hidradenitis suppurativa (acne inversa) in adults with an inadequate response to conventional systemic HS therapy (see section 5.1).

Psoriatic arthritis

Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate (see section 5.1).

Axial spondyloarthritis (axSpA)

Ankylosing spondylitis (AS, radiographic axial spondyloarthritis)
Cosentyx is indicated for the treatment of active ankylosing spondylitis in adults who have responded inadequately to conventional therapy.

Non-radiographic axial spondyloarthritis (nr-axSpA)
Cosentyx is indicated for the treatment of active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) evidence in adults who have responded inadequately to non-steroidal anti-inflammatory drugs (NSAIDs).

Juvenile idiopathic arthritis (JIA)

Enthesitis-related arthritis (ERA)
Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active enthesitis-related arthritis in patients 6 years and older whose disease has responded inadequately to, or who cannot tolerate, conventional therapy (see section 5.1).

Juvenile psoriatic arthritis (JPsA)
Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active juvenile psoriatic arthritis in patients 6 years and older whose disease has responded inadequately to, or who cannot tolerate, conventional therapy (see section 5.1).

4.2 Posology and method of administration

Cosentyx is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of conditions for which Cosentyx is indicated.

Posology

Adult plaque psoriasis
The recommended dose is 300 mg of secukinumab by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Based on clinical response, a maintenance dose of 300 mg every 2 weeks may provide additional benefit for patients with a body weight of 90 kg or higher. Each 300 mg dose is given as one subcutaneous injection of 300 mg or as two subcutaneous injections of 150 mg.

Paediatric plaque psoriasis (adolescents and children from the age of 6 years)
The recommended dose is based on body weight (Table 1) and administered by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 75 mg dose is given as one subcutaneous injection of 75 mg. Each 150 mg dose is given as one subcutaneous injection of 150 mg. Each 300 mg dose is given as one subcutaneous injection of 300 mg or as two subcutaneous injections of 150 mg.

Table 1 Recommended dose for paediatric plaque psoriasis

Body weight at time of dosing	Recommended dose
<25 kg	75 mg
25 to <50 kg	75 mg
≥50 kg	150 mg (*may be increased to 300 mg)

*Some patients may derive additional benefit from the higher dose.

The 150 mg and 300 mg solution for injection in pre-filled syringe and in pre-filled pen are not indicated for administration to paediatric patients with a weight <50 kg. Cosentyx may be available in other strengths and/or presentations depending on the individual treatment needs.

Hidradenitis suppurativa (HS)
The recommended dose is 300 mg of secukinumab by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3, and 4, followed by monthly maintenance dosing. Based on clinical response, the maintenance dose can be increased to 300 mg every 2 weeks. Each 300 mg dose is given as one subcutaneous injection of 300 mg or as two subcutaneous injections of 150 mg.

Psoriatic arthritis
For patients with concomitant moderate to severe plaque psoriasis, please refer to adult plaque psoriasis recommendation.

For patients who are anti-TNFα inadequate responders (IR), the recommended dose is 300 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 300 mg dose is given as one subcutaneous injection of 300 mg or as two subcutaneous injections of 150 mg.

For other patients, the recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Based on clinical response, the dose can be increased to 300 mg.

Axial spondyloarthritis (axSpA)
Ankylosing spondylitis (AS, radiographic axial spondyloarthritis)
The recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Based on clinical response, the dose can be increased to 300 mg. Each 300 mg dose is given as one subcutaneous injection of 300 mg or as two subcutaneous injections of 150 mg.

Non-radiographic axial spondyloarthritis (nr-axSpA)
The recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing.

Juvenile idiopathic arthritis (JIA)

Enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA)
The recommended dose is based on body weight (Table 2) and administered by subcutaneous injection at weeks 0, 1, 2, 3, and 4, followed by monthly maintenance dosing. Each 75 mg dose is given as one subcutaneous injection of 75 mg. Each 150 mg dose is given as one subcutaneous injection of 150 mg.

Table 2 Recommended dose for juvenile idiopathic arthritis

Body weight at time of dosing	Recommended dose
<50 kg	75 mg
≥50 kg	150 mg

The 150 mg and 300 mg solution for injection in pre-filled syringe and in pre-filled pen are not indicated for administration to paediatric patients with a weight <50 kg. Cosentyx may be available in other strengths and/or presentations depending on the individual treatment needs.

For all of the above indications, available data suggest that a clinical response is usually achieved within 16 weeks of treatment. Consideration should be given to discontinuing treatment in patients who have shown no response by 16 weeks of treatment. Some patients with an initial partial response may subsequently improve with continued treatment beyond 16 weeks.

Special populations

Elderly patients (aged 65 years and over)
No dose adjustment is required (see section 5.2).

Renal impairment / hepatic impairment
Cosentyx has not been studied in these patient populations. No dose recommendations can be made.

Paediatric population
The safety and efficacy of Cosentyx in children with plaque psoriasis and in the juvenile idiopathic arthritis (JIA) categories of ERA and JPsA below the age of 6 years have not been established.

The safety and efficacy of Cosentyx in children below the age of 18 years in other indications have not yet been established. No data are available.

Method of administration

Cosentyx is to be administered by subcutaneous injection. If possible, areas of the skin that show psoriasis should be avoided as injection sites. The syringe or the pen must not be shaken.

After proper training in subcutaneous injection technique, patients may self-inject Cosentyx or be injected by a caregiver if a physician determines that this is appropriate. However, the physician should ensure appropriate follow-up of patients. Patients or caregivers should be instructed to inject the full amount of Cosentyx according to the instructions provided in the package leaflet. Comprehensive instructions for administration are given in the package leaflet.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Clinically important, active infection, e.g. active tuberculosis (see section 4.4).

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Infections

Secukinumab has the potential to increase the risk of infections. Serious infections have been observed in patients receiving secukinumab in the post-marketing setting. Caution should be exercised when considering the use of secukinumab in patients with a chronic infection or a history of recurrent infection.

Patients should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, the patient should be closely monitored and secukinumab should not be administered until the infection resolves.

In clinical studies, infections have been observed in patients receiving secukinumab (see section 4.8). Most of these were mild or moderate upper respiratory tract infections such as nasopharyngitis and did not require treatment discontinuation.

Related to the mechanism of action of secukinumab, non-serious mucocutaneous candida infections were more frequently reported for secukinumab than placebo in the psoriasis clinical studies (3.55 per 100 patient years for secukinumab 300 mg versus 1.00 per 100 patient years for placebo) (see section 4.8).

No increased susceptibility to tuberculosis was reported from clinical studies. However, secukinumab should not be given to patients with active tuberculosis. Anti-tuberculosis therapy should be considered prior to initiation of secukinumab in patients with latent tuberculosis.

Inflammatory bowel disease (including Crohn's disease and ulcerative colitis)

Cases of new or exacerbations of inflammatory bowel disease have been reported with secukinumab (see section 4.8). Secukinumab is not recommended in patients with inflammatory bowel disease. If a patient develops signs and symptoms of inflammatory bowel disease or experiences an exacerbation of pre-existing inflammatory bowel disease, secukinumab should be discontinued and appropriate medical management should be initiated.

Hypersensitivity reactions

In clinical studies, rare cases of anaphylactic reactions have been observed in patients receiving secukinumab. If an anaphylactic or other serious allergic reactions occur, administration of secukinumab should be discontinued immediately and appropriate therapy initiated.

Latex-sensitive individuals – Cosentyx 150 mg solution for injection in pre-filled syringe and 150 mg solution for injection in pre-filled pen only

The removable needle cap of Cosentyx 150 mg solution for injection in pre-filled syringe and Cosentyx 150 mg solution for injection in pre-filled pen contains a derivative of natural rubber latex. No natural rubber latex has to date been detected in the removable needle cap. Nevertheless, the use of Cosentyx 150 mg solution for injection in pre-filled syringe and Cosentyx 150 mg solution for injection in pre-filled pen in latex-sensitive individuals has not been studied and there is therefore a potential risk of hypersensitivity reactions which cannot be completely ruled out.

Vaccinations

Live vaccines should not be given concurrently with secukinumab.

Patients receiving secukinumab may receive concurrent inactivated or non-live vaccinations. In a study, after *meningococcal* and inactivated *influenza* vaccinations, a similar proportion of healthy volunteers treated with 150 mg of secukinumab and those treated with placebo were able to mount an adequate immune response of at least a 4-fold increase in antibody titres to *meningococcal* and *influenza* vaccines. The data suggest that secukinumab does not suppress the humoral immune response to the *meningococcal* or *influenza* vaccines.

Prior to initiating therapy with Cosentyx, it is recommended that paediatric patients receive all age-appropriate immunisations as per current immunisation guidelines.

Concomitant immunosuppressive therapy

In psoriasis studies, the safety and efficacy of secukinumab in combination with immunosuppressants, including biologics, or phototherapy have not been evaluated. Secukinumab was administered concomitantly with methotrexate (MTX), sulfasalazine and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and ankylosing spondylitis). Caution should be exercised when considering concomitant use of other immunosuppressants and secukinumab (see also section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

Live vaccines should not be given concurrently with secukinumab (see also section 4.4).

In a study in adult subjects with plaque psoriasis, no interaction was observed between secukinumab and midazolam (CYP3A4 substrate).

No interaction was seen when secukinumab was administered concomitantly with methotrexate (MTX) and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and axial spondyloarthritis).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 20 weeks after treatment.

Pregnancy

There are no adequate data from the use of secukinumab in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Cosentyx during pregnancy.

Breast-feeding

It is not known whether secukinumab is excreted in human milk. Immunoglobulins are excreted in human milk and it is not known if secukinumab is absorbed systemically after ingestion. Because of the potential for adverse reactions in nursing infants from secukinumab, a decision on whether to discontinue breast-feeding during treatment and up to 20 weeks after treatment or to discontinue therapy with Cosentyx must be made taking into account the benefit of breast-feeding to the child and the benefit of therapy to the woman.

Fertility

The effect of secukinumab on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility.

4.7 Effects on ability to drive and use machines

Cosentyx has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse reactions are upper respiratory tract infections (17.1%) (most frequently nasopharyngitis, rhinitis).

Tabulated list of adverse reactions

Adverse reactions from clinical studies and post-marketing reports (Table 3) are listed by MedDRA system organ class. Within each system organ class, the adverse reactions are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse reaction is based on the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1 000 to <1/100); rare (≥1/10 000 to <1/1 000); very rare (<1/10 000); and not known (cannot be estimated from the available data).

Over 20 000 patients have been treated with secukinumab in blinded and open-label clinical studies in various indications (plaque psoriasis, psoriatic arthritis, axial spondyloarthritis, hidradenitis suppurativa and other autoimmune conditions), representing 34 908 patient years of exposure. Of these, over 14 000 patients were exposed to secukinumab for at least one year. The safety profile of secukinumab is consistent across all indications.

Table 3 List of adverse reactions in clinical studies[1)] and post-marketing experience

System organ class	Frequency	Adverse reaction
Infections and infestations	Very common	Upper respiratory tract infections
	Common	Oral herpes
	Uncommon	Oral candidiasis
		Otitis externa
		Lower respiratory tract infections
		Tinea pedis
	Not known	Mucosal and cutaneous candidiasis (including oesophageal candidiasis)
Blood and lymphatic system disorders	Uncommon	Neutropenia
Immune system disorders	Rare	Anaphylactic reactions
Nervous system disorders	Common	Headache
Eye disorders	Uncommon	Conjunctivitis
Respiratory, thoracic and mediastinal disorders	Common	Rhinorrhoea
Gastrointestinal disorders	Common	Diarrhoea
	Common	Nausea
	Uncommon	Inflammatory bowel disease
Skin and subcutaneous tissue disorders	Uncommon	Urticaria
		Dyshidrotic eczema
	Rare	Exfoliative dermatitis[2)]
		Hypersensitivity vasculitis
	Not known	Pyoderma gangrenosum
General disorders and administration site conditions	Common	Fatigue

[1)] Placebo-controlled clinical studies (phase III) in plaque psoriasis, PsA, AS, nr-axSpA and HS patients exposed to 300 mg, 150 mg, 75 mg or placebo up to 12 weeks (psoriasis) or 16 weeks (PsA, AS, nr-axSpA and HS) treatment duration

[2)] Cases were reported in patients with psoriasis diagnosis

Description of selected adverse reactions

Infections
In the placebo-controlled period of clinical studies in plaque psoriasis (a total of 1 382 patients treated with secukinumab and 694 patients treated with placebo for up to 12 weeks), infections were reported in 28.7% of patients treated with secukinumab compared with 18.9% of patients treated with placebo. The majority of infections consisted of non-serious and mild to moderate upper respiratory tract infections, such as nasopharyngitis, which did not necessitate treatment discontinuation. There was an increase in mucosal or cutaneous candidiasis, consistent with the mechanism of action, but the cases were mild or moderate in severity, non-serious, responsive to standard treatment and did not necessitate treatment discontinuation. Serious infections occurred in 0.14% of patients treated with secukinumab and in 0.3% of patients treated with placebo (see section 4.4).

Over the entire treatment period (a total of 3 430 patients treated with secukinumab for up to 52 weeks for the majority of patients), infections were reported in 47.5% of patients treated with secukinumab (0.9 per patient-year of follow-up). Serious infections were reported in 1.2% of patients treated with secukinumab (0.015 per patient-year of follow-up).

Infection rates observed in psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) clinical studies were similar to those observed in the psoriasis studies.

Patients with hidradenitis suppurativa are more susceptible to infections. In the placebo-controlled period of clinical studies in hidradenitis suppurativa (a total of 721 patients treated with secukinumab and 363 patients treated with placebo for up to 16 weeks), infections were numerically higher compared to those observed in the psoriasis studies (30.7% of patients treated with secukinumab compared with 31.7% in patients treated with placebo). Most of these were non-serious, mild or moderate in severity and did not require treatment discontinuation or interruption.

Neutropenia
In psoriasis phase III clinical studies, neutropenia was more frequently observed with secukinumab than with placebo, but most cases were mild, transient and reversible. Neutropenia $<1.0\text{-}0.5 \times 10^9/l$ (CTCAE grade 3) was reported in 18 out of 3 430 (0.5%) patients on secukinumab, with no dose dependence and no temporal relationship to infections in 15 out of 18 cases. There were no reported cases of more severe neutropenia. Non-serious infections with usual response to standard care and not requiring discontinuation of secukinumab were reported in the remaining 3 cases.

The frequency of neutropenia in psoriatic arthritis, axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) and hidradenitis suppurativa was similar to psoriasis.

Rare cases of neutropenia $<0.5 \times 10^9/l$ (CTCAE grade 4) were reported.

Hypersensitivity reactions
In clinical studies, urticaria and rare cases of anaphylactic reaction to secukinumab were observed (see also section 4.4).

Immunogenicity
In psoriasis, psoriatic arthritis, axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) and hidradenitis suppurativa clinical studies, less than 1% of patients treated with secukinumab developed antibodies to secukinumab up to 52 weeks of treatment. About half of the treatment-emergent anti-drug antibodies were neutralising, but this was not associated with loss of efficacy or pharmacokinetic abnormalities.

Paediatric population

Undesirable effects in paediatric patients from the age of 6 years with plaque psoriasis
The safety of secukinumab was assessed in two phase III studies in paediatric patients with plaque psoriasis. The first study (paediatric study 1) was a double-blind, placebo-controlled study of 162 patients from 6 to less than 18 years of age with severe plaque psoriasis. The second study (paediatric study 2) is an open-label study of 84 patients from 6 to less than 18 years of age with moderate to severe plaque psoriasis. The safety profile reported in these two studies was consistent with the safety profile reported in adult plaque psoriasis patients.

Undesirable effects in paediatric patients with JIA
The safety of secukinumab was also assessed in a phase III study in 86 juvenile idiopathic arthritis patients with ERA and JPsA from 2 to less than 18 years of age. The safety profile reported in this study was consistent with the safety profile reported in adult patients.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Doses up to 30 mg/kg (approximately 2000 to 3000 mg) have been administered intravenously in clinical studies without dose-limiting toxicity. In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC10

Mechanism of action

Secukinumab is a fully human IgG1/κ monoclonal antibody that selectively binds to and neutralises the proinflammatory cytokine interleukin-17A (IL-17A). Secukinumab works by targeting IL-17A and inhibiting its interaction with the IL-17 receptor, which is expressed on various cell types including keratinocytes. As a result, secukinumab inhibits the release of proinflammatory cytokines, chemokines and mediators of tissue damage and reduces IL-17A-mediated contributions to autoimmune and inflammatory diseases. Clinically relevant levels of secukinumab reach the skin and reduce local inflammatory markers. As a direct consequence treatment with secukinumab reduces erythema, induration and desquamation present in plaque psoriasis lesions.

IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. IL-17A plays a key role in the pathogenesis of plaque psoriasis, hidradenitis suppurativa, psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) and is up-regulated in lesional skin in contrast to non-lesional skin of plaque psoriasis patients and in synovial tissue of psoriatic arthritis patients. IL-17A is also upregulated in hidradenitis suppurativa lesions and increased IL-17A serum levels have been observed in affected patients. The frequency of IL-17-producing cells was also significantly higher in the subchondral bone marrow of facet joints from patients with ankylosing spondylitis. Increased numbers of IL-17A producing lymphocytes have also been found in patients with non-radiographic axial spondyloarthritis.

Inhibition of IL-17A was shown to be effective in the treatment of ankylosing spondylitis, thus establishing the key role of this cytokine in axial spondyloarthritis.

Pharmacodynamic effects

Serum levels of total IL-17A (free and secukinumab-bound IL-17A) are initially increased in patients receiving secukinumab. This is followed by a slow decrease due to reduced clearance of secukinumab-bound IL-17A, indicating that secukinumab selectively captures free IL-17A, which plays a key role in the pathogenesis of plaque psoriasis.

In a study with secukinumab, infiltrating epidermal neutrophils and various neutrophil-associated markers that are increased in lesional skin of plaque psoriasis patients were significantly reduced after one to two weeks of treatment.

Secukinumab has been shown to lower (within 1 to 2 weeks of treatment) levels of C-reactive protein, which is a marker of inflammation.

Clinical efficacy and safety

Adult plaque psoriasis
The safety and efficacy of secukinumab were assessed in four randomised, double-blind, placebo-controlled phase III studies in patients with moderate to severe plaque psoriasis who were candidates for phototherapy or systemic therapy [ERASURE, FIXTURE, FEATURE, JUNCTURE]. The efficacy and safety of secukinumab 150 mg and 300 mg were evaluated versus either placebo or etanercept. In addition, one study assessed a chronic treatment regimen versus a "retreatment as needed" regimen [SCULPTURE].

Of the 2 403 patients who were included in the placebo-controlled studies, 79% were biologic-naive, 45% were non-biologic failures and 8% were biologic failures (6% were anti-TNF failures, and 2% were anti-p40 failures). Approximately 15 to 25% of patients in phase III studies had psoriatic arthritis (PsA) at baseline.

Psoriasis study 1 (ERASURE) evaluated 738 patients. Patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Psoriasis study 2 (FIXTURE) evaluated 1 306 patients. Patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients randomised to etanercept received 50 mg doses twice per week for 12 weeks followed by 50 mg every week. In both study 1 and study 2, patients randomised to receive placebo who were non-responders at week 12 then crossed over to receive secukinumab (either 150 mg or 300 mg) at weeks 12, 13, 14, and 15, followed by the same dose every month starting at week 16. All patients were followed for up to 52 weeks following first administration of study treatment.

Psoriasis study 3 (FEATURE) evaluated 177 patients using a pre-filled syringe compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of secukinumab self-administration via the pre-filled syringe. Psoriasis study 4 (JUNCTURE) evaluated 182 patients using a pre-filled pen compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of secukinumab self-administration via the pre-filled pen. In both study 3 and study 4, patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients were also randomised to receive placebo at weeks 0, 1, 2, 3 and 4, followed by the same dose every month.

Psoriasis study 5 (SCULPTURE) evaluated 966 patients. All patients received secukinumab 150 mg or 300 mg doses at weeks 0, 1, 2, 3, 4, 8 and 12 and then were randomised to receive either a maintenance regimen of the same dose every month starting at week 12 or a "retreatment as needed" regimen of the same dose. Patients randomised to "retreatment as needed" did not achieve adequate maintenance of response and therefore a fixed monthly maintenance regimen is recommended.

The co-primary endpoints in the placebo and active-controlled studies were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 "clear" or "almost clear" response versus placebo at week 12 (see Tables 4 and 5). The 300 mg dose provided improved skin clearance particularly for "clear" or "almost clear" skin across the efficacy endpoints of PASI 90, PASI 100, and IGA mod 2011 0 or 1 response across all studies with peak effects seen at week 16, therefore this dose is recommended.

Table 4 Summary of PASI 50/75/90/100 & IGA* mod 2011 "clear" or "almost clear" clinical response in psoriasis studies 1, 3 and 4 (ERASURE, FEATURE and JUNCTURE)

		Week 12		Week 16		Week 52	
	Placebo	**150 mg**	**300 mg**	**150 mg**	**300 mg**	**150 mg**	**300 mg**
Study 1							
Number of patients	246	244	245	244	245	244	245
PASI 50 response n (%)	22 (8.9%)	203 (83.5%)	222 (90.6%)	212 (87.2%)	224 (91.4%)	187 (77%)	207 (84.5%)
PASI 75 response n (%)	11 (4.5%)	174 (71.6%)**	200 (81.6%)**	188 (77.4%)	211 (86.1%)	146 (60.1%)	182 (74.3%)
PASI 90 response n (%)	3 (1.2%)	95 (39.1%)**	145 (59.2%)**	130 (53.5%)	171 (69.8%)	88 (36.2%)	147 (60.0%)
PASI 100 response n (%)	2 (0.8%)	31 (12.8%)	70 (28.6%)	51 (21.0%)	102 (41.6%)	49 (20.2%)	96 (39.2%)
IGA mod 2011 "clear" or "almost clear" response n (%)	6 (2.40%)	125 (51.2%)**	160 (65.3%)**	142 (58.2%)	180 (73.5%)	101 (41.4%)	148 (60.4%)
Study 3							
Number of patients	59	59	58	-	-	-	-
PASI 50 response n (%)	3 (5.1%)	51 (86.4%)	51 (87.9%)	-	-	-	-
PASI 75 response n (%)	0 (0.0%)	41 (69.5%)**	44 (75.9%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	27 (45.8%)	35 (60.3%)	-	-	-	-
PASI 100 response n (%)	0 (0.0%)	5 (8.5%)	25 (43.1%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	31 (52.5%)**	40 (69.0%)**	-	-	-	-
Study 4							
Number of patients	61	60	60	-	-	-	-
PASI 50 response n (%)	5 (8.2%)	48 (80.0%)	58 (96.7%)	-	-	-	-
PASI 75 response n (%)	2 (3.3%)	43 (71.7%)**	52 (86.7%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	24 (40.0%)	33 (55.0%)	-	-	-	-
PASI 100 response n(%)	0 (0.0%)	10 (16.7%)	16 (26.7%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	32 (53.3%)**	44 (73.3%)**	-	-	-	-

* The IGA mod 2011 is a 5-category scale including "0 = clear", "1 = almost clear", "2 = mild", "3 = moderate" or "4 = severe", indicating the physician's overall assessment of the psoriasis severity focusing on induration, erythema and scaling. Treatment success of "clear" or "almost clear" consisted of no signs of psoriasis or normal to pink colouration of lesions, no thickening of the plaque and none to minimal focal scaling.

** p-values versus placebo and adjusted for multiplicity: $p<0.0001$.

Table 5 Summary of clinical response on psoriasis study 2 (FIXTURE)

	Week 12				Week 16			Week 52		
	Placebo	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**
Number of patients	324	327	323	323	327	323	323	327	323	323
PASI 50 response n (%)	49 (15.1%)	266 (81.3%)	296 (91.6%)	226 (70.0%)	290 (88.7%)	302 (93.5%)	257 (79.6%)	249 (76.1%)	274 (84.8%)	234 (72.4%)
PASI 75 response n (%)	16 (4.9%)	219 (67.0%) **	249 (77.1%) **	142 (44.0%)	247 (75.5%)	280 (86.7%)	189 (58.5%)	215 (65.7%)	254 (78.6%)	179 (55.4%)
PASI 90 response n (%)	5 (1.5%)	137 (41.9%)	175 (54.2%)	67 (20.7%)	176 (53.8%)	234 (72.4%)	101 (31.3%)	147 (45.0%)	210 (65.0%)	108 (33.4%)
PASI 100 response n (%)	0 (0%)	47 (14.4%)	78 (24.1%)	14 (4.3%)	84 (25.7%)	119 (36.8%)	24 (7.4%)	65 (19.9%)	117 (36.2%)	32 (9.9%)
IGA mod 2011 “clear” or “almost clear” response n (%)	9 (2.8%)	167 (51.1%) **	202 (62.5%) **	88 (27.2%)	200 (61.2%)	244 (75.5%)	127 (39.3%)	168 (51.4%)	219 (67.8%)	120 (37.2%)

** p-values versus etanercept: p=0.0250

In an additional psoriasis study (CLEAR) 676 patients were evaluated. Secukinumab 300 mg met the primary and secondary endpoints by showing superiority to ustekinumab based on PASI 90 response at week 16 (primary endpoint), speed of onset of PASI 75 response at week 4, and long-term PASI 90 response at week 52. Greater efficacy of secukinumab compared to ustekinumab for the endpoints PASI 75/90/100 and IGA mod 2011 0 or 1 response (“clear” or “almost clear”) was observed early and continued through to week 52 (Table 6).

Table 6 Summary of clinical response on CLEAR study

	Week 4		Week 16		Week 52	
	Secukinumab 300 mg	**Ustekinumab***	**Secukinumab 300 mg**	**Ustekinumab***	**Secukinumab 300 mg**	**Ustekinumab***
Number of patients	334	335	334	335	334	335
PASI 75 response n (%)	166 (49.7%)**	69 (20.6%)	311 (93.1%)	276 (82.4%)	306 (91.6%)	262 (78.2%)
PASI 90 response n (%)	70 (21.0%)	18 (5.4%)	264 (79.0%)**	192 (57.3%)	250 (74.9%)***	203 (60.6%)
PASI 100 response n (%)	14 (4.2%)	3 (0.9%)	148 (44.3%)	95 (28.4%)	150 (44.9%)	123 (36.7%)
IGA mod 2011 “clear” or “almost clear” response n (%)	128 (38.3%)	41 (12.2%)	278 (83.2%)	226 (67.5%)	261 (78.1%)	213 (63.6%)

* Patients treated with secukinumab received 300 mg doses at weeks 0, 1, 2 3 and 4, followed by the same dose every 4 weeks until week 52. Patients treated with ustekinumab received 45 mg or 90 mg at weeks 0 and 4, then every 12 weeks until week 52 (dosed by weight as per approved posology)

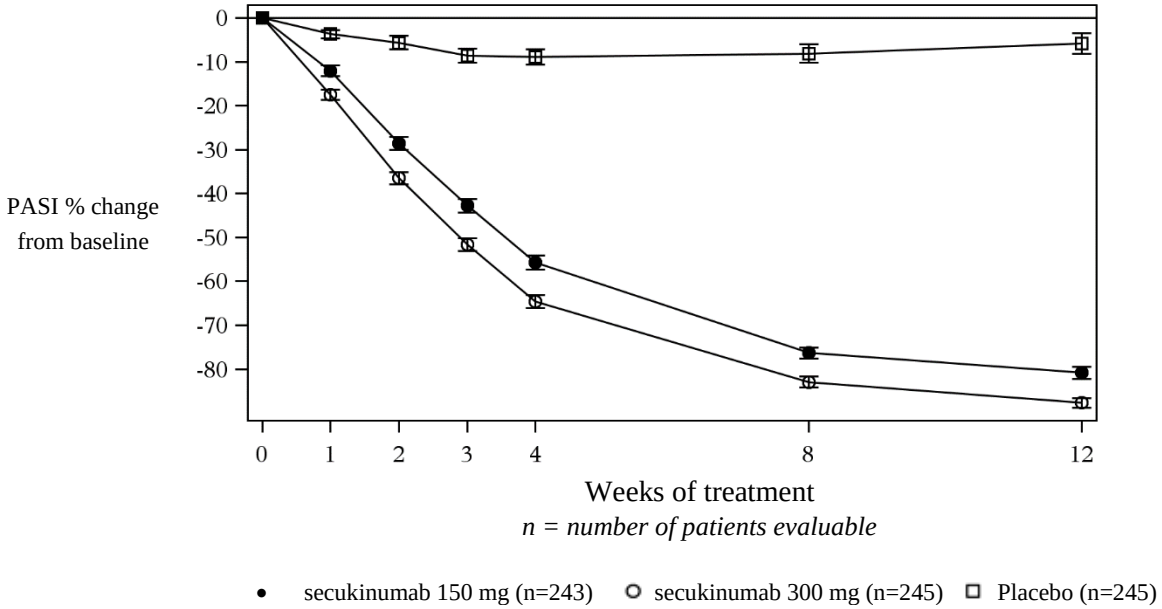
** p-values versus ustekinumab: p<0.0001 for primary endpoint of PASI 90 at week 16 and secondary endpoint of PASI 75 at week 4

*** p-values versus ustekinumab: p=0.0001 for secondary endpoint of PASI 90 at week 52

Secukinumab was efficacious in systemic treatment-naive, biologic-naive, biologic/anti-TNF-exposed and biologic/anti-TNF-failure patients. Improvements in PASI 75 in patients with concurrent psoriatic arthritis at baseline were similar to those in the overall plaque psoriasis population.

Secukinumab was associated with a fast onset of efficacy with a 50% reduction in mean PASI by week 3 for the 300 mg dose.

Figure 1 Time course of percentage change from baseline of mean PASI score in study 1 (ERASURE)



Specific locations/forms of plaque psoriasis
In two additional placebo-controlled studies, improvement was seen in both nail psoriasis (TRANSFIGURE, 198 patients) and palmoplantar plaque psoriasis (GESTURE, 205 patients). In the TRANSFIGURE study, secukinumab was superior to placebo at week 16 (46.1% for 300 mg, 38.4% for 150 mg and 11.7% for placebo) as assessed by significant improvement from baseline in the Nail Psoriasis Severity Index (NAPSI %) for patients with moderate to severe plaque psoriasis with nail involvement. In the GESTURE study, secukinumab was superior to placebo at week 16 (33.3% for 300 mg, 22.1% for 150 mg, and 1.5% for placebo) as assessed by significant improvement of ppIGA 0 or 1 response ("clear" or "almost clear") for patients with moderate to severe palmoplantar plaque psoriasis.

A placebo-controlled study evaluated 102 patients with moderate to severe scalp psoriasis, defined as having a Psoriasis Scalp Severity Index (PSSI) score of ≥12, an IGA mod 2011 scalp only score of 3 or greater and at least 30% of the scalp surface area affected. Secukinumab 300 mg was superior to placebo at week 12 as assessed by significant improvement from baseline in both the PSSI 90 response (52.9% versus 2.0%) and IGA mod 2011 0 or 1 scalp only response (56.9% versus 5.9%). Improvement in both endpoints was sustained for secukinumab patients who continued treatment through to week 24.

Quality of life/patient-reported outcomes
Statistically significant improvements at week 12 (studies 1-4) from baseline compared to placebo were demonstrated in the DLQI (Dermatology Life Quality Index). Mean decreases (improvements) in DLQI from baseline ranged from -10.4 to -11.6 with secukinumab 300 mg, from -7.7 to -10.1 with secukinumab 150 mg, versus -1.1 to -1.9 for placebo at week 12. These improvements were maintained for 52 weeks (studies 1 and 2).

Forty percent of the participants in studies 1 and 2 completed the Psoriasis Symptom Diary©. For the participants completing the diary in each of these studies, statistically significant improvements at week 12 from baseline compared to placebo in patient-reported signs and symptoms of itching, pain and scaling were demonstrated.

Statistically significant improvements at week 4 from baseline in patients treated with secukinumab compared to patients treated with ustekinumab (CLEAR) were demonstrated in the DLQI and these improvements were maintained for up to 52 weeks.

Statistically significant improvements in patient-reported signs and symptoms of itching, pain and scaling at week 16 and week 52 (CLEAR) were demonstrated in the Psoriasis Symptom Diary© in patients treated with secukinumab compared to patients treated with ustekinumab.

Statistically significant improvements (decreases) at week 12 from baseline in the scalp psoriasis study were demonstrated in patient reported signs and symptoms of scalp itching, pain and scaling compared to placebo.

Plaque psoriasis dose flexibility
A randomised, double-blind, multicentre study evaluated two maintenance dosing regimens (300 mg every 2 weeks [Q2W] and 300 mg every 4 weeks [Q4W]) administered by 150 mg pre-filled syringe in 331 patients weighing ≥90 kg with moderate to severe psoriasis. Patients were randomised 1:1 as follows:

- secukinumab 300 mg at weeks 0, 1, 2, 3, and 4 followed by the same dose every 2 weeks (Q2W) up to week 52 (n=165).
- secukinumab 300 mg at weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks (Q4W) up to week 16 (n=166).
    - Patients randomised to receive secukinumab 300 mg Q4W who were PASI 90 responders at week 16 continued to receive the same dosing regimen up to week 52. Patients randomised to receive secukinumab 300 mg Q4W who were PASI 90 non-responders at week 16 either continued on the same dosing regimen, or were reassigned to receive secukinumab 300 mg Q2W up to week 52.

Overall, the efficacy response rates for the group treated with the every 2 weeks regimen were higher compared to the group treated with the every 4 weeks regimen (Table 7).

Table 7 Summary of clinical response in the plaque psoriasis dose flexibility study*

	Week 16		**Week 52**	
	secukinumab 300 mg Q2W	**secukinumab 300 mg Q4W**	**secukinumab 300 mg Q2W**	**secukinumab 300 mg Q4W**[1]
Number of patients	165	166	165	83
PASI 90 response n (%)	121 (73.2%) **	92 (55.5%)	126 (76.4%)	44 (52.4%)
IGA mod 2011 "clear" or "almost clear" response n (%)	122 (74.2%)[2]	109 (65.9%)[2]	125 (75.9%)	46 (55.6%)

* Multiple imputation
[1] 300 mg Q4W:patients continuously treated with 300 mg Q4W regardless of PASI 90 response status at week 16; 43 patients were PASI 90 responder at week 16 and 40 patients were PASI 90 non-responders at week 16
** One sided p-value = 0.0003 for primary endpoint of PASI 90 at week 16
[2] Not statistically significant

In the PASI 90 non-responders at week 16 who were up-titrated to secukinumab 300 mg Q2W, the PASI 90 response rates improved compared to those who remained on the secukinumab 300 mg Q4W dosing regimen, while the IGA mod 2011 0/1 response rates remained stable over time in both treatment groups.

The safety profiles of the two dosing regimens, Cosentyx 300 mg administered every 4 weeks and Cosentyx 300 mg administered every 2 weeks, in patients weighing ≥90 kg were comparable and consistent with the safety profile reported in psoriasis patients.

Hidradenitis suppurativa

The safety and efficacy of secukinumab were assessed in 1 084 patients in two randomised, double-blind, placebo-controlled phase III studies in adult patients with moderate to severe hidradenitis suppurativa (HS) who were candidates for systemic biologic therapy. Patients were required to have at least five inflammatory lesions affecting at least two anatomical areas at baseline. In HS study 1 (SUNSHINE) and HS study 2 (SUNRISE), respectively, 4.6% and 2.8% of patients were Hurley stage I, 61.4% and 56.7% were Hurley stage II, and 34.0% and 40.5% were Hurley stage III.The proportion of patients weighing ≥90 kg was 54.7% in HS study 1 and 50.8% in HS study 2. Patients in these studies had a diagnosis of moderate to severe HS for a mean of 7.3 years and 56.3% of the study participants were female.

In HS study 1 and HS study 2, 23,8% and 23,2% of patients, respectively, were previously treated with a biologic. 82.3% and 83.6% of patients, respectively, were previously treated with systemic antibiotics.

HS study 1 evaluated 541 patients and HS study 2 evaluated 543 patients, of whom 12.8% and 10.7%, respectively, received concomitant stable-dose antibiotics. In both studies, patients randomised to secukinumab received 300 mg subcutaneously at weeks 0, 1, 2, 3 and 4, followed by 300 mg every 2 weeks (Q2W) or every 4 weeks (Q4W). At week 16, patients who were randomised to placebo were reassigned to receive secukinumab 300 mg at weeks 16, 17, 18, 19 and 20 followed by either secukinumab 300 mg Q2W or secukinumab 300 mg Q4W.

The primary endpoint in both studies (HS study 1 and HS study 2) was the proportion of patients achieving a Hidradenitis Suppurativa Clinical Response defined as at least a 50% decrease in abscesses and inflammatory nodules count with no increase in the number of abscesses and/or in the number of draining fistulae relative to baseline (HiSCR50) at week 16. Reduction in HS-related skin pain was assessed as a secondary endpoint on the pooled data of HS study 1 and HS study 2 using a Numerical Rating Scale (NRS) in patients who entered the studies with an initial baseline score of 3 or greater.

In HS study 1 and HS study 2, a higher proportion of patients treated with secukinumab 300 mg Q2W achieved a HiSCR50 response with a decrease in abscesses and inflammatory nodules (AN) count compared to placebo at week 16. In HS study 2, a difference in HiSCR50 response and AN count was also observed with the secukinumab 300 mg Q4W regimen. In the secukinumab 300 mg Q2W group in HS study 1 and in the secukinumab 300 mg Q4W group in HS study 2, a lower rate of patients experienced flares compared to placebo up to week 16. A higher proportion of patients treated with secukinumab 300 mg Q2W (pooled data) experienced a clinically relevant decrease in HS-related skin pain compared to placebo at week 16 (Table 8).

Table 8 Clinical response in HS study 1 and HS study 2 at week 16[1]

	HS study 1			HS study 2		
	Placebo	300 mg Q4W	300 mg Q2W	Placebo	300 mg Q4W	300 mg Q2W
Number of patients randomised	180	180	181	183	180	180
HiSCR50, n (%)	61 (33.7)	75 (41.8)	82 (45.0*)	57 (31.2)	83 (46.1*)	76 (42.3*)
AN count, mean % change from baseline	-24.3	-42.4	-46.8*	-22.4	-45.5*	-39.3*
Flares, n (%)	52 (29.0)	42 (23.2)	28 (15.4*)	50 (27.0)	28 (15.6*)	36 (20.1)
	Pooled data (HS study 1 and HS study 2)					
	Placebo		300 mg Q4W		300 mg Q2W	
Number of patients with NRS ≥3 at baseline	251		252		266	
≥30% reduction in skin pain, NRS30 response, n (%)	58 (23.0)		84 (33.5)		97 (36.6*)	

[1] Multiple imputation was implemented to handle missing data
n: Rounded average number of subjects with responses in 100 imputations
*Statistically significant versus placebo based on the pre-defined hierarchy with overall alpha=0.05
AN: Abscesses and inflammatory Nodules; HiSCR: Hidradenitis Suppurativa Clinical Response; NRS: Numerical Rating Scale

In both studies, the onset of action of secukinumab occurred as early as week 2, the efficacy progressively increased to week 16 and was maintained up to week 52.

Improvements were seen for the primary and key secondary endpoints in HS patients regardless of previous or concomitant antibiotic treatment.

HiSCR50 responses were improved at week 16 in both biologic-naïve and biologic-exposed patients.

Greater improvements at week 16 from baseline compared to placebo were demonstrated in health-related quality of life as measured by the Dermatology Life Quality Index.

Psoriatic arthritis
The safety and efficacy of secukinumab were assessed in 1 999 patients in three randomised, double-blind, placebo-controlled phase III studies in patients with active psoriatic arthritis (≥3 swollen and ≥3 tender joints) despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients with each subtype of PsA were enrolled in these studies, including polyarticular arthritis with no evidence of rheumatoid nodules, spondylitis with peripheral arthritis, asymmetric peripheral arthritis, distal interphalangeal involvement and arthritis mutilans. Patients in these studies had a diagnosis of PsA of at least five years. The majority of patients also had active psoriasis skin lesions or a documented history of psoriasis. Over 61% and 42% of the PsA patients had enthesitis and dactylitis at baseline, respectively. For all studies, the primary endpoint was American College of Rheumatology (ACR) 20 response. For Psoriatic Arthritis study 1 (PsA study 1) and Psoriatic Arthritis study 2 (PsA study 2), the primary endpoint was at week 24. For Psoriatic Arthritis study 3 (PsA study 3), the primary endpoint was at week 16 with the key secondary endpoint, the change from baseline in modified Total Sharp Score (mTSS), at week 24.

In PsA study 1, PsA study 2 and PsA study 3, 29%, 35% and 30% of patients, respectively, were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

PsA study 1 (FUTURE 1) evaluated 606 patients, of whom 60.7% had concomitant MTX. Patients randomised to secukinumab received 10 mg/kg intravenously at weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously every month starting at week 8. Patients randomised to placebo who were non-responders at week 16 (early rescue) and other placebo patients at week 24 were crossed over to receive secukinumab (either 75 mg or 150 mg subcutaneously) followed by the same dose every month.

PsA study 2 (FUTURE 2) evaluated 397 patients, of whom 46.6% had concomitant MTX. Patients randomised to secukinumab received 75 mg, 150 mg or 300 mg subcutaneously at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients randomised to receive placebo who were non-responders at week 16 (early rescue) were crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 16 followed by the same dose every month. Patients randomised to receive placebo who were responders at week 16 were crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 24 followed by the same dose every month.

PsA study 3 (FUTURE 5) evaluated 996 patients, of whom 50.1% had concomitant MTX. Patients were randomised to receive secukinumab 150 mg, 300 mg or placebo subcutaneously at weeks 0, 1, 2, 3 and 4, followed by the same dose every month, or a once monthly injection of secukinumab 150 mg (without loading). Patients randomised to receive placebo who were non-responders at week 16 (early rescue) were then crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 16 followed by the same dose every month. Patients randomised to receive placebo who were responders at week 16 were crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 24 followed by the same dose every month.

Signs and symptoms
Treatment with secukinumab resulted in significant improvement in measures of disease activity compared to placebo at weeks 16 and 24 (see Table 9).

Table 9 Clinical response in PsA study 2 and PsA study 3 at week 16 and week 24

	PsA study 2			**PsA study 3**		
	Placebo	150 mg[1]	300 mg[1]	Placebo	150 mg[1]	300 mg[1]
Number of patients randomised	98	100	100	332	220	222
ACR20 response n (%)						
Week 16	18 (18.4%)	60 (60.0%***)	57 (57.0%***)	91◊ (27.4%)	122◊ (55.5%***)	139◊ (62.6%***)
Week 24	15◊ (15.3%)	51◊ (51.0%***)	54◊ (54.0%***)	78 (23.5%)	117 (53.2%***)	141 (63.5%***)
ACR50 response n (%)						
Week 16	6 (6.1%)	37 (37.0%***)	35 (35.0%***)	27 (8.1%)	79 (35.9%*)	88 (39.6%*)
Week 24	7 (7.1%)	35 (35.0%)	35 (35.0%**)	29 (8.7%)	86 (39.1%***)	97 (43.7%***)
ACR70 response n (%)						
Week 16	2 (2.0%)	17 (17.0%**)	15 (15.0%**)	14 (4.2%)	40 (18.2%***)	45 (20.3%***)
Week 24	1 (1.0%)	21 (21.0%**)	20 (20.0%**)	13 (3.9%)	53 (24.1%***)	57 (25.7%***)
DAS28-CRP						
Week 16	-0.50	-1.45***	-1.51***	-0.63	-1.29*	-1.49*
Week 24	-0.96	-1.58**	-1.61**	-0.84	-1.57***	-1.68***

Number of patients with ≥3% BSA psoriasis skin involvement at baseline	43 (43.9%)	58 (58.0%)	41 (41.0%)	162 (48.8%)	125 (56.8%)	110 (49.5%)
PASI 75 response n (%)						
Week 16	3 (7.0%)	33 (56.9%***)	27 (65.9%***)	20 (12.3%)	75 (60.0%*)	77 (70.0%*)
Week 24	7 (16.3%)	28 (48.3%**)	26 (63.4%***)	29 (17.9%)	80 (64.0%***)	78 (70.9%***)
PASI 90 response n (%)						
Week 16	3 (7.0%)	22 (37.9%***)	18 (43.9%***)	15 (9.3%)	46 (36.8%*)	59 (53.6%*)
Week 24	4 (9.3%)	19 (32.8%**)	20 (48.8%***)	19 (11.7%)	51 (40.8%***)	60 (54.5%***)
Dactylitis resolution n (%) †						
Week 16	10 (37%)	21 (65.6%*)	26 (56.5%)	40 (32.3%)	46 (57.5%*)	54 (65.9%*)
Week 24	4 (14.8%)	16 (50.0%**)	26 (56.5%**)	42 (33.9%)	51 (63.8%***)	52 (63.4%***)
Enthesitis resolution n (%) ‡						
Week 16	17 (26.2%)	32 (50.0%**)	32 (57.1%***)	68 (35.4%)	77 (54.6%*)	78 (55.7%*)
Week 24	14 (21.5%)	27 (42.2%*)	27 (48.2%**)	66 (34.4%)	77 (54.6%***)	86 (61.4%***)

* p<0.05, ** p<0.01, *** p<0.001; versus placebo
All p-values are adjusted for multiplicity of testing based on pre-defined hierarchy at week 24 for PsA study 2, except for ACR70, Dactylitis and Enthesitis, which were exploratory endpoints and all endpoints at week 16.
All p-values are adjusted for multiplicity of testing based on pre-defined hierarchy at week 16 for PsA study 3, except for ACR70 which was an exploratory endpoint and all endpoints at week 24.
Non-responder imputation used for missing binary endpoint.
ACR: American College of Rheumatology; PASI: Psoriasis Area and Severity Index; DAS: Disease Activity Score; BSA: Body Surface Area

[◊]Primary Endpoint

[1]Secukinumab 150 mg or 300 mg s.c. at weeks 0, 1, 2, 3, and 4 followed by the same dose every month

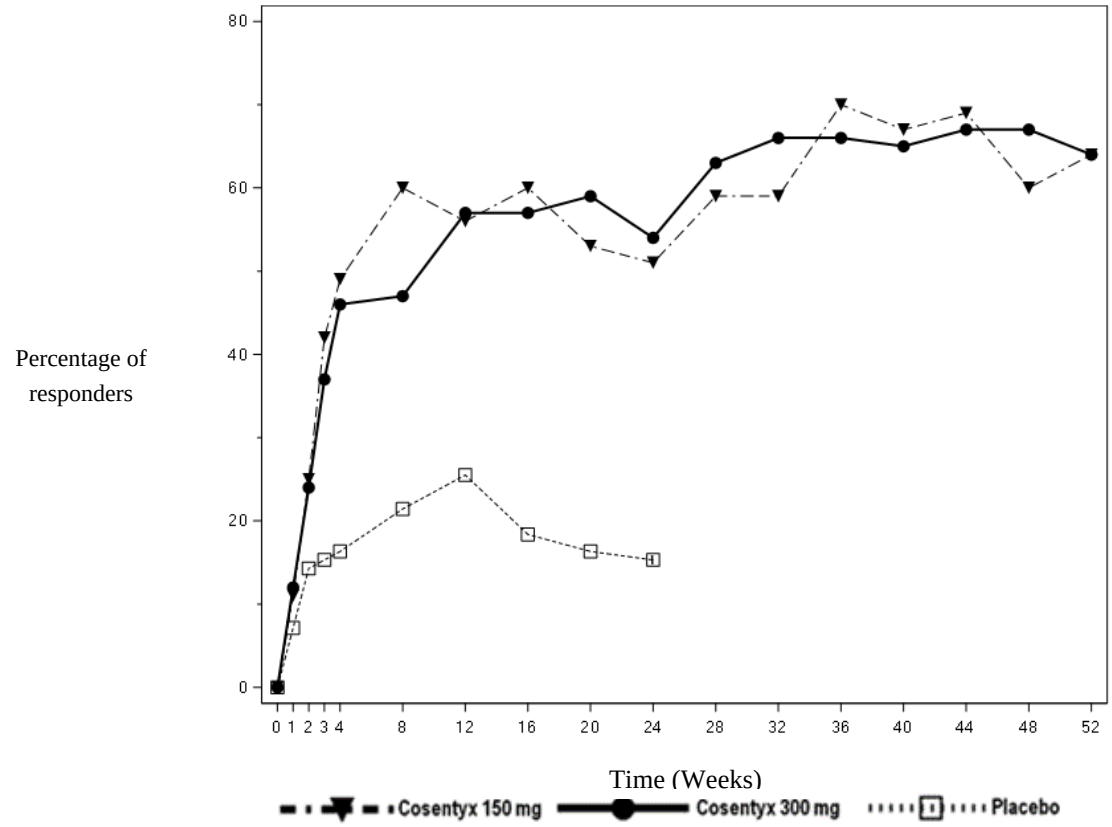
†In patients with dactylitis at baseline (n=27, 32, 46, respectively for PsA study 2 and n=124, 80, 82, respectively for PsA study 3)

‡In patients with enthesitis at baseline (n=65, 64, 56, respectively for PsA study 2 and n=192, 141, 140, respectively for PsA study 3)

The onset of action of secukinumab occurred as early as week 2. Statistically significant difference in ACR 20 versus placebo was reached at week 3.

The percentage of patients achieving ACR 20 response by visit is shown in Figure 2.

Figure 2 ACR20 response in PsA study 2 over time up to week 52



Similar responses for primary and key secondary endpoints were seen in PsA patients regardless of whether they were on concomitant MTX treatment or not. In PsA study 2, at week 24, secukinumab-treated patients with concomitant MTX use had a higher ACR 20 response (47.7% and 54.4% for 150 mg and 300 mg, respectively, compared to placebo 20.0%) and ACR 50 response (31.8% and 38.6% for 150 mg and 300 mg, respectively, compared to placebo 8.0%). Secukinumab-treated patients without concomitant MTX use had a higher ACR 20 response (53.6% and 53.6% for 150 mg and 300 mg, respectively, compared to placebo 10.4%) and ACR 50 response (37.5% and 32.1% for 150 mg and 300 mg, respectively, compared to placebo 6.3%).

In PsA study 2, both anti-TNFα-naive and anti-TNFα-IR secukinumab-treated patients had a significantly higher ACR 20 response compared to placebo at week 24, with a slightly higher response in the anti-TNFα-naive group (anti-TNFα-naive: 64% and 58% for 150 mg and 300 mg, respectively, compared to placebo 15.9%; anti-TNFα-IR: 30% and 46% for 150 mg and 300 mg, respectively, compared to placebo 14.3%). In the anti-TNFα-IR patients subgroup, only the 300 mg dose showed significantly higher response rate for ACR 20 compared to placebo ($p<0.05$) and demonstrated clinical meaningful benefit over 150 mg on multiple secondary endpoints. Improvements in the PASI 75 response were seen in both subgroups and the 300 mg dose showed statistically significant benefit in the anti-TNFα-IR patients.

Improvements were shown in all components of the ACR scores, including patient assessment of pain. In PsA study 2, the proportion of patients achieving a modified PsA Response Criteria (PsARC) response was greater in the secukinumab-treated patients (59.0% and 61.0% for 150 mg and 300 mg, respectively) compared to placebo (26.5%) at week 24.

In PsA study 1 and PsA study 2, efficacy was maintained up to week 104. In PsA study 2, among 200 patients initially randomised to secukinumab 150 mg and 300 mg, 178 (89%) patients were still on treatment at week 52. Of the 100 patients randomised to secukinumab 150 mg, 64, 39 and 20 had an ACR 20/50/70 response, respectively. Of the 100 patients randomised to secukinumab 300 mg, 64, 44 and 24 had an ACR 20/50/70 response, respectively.

Radiographic response
In PsA study 3, inhibition of progression of structural damage was assessed radiographically and expressed by the modified Total Sharp Score (mTSS) and its components, the Erosion Score (ES) and the Joint Space Narrowing Score (JSN). Radiographs of hands, wrists, and feet were obtained at baseline, week 16 and/or week 24 and scored independently by at least two readers who were blinded to treatment group and visit number. Secukinumab 150 mg and 300 mg treatment significantly inhibited the rate of progression of peripheral joint damage compared with placebo treatment as measured by change from baseline in mTSS at week 24 (Table 10).

Inhibition of progression of structural damage was also assessed in PsA study 1 at weeks 24 and 52, compared to baseline. Week 24 data are presented in Table 10.

Table 10 Change in modified Total Sharp Score in psoriatic arthritis

	PsA study 3			**PsA study 1**	
	Placebo n=296	**secukinumab 150 mg[1] n=213**	**secukinumab 300 mg[1] n=217**	**Placebo n=179**	**secukinumab 150 mg[2] n=185**
Total score					
Baseline (SD)	15.0 (38.2)	13.5 (25.6)	12.9 (23.8)	28.4 (63.5)	22.3 (48.0)
Mean change at week 24	0.50	0.13*	0.02*	0.57	0.13*
*p<0.05 based on nominal, but non adjusted, p-value [1]secukinumab 150 mg or 300 mg s.c. at weeks 0, 1, 2, 3, and 4 followed by the same dose every month [2]10 mg/kg at weeks 0, 2 and 4 followed by subcutaneous doses of 75 mg or 150 mg					

In PsA study 1, inhibition of structural damage was maintained with secukinumab treatment up to week 52.

In PsA study 3, the percentage of patients with no disease progression (defined as a change from baseline in mTSS of ≤0.5) from randomisation to week 24 was 80.3%, 88.5% and 73.6% for secukinumab 150 mg, 300 mg and placebo, respectively. An effect of inhibition of structural damage was observed in anti-TNFα-naïve and anti-TNFα-IR patients and in patients treated with and without concomitant MTX.

In PsA study 1, the percentage of patients with no disease progression (defined as a change from baseline in mTSS of ≤0.5) from randomisation to week 24 was 82.3% in secukinumab 10 mg/kg intravenous load – 150 mg subcutaneous maintenance and 75.7% in placebo. The percentage of patients with no disease progression from week 24 to week 52 for secukinumab 10 mg/kg intravenous load – followed by 150 mg subcutaneous maintenance and for placebo patients who switched to 75 mg or 150 mg subcutaneous every 4 weeks at week 16 or week 24 was 85.7% and 86.8%, respectively.

Axial manifestations in PsA
A randomised, double-blind, placebo-controlled study (MAXIMISE) assessed the efficacy of secukinumab in 485 PsA patients with axial manifestations who were naive to biologic treatment and responded inadequately to NSAIDs. The primary variable of at least a 20% improvement in Assessment of SpondyloArthritis International Society (ASAS 20) criteria at week 12 was met. Treatment with secukinumab 300 mg and 150 mg compared to placebo also resulted in greater improvement in signs and symptoms (including decreases from baseline in spinal pain) and improvement in physical function (see Table 11).

Table 11 Clinical response on MAXIMISE study at week 12

	Placebo (n=164)	**150 mg (n=157)**	**300 mg (n=164)**
ASAS 20 response, % (95% CI)	31.2 (24.6, 38.7)	66.3 (58.4, 73.3)*	62.9 (55.2, 70.0)*
ASAS 40 response, % (95% CI)	12.2 (7.8, 18.4)	39.5 (32.1, 47.4)**	43.6 (36.2, 51.3)**
BASDAI 50, % (95% CI)	9.8 (5.9, 15.6)	32.7 (25.8, 40.5)**	37.4 (30.1, 45.4)**
Spinal pain, VAS (95% CI)	-13.6 (-17.2, -10.0)	-28.5 (-32.2, -24.8)**	-26.5 (-30.1, -22.9)**
Physical function, HAQ-DI (95% CI)	-0.155 (-0.224, -0.086)	-0.330 (-0.401, -0.259)**	-0.389 (-0.458, -0.320)**
* p<0.0001; versus placebo using multiple imputation. ** Comparison versus placebo was not adjusted for multiplicity. ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; VAS: Visual Analog Scale; HAQ-DI: Health Assessment Questionnaire – Disability Index.			

Improvement in ASAS 20 and ASAS 40 for both secukinumab doses were observed by week 4 and were maintained up to 52 weeks.

Physical function and health-related quality of life
In PsA study 2 and PsA study 3, patients treated with secukinumab 150 mg (p=0.0555 and p<0.0001) and 300 mg (p=0.0040 and p<0.0001) showed improvement in physical function compared to patients treated with placebo as assessed by Health Assessment Questionnaire-Disability Index (HAQ-DI) at week 24 and week 16, respectively. Improvements in HAQ-DI scores were seen regardless of previous anti-TNFα exposure. Similar responses were seen in PsA study 1.

Secukinumab-treated patients reported significant improvements in health-related quality of life as measured by the Short Form-36 Health Survey Physical Component Summary (SF-36 PCS) score (p<0.001). There were also statistically significant improvements demonstrated in exploratory endpoints assessed by the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) scores for 150 mg and 300 mg compared to placebo (7.97, 5.97 versus 1.63, respectively) and these improvements were maintained up to week 104 in PsA study 2.

Similar responses were seen in PsA study 1 and efficacy was maintained up to week 52.

Axial spondyloarthritis (axSpA)
Ankylosing spondylitis (AS) / Radiographic axial spondyloarthritis
The safety and efficacy of secukinumab were assessed in 816 patients in three randomised, double-blind, placebo-controlled phase III studies in patients with active ankylosing spondylitis (AS) with a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4 despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients in Ankylosing Spondylitis study 1 (AS study 1) and Ankylosing Spondylitis study 2 (AS study 2) had a diagnosis of AS for a median of 2.7 to 5.8 years. For both studies, the primary endpoint was at least a 20% improvement in Assessment of SpondyloArthritis International Society (ASAS 20) criteria at week 16.

In Ankylosing Spondylitis study 1 (AS study 1), Ankylosing Spondylitis study 2 (AS study 2), and Ankylosing Spondylitis study 3 (AS study 3), 27.0%, 38.8%, and 23.5% of patients, respectively, were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

AS study 1 (MEASURE 1) evaluated 371 patients, of whom 14.8% and 33.4% used concomitant MTX or sulfasalazine, respectively. Patients randomised to secukinumab received 10 mg/kg intravenously at weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously every month starting at week 8. Patients randomised to placebo who were non-responders at week 16 (early rescue) and all other placebo patients at week 24 were crossed over to receive secukinumab (either 75 mg or 150 mg subcutaneously), followed by the same dose every month.

AS study 2 (MEASURE 2) evaluated 219 patients, of whom 11.9% and 14.2% used concomitant MTX or sulfasalazine, respectively. Patients randomised to secukinumab received 75 mg or 150 mg subcutaneously at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. At week 16, patients who were randomised to placebo at baseline were re-randomised to receive secukinumab (either 75 mg or 150 mg subcutaneously) every month.

AS study 3 (MEASURE 3) evaluated 226 patients, of whom 13.3% and 23.5% used concomitant MTX or sulfasalazine, respectively. Patients randomised to secukinumab received 10 mg/kg intravenously at weeks 0, 2, and 4, followed by either 150 mg or 300 mg subcutaneously every month. At week 16, patients who were randomised to placebo at baseline were re-randomised to receive secukinumab (either 150 mg or 300 mg subcutaneously) every month. The primary endpoint was ASAS 20 at week 16. Patients were blinded to the treatment regimen up to week 52, and the study continued to week 156.

Signs and symptoms:
In AS study 2, treatment with secukinumab 150 mg resulted in greater improvement in measures of disease activity compared with placebo at week 16 (see Table 12).

Table 12 Clinical response in AS study 2 at week 16

Outcome (p-value versus placebo)	**Placebo (n = 74)**	**75 mg (n = 73)**	**150 mg (n = 72)**
ASAS 20 response, %	28.4	41.1	61.1***
ASAS 40 response, %	10.8	26.0	36.1***
hsCRP, (post-BSL/BSL ratio)	1.13	0.61	0.55***
ASAS 5/6, %	8.1	34.2	43.1***
ASAS partial remission, %	4.1	15.1	13.9
BASDAI 50, %	10.8	24.7*	30.6**
ASDAS-CRP major improvement	4.1	15.1*	25.0***

* $p<0.05$, ** $p<0.01$, *** $p<0.001$; versus placebo
All p-values adjusted for multiplicity of testing based on pre-defined hierarchy, except BASDAI 50 and ASDAS-CRP
Non-responder imputation used for missing binary endpoint

ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; hsCRP: high-sensitivity C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score; BSL: baseline

The onset of action of secukinumab 150 mg occurred as early as week 1 for ASAS 20 and week 2 for ASAS 40 (superior to placebo) in AS study 2.

ASAS 20 responses were improved at week 16 in both anti-TNFα-naïve patients (68.2% versus 31.1%; $p<0.05$) and anti-TNFα-IR patients (50.0% versus 24.1%; $p<0.05$) for secukinumab 150 mg compared with placebo, respectively.

In AS study 1 and AS study 2, secukinumab-treated patients (150 mg in AS study 2 and both regimens in AS study 1) demonstrated significantly improved signs and symptoms at week 16, with comparable magnitude of response and efficacy maintained up to week 52 in both anti-TNFα-naive and anti-TNFα-IR patients. In AS study 2, among 72 patients initially randomised to secukinumab 150 mg, 61 (84.7%) patients were still on treatment at week 52. Of the 72 patients randomised to secukinumab 150 mg, 45 and 35 had an ASAS 20/40 response, respectively.

In AS study 3, patients treated with secukinumab (150 mg and 300 mg) demonstrated improved signs and symptoms, and had comparable efficacy responses regardless of dose that were superior to placebo at week 16 for the primary endpoint (ASAS 20). Overall, the efficacy response rates for the 300 mg group were consistently greater compared to the 150 mg group for the secondary endpoints. During the blinded period, the ASAS 20 and ASAS 40 responses were 69.7% and 47.6% for 150 mg and 74.3% and 57.4% for 300 mg at week 52, respectively. The ASAS 20 and ASAS 40 responses were maintained up to week 156 (69.5% and 47.6% for 150 mg versus 74.8% and 55.6% for 300 mg). Greater response rates favouring 300 mg were also observed for ASAS partial remission (ASAS PR) response at week 16 and were maintained up to week 156. Larger differences in response rates, favouring 300 mg over 150 mg, were observed in anti-TNFα-IR patients (n=36) compared to anti-TNFα-naïve patients (n=114).

Spinal mobility:
Patients treated with secukinumab 150 mg showed improvements in spinal mobility as measured by change from baseline in BASMI at week 16 for both AS study 1 (-0.40 versus -0.12 for placebo; p=0.0114) and AS study 2 (-0.51 versus -0.22 for placebo; p=0.0533). These improvements were sustained up to week 52.

Physical function and health-related quality of life:
In AS study 1 and study 2, patients treated with secukinumab 150 mg showed improvements in health-related quality of life as measured by AS Quality of Life Questionnaire (ASQoL) (p=0.001) and SF-36 Physical Component Summary (SF-36PCS) (p<0.001). Patients treated with secukinumab 150 mg also showed statistically significant improvements on exploratory endpoints in physical function as assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI) compared to placebo (-2.15 versus -0.68), and in fatigue as assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale compared to placebo (8.10 versus 3.30). These improvements were sustained up to week 52.

Non-radiographic axial spondyloarthritis (nr-axSpA)
The safety and efficacy of secukinumab were assessed in 555 patients in one randomised, double-blind, placebo-controlled phase III study (PREVENT), consisting of a 2-year core phase and a 2-year extension phase, in patients with active non-radiographic axial spondyloarthritis (nr-axSpA) fulfilling the Assessment of SpondyloArthritis International Society (ASAS) classification criteria for axial spondyloarthritis (axSpA) with no radiographic evidence of changes in the sacroiliac joints that would meet the modified New York criteria for ankylosing spondylitis (AS). Patients enrolled had active disease, defined as a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4, a Visual Analogue Scale (VAS) for total back pain of ≥40 (on a scale of 0-100 mm), despite current or previous non-steroidal anti-inflammatory drug (NSAID) therapy and increased C-reactive protein (CRP) and/or evidence of sacroiliitis on Magnetic Resonance Imaging (MRI). Patients in this study had a diagnosis of axSpA for a mean of 2.1 to 3.0 years and 54% of the study participants were female.

In the PREVENT study, 9.7% of patients were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

In the PREVENT study, 9.9% and 14.8% of patients used concomitant MTX or sulfasalazine, respectively. In the double-blind period, patients received either placebo or secukinumab for 52 weeks. Patients randomised to secukinumab received 150 mg subcutaneously at weeks 0, 1, 2, 3 and 4 followed by the same dose every month, or a once monthly injection of secukinumab 150 mg. The primary endpoint was at least 40% improvement in Assessment of SpondyloArthritis International Society (ASAS 40) at Week 16 in anti-TNFα-naive patients.

Signs and symptoms:
In the PREVENT study, treatment with secukinumab 150 mg resulted in significant improvements in the measures of disease activity compared to placebo at week 16. These measures include ASAS 40, ASAS 5/6, BASDAI score, BASDAI 50, high-sensitivity CRP (hsCRP), ASAS 20 and ASAS partial remission response compared to placebo (Table 13). Responses were maintained up to week 52.

Table 13 Clinical response in the PREVENT study at week 16

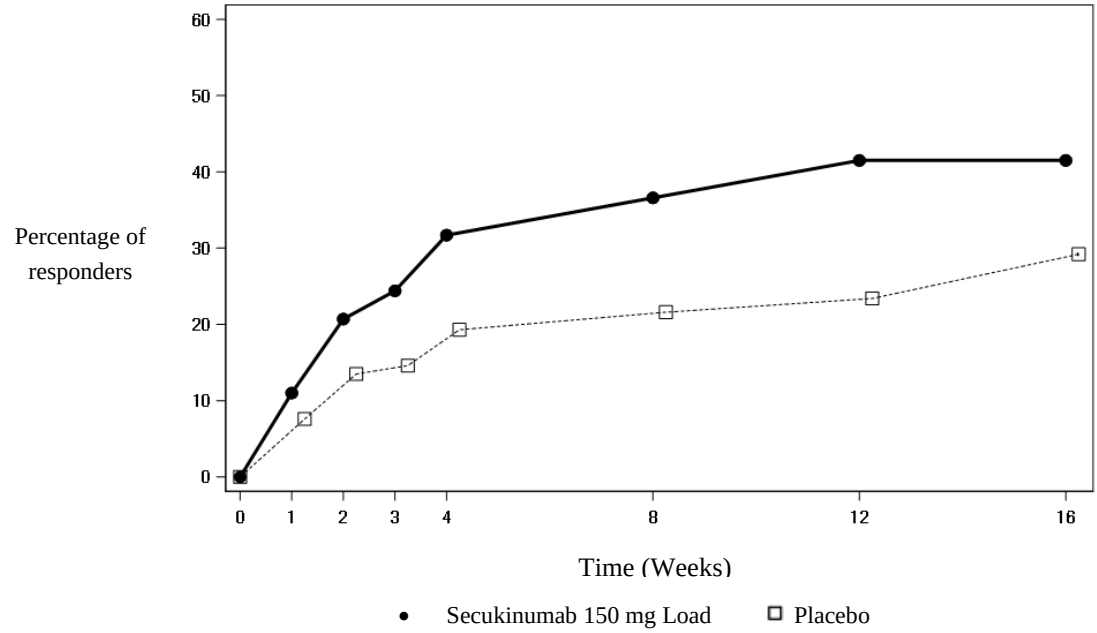
Outcome (p-value versus placebo)	**Placebo**	**150 mg[1]**
Number of anti-TNFα-naive patients randomised	**171**	**164**
ASAS 40 response, %	29.2	41.5*
Total number of patients randomised	**186**	**185**
ASAS 40 response, %	28.0	40.0*
ASAS 5/6, %	23.7	40.0*
BASDAI, LS mean change from baseline score	-1.46	-2.35*
BASDAI 50, %	21.0	37.3*
hsCRP, (post-BSL/BSL ratio)	0.91	0.64*
ASAS 20 response, %	45.7	56.8*
ASAS partial remission, %	7.0	21.6*

*p<0.05 versus placebo
All p-values adjusted for multiplicity of testing based on pre-defined hierarchy
Non-responder imputation used for missing binary endpoint
[1]secukinumab 150 mg s.c. at weeks 0, 1, 2, 3, and 4 followed by the same dose every month

ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; hsCRP: high-sensitivity C-reactive protein; BSL: baseline; LS: Least square

The onset of action of secukinumab 150 mg occurred as early as week 3 for ASAS 40 in anti-TNFα naive patients (superior to placebo) in the PREVENT study. The percentage of patients achieving an ASAS 40 response in anti-TNFα naive patients by visit is shown in Figure 3.

Figure 3 ASAS 40 responses in anti-TNFα naive patients in the PREVENT study over time up to week 16



ASAS 40 responses were also improved at week 16 in anti-TNFα-IR patients for secukinumab 150 mg compared with placebo.

Physical function and health-related quality of life:
Patients treated with secukinumab 150 mg showed statistically significant improvements by week 16 compared to placebo-treated patients in physical function as assessed by the BASFI (week 16: -1.75 versus -1.01, $p<0.05$). Patients treated with secukinumab reported significant improvements compared to placebo-treated patients by week 16 in health-related quality of life as measured by ASQoL (LS mean change: week 16: -3.45 versus -1.84, $p<0.05$) and SF-36 Physical Component Summary (SF-36 PCS) (LS mean change: week 16: 5.71 versus 2.93, $p<0.05$). These improvements were sustained up to week 52.

Spinal mobility:
Spinal mobility was assessed by BASMI up to week 16. Numerically greater improvements were demonstrated in patients treated with secukinumab compared with placebo-treated patients at weeks 4, 8, 12 and 16.

Inhibition of inflammation in magnetic resonance imaging (MRI):
Signs of inflammation were assessed by MRI at baseline and week 16 and expressed as change from baseline in Berlin SI-joint oedema score for sacroiliac joints and ASspiMRI-a score and Berlin spine score for the spine. Inhibition of inflammatory signs in both sacroiliac joints and the spine was observed in patients treated with secukinumab. Mean change from baseline in Berlin SI-joint oedema score was -1.68 for patients treated with secukinumab 150 mg (n=180) versus -0.39 for the placebo-treated patients (n=174) ($p<0.05$).

Paediatric population

Paediatric plaque psoriasis
Secukinumab has been shown to improve signs and symptoms, and health-related quality of life in paediatric patients 6 years and older with plaque psoriasis (see Tables 15 and 17).

Severe plaque psoriasis
The safety and efficacy of secukinumab were assessed in a randomised, double-blind, placebo and etanercept-controlled phase III study in paediatric patients from 6 to <18 years of age with severe plaque psoriasis, as defined by a PASI score ≥20, an IGA mod 2011 score of 4, and BSA involvement of ≥10%, who were candidates for systemic therapy. Approximately 43% of the patients had prior exposure to phototherapy, 53% to conventional systemic therapy, 3% to biologics, and 9% had concomitant psoriatic arthritis.

The paediatric psoriasis study 1 evaluated 162 patients who were randomised to receive low dose secukinumab (75 mg for body weight <50 kg or 150 mg for body weight ≥50 kg), high dose secukinumab (75 mg for body weight <25 kg, 150 mg for body weight between ≥25 kg and <50 kg, or 300 mg for body weight ≥50 kg), or placebo at weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks, or etanercept. Patients randomised to etanercept received 0.8 mg/kg weekly (up to a maximum of 50 mg). Patient distribution by weight and age at randomisation is described in Table 14.

Table 14 Patient distribution by weight and age for paediatric psoriasis study 1

Randomisation strata	**Description**	**Secukinumab low dose n=40**	**Secukinumab high dose n=40**	**Placebo n=41**	**Etanercept n=41**	**Total N=162**
Age	6-<12 years	8	9	10	10	37
	≥12-<18 years	32	31	31	31	125
Weight	<25 kg	2	3	3	4	12
	≥25-<50 kg	17	15	17	16	65
	≥50 kg	21	22	21	21	85

Patients randomised to receive placebo who were non-responders at week 12 were switched to either the secukinumab low or high dose group (dose based on body weight group) and received study drug at weeks 12, 13, 14, and 15, followed by the same dose every 4 weeks starting at week 16. The co-primary endpoints were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 ‘clear’ or ‘almost clear’ (0 or 1) response at week 12.

During the 12 week placebo-controlled period, the efficacy of both the low and the high dose of secukinumab was comparable for the co-primary endpoints. The odds ratio estimates in favour of both secukinumab doses were statistically significant for both the PASI 75 and IGA mod 2011 0 or 1 responses.

All patients were followed for efficacy and safety during the 52 weeks following the first dose. The proportion of patients achieving PASI 75 and IGA mod 2011 ‘clear’ or ‘almost clear’ (0 or 1) responses showed separation between secukinumab treatment groups and placebo at the first post-baseline visit at week 4, the difference becoming more prominent at week 12. The response was maintained throughout the 52 week time period (see Table 15). Improvement in PASI 50, 90, 100 responder rates and Children’s Dermatology Life Quality Index (CDLQI) scores of 0 or 1 were also maintained throughout the 52 week time period.

In addition, PASI 75, IGA 0 or 1, PASI 90 response rates at weeks 12 and 52 for both secukinumab low and high dose groups were higher than the rates for patients treated with etanercept (see Table 15).

Beyond week 12, efficacy of both the low and the high dose of secukinumab was comparable although the efficacy of the high dose was higher for patients ≥50 kg. The safety profiles of the low dose and the high dose were comparable and consistent with the safety profile in adults.

Table 15 Summary of clinical response in severe paediatric psoriasis at weeks 12 and 52 (paediatric psoriasis study 1)*

Response criterion	Treatment comparison 'test' vs. 'control'	'test' n**/m (%)	'control' n**/m (%)	odds ratio estimate (95% CI)	p-value
At week 12* **					
PASI 75	secukinumab low dose vs. placebo	32/40 (80.0)	6/41 (14.6)	25.78 (7.08, 114.66)	<0.0001
	secukinumab high dose vs. placebo	31/40 (77.5)	6/41 (14.6)	22.65 (6.31, 98.93)	<0.0001
	secukinumab low dose vs. etanercept	32/40 (80.0)	26/41 (63.4)	2.25 (0.73, 7.38)	
	secukinumab high dose vs. etanercept	31/40 (77.5)	26/41 (63.4)	1.92 (0.64, 6.07)	
IGA 0/1	secukinumab low dose vs. placebo	28/40 (70.0)	2/41 (4.9)	51.77 (10.02, 538.64)	<0.0001
	secukinumab high dose vs. placebo	24/40 (60.0)	2/41 (4.9)	32.52 (6.48, 329.52)	<0.0001
	secukinumab low dose vs. etanercept	28/40 (70.0)	14/41 (34.1)	4.49 (1.60, 13.42)	
	secukinumab high dose vs. etanercept	24/40 (60.0)	14/41 (34.1)	2.86 (1.05, 8.13)	
PASI 90	secukinumab low dose vs. placebo	29/40 (72.5)	1/41 (2.4)	133.67 (16.83, 6395.22)	<0.0001
	secukinumab high dose vs. placebo	27/40 (67.5)	1/41 (2.4)	102.86 (13.22, 4850.13)	<0.0001
	secukinumab low dose vs. etanercept	29/40 (72.5)	12/41 (29.3)	7.03 (2.34, 23.19)	
	secukinumab high dose vs. etanercept	27/40 (67.5)	12/41 (29.3)	5.32 (1.82, 16.75)	
At week 52					
PASI 75	secukinumab low dose vs. etanercept	35/40 (87.5)	28/41 (68.3)	3.12 (0.91, 12.52)	
	secukinumab high dose vs. etanercept	35/40 (87.5)	28/41 (68.3)	3.09 (0.90, 12.39)	
IGA 0/1	secukinumab low dose vs. etanercept	29/40 (72.5)	23/41 (56.1)	2.02 (0.73, 5.77)	
	secukinumab high dose vs. etanercept	30/40 (75.0)	23/41 (56.1)	2.26 (0.81, 6.62)	
PASI 90	secukinumab low dose vs. etanercept	30/40 (75.0)	21/41 (51.2)	2.85 (1.02, 8.38)	
	secukinumab high dose vs. etanercept	32/40 (80.0)	21/41 (51.2)	3.69 (1.27, 11.61)	

* non-responder imputation was used to handle missing values
** n is the number of responders, m = number of patients evaluable
*** extended visit window at week 12
Odds ratio, 95% confidence interval, and p-value are from an exact logistic regression model with treatment group, baseline body-weight category and age category as factors

A higher proportion of paediatric patients treated with secukinumab reported improvement in health-related quality of life as measured by a CDLQI score of 0 or 1 compared to placebo at week 12 (low dose 44.7%, high dose 50%, placebo 15%). Over time up to and including week 52 both secukinumab dose groups were numerically higher than the etanercept group (low dose 60.6%, high dose 66.7%, etanercept 44.4%).

Moderate to severe plaque psoriasis
Secukinumab was predicted to be effective for the treatment of paediatric patients with moderate plaque psoriasis based on the demonstrated efficacy and exposure response relationship in adult patients with moderate to severe plaque psoriasis, and the similarity of the disease course, pathophysiology, and drug effect in adult and paediatric patients at the same exposure levels.

Moreover, the safety and efficacy of secukinumab was assessed in an open-label, two-arm, parallel-group, multicentre phase III study in paediatric patients from 6 to <18 years of age with moderate to severe plaque psoriasis, as defined by a PASI score ≥12, an IGA mod 2011 score of ≥3, and BSA involvement of ≥10%, who were candidates for systemic therapy.

The paediatric psoriasis study 2 evaluated 84 patients who were randomised to receive low dose secukinumab (75 mg for body weight <50 kg or 150 mg for body weight ≥50 kg) or high dose secukinumab (75 mg for body weight <25 kg, 150 mg for body weight between ≥25 kg and <50 kg, or 300 mg for body weight ≥50 kg) at weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks. Patient distribution by weight and age at randomisation is described in Table 16.

Table 16 Patient distribution by weight and age for paediatric psoriasis study 2

Sub-groups	Description	Secukinumab low dose n=42	Secukinumab high dose n=42	Total N=84
Age	6-<12 years	17	16	33
	≥12-<18 years	25	26	51
Weight	<25 kg	4	4	8
	≥25-<50 kg	13	12	25
	≥50 kg	25	26	51

The co-primary endpoints were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 'clear' or 'almost clear' (0 or 1) response at week 12.

The efficacy of both the low and the high dose of secukinumab was comparable and showed statistically significant improvement compared to historical placebo for the co-primary endpoints. The estimated posterior probability of a positive treatment effect was 100%.

Patients were followed for efficacy over a 52 week period after first administration. Efficacy (defined as PASI 75 response and IGA mod 2011 'clear' or 'almost clear' [0 or 1]) was observed as early as the first post-baseline visit at week 2, and the proportion of patients who achieved a PASI 75 response and IGA mod 2011 'clear' or 'almost clear' (0 or 1) increased up to week 24 and were sustained until week 52. Improvement in PASI 90 and PASI 100 were also observed at week 12, increased up to week 24, and were sustained until week 52 (see Table 17).

The safety profiles of the low dose and the high dose were comparable and consistent with the safety profile in adults.

Table 17 Summary of clinical response in moderate to severe paediatric psoriasis at weeks 12 and 52 (paediatric psoriasis study 2)*

	Week 12		Week 52	
	Secukinumab low dose	Secukinumab high dose	Secukinumab low dose	Secukinumab high dose
Number of patients	42	42	42	42
PASI 75 response n (%)	39 (92.9%)	39 (92.9%)	37 (88.1%)	38 (90.5%)
IGA mod 2011 'clear' or 'almost clear' response n (%)	33 (78.6%)	35 (83.3%)	36 (85.7%)	35 (83.3%)
PASI 90 response n (%)	29 (69%)	32 (76.2%)	32 (76.2%)	35 (83.3%)
PASI 100 response n (%)	25 (59.5%)	23 (54.8%)	22 (52.4%)	29 (69.0%)
* non-responder imputation was used to handle missing values				

These outcomes in the paediatric moderate to severe plaque psoriasis population confirmed the predictive assumptions based on the efficacy and exposure response relationship in adult patients, mentioned above.

In the low dose group, 50% and 70.7% of patients achieved a CDLQI 0 or 1 score at weeks 12 and 52, respectively. In the high dose group, 61.9% and 70.3% achieved a CDLQI 0 or 1 score at weeks 12 and 52, respectively.

Juvenile idiopathic arthritis (JIA)

Enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA)
The efficacy and safety of secukinumab were assessed in 86 patients in a 3-part, double-blind, placebo-controlled, event-driven, randomised, phase III study in patients 2 to <18 years of age with active ERA or JPsA as diagnosed based on a modified International League of Associations for Rheumatology (ILAR) JIA classification criteria. The study consisted of an open-label portion (Part 1) where all patients received secukinumab until week 12. Patients demonstrating a JIA ACR 30 response at week 12 entered into the Part 2 double-blind phase and were randomised 1:1 to continue treatment with secukinumab or to begin treatment with placebo (randomised withdrawal) until week 104 or until a flare occured. Patients who flared then entered open-label secukinumab treatment until week 104 (Part 3).

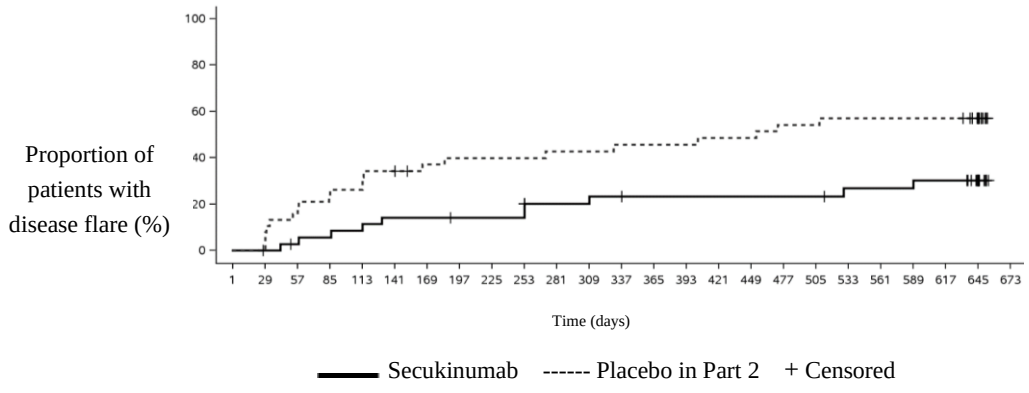
The JIA patient subtypes at study entry were: 60.5% ERA and 39.5% JPsA, who either had inadequate response or were intolerant to ≥1 disease-modifying antirheumatic drugs (DMARDs) and ≥1 non-steroidal anti-inflammatory drugs (NSAIDs). At baseline, MTX use was reported for 65.1% of patients; (63.5% [33/52] of ERA patients and 67.6% [23/34] of JPsA patients). There were 12 out of 52 ERA patients concomitantly treated with sulfasalazine (23.1%). Patients with a body weight at baseline <50 kg (n=30) were given a dose of 75 mg and patients with a body weight ≥50 kg (n=56) were given a dose of 150 mg. Age at baseline ranged from 2 to 17 years, with 3 patients between 2 to <6 years, 22 patients 6 to <12 years and 61 patients 12 to <18 years. At baseline the Juvenile Arthritis Disease Activity Score (JADAS)-27 was 15.1 (SD:7.1).

The primary endpoint was time to flare in the randomised withdrawal period (Part 2). Disease flare was defined as a ≥30% worsening in at least three of the six JIA ACR response criteria and ≥30% improvement in not more than one of the six JIA ACR response criteria and a minimum of two active joints.

At the end of Part 1, 75 out of 86 (87.2%) patients demonstrated a JIA ACR 30 response and entered into Part 2.

The study met its primary endpoint by demonstrating a statistically significant prolongation in the time to disease flare in patients treated with secukinumab compared to placebo in Part 2. The risk of flare was reduced by 72% for patients on secukinumab compared with patients on placebo in Part 2 (Hazard ratio=0.28, 95% CI: 0.13 to 0.63, p<0.001) (Figure 4 and Table 18). During Part 2, a total of 21 patients in the placebo group experienced a flare event (11 JPsA and 10 ERA) compared with 10 patients in the secukinumab group (4 JPsA and 6 ERA).

Figure 4 Kaplan-Meier estimates of the time to disease flare in Part 2



Number of patients at risk

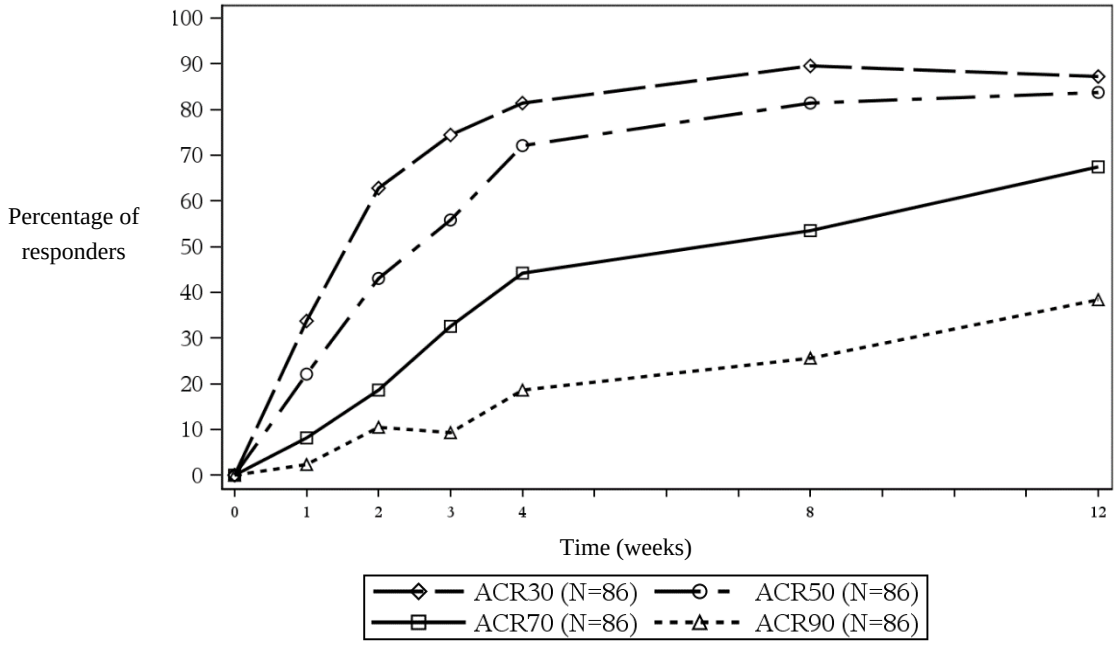
Secukinumab	37	36	34	33	32	30	30	29	29	29	25	25	24	23	23	23	23	23	23	21	21	21	20	14	0
Placebo in Part 2	38	38	32	29	28	25	22	21	21	21	20	20	19	19	19	18	18	16	16	15	15	15	15	10	0

Table 18 Survival analysis of time to disease flare – Part 2

	Secukinumab (N=37)	**Placebo in Part 2** (N=38)
Number of flare events at the end of Part 2, n (%)	10 (27.0)	21 (55.3)
Kaplan-Meier estimates:		
Median, in days (95% CI)	NC (NC, NC)	453.0 (114.0, NC)
Flare-free rate at 6 months (95% CI)	85.8 (69.2, 93.8)	60.1 (42.7, 73.7)
Flare-free rate at 12 months (95% CI)	76.7 (58.7, 87.6)	54.3 (37.1, 68.7)
Flare-free rate at 18 months (95% CI)	73.2 (54.6, 85.1)	42.9 (26.7, 58.1)
Hazard ratio to placebo: Estimate (95% CI)	0.28 (0.13, 0.63)	
Stratified log-rank test p-value	<0.001**	
Analysis was conducted on all randomised patients who received at least one dose of study drug in Part 2. Secukinumab: all patients who did not take any placebo. Placebo in Part 2: all patients who took placebo in Part 2 and secukinumab in other period/s. NC = Not calculable. ** = Statistically significant on one-sided significance level 0.025.		

In open-label Part 1, all patients received secukinumab until week 12. At week 12, 83.7%, 67.4%, and 38.4% of children were JIA ACR 50, 70 and 90 responders, respectively (Figure 5). The onset of action of secukinumab occurred as early as week 1. At week 12 the JADAS-27 score was 4.64 (SD:4.73) and the mean decrease from baseline in JADAS-27 was -10.487 (SD:7.23).

Figure 5 JIA ACR 30/50/70/90 response for subjects up to week 12 in Part 1*



*non-responder imputation was used to handle missing values

The data in the 2 to <6 age group were inconclusive due to the low number of patients below 6 years of age enrolled in the study.

The European Medicines Agency has waived the obligation to submit the results of studies with Cosentyx in plaque psoriasis in paediatric patients aged from birth to less than 6 years and in chronic idiopathic arthritis for paediatric patients aged from birth to less than 2 years (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Most pharmacokinetics properties observed in patients with plaque psoriasis, psoriatic arthritis and ankylosing spondylitis were similar.

Absorption

Following a single subcutaneous dose of 300 mg as a liquid formulation in healthy volunteers, secukinumab reached peak serum concentrations of 43.2±10.4 µg/ml between 2 and 14 days post dose.

Based on population pharmacokinetic analysis, following a single subcutaneous dose of either 150 mg or 300 mg in plaque psoriasis patients, secukinumab reached peak serum concentrations of 13.7±4.8 µg/ml or 27.3±9.5 µg/ml, respectively, between 5 and 6 days post dose.

After initial weekly dosing during the first month, time to reach the maximum concentration was between 31 and 34 days based on population pharmacokinetic analysis.

On the basis of simulated data, peak concentrations at steady-state ($C_{max,ss}$) following subcutaneous administration of 150 mg or 300 mg were 27.6 µg/ml and 55.2 µg/ml, respectively. Population pharmacokinetic analysis suggests that steady-state is reached after 20 weeks with monthly dosing regimens.

Compared with exposure after a single dose, the population pharmacokinetic analysis showed that patients exhibited a 2-fold increase in peak serum concentrations and area under the curve (AUC) following repeated monthly dosing during maintenance.

Population pharmacokinetic analysis showed that secukinumab was absorbed with an average absolute bioavailability of 73% in patients with plaque psoriasis. Across studies, absolute bioavailabilities in the range between 60 and 77% were calculated.

The bioavailability of secukinumab in PsA patients was 85% on the basis of the population pharmacokinetic model.

Following a single subcutaneous injection of 300 mg solution for injection in pre-filled syringe in plaque psoriasis patients, secukinumab systemic exposure was similar to what was observed previously with two injections of 150 mg.

Following subcutaneous administration of 300 mg at weeks 0, 1, 2, 3 and 4 followed by 300 mg every 2 weeks, the mean ± SD steady-state secukinumab trough concentration at week 16 was approximately 55.1±26.7 µg/ml and 58.1±30.1 µg/ml in HS study 1 and HS study 2, respectively.

Distribution

The mean volume of distribution during the terminal phase (V_z) following single intravenous administration ranged from 7.10 to 8.60 litres in plaque psoriasis patients, suggesting that secukinumab undergoes limited distribution to peripheral compartments.

Biotransformation

The majority of IgG elimination occurs via intracellular catabolism, following fluid-phase or receptor mediated endocytosis.

Elimination

Mean systemic clearance (CL) following a single intravenous administration to patients with plaque psoriasis ranged from 0.13 to 0.36 l/day. In a population pharmacokinetic analysis, the mean systemic clearance (CL) was 0.19 l/day in plaque psoriasis patients. The CL was not impacted by gender. Clearance was dose- and time-independent.

The mean elimination half-life, as estimated from population pharmacokinetic analysis, was 27 days in plaque psoriasis patients, ranging from 18 to 46 days across psoriasis studies with intravenous administration.

In a population pharmacokinetic analysis, the mean systemic CL following subcutaneous administration of 300 mg at weeks 0, 1, 2, 3, and 4 followed by 300 mg every 2 weeks to patients with hidradenitis suppurativa was 0.26 l/day.

The mean elimination half-life, as estimated from population pharmacokinetic analysis, was 23 days in hidradenitis suppurativa patients.

Linearity/non-linearity

The single and multiple dose pharmacokinetics of secukinumab in plaque psoriasis patients were determined in several studies with intravenous doses ranging from 1x 0.3 mg/kg to 3x 10 mg/kg and with subcutaneous doses ranging from 1x 25 mg to multiple doses of 300 mg. Exposure was dose proportional across all dosing regimens.

Special populations

Elderly patients
Based on population pharmacokinetic analysis with a limited number of elderly patients (n=71 for age ≥65 years and n=7 for age ≥75 years), clearance in elderly patients and patients less than 65 years of age was similar.

Patients with renal or hepatic impairment
No pharmacokinetic data are available in patients with renal or hepatic impairment. The renal elimination of intact secukinumab, an IgG monoclonal antibody, is expected to be low and of minor importance. IgGs are mainly eliminated via catabolism and hepatic impairment is not expected to influence clearance of secukinumab.

Effect of weight on pharmacokinetics
Secukinumab clearance and volume of distribution increase as body weight increases.

Paediatric population
Plaque psoriasis
In a pool of the two paediatric studies, patients with moderate to severe plaque psoriasis (6 to less than 18 years of age) were administered secukinumab at the recommended paediatric dosing regimen. At week 24, patients weighing ≥25 and <50 kg had a mean ± SD steady-state trough concentration of 19.8 ± 6.96 µg/ml (n=24) after 75 mg of secukinumab and patients weighing ≥50 kg had mean ±SD trough concentration of 27.3 ± 10.1 µg/ml (n=36) after 150 mg of secukinumab. The mean ± SD steady-state trough concentration in patients weighing <25 kg (n=8) was 32.6 ± 10.8 µg/ml at week 24 after 75 mg dose.

Juvenile idiopathic arthritis
In a paediatric study, ERA and JPsA patients (2 to less than 18 years of age) were administered secukinumab at the recommended paediatric dosing regimen. At week 24, patients weighing <50 kg, and weighing ≥50 kg had a mean ± SD steady-state trough concentration of 25.2±5.45 µg/ml (n=10) and 27.9±9.57 µg/ml (n=19), respectively.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans (adult or paediatric) based on conventional studies of safety pharmacology, repeated dose and reproductive toxicity, or tissue cross-reactivity.

Animal studies have not been conducted to evaluate the carcinogenic potential of secukinumab.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Trehalose dihydrate
Histidine
Histidine hydrochloride monohydrate
Methionine
Polysorbate 80
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years
If necessary, Cosentyx may be stored unrefrigerated for a single period of up to 4 days at room temperature, not above 30°C.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). Do not freeze.
Store in the original package in order to protect from light.

6.5 Nature and contents of container

Cosentyx 150 mg solution for injection in pre-filled syringe

Cosentyx 150 mg solution for injection in pre-filled syringe is supplied in a pre-filled 1 ml glass syringe with a silicone-coated bromobutyl rubber plunger stopper, staked 27G x ½″ needle and rigid needle shield of styrene butadiene rubber assembled in an automatic needle guard of polycarbonate.

Cosentyx 150 mg solution for injection in pre-filled syringe is available in unit packs containing 1 or 2 pre-filled syringes and in multipacks containing 6 (3 packs of 2) pre-filled syringes.

Cosentyx 300 mg solution for injection in pre-filled syringe

Cosentyx 300 mg solution for injection in pre-filled syringe is supplied in a pre-filled 2.25 ml glass syringe with a silicone-coated bromobutyl rubber plunger stopper, staked 27G x ½″ needle and rigid needle shield of synthetic polyisoprene rubber assembled in an automatic needle guard of polycarbonate.

Cosentyx 300 mg solution for injection in pre-filled syringe is available in unit packs containing 1 pre-filled syringe and in multipacks containing 3 (3 packs of 1) pre-filled syringes.

Cosentyx 150 mg solution for injection in pre-filled pen

Cosentyx 150 mg solution for injection in pre-filled pen is supplied in a single-use pre-filled syringe assembled into a triangular-shaped pen with transparent window and label. The pre-filled syringe inside the pen is a 1 ml glass syringe with a silicone-coated bromobutyl rubber plunger stopper, staked 27G x ½″ needle and rigid needle shield of styrene butadiene rubber.

Cosentyx 150 mg solution for injection in pre-filled pen is available in unit packs containing 1 or 2 pre-filled pens and in multipacks containing 6 (3 packs of 2) pre-filled pens.

Cosentyx 300 mg solution for injection in pre-filled pen

Cosentyx 300 mg solution for injection in pre-filled pen is supplied in a single-use pre-filled syringe assembled into a squared-shaped pen with transparent window and label. The pre-filled syringe inside the pen is a 2.25 ml glass syringe with a silicone-coated bromobutyl rubber plunger stopper, staked 27G x ½″ needle and rigid needle shield of synthetic polyisoprene rubber.

Cosentyx 300 mg solution for injection in pre-filled pen is available in unit packs containing 1 pre-filled pen and in multipacks containing 3 (3 packs of 1) pre-filled pens.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Cosentyx 150 mg solution for injection in pre-filled syringe

Cosentyx 150 mg solution for injection is supplied in a single-use pre-filled syringe for individual use. The syringe should be taken out of the refrigerator 20 minutes before injecting to allow it to reach room temperature.

Cosentyx 300 mg solution for injection in pre-filled syringe

Cosentyx 300 mg solution for injection is supplied in a single-use pre-filled syringe for individual use. The syringe should be taken out of the refrigerator 30-45 minutes before injecting to allow it to reach room temperature.

Cosentyx 150 mg solution for injection in pre-filled pen

Cosentyx 150 mg solution for injection is supplied in a single-use pre-filled pen for individual use. The pen should be taken out of the refrigerator 20 minutes before injecting to allow it to reach room temperature.

Cosentyx 300 mg solution for injection in pre-filled pen

Cosentyx 300 mg solution for injection is supplied in a single-use pre-filled pen for individual use. The pen should be taken out of the refrigerator 30-45 minutes before injecting to allow it to reach room temperature.

Prior to use, a visual inspection of the pre-filled syringe or pre-filled pen is recommended. The liquid should be clear. Its colour may vary from colourless to slightly yellow. You may see a small air bubble, which is normal. Do not use if the liquid contains easily visible particles, is cloudy or is distinctly brown.
Detailed instructions for use are provided in the package leaflet.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

Cosentyx 150 mg solution for injection in pre-filled syringe

EU/1/14/980/002
EU/1/14/980/003
EU/1/14/980/006

Cosentyx 300 mg solution for injection in pre-filled syringe

EU/1/14/980/008-009

Cosentyx150 mg solution for injection in pre-filled pen

EU/1/14/980/004
EU/1/14/980/005
EU/1/14/980/007

Cosentyx 300 mg solution for injection in pre-filled pen

EU/1/14/980/010-011

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15 January 2015
Date of latest renewal: 03 September 2019

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg powder for solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial of powder contains 150 mg secukinumab. After reconstitution, 1 ml of solution contains 150 mg secukinumab.

Secukinumab is a recombinant fully human monoclonal antibody produced in Chinese Hamster Ovary (CHO) cells.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for solution for injection

The powder is a white solid lyophilisate.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Adult plaque psoriasis

Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

Paediatric plaque psoriasis

Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years who are candidates for systemic therapy.

Hidradenitis suppurativa (HS)

Cosentyx is indicated for the treatment of active moderate to severe hidradenitis suppurativa (acne inversa) in adults with an inadequate response to conventional systemic HS therapy (see section 5.1).

Psoriatic arthritis

Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate (see section 5.1).

Axial spondyloarthritis (axSpA)

Ankylosing spondylitis (AS, radiographic axial spondyloarthritis)
Cosentyx is indicated for the treatment of active ankylosing spondylitis in adults who have responded inadequately to conventional therapy.

Non-radiographic axial spondyloarthritis (nr-axSpA)
Cosentyx is indicated for the treatment of active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) evidence in adults who have responded inadequately to non-steroidal anti-inflammatory drugs (NSAIDs).

Juvenile idiopathic arthritis (JIA)

Enthesitis-related arthritis (ERA)
Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active enthesitis-related arthritis in patients 6 years and older whose disease has responded inadequately to, or who cannot tolerate, conventional therapy (see section 5.1).

Juvenile psoriatic arthritis (JPsA)
Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active juvenile psoriatic arthritis in patients 6 years and older whose disease has responded inadequately to, or who cannot tolerate, conventional therapy (see section 5.1).

4.2 Posology and method of administration

Cosentyx is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of conditions for which Cosentyx is indicated.

Posology

Adult plaque psoriasis
The recommended dose is 300 mg of secukinumab by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Based on clinical response, a maintenance dose of 300 mg every 2 weeks may provide additional benefit for patients with a body weight of 90 kg or higher. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

Paediatric plaque psoriasis (adolescents and children from the age of 6 years)
The recommended dose is based on body weight (Table 1) and administered by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 75 mg dose is given as one subcutaneous injection of 75 mg. Each 150 mg dose is given as one subcutaneous injection of 150 mg. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

Table 1 Recommended dose for paediatric plaque psoriasis

Body weight at time of dosing	**Recommended dose**
<25 kg	75 mg
25 to <50 kg	75 mg
≥50 kg	150 mg (*may be increased to 300 mg)

*Some patients may derive additional benefit from the higher dose.

Cosentyx may be available in other strengths and/or presentations depending on the individual treatment needs.

Hidradenitis suppurativa (HS)
The recommended dose is 300 mg of secukinumab by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3, and 4, followed by monthly maintenance dosing. Based on clinical response, the maintenance dose can be increased to 300 mg every 2 weeks. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

Psoriatic arthritis
For patients with concomitant moderate to severe plaque psoriasis, please refer to adult plaque psoriasis recommendation.

For patients who are anti-TNFα inadequate responders (IR), the recommended dose is 300 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

For other patients, the recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Based on clinical response, the dose can be increased to 300 mg.

Axial spondyloarthritis (axSpA)
Ankylosing spondylitis (AS, radiographic axial spondyloarthritis)
The recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Based on clinical response, the dose can be increased to 300 mg. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

Non-radiographic axial spondyloarthritis (nr-axSpA)
The recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing.

Juvenile idiopathic arthritis (JIA)

Enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA)
The recommended dose is based on body weight (Table 2) and administered by subcutaneous injection at weeks 0, 1, 2, 3, and 4, followed by monthly maintenance dosing. Each 75 mg dose is given as one subcutaneous injection of 75 mg. Each 150 mg dose is given as one subcutaneous injection of 150 mg.

Table 2 Recommended dose for juvenile idiopathic arthritis

Body weight at time of dosing	**Recommended dose**
<50 kg	75 mg
≥50 kg	150 mg

Cosentyx may be available in other strengths and/or presentations depending on the individual treatment needs.

For all of the above indications, available data suggest that a clinical response is usually achieved within 16 weeks of treatment. Consideration should be given to discontinuing treatment in patients who have shown no response by 16 weeks of treatment. Some patients with an initial partial response may subsequently improve with continued treatment beyond 16 weeks.

Special populations

Elderly patients (aged 65 years and over)
No dose adjustment is required (see section 5.2).

Renal impairment / hepatic impairment
Cosentyx has not been studied in these patient populations. No dose recommendations can be made.

Paediatric population
The safety and efficacy of Cosentyx in children with plaque psoriasis and in the juvenile idiopathic arthritis (JIA) categories of ERA and JPsA below the age of 6 years have not been established.

The safety and efficacy of Cosentyx in children below the age of 18 years in other indications have not yet been established. No data are available.

Method of administration

Cosentyx is to be administered by subcutaneous injection. If possible, areas of the skin that show psoriasis should be avoided as injection sites. The powder for solution for injection must be reconstituted before use.

The reconstitution, dose preparation and administration of the powder for solution for injection is to be done by a healthcare professional. For instructions on reconstitution of the medicinal product before administration, see section 6.6 and the Instructions for Use in the package leaflet.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Clinically important, active infection, e.g. active tuberculosis (see section 4.4).

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Infections

Secukinumab has the potential to increase the risk of infections. Serious infections have been observed in patients receiving secukinumab in the post-marketing setting. Caution should be exercised when considering the use of secukinumab in patients with a chronic infection or a history of recurrent infection.

Patients should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, the patient should be closely monitored and secukinumab should not be administered until the infection resolves.

In clinical studies, infections have been observed in patients receiving secukinumab (see section 4.8). Most of these were mild or moderate upper respiratory tract infections such as nasopharyngitis and did not require treatment discontinuation.

Related to the mechanism of action of secukinumab, non-serious mucocutaneous candida infections were more frequently reported for secukinumab than placebo in the psoriasis clinical studies (3.55 per 100 patient years for secukinumab 300 mg versus 1.00 per 100 patient years for placebo) (see section 4.8).

No increased susceptibility to tuberculosis was reported from clinical studies. However, secukinumab should not be given to patients with active tuberculosis. Anti-tuberculosis therapy should be considered prior to initiation of secukinumab in patients with latent tuberculosis.

Inflammatory bowel disease (including Crohn’s disease and ulcerative colitis)

Cases of new or exacerbations of inflammatory bowel disease have been reported with secukinumab (see section 4.8). Secukinumab is not recommended in patients with inflammatory bowel disease. If a patient develops signs and symptoms of inflammatory bowel disease or experiences an exacerbation of pre-existing inflammatory bowel disease, secukinumab should be discontinued and appropriate medical management should be initiated.

Hypersensitivity reactions

In clinical studies, rare cases of anaphylactic reactions have been observed in patients receiving secukinumab. If an anaphylactic or other serious allergic reactions occur, administration of secukinumab should be discontinued immediately and appropriate therapy initiated.

Vaccinations

Live vaccines should not be given concurrently with secukinumab.

Patients receiving secukinumab may receive concurrent inactivated or non-live vaccinations. In a study, after *meningococcal* and inactivated *influenza* vaccinations, a similar proportion of healthy volunteers treated with 150 mg of secukinumab and those treated with placebo were able to mount an adequate immune response of at least a 4-fold increase in antibody titres to *meningococcal* and *influenza* vaccines. The data suggest that secukinumab does not suppress the humoral immune response to the *meningococcal* or *influenza* vaccines.

Prior to initiating therapy with Cosentyx, it is recommended that paediatric patients receive all age-appropriate immunisations as per current immunisation guidelines.

Concomitant immunosuppressive therapy

In psoriasis studies, the safety and efficacy of secukinumab in combination with immunosuppressants, including biologics, or phototherapy have not been evaluated. Secukinumab was administered concomitantly with methotrexate (MTX), sulfasalazine and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and ankylosing spondylitis). Caution should be exercised when considering concomitant use of other immunosuppressants and secukinumab (see also section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

Live vaccines should not be given concurrently with secukinumab (see also section 4.4).

In a study in adult subjects with plaque psoriasis, no interaction was observed between secukinumab and midazolam (CYP3A4 substrate).

No interaction was seen when secukinumab was administered concomitantly with methotrexate (MTX) and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and axial spondyloarthritis).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 20 weeks after treatment.

Pregnancy

There are no adequate data from the use of secukinumab in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Cosentyx during pregnancy.

Breast-feeding

It is not known whether secukinumab is excreted in human milk. Immunoglobulins are excreted in human milk and it is not known if secukinumab is absorbed systemically after ingestion. Because of the potential for adverse reactions in nursing infants from secukinumab, a decision on whether to discontinue breast-feeding during treatment and up to 20 weeks after treatment or to discontinue therapy with Cosentyx must be made taking into account the benefit of breast-feeding to the child and the benefit of therapy to the woman.

Fertility

The effect of secukinumab on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility.

4.7 Effects on ability to drive and use machines

Cosentyx has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse reactions are upper respiratory tract infections (17.1%) (most frequently nasopharyngitis, rhinitis).

Tabulated list of adverse reactions

Adverse reactions from clinical studies and post-marketing reports (Table 3) are listed by MedDRA system organ class. Within each system organ class, the adverse reactions are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse reaction is based on the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1 000 to <1/100); rare (≥1/10 000 to <1/1 000); very rare (<1/10 000); and not known (cannot be estimated from the available data).

Over 20 000 patients have been treated with secukinumab in blinded and open-label clinical studies in various indications (plaque psoriasis, psoriatic arthritis, axial spondyloarthritis, hidradenitis suppurativa and other autoimmune conditions), representing 34 908 patient years of exposure. Of these, over 14 000 patients were exposed to secukinumab for at least one year. The safety profile of secukinumab is consistent across all indications.

Table 3 List of adverse reactions in clinical studies[1)] and post-marketing experience

System organ class	Frequency	Adverse reaction
Infections and infestations	Very common	Upper respiratory tract infections
	Common	Oral herpes
	Uncommon	Oral candidiasis
		Otitis externa
		Lower respiratory tract infections
		Tinea pedis
	Not known	Mucosal and cutaneous candidiasis (including oesophageal candidiasis)
Blood and lymphatic system disorders	Uncommon	Neutropenia
Immune system disorders	Rare	Anaphylactic reactions
Nervous system disorders	Common	Headache
Eye disorders	Uncommon	Conjunctivitis
Respiratory, thoracic and mediastinal disorders	Common	Rhinorrhoea
Gastrointestinal disorders	Common	Diarrhoea
	Common	Nausea
	Uncommon	Inflammatory bowel disease
Skin and subcutaneous tissue disorders	Uncommon	Urticaria
		Dyshidrotic eczema
	Rare	Exfoliative dermatitis[2)]
		Hypersensitivity vasculitis
	Not known	Pyoderma gangrenosum
General disorders and administration site conditions	Common	Fatigue

[1)] Placebo-controlled clinical studies (phase III) in plaque psoriasis, PsA, AS, nr-axSpA and HS patients exposed to 300 mg, 150 mg, 75 mg or placebo up to 12 weeks (psoriasis) or 16 weeks (PsA, AS, nr-axSpA and HS) treatment duration
[2)] Cases were reported in patients with psoriasis diagnosis

Description of selected adverse reactions

Infections
In the placebo-controlled period of clinical studies in plaque psoriasis (a total of 1 382 patients treated with secukinumab and 694 patients treated with placebo for up to 12 weeks), infections were reported in 28.7% of patients treated with secukinumab compared with 18.9% of patients treated with placebo. The majority of infections consisted of non-serious and mild to moderate upper respiratory tract infections, such as nasopharyngitis, which did not necessitate treatment discontinuation. There was an increase in mucosal or cutaneous candidiasis, consistent with the mechanism of action, but the cases were mild or moderate in severity, non-serious, responsive to standard treatment and did not necessitate treatment discontinuation. Serious infections occurred in 0.14% of patients treated with secukinumab and in 0.3% of patients treated with placebo (see section 4.4).

Over the entire treatment period (a total of 3 430 patients treated with secukinumab for up to 52 weeks for the majority of patients), infections were reported in 47.5% of patients treated with secukinumab (0.9 per patient-year of follow-up). Serious infections were reported in 1.2% of patients treated with secukinumab (0.015 per patient-year of follow-up).

Infection rates observed in psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) clinical studies were similar to those observed in the psoriasis studies.

Patients with hidradenitis suppurativa are more susceptible to infections. In the placebo-controlled period of clinical studies in hidradenitis suppurativa (a total of 721 patients treated with secukinumab and 363 patients treated with placebo for up to 16 weeks), infections were numerically higher compared to those observed in the psoriasis studies (30.7% of patients treated with secukinumab compared with 31.7% in patients treated with placebo). Most of these were non-serious, mild or moderate in severity and did not require treatment discontinuation or interruption.

Neutropenia
In psoriasis phase III clinical studies, neutropenia was more frequently observed with secukinumab than with placebo, but most cases were mild, transient and reversible. Neutropenia <1.0-0.5x10^9/l (CTCAE grade 3) was reported in 18 out of 3 430 (0.5%) patients on secukinumab, with no dose dependence and no temporal relationship to infections in 15 out of 18 cases. There were no reported cases of more severe neutropenia. Non-serious infections with usual response to standard care and not requiring discontinuation of secukinumab were reported in the remaining 3 cases.

The frequency of neutropenia in psoriatic arthritis, axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) and hidradenitis suppurativa was similar to psoriasis.

Rare cases of neutropenia <0.5x10^9/l (CTCAE grade 4) were reported.

Hypersensitivity reactions
In clinical studies, urticaria and rare cases of anaphylactic reaction to secukinumab were observed (see also section 4.4).

Immunogenicity
In psoriasis, psoriatic arthritis, axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) and hidradenitis suppurativa clinical studies, less than 1% of patients treated with secukinumab developed antibodies to secukinumab up to 52 weeks of treatment. About half of the treatment-emergent anti-drug antibodies were neutralising, but this was not associated with loss of efficacy or pharmacokinetic abnormalities.

Paediatric population

Undesirable effects in paediatric patients from the age of 6 years with plaque psoriasis
The safety of secukinumab was assessed in two phase III studies in paediatric patients with plaque psoriasis. The first study (paediatric study 1) was a double-blind, placebo-controlled study of 162 patients from 6 to less than 18 years of age with severe plaque psoriasis. The second study (paediatric study 2) is an open-label study of 84 patients from 6 to less than 18 years of age with moderate to severe plaque psoriasis. The safety profile reported in these two studies was consistent with the safety profile reported in adult plaque psoriasis patients.

Undesirable effects in paediatric patients with JIA
The safety of secukinumab was also assessed in a phase III study in 86 juvenile idiopathic arthritis patients with ERA and JPsA from 2 to less than 18 years of age. The safety profile reported in this study was consistent with the safety profile reported in adult patients.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Doses up to 30 mg/kg (approximately 2000 to 3000 mg) have been administered intravenously in clinical studies without dose-limiting toxicity. In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC10

Mechanism of action

Secukinumab is a fully human IgG1/κ monoclonal antibody that selectively binds to and neutralises the proinflammatory cytokine interleukin-17A (IL-17A). Secukinumab works by targeting IL-17A and inhibiting its interaction with the IL-17 receptor, which is expressed on various cell types including keratinocytes. As a result, secukinumab inhibits the release of proinflammatory cytokines, chemokines and mediators of tissue damage and reduces IL-17A-mediated contributions to autoimmune and inflammatory diseases. Clinically relevant levels of secukinumab reach the skin and reduce local inflammatory markers. As a direct consequence treatment with secukinumab reduces erythema, induration and desquamation present in plaque psoriasis lesions.

IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. IL-17A plays a key role in the pathogenesis of plaque psoriasis, hidradenitis suppurativa, psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) and is up-regulated in lesional skin in contrast to non-lesional skin of plaque psoriasis patients and in synovial tissue of psoriatic arthritis patients. IL-17A is also upregulated in hidradenitis suppurativa lesions and increased IL-17A serum levels have been observed in affected patients. The frequency of IL-17-producing cells was also significantly higher in the subchondral bone marrow of facet joints from patients with ankylosing spondylitis. Increased numbers of IL-17A producing lymphocytes have also been found in patients with non-radiographic axial spondyloarthritis. Inhibition of IL-17A was shown to be effective in the treatment of ankylosing spondylitis, thus establishing the key role of this cytokine in axial spondyloarthritis.

Pharmacodynamic effects

Serum levels of total IL-17A (free and secukinumab-bound IL-17A) are initially increased in patients receiving secukinumab. This is followed by a slow decrease due to reduced clearance of secukinumab-bound IL-17A, indicating that secukinumab selectively captures free IL-17A, which plays a key role in the pathogenesis of plaque psoriasis.

In a study with secukinumab, infiltrating epidermal neutrophils and various neutrophil-associated markers that are increased in lesional skin of plaque psoriasis patients were significantly reduced after one to two weeks of treatment.

Secukinumab has been shown to lower (within 1 to 2 weeks of treatment) levels of C-reactive protein, which is a marker of inflammation.

Clinical efficacy and safety

Adult plaque psoriasis
The safety and efficacy of secukinumab were assessed in four randomised, double-blind, placebo-controlled phase III studies in patients with moderate to severe plaque psoriasis who were candidates for phototherapy or systemic therapy [ERASURE, FIXTURE, FEATURE, JUNCTURE]. The efficacy and safety of secukinumab 150 mg and 300 mg were evaluated versus either placebo or etanercept. In addition, one study assessed a chronic treatment regimen versus a "retreatment as needed" regimen [SCULPTURE].

Of the 2 403 patients who were included in the placebo-controlled studies, 79% were biologic-naive, 45% were non-biologic failures and 8% were biologic failures (6% were anti-TNF failures, and 2% were anti-p40 failures). Approximately 15 to 25% of patients in phase III studies had psoriatic arthritis (PsA) at baseline.

Psoriasis study 1 (ERASURE) evaluated 738 patients. Patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Psoriasis study 2 (FIXTURE) evaluated 1 306 patients. Patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients randomised to etanercept received 50 mg doses twice per week for 12 weeks followed by 50 mg every week. In both study 1 and study 2, patients randomised to receive placebo who were non-responders at week 12 then crossed over to receive secukinumab (either 150 mg or 300 mg) at weeks 12, 13, 14, and 15, followed by the same dose every month starting at week 16. All patients were followed for up to 52 weeks following first administration of study treatment.

Psoriasis study 3 (FEATURE) evaluated 177 patients using a pre-filled syringe compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of secukinumab self-administration via the pre-filled syringe. Psoriasis study 4 (JUNCTURE) evaluated 182 patients using a pre-filled pen compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of secukinumab self-administration via the pre-filled pen. In both study 3 and study 4, patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients were also randomised to receive placebo at weeks 0, 1, 2, 3 and 4, followed by the same dose every month.

Psoriasis study 5 (SCULPTURE) evaluated 966 patients. All patients received secukinumab 150 mg or 300 mg doses at weeks 0, 1, 2, 3, 4, 8 and 12 and then were randomised to receive either a maintenance regimen of the same dose every month starting at week 12 or a "retreatment as needed" regimen of the same dose. Patients randomised to "retreatment as needed" did not achieve adequate maintenance of response and therefore a fixed monthly maintenance regimen is recommended.

The co-primary endpoints in the placebo and active-controlled studies were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 "clear" or "almost clear" response versus placebo at week 12 (see Tables 4 and 5). The 300 mg dose provided improved skin clearance particularly for "clear" or "almost clear" skin across the efficacy endpoints of PASI 90, PASI 100, and IGA mod 2011 0 or 1 response across all studies with peak effects seen at week 16, therefore this dose is recommended.

Table 4 Summary of PASI 50/75/90/100 & IGA* mod 2011 "clear" or "almost clear" clinical response in psoriasis studies 1, 3 and 4 (ERASURE, FEATURE and JUNCTURE)

		Week 12		Week 16		Week 52	
	Placebo	**150 mg**	**300 mg**	**150 mg**	**300 mg**	**150 mg**	**300 mg**
Study 1							
Number of patients	246	244	245	244	245	244	245
PASI 50 response n (%)	22 (8.9%)	203 (83.5%)	222 (90.6%)	212 (87.2%)	224 (91.4%)	187 (77%)	207 (84.5%)
PASI 75 response n (%)	11 (4.5%)	174 (71.6%)**	200 (81.6%)**	188 (77.4%)	211 (86.1%)	146 (60.1%)	182 (74.3%)
PASI 90 response n (%)	3 (1.2%)	95 (39.1%)**	145 (59.2%)**	130 (53.5%)	171 (69.8%)	88 (36.2%)	147 (60.0%)
PASI 100 response n (%)	2 (0.8%)	31 (12.8%)	70 (28.6%)	51 (21.0%)	102 (41.6%)	49 (20.2%)	96 (39.2%)
IGA mod 2011 "clear" or "almost clear" response n (%)	6 (2.40%)	125 (51.2%)**	160 (65.3%)**	142 (58.2%)	180 (73.5%)	101 (41.4%)	148 (60.4%)
Study 3							
Number of patients	59	59	58	-	-	-	-
PASI 50 response n (%)	3 (5.1%)	51 (86.4%)	51 (87.9%)	-	-	-	-
PASI 75 response n (%)	0 (0.0%)	41 (69.5%)**	44 (75.9%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	27 (45.8%)	35 (60.3%)	-	-	-	-
PASI 100 response n (%)	0 (0.0%)	5 (8.5%)	25 (43.1%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	31 (52.5%)**	40 (69.0%)**	-	-	-	-
Study 4							
Number of patients	61	60	60	-	-	-	-
PASI 50 response n (%)	5 (8.2%)	48 (80.0%)	58 (96.7%)	-	-	-	-
PASI 75 response n (%)	2 (3.3%)	43 (71.7%)**	52 (86.7%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	24 (40.0%)	33 (55.0%)	-	-	-	-
PASI 100 response n(%)	0 (0.0%)	10 (16.7%)	16 (26.7%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	32 (53.3%)**	44 (73.3%)**	-	-	-	-

* The IGA mod 2011 is a 5-category scale including "0 = clear", "1 = almost clear", "2 = mild", "3 = moderate" or "4 = severe", indicating the physician's overall assessment of the psoriasis severity focusing on induration, erythema and scaling. Treatment success of "clear" or "almost clear" consisted of no signs of psoriasis or normal to pink colouration of lesions, no thickening of the plaque and none to minimal focal scaling.

** p-values versus placebo and adjusted for multiplicity: $p<0.0001$.

Table 5 Summary of clinical response on psoriasis study 2 (FIXTURE)

	Week 12				Week 16			Week 52		
	Placebo	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**
Number of patients	324	327	323	323	327	323	323	327	323	323
PASI 50 response n (%)	49 (15.1%)	266 (81.3%)	296 (91.6%)	226 (70.0%)	290 (88.7%)	302 (93.5%)	257 (79.6%)	249 (76.1%)	274 (84.8%)	234 (72.4%)
PASI 75 response n (%)	16 (4.9%)	219 (67.0%) **	249 (77.1%) **	142 (44.0%)	247 (75.5%)	280 (86.7%)	189 (58.5%)	215 (65.7%)	254 (78.6%)	179 (55.4%)
PASI 90 response n (%)	5 (1.5%)	137 (41.9%)	175 (54.2%)	67 (20.7%)	176 (53.8%)	234 (72.4%)	101 (31.3%)	147 (45.0%)	210 (65.0%)	108 (33.4%)
PASI 100 response n (%)	0 (0%)	47 (14.4%)	78 (24.1%)	14 (4.3%)	84 (25.7%)	119 (36.8%)	24 (7.4%)	65 (19.9%)	117 (36.2%)	32 (9.9%)
IGA mod 2011 “clear” or “almost clear” response n (%)	9 (2.8%)	167 (51.1%) **	202 (62.5%) **	88 (27.2%)	200 (61.2%)	244 (75.5%)	127 (39.3%)	168 (51.4%)	219 (67.8%)	120 (37.2%)

** p-values versus etanercept: p=0.0250

In an additional psoriasis study (CLEAR) 676 patients were evaluated. Secukinumab 300 mg met the primary and secondary endpoints by showing superiority to ustekinumab based on PASI 90 response at week 16 (primary endpoint), speed of onset of PASI 75 response at week 4, and long-term PASI 90 response at week 52. Greater efficacy of secukinumab compared to ustekinumab for the endpoints PASI 75/90/100 and IGA mod 2011 0 or 1 response (“clear” or “almost clear”) was observed early and continued through to week 52 (Table 6).

Table 6 Summary of clinical response on CLEAR study

	Week 4		Week 16		Week 52	
	Secukinumab 300 mg	**Ustekinumab***	**Secukinumab 300 mg**	**Ustekinumab***	**Secukinumab 300 mg**	**Ustekinumab***
Number of patients	334	335	334	335	334	335
PASI 75 response n (%)	166 (49.7%)**	69 (20.6%)	311 (93.1%)	276 (82.4%)	306 (91.6%)	262 (78.2%)
PASI 90 response n (%)	70 (21.0%)	18 (5.4%)	264 (79.0%)**	192 (57.3%)	250 (74.9%)***	203 (60.6%)
PASI 100 response n (%)	14 (4.2%)	3 (0.9%)	148 (44.3%)	95 (28.4%)	150 (44.9%)	123 (36.7%)
IGA mod 2011 “clear” or “almost clear” response n (%)	128 (38.3%)	41 (12.2%)	278 (83.2%)	226 (67.5%)	261 (78.1%)	213 (63.6%)

* Patients treated with secukinumab received 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every 4 weeks until week 52. Patients treated with ustekinumab received 45 mg or 90 mg at weeks 0 and 4, then every 12 weeks until week 52 (dosed by weight as per approved posology)

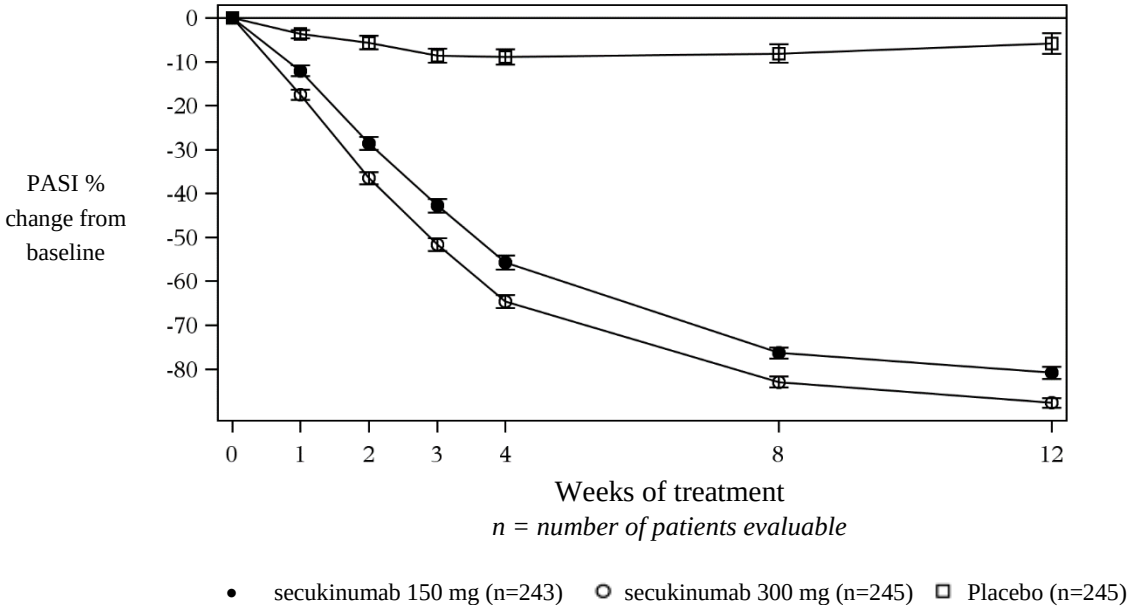
** p-values versus ustekinumab: p<0.0001 for primary endpoint of PASI 90 at week 16 and secondary endpoint of PASI 75 at week 4

*** p-values versus ustekinumab: p=0.0001 for secondary endpoint of PASI 90 at week 52

Secukinumab was efficacious in systemic treatment-naive, biologic-naive, biologic/anti-TNF-exposed and biologic/anti-TNF-failure patients. Improvements in PASI 75 in patients with concurrent psoriatic arthritis at baseline were similar to those in the overall plaque psoriasis population.

Secukinumab was associated with a fast onset of efficacy with a 50% reduction in mean PASI by week 3 for the 300 mg dose.

Figure 1 Time course of percentage change from baseline of mean PASI score in study 1 (ERASURE)



Specific locations/forms of plaque psoriasis
In two additional placebo-controlled studies, improvement was seen in both nail psoriasis (TRANSFIGURE, 198 patients) and palmoplantar plaque psoriasis (GESTURE, 205 patients). In the TRANSFIGURE study, secukinumab was superior to placebo at week 16 (46.1% for 300 mg, 38.4% for 150 mg and 11.7% for placebo) as assessed by significant improvement from baseline in the Nail Psoriasis Severity Index (NAPSI %) for patients with moderate to severe plaque psoriasis with nail involvement. In the GESTURE study, secukinumab was superior to placebo at week 16 (33.3% for 300 mg, 22.1% for 150 mg, and 1.5% for placebo) as assessed by significant improvement of ppIGA 0 or 1 response ("clear" or "almost clear") for patients with moderate to severe palmoplantar plaque psoriasis.

A placebo-controlled study evaluated 102 patients with moderate to severe scalp psoriasis, defined as having a Psoriasis Scalp Severity Index (PSSI) score of ≥12, an IGA mod 2011 scalp only score of 3 or greater and at least 30% of the scalp surface area affected. Secukinumab 300 mg was superior to placebo at week 12 as assessed by significant improvement from baseline in both the PSSI 90 response (52.9% versus 2.0%) and IGA mod 2011 0 or 1 scalp only response (56.9% versus 5.9%). Improvement in both endpoints was sustained for secukinumab patients who continued treatment through to week 24.

Quality of life/patient-reported outcomes
Statistically significant improvements at week 12 (studies 1-4) from baseline compared to placebo were demonstrated in the DLQI (Dermatology Life Quality Index). Mean decreases (improvements) in DLQI from baseline ranged from -10.4 to -11.6 with secukinumab 300 mg, from -7.7 to -10.1 with secukinumab 150 mg, versus -1.1 to -1.9 for placebo at week 12. These improvements were maintained for 52 weeks (studies 1 and 2).

Forty percent of the participants in studies 1 and 2 completed the Psoriasis Symptom Diary©. For the participants completing the diary in each of these studies, statistically significant improvements at week 12 from baseline compared to placebo in patient-reported signs and symptoms of itching, pain and scaling were demonstrated.

Statistically significant improvements at week 4 from baseline in patients treated with secukinumab compared to patients treated with ustekinumab (CLEAR) were demonstrated in the DLQI and these improvements were maintained for up to 52 weeks.

Statistically significant improvements in patient-reported signs and symptoms of itching, pain and scaling at week 16 and week 52 (CLEAR) were demonstrated in the Psoriasis Symptom Diary© in patients treated with secukinumab compared to patients treated with ustekinumab.

Statistically significant improvements (decreases) at week 12 from baseline in the scalp psoriasis study were demonstrated in patient reported signs and symptoms of scalp itching, pain and scaling compared to placebo.

Plaque psoriasis dose flexibility
A randomised, double-blind, multicentre study evaluated two maintenance dosing regimens (300 mg every 2 weeks [Q2W] and 300 mg every 4 weeks [Q4W]) administered by 150 mg pre-filled syringe in 331 patients weighing ≥90 kg with moderate to severe psoriasis. Patients were randomised 1:1 as follows:

- secukinumab 300 mg at weeks 0, 1, 2, 3, and 4 followed by the same dose every 2 weeks (Q2W) up to week 52 (n=165).
- secukinumab 300 mg at weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks (Q4W) up to week 16 (n=166).
    - Patients randomised to receive secukinumab 300 mg Q4W who were PASI 90 responders at week 16 continued to receive the same dosing regimen up to week 52. Patients randomised to receive secukinumab 300 mg Q4W who were PASI 90 non-responders at week 16 either continued on the same dosing regimen, or were reassigned to receive secukinumab 300 mg Q2W up to week 52.

Overall, the efficacy response rates for the group treated with the every 2 weeks regimen were higher compared to the group treated with the every 4 weeks regimen (Table 7).

Table 7 Summary of clinical response in the plaque psoriasis dose flexibility study*

	Week 16		**Week 52**	
	secukinumab 300 mg Q2W	**secukinumab 300 mg Q4W**	**secukinumab 300 mg Q2W**	**secukinumab 300 mg Q4W**[1]
Number of patients	165	166	165	83
PASI 90 response n (%)	121 (73.2%) **	92 (55.5%)	126 (76.4%)	44 (52.4%)
IGA mod 2011 "clear" or "almost clear" response n (%)	122 (74.2%)[2]	109 (65.9%)[2]	125 (75.9%)	46 (55.6%)

* Multiple imputation
[1] 300 mg Q4W:patients continuously treated with 300 mg Q4W regardless of PASI 90 response status at week 16; 43 patients were PASI 90 responder at week 16 and 40 patients were PASI 90 non-responders at week 16
** One sided p-value = 0.0003 for primary endpoint of PASI 90 at week 16
[2] Not statistically significant

In the PASI 90 non-responders at week 16 who were up-titrated to secukinumab 300 mg Q2W, the PASI 90 response rates improved compared to those who remained on the secukinumab 300 mg Q4W dosing regimen, while the IGA mod 2011 0/1 response rates remained stable over time in both treatment groups.

The safety profiles of the two dosing regimens, Cosentyx 300 mg administered every 4 weeks and Cosentyx 300 mg administered every 2 weeks, in patients weighing ≥90 kg were comparable and consistent with the safety profile reported in psoriasis patients.

Hidradenitis suppurativa

The safety and efficacy of secukinumab were assessed in 1 084 patients in two randomised, double-blind, placebo-controlled phase III studies in adult patients with moderate to severe hidradenitis suppurativa (HS) who were candidates for systemic biologic therapy. Patients were required to have at least five inflammatory lesions affecting at least two anatomical areas at baseline. In HS study 1 (SUNSHINE) and HS study 2 (SUNRISE), respectively, 4.6% and 2.8% of patients were Hurley stage I, 61.4% and 56.7% were Hurley stage II, and 34.0% and 40.5% were Hurley stage III.The proportion of patients weighing ≥90 kg was 54.7% in HS study 1 and 50.8% in HS study 2. Patients in these studies had a diagnosis of moderate to severe HS for a mean of 7.3 years and 56.3% of the study participants were female.

In HS study 1 and HS study 2, 23,8% and 23,2% of patients, respectively, were previously treated with a biologic. 82.3% and 83.6% of patients, respectively, were previously treated with systemic antibiotics.

HS study 1 evaluated 541 patients and HS study 2 evaluated 543 patients, of whom 12.8% and 10.7%, respectively, received concomitant stable-dose antibiotics. In both studies, patients randomised to secukinumab received 300 mg subcutaneously at weeks 0, 1, 2, 3 and 4, followed by 300 mg every 2 weeks (Q2W) or every 4 weeks (Q4W). At week 16, patients who were randomised to placebo were reassigned to receive secukinumab 300 mg at weeks 16, 17, 18, 19 and 20 followed by either secukinumab 300 mg Q2W or secukinumab 300 mg Q4W.

The primary endpoint in both studies (HS study 1 and HS study 2) was the proportion of patients achieving a Hidradenitis Suppurativa Clinical Response defined as at least a 50% decrease in abscesses and inflammatory nodules count with no increase in the number of abscesses and/or in the number of draining fistulae relative to baseline (HiSCR50) at week 16. Reduction in HS-related skin pain was assessed as a secondary endpoint on the pooled data of HS study 1 and HS study 2 using a Numerical Rating Scale (NRS) in patients who entered the studies with an initial baseline score of 3 or greater.

In HS study 1 and HS study 2, a higher proportion of patients treated with secukinumab 300 mg Q2W achieved a HiSCR50 response with a decrease in abscesses and inflammatory nodules (AN) count compared to placebo at week 16. In HS study 2, a difference in HiSCR50 response and AN count was also observed with the secukinumab 300 mg Q4W regimen. In the secukinumab 300 mg Q2W group in HS study 1 and in the secukinumab 300 mg Q4W group in HS study 2, a lower rate of patients experienced flares compared to placebo up to week 16. A higher proportion of patients treated with secukinumab 300 mg Q2W (pooled data) experienced a clinically relevant decrease in HS-related skin pain compared to placebo at week 16 (Table 8).

Table 8 Clinical response in HS study 1 and HS study 2 at week 16[1]

	HS study 1			HS study 2		
	Placebo	300 mg Q4W	300 mg Q2W	Placebo	300 mg Q4W	300 mg Q2W
Number of patients randomised	180	180	181	183	180	180
HiSCR50, n (%)	61 (33.7)	75 (41.8)	82 (45.0*)	57 (31.2)	83 (46.1*)	76 (42.3*)
AN count, mean % change from baseline	-24.3	-42.4	-46.8*	-22.4	-45.5*	-39.3*
Flares, n (%)	52 (29.0)	42 (23.2)	28 (15.4*)	50 (27.0)	28 (15.6*)	36 (20.1)
	Pooled data (HS study 1 and HS study 2)					
	Placebo		300 mg Q4W		300 mg Q2W	
Number of patients with NRS ≥3 at baseline	251		252		266	
≥30% reduction in skin pain, NRS30 response, n (%)	58 (23.0)		84 (33.5)		97 (36.6*)	

[1] Multiple imputation was implemented to handle missing data
n: Rounded average number of subjects with responses in 100 imputations
*Statistically significant versus placebo based on the pre-defined hierarchy with overall alpha=0.05
AN: Abscesses and inflammatory Nodules; HiSCR: Hidradenitis Suppurativa Clinical Response; NRS: Numerical Rating Scale

In both studies, the onset of action of secukinumab occurred as early as week 2, the efficacy progressively increased to week 16 and was maintained up to week 52.

Improvements were seen for the primary and key secondary endpoints in HS patients regardless of previous or concomitant antibiotic treatment.

HiSCR50 responses were improved at week 16 in both biologic-naïve and biologic-exposed patients.

Greater improvements at week 16 from baseline compared to placebo were demonstrated in health-related quality of life as measured by the Dermatology Life Quality Index.

Psoriatic arthritis

The safety and efficacy of secukinumab were assessed in 1 999 patients in three randomised, double-blind, placebo-controlled phase III studies in patients with active psoriatic arthritis (≥3 swollen and ≥3 tender joints) despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients with each subtype of PsA were enrolled in these studies, including polyarticular arthritis with no evidence of rheumatoid nodules, spondylitis with peripheral arthritis, asymmetric peripheral arthritis, distal interphalangeal involvement and arthritis mutilans. Patients in these studies had a diagnosis of PsA of at least five years. The majority of patients also had active psoriasis skin lesions or a documented history of psoriasis. Over 61% and 42% of the PsA patients had enthesitis and dactylitis at baseline, respectively. For all studies, the primary endpoint was American College of Rheumatology (ACR) 20 response. For Psoriatic Arthritis study 1 (PsA study 1) and Psoriatic Arthritis study 2 (PsA study 2), the primary endpoint was at week 24. For Psoriatic Arthritis study 3 (PsA study 3), the primary endpoint was at week 16 with the key secondary endpoint, the change from baseline in modified Total Sharp Score (mTSS), at week 24.

In PsA study 1, PsA study 2 and PsA study 3, 29%, 35% and 30% of patients, respectively, were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

PsA study 1 (FUTURE 1) evaluated 606 patients, of whom 60.7% had concomitant MTX. Patients randomised to secukinumab received 10 mg/kg intravenously at weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously every month starting at week 8. Patients randomised to placebo who were non-responders at week 16 (early rescue) and other placebo patients at week 24 were crossed over to receive secukinumab (either 75 mg or 150 mg subcutaneously) followed by the same dose every month.

PsA study 2 (FUTURE 2) evaluated 397 patients, of whom 46.6% had concomitant MTX. Patients randomised to secukinumab received 75 mg, 150 mg or 300 mg subcutaneously at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients randomised to receive placebo who were non-responders at week 16 (early rescue) were crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 16 followed by the same dose every month. Patients randomised to receive placebo who were responders at week 16 were crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 24 followed by the same dose every month.

PsA study 3 (FUTURE 5) evaluated 996 patients, of whom 50.1% had concomitant MTX. Patients were randomised to receive secukinumab 150 mg, 300 mg or placebo subcutaneously at weeks 0, 1, 2, 3 and 4, followed by the same dose every month, or a once monthly injection of secukinumab 150 mg (without loading). Patients randomised to receive placebo who were non-responders at week 16 (early rescue) were then crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 16 followed by the same dose every month. Patients randomised to receive placebo who were responders at week 16 were crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 24 followed by the same dose every month.

Signs and symptoms
Treatment with secukinumab resulted in significant improvement in measures of disease activity compared to placebo at weeks 16 and 24 (see Table 9).

Table 9 Clinical response in PsA study 2 and PsA study 3 at week 16 and week 24

	PsA study 2			**PsA study 3**		
	Placebo	150 mg[1]	300 mg[1]	Placebo	150 mg[1]	300 mg[1]
Number of patients randomised	98	100	100	332	220	222
ACR20 response n (%)						
Week 16	18 (18.4%)	60 (60.0%***)	57 (57.0%***)	91◊ (27.4%)	122◊ (55.5%***)	139◊ (62.6%***)
Week 24	15◊ (15.3%)	51◊ (51.0%***)	54◊ (54.0%***)	78 (23.5%)	117 (53.2%***)	141 (63.5%***)
ACR50 response n (%)						
Week 16	6 (6.1%)	37 (37.0%***)	35 (35.0%***)	27 (8.1%)	79 (35.9%*)	88 (39.6%*)
Week 24	7 (7.1%)	35 (35.0%)	35 (35.0%**)	29 (8.7%)	86 (39.1%***)	97 (43.7%***)
ACR70 response n (%)						
Week 16	2 (2.0%)	17 (17.0%**)	15 (15.0%**)	14 (4.2%)	40 (18.2%***)	45 (20.3%***)
Week 24	1 (1.0%)	21 (21.0%**)	20 (20.0%**)	13 (3.9%)	53 (24.1%***)	57 (25.7%***)

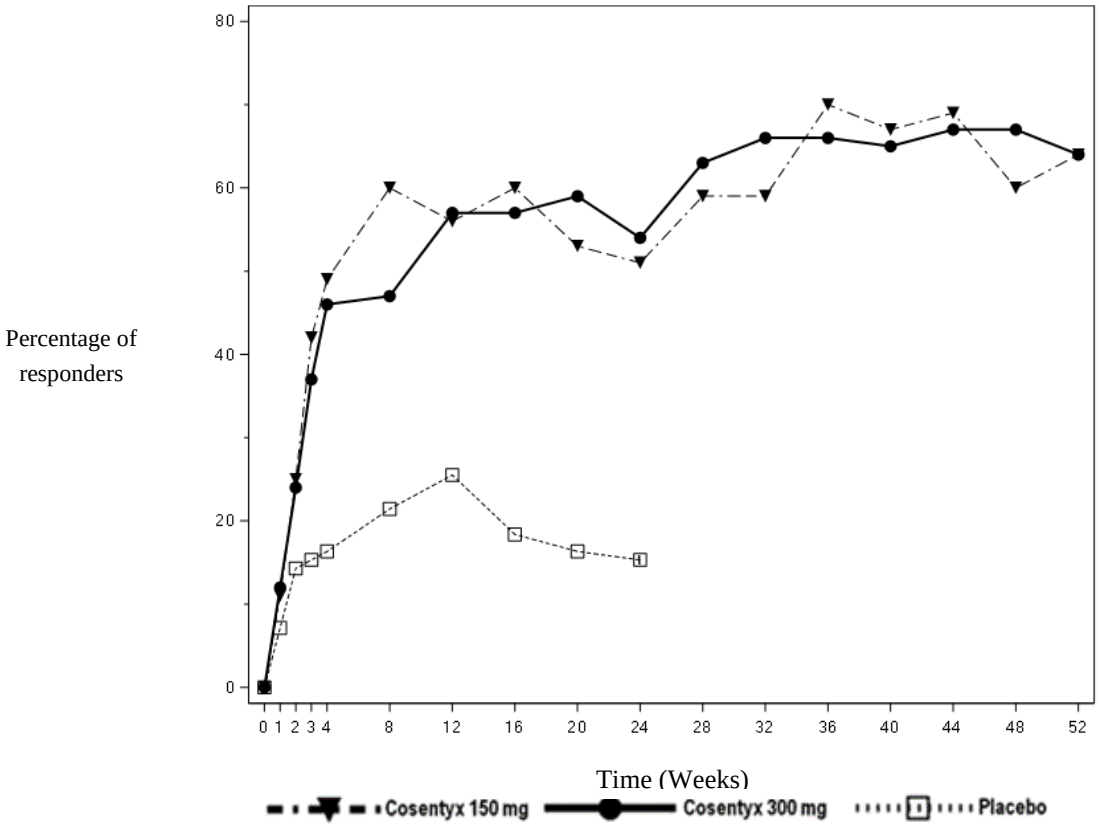
DAS28-CRP						
Week 16	-0.50	-1.45***	-1.51***	-0.63	-1.29*	-1.49*
Week 24	-0.96	-1.58**	-1.61**	-0.84	-1.57***	-1.68***
Number of patients with ≥3% BSA psoriasis skin involvement at baseline	43 (43.9%)	58 (58.0%)	41 (41.0%)	162 (48.8%)	125 (56.8%)	110 (49.5%)
PASI 75 response n (%)						
Week 16	3 (7.0%)	33 (56.9%***)	27 (65.9%***)	20 (12.3%)	75 (60.0%*)	77 (70.0%*)
Week 24	7 (16.3%)	28 (48.3%**)	26 (63.4%***)	29 (17.9%)	80 (64.0%***)	78 (70.9%***)
PASI 90 response n (%)						
Week 16	3 (7.0%)	22 (37.9%***)	18 (43.9%***)	15 (9.3%)	46 (36.8%*)	59 (53.6%*)
Week 24	4 (9.3%)	19 (32.8%**)	20 (48.8%***)	19 (11.7%)	51 (40.8%***)	60 (54.5%***)
Dactylitis resolution n (%) †						
Week 16	10 (37%)	21 (65.6%*)	26 (56.5%)	40 (32.3%)	46 (57.5%*)	54 (65.9%*)
Week 24	4 (14.8%)	16 (50.0%**)	26 (56.5%**)	42 (33.9%)	51 (63.8%***)	52 (63.4%***)
Enthesitis resolution n (%) ‡						
Week 16	17 (26.2%)	32 (50.0%**)	32 (57.1%***)	68 (35.4%)	77 (54.6%*)	78 (55.7%*)
Week 24	14 (21.5%)	27 (42.2%*)	27 (48.2%**)	66 (34.4%)	77 (54.6%***)	86 (61.4%***)

* p<0.05, ** p<0.01, *** p<0.001; versus placebo
All p-values are adjusted for multiplicity of testing based on pre-defined hierarchy at week 24 for PsA study 2, except for ACR70, Dactylitis and Enthesitis, which were exploratory endpoints and all endpoints at week 16.
All p-values are adjusted for multiplicity of testing based on pre-defined hierarchy at week 16 for PsA study 3, except for ACR70 which was an exploratory endpoint and all endpoints at week 24.
Non-responder imputation used for missing binary endpoint.
ACR: American College of Rheumatology; PASI: Psoriasis Area and Severity Index; DAS: Disease Activity Score; BSA: Body Surface Area
◊Primary Endpoint
[1]Secukinumab 150 mg or 300 mg s.c. at weeks 0, 1, 2, 3, and 4 followed by the same dose every month
†In patients with dactylitis at baseline (n=27, 32, 46, respectively for PsA study 2 and n=124, 80, 82, respectively for PsA study 3)
‡In patients with enthesitis at baseline (n=65, 64, 56, respectively for PsA study 2 and n=192, 141, 140, respectively for PsA study 3)

The onset of action of secukinumab occurred as early as week 2. Statistically significant difference in ACR 20 versus placebo was reached at week 3.

The percentage of patients achieving ACR 20 response by visit is shown in Figure 2.

Figure 2 ACR20 response in PsA study 2 over time up to week 52



Similar responses for primary and key secondary endpoints were seen in PsA patients regardless of whether they were on concomitant MTX treatment or not. In PsA study 2, at week 24, secukinumab-treated patients with concomitant MTX use had a higher ACR 20 response (47.7% and 54.4% for 150 mg and 300 mg, respectively, compared to placebo 20.0%) and ACR 50 response (31.8% and 38.6% for 150 mg and 300 mg, respectively, compared to placebo 8.0%). Secukinumab-treated patients without concomitant MTX use had a higher ACR 20 response (53.6% and 53.6% for 150 mg and 300 mg, respectively, compared to placebo 10.4%) and ACR 50 response (37.5% and 32.1% for 150 mg and 300 mg, respectively, compared to placebo 6.3%).

In PsA study 2, both anti-TNFα-naive and anti-TNFα-IR secukinumab-treated patients had a significantly higher ACR 20 response compared to placebo at week 24, with a slightly higher response in the anti-TNFα-naive group (anti-TNFα-naive: 64% and 58% for 150 mg and 300 mg, respectively, compared to placebo 15.9%; anti-TNFα-IR: 30% and 46% for 150 mg and 300 mg, respectively, compared to placebo 14.3%). In the anti-TNFα-IR patients subgroup, only the 300 mg dose showed significantly higher response rate for ACR 20 compared to placebo ($p<0.05$) and demonstrated clinical meaningful benefit over 150 mg on multiple secondary endpoints. Improvements in the PASI 75 response were seen in both subgroups and the 300 mg dose showed statistically significant benefit in the anti-TNFα-IR patients.

Improvements were shown in all components of the ACR scores, including patient assessment of pain. In PsA study 2, the proportion of patients achieving a modified PsA Response Criteria (PsARC) response was greater in the secukinumab-treated patients (59.0% and 61.0% for 150 mg and 300 mg, respectively) compared to placebo (26.5%) at week 24.

In PsA study 1 and PsA study 2, efficacy was maintained up to week 104. In PsA study 2, among 200 patients initially randomised to secukinumab 150 mg and 300 mg, 178 (89%) patients were still on treatment at week 52. Of the 100 patients randomised to secukinumab 150 mg, 64, 39 and 20 had an ACR 20/50/70 response, respectively. Of the 100 patients randomised to secukinumab 300 mg, 64, 44 and 24 had an ACR 20/50/70 response, respectively.

Radiographic response
In PsA study 3, inhibition of progression of structural damage was assessed radiographically and expressed by the modified Total Sharp Score (mTSS) and its components, the Erosion Score (ES) and the Joint Space Narrowing Score (JSN). Radiographs of hands, wrists, and feet were obtained at baseline, week 16 and/or week 24 and scored independently by at least two readers who were blinded to treatment group and visit number. Secukinumab 150 mg and 300 mg treatment significantly inhibited the rate of progression of peripheral joint damage compared with placebo treatment as measured by change from baseline in mTSS at week 24 (Table 10).

Inhibition of progression of structural damage was also assessed in PsA study 1 at weeks 24 and 52, compared to baseline. Week 24 data are presented in Table 10.

Table 10 Change in modified Total Sharp Score in psoriatic arthritis

	PsA study 3			**PsA study 1**	
	Placebo n=296	**secukinumab 150 mg[1] n=213**	**secukinumab 300 mg[1] n=217**	**Placebo n=179**	**secukinumab 150 mg[2] n=185**
Total score					
Baseline (SD)	15.0 (38.2)	13.5 (25.6)	12.9 (23.8)	28.4 (63.5)	22.3 (48.0)
Mean change at week 24	0.50	0.13*	0.02*	0.57	0.13*
*p<0.05 based on nominal, but non adjusted, p-value [1]secukinumab 150 mg or 300 mg s.c. at weeks 0, 1, 2, 3, and 4 followed by the same dose every month [2]10 mg/kg at weeks 0, 2 and 4 followed by subcutaneous doses of 75 mg or 150 mg					

In PsA study 1, inhibition of structural damage was maintained with secukinumab treatment up to week 52.

In PsA study 3, the percentage of patients with no disease progression (defined as a change from baseline in mTSS of ≤0.5) from randomisation to week 24 was 80.3%, 88.5% and 73.6% for secukinumab 150 mg, 300 mg and placebo, respectively. An effect of inhibition of structural damage was observed in anti-TNFα-naïve and anti-TNFα-IR patients and in patients treated with and without concomitant MTX.

In PsA study 1, the percentage of patients with no disease progression (defined as a change from baseline in mTSS of ≤0.5) from randomisation to week 24 was 82.3% in secukinumab 10 mg/kg intravenous load – 150 mg subcutaneous maintenance and 75.7% in placebo. The percentage of patients with no disease progression from week 24 to week 52 for secukinumab 10 mg/kg intravenous load – followed by 150 mg subcutaneous maintenance and for placebo patients who switched to 75 mg or 150 mg subcutaneous every 4 weeks at week 16 or week 24 was 85.7% and 86.8%, respectively.

Axial manifestations in PsA
A randomised, double-blind, placebo-controlled study (MAXIMISE) assessed the efficacy of secukinumab in 485 PsA patients with axial manifestations who were naive to biologic treatment and responded inadequately to NSAIDs. The primary variable of at least a 20% improvement in Assessment of SpondyloArthritis International Society (ASAS 20) criteria at week 12 was met. Treatment with secukinumab 300 mg and 150 mg compared to placebo also resulted in greater improvement in signs and symptoms (including decreases from baseline in spinal pain) and improvement in physical function (see Table 11).

Table 11 Clinical response on MAXIMISE study at week 12

	Placebo (n=164)	**150 mg (n=157)**	**300 mg (n=164)**
ASAS 20 response, % (95% CI)	31.2 (24.6, 38.7)	66.3 (58.4, 73.3)*	62.9 (55.2, 70.0)*
ASAS 40 response, % (95% CI)	12.2 (7.8, 18.4)	39.5 (32.1, 47.4)**	43.6 (36.2, 51.3)**
BASDAI 50, % (95% CI)	9.8 (5.9, 15.6)	32.7 (25.8, 40.5)**	37.4 (30.1, 45.4)**
Spinal pain, VAS (95% CI)	-13.6 (-17.2, -10.0)	-28.5 (-32.2, -24.8)**	-26.5 (-30.1, -22.9)**
Physical function, HAQ-DI (95% CI)	-0.155 (-0.224, -0.086)	-0.330 (-0.401, -0.259)**	-0.389 (-0.458, -0.320)**
* p<0.0001; versus placebo using multiple imputation. ** Comparison versus placebo was not adjusted for multiplicity. ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; VAS: Visual Analog Scale; HAQ-DI: Health Assessment Questionnaire – Disability Index.			

Improvement in ASAS 20 and ASAS 40 for both secukinumab doses were observed by week 4 and were maintained up to 52 weeks.

Physical function and health-related quality of life
In PsA study 2 and PsA study 3, patients treated with secukinumab 150 mg (p=0.0555 and p<0.0001) and 300 mg (p=0.0040 and p<0.0001) showed improvement in physical function compared to patients treated with placebo as assessed by Health Assessment Questionnaire-Disability Index (HAQ-DI) at week 24 and week 16, respectively. Improvements in HAQ-DI scores were seen regardless of previous anti-TNFα exposure. Similar responses were seen in PsA study 1.

Secukinumab-treated patients reported significant improvements in health-related quality of life as measured by the Short Form-36 Health Survey Physical Component Summary (SF-36 PCS) score (p<0.001). There were also statistically significant improvements demonstrated in exploratory endpoints assessed by the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) scores for 150 mg and 300 mg compared to placebo (7.97, 5.97 versus 1.63, respectively) and these improvements were maintained up to week 104 in PsA study 2.

Similar responses were seen in PsA study 1 and efficacy was maintained up to week 52.

Axial spondyloarthritis (axSpA)
Ankylosing spondylitis (AS) / Radiographic axial spondyloarthritis
The safety and efficacy of secukinumab were assessed in 816 patients in three randomised, double-blind, placebo-controlled phase III studies in patients with active ankylosing spondylitis (AS) with a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4 despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients in Ankylosing Spondylitis study 1 (AS study 1) and Ankylosing Spondylitis study 2 (AS study 2) had a diagnosis of AS for a median of 2.7 to 5.8 years. For both studies, the primary endpoint was at least a 20% improvement in Assessment of SpondyloArthritis International Society (ASAS 20) criteria at week 16.

In Ankylosing Spondylitis study 1 (AS study 1), Ankylosing Spondylitis study 2 (AS study 2), and Ankylosing Spondylitis study 3 (AS study 3), 27.0%, 38.8%, and 23.5% of patients, respectively, were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

AS study 1 (MEASURE 1) evaluated 371 patients, of whom 14.8% and 33.4% used concomitant MTX or sulfasalazine, respectively. Patients randomised to secukinumab received 10 mg/kg intravenously at weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously every month starting at week 8. Patients randomised to placebo who were non-responders at week 16 (early rescue) and all other placebo patients at week 24 were crossed over to receive secukinumab (either 75 mg or 150 mg subcutaneously), followed by the same dose every month.

AS study 2 (MEASURE 2) evaluated 219 patients, of whom 11.9% and 14.2% used concomitant MTX or sulfasalazine, respectively. Patients randomised to secukinumab received 75 mg or 150 mg subcutaneously at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. At week 16, patients who were randomised to placebo at baseline were re-randomised to receive secukinumab (either 75 mg or 150 mg subcutaneously) every month.

AS study 3 (MEASURE 3) evaluated 226 patients, of whom 13.3% and 23.5% used concomitant MTX or sulfasalazine, respectively. Patients randomised to secukinumab received 10 mg/kg intravenously at weeks 0, 2, and 4, followed by either 150 mg or 300 mg subcutaneously every month. At week 16, patients who were randomised to placebo at baseline were re-randomised to receive secukinumab (either 150 mg or 300 mg subcutaneously) every month. The primary endpoint was ASAS 20 at week 16. Patients were blinded to the treatment regimen up to week 52, and the study continued to week 156.

Signs and symptoms:
In AS study 2, treatment with secukinumab 150 mg resulted in greater improvement in measures of disease activity compared with placebo at week 16 (see Table 12).

Table 12 Clinical response in AS study 2 at week 16

Outcome (p-value versus placebo)	**Placebo (n = 74)**	**75 mg (n = 73)**	**150 mg (n = 72)**
ASAS 20 response, %	28.4	41.1	61.1***
ASAS 40 response, %	10.8	26.0	36.1***
hsCRP, (post-BSL/BSL ratio)	1.13	0.61	0.55***
ASAS 5/6, %	8.1	34.2	43.1***
ASAS partial remission, %	4.1	15.1	13.9
BASDAI 50, %	10.8	24.7*	30.6**
ASDAS-CRP major improvement	4.1	15.1*	25.0***

* $p<0.05$, ** $p<0.01$, *** $p<0.001$; versus placebo
All p-values adjusted for multiplicity of testing based on pre-defined hierarchy, except BASDAI 50 and ASDAS-CRP
Non-responder imputation used for missing binary endpoint

ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; hsCRP: high-sensitivity C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score; BSL: baseline

The onset of action of secukinumab 150 mg occurred as early as week 1 for ASAS 20 and week 2 for ASAS 40 (superior to placebo) in AS study 2.

ASAS 20 responses were improved at week 16 in both anti-TNFα-naïve patients (68.2% versus 31.1%; $p<0.05$) and anti-TNFα-IR patients (50.0% versus 24.1%; $p<0.05$) for secukinumab 150 mg compared with placebo, respectively.

In AS study 1 and AS study 2, secukinumab-treated patients (150 mg in AS study 2 and both regimens in AS study 1) demonstrated significantly improved signs and symptoms at week 16, with comparable magnitude of response and efficacy maintained up to week 52 in both anti-TNFα-naive and anti-TNFα-IR patients. In AS study 2, among 72 patients initially randomised to secukinumab 150 mg, 61 (84.7%) patients were still on treatment at week 52. Of the 72 patients randomised to secukinumab 150 mg, 45 and 35 had an ASAS 20/40 response, respectively.

In AS study 3, patients treated with secukinumab (150 mg and 300 mg) demonstrated improved signs and symptoms, and had comparable efficacy responses regardless of dose that were superior to placebo at week 16 for the primary endpoint (ASAS 20). Overall, the efficacy response rates for the 300 mg group were consistently greater compared to the 150 mg group for the secondary endpoints. During the blinded period, the ASAS 20 and ASAS 40 responses were 69.7% and 47.6% for 150 mg and 74.3% and 57.4% for 300 mg at week 52, respectively. The ASAS 20 and ASAS 40 responses were maintained up to week 156 (69.5% and 47.6% for 150 mg versus 74.8% and 55.6% for 300 mg). Greater response rates favouring 300 mg were also observed for ASAS partial remission (ASAS PR) response at week 16 and were maintained up to week 156. Larger differences in response rates, favouring 300 mg over 150 mg, were observed in anti-TNFα-IR patients (n=36) compared to anti-TNFα-naïve patients (n=114).

Spinal mobility:
Patients treated with secukinumab 150 mg showed improvements in spinal mobility as measured by change from baseline in BASMI at week 16 for both AS study 1 (-0.40 versus -0.12 for placebo; p=0.0114) and AS study 2 (-0.51 versus -0.22 for placebo; p=0.0533). These improvements were sustained up to week 52.

Physical function and health-related quality of life:
In AS study 1 and study 2, patients treated with secukinumab 150 mg showed improvements in health-related quality of life as measured by AS Quality of Life Questionnaire (ASQoL) (p=0.001) and SF-36 Physical Component Summary (SF-36PCS) (p<0.001). Patients treated with secukinumab 150 mg also showed statistically significant improvements on exploratory endpoints in physical function as assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI) compared to placebo (-2.15 versus -0.68), and in fatigue as assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale compared to placebo (8.10 versus 3.30). These improvements were sustained up to week 52.

Non-radiographic axial spondyloarthritis (nr-axSpA)
The safety and efficacy of secukinumab were assessed in 555 patients in one randomised, double-blind, placebo-controlled phase III study (PREVENT), consisting of a 2-year core phase and a 2-year extension phase, in patients with active non-radiographic axial spondyloarthritis (nr-axSpA) fulfilling the Assessment of SpondyloArthritis International Society (ASAS) classification criteria for axial spondyloarthritis (axSpA) with no radiographic evidence of changes in the sacroiliac joints that would meet the modified New York criteria for ankylosing spondylitis (AS). Patients enrolled had active disease, defined as a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4, a Visual Analogue Scale (VAS) for total back pain of ≥40 (on a scale of 0-100 mm), despite current or previous non-steroidal anti-inflammatory drug (NSAID) therapy and increased C-reactive protein (CRP) and/or evidence of sacroiliitis on Magnetic Resonance Imaging (MRI). Patients in this study had a diagnosis of axSpA for a mean of 2.1 to 3.0 years and 54% of the study participants were female.

In the PREVENT study, 9.7% of patients were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

In the PREVENT study, 9.9% and 14.8% of patients used concomitant MTX or sulfasalazine, respectively. In the double-blind period, patients received either placebo or secukinumab for 52 weeks. Patients randomised to secukinumab received 150 mg subcutaneously at weeks 0, 1, 2, 3 and 4 followed by the same dose every month, or a once monthly injection of secukinumab 150 mg. The primary endpoint was at least 40% improvement in Assessment of SpondyloArthritis International Society (ASAS 40) at Week 16 in anti-TNFα-naive patients.

Signs and symptoms:
In the PREVENT study, treatment with secukinumab 150 mg resulted in significant improvements in the measures of disease activity compared to placebo at week 16. These measures include ASAS 40, ASAS 5/6, BASDAI score, BASDAI 50, high-sensitivity CRP (hsCRP), ASAS 20 and ASAS partial remission response compared to placebo (Table 13). Responses were maintained up to week 52.

Table 13 Clinical response in the PREVENT study at week 16

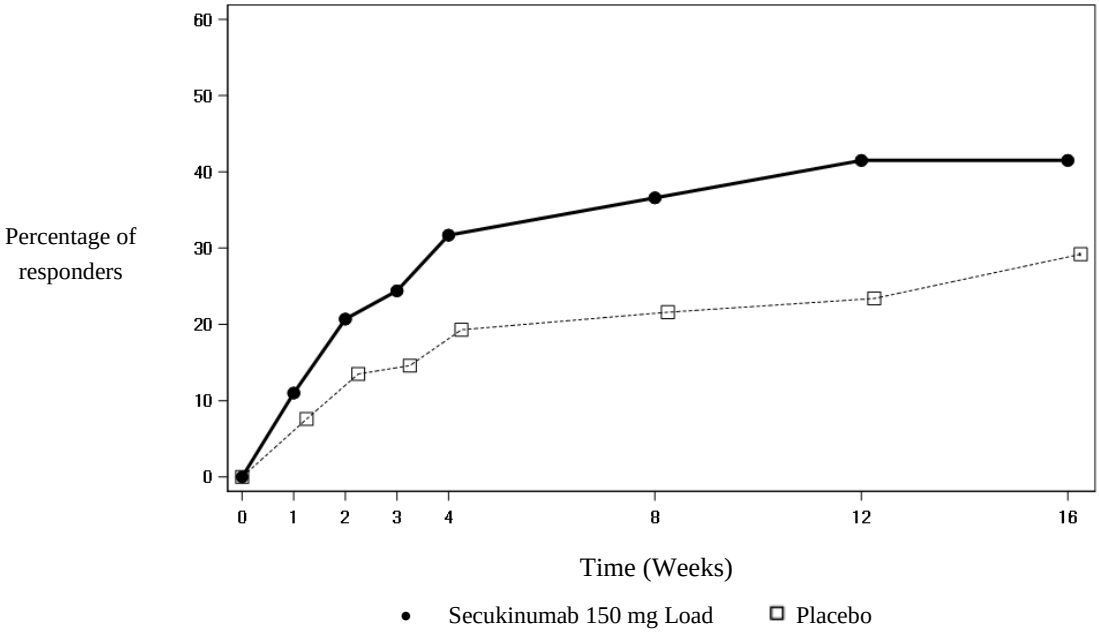
Outcome (p-value versus placebo)	**Placebo**	**150 mg[1]**
Number of anti-TNFα-naive patients randomised	**171**	**164**
ASAS 40 response, %	29.2	41.5*
Total number of patients randomised	**186**	**185**
ASAS 40 response, %	28.0	40.0*
ASAS 5/6, %	23.7	40.0*
BASDAI, LS mean change from baseline score	-1.46	-2.35*
BASDAI 50, %	21.0	37.3*
hsCRP, (post-BSL/BSL ratio)	0.91	0.64*
ASAS 20 response, %	45.7	56.8*
ASAS partial remission, %	7.0	21.6*

*p<0.05 versus placebo
All p-values adjusted for multiplicity of testing based on pre-defined hierarchy
Non-responder imputation used for missing binary endpoint
[1]secukinumab 150 mg s.c. at weeks 0, 1, 2, 3, and 4 followed by the same dose every month

ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; hsCRP: high-sensitivity C-reactive protein; BSL: baseline; LS: Least square

The onset of action of secukinumab 150 mg occurred as early as week 3 for ASAS 40 in anti-TNFα naive patients (superior to placebo) in the PREVENT study. The percentage of patients achieving an ASAS 40 response in anti-TNFα naive patients by visit is shown in Figure 3.

Figure 3 ASAS 40 responses in anti-TNFα naive patients in the PREVENT study over time up to week 16



ASAS 40 responses were also improved at week 16 in anti-TNFα-IR patients for secukinumab 150 mg compared with placebo.

Physical function and health-related quality of life:
Patients treated with secukinumab 150 mg showed statistically significant improvements by week 16 compared to placebo-treated patients in physical function as assessed by the BASFI (week 16: -1.75 versus -1.01, $p<0.05$). Patients treated with secukinumab reported significant improvements compared to placebo-treated patients by week 16 in health-related quality of life as measured by ASQoL (LS mean change: week 16: -3.45 versus -1.84, $p<0.05$) and SF-36 Physical Component Summary (SF-36 PCS) (LS mean change: week 16: 5.71 versus 2.93, $p<0.05$). These improvements were sustained up to week 52.

Spinal mobility:
Spinal mobility was assessed by BASMI up to week 16. Numerically greater improvements were demonstrated in patients treated with secukinumab compared with placebo-treated patients at weeks 4, 8, 12 and 16.

Inhibition of inflammation in magnetic resonance imaging (MRI):
Signs of inflammation were assessed by MRI at baseline and week 16 and expressed as change from baseline in Berlin SI-joint oedema score for sacroiliac joints and ASspiMRI-a score and Berlin spine score for the spine. Inhibition of inflammatory signs in both sacroiliac joints and the spine was observed in patients treated with secukinumab. Mean change from baseline in Berlin SI-joint oedema score was -1.68 for patients treated with secukinumab 150 mg (n=180) versus -0.39 for the placebo-treated patients (n=174) ($p<0.05$).

Paediatric population

Paediatric plaque psoriasis
Secukinumab has been shown to improve signs and symptoms, and health-related quality of life in paediatric patients 6 years and older with plaque psoriasis (see Tables 15 and 17).

Severe plaque psoriasis
The safety and efficacy of secukinumab were assessed in a randomised, double-blind, placebo and etanercept-controlled phase III study in paediatric patients from 6 to <18 years of age with severe plaque psoriasis, as defined by a PASI score ≥20, an IGA mod 2011 score of 4, and BSA involvement of ≥10%, who were candidates for systemic therapy. Approximately 43% of the patients had prior exposure to phototherapy, 53% to conventional systemic therapy, 3% to biologics, and 9% had concomitant psoriatic arthritis.

The paediatric psoriasis study 1 evaluated 162 patients who were randomised to receive low dose secukinumab (75 mg for body weight <50 kg or 150 mg for body weight ≥50 kg), high dose secukinumab (75 mg for body weight <25 kg, 150 mg for body weight between ≥25 kg and <50 kg, or 300 mg for body weight ≥50 kg), or placebo at weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks, or etanercept. Patients randomised to etanercept received 0.8 mg/kg weekly (up to a maximum of 50 mg). Patient distribution by weight and age at randomisation is described in Table 14.

Table 14 Patient distribution by weight and age for paediatric psoriasis study 1

Randomisation strata	**Description**	**Secukinumab low dose n=40**	**Secukinumab high dose n=40**	**Placebo n=41**	**Etanercept n=41**	**Total N=162**
Age	6-<12 years	8	9	10	10	37
	≥12-<18 years	32	31	31	31	125
Weight	<25 kg	2	3	3	4	12
	≥25-<50 kg	17	15	17	16	65
	≥50 kg	21	22	21	21	85

Patients randomised to receive placebo who were non-responders at week 12 were switched to either the secukinumab low or high dose group (dose based on body weight group) and received study drug at weeks 12, 13, 14, and 15, followed by the same dose every 4 weeks starting at week 16. The co-primary endpoints were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 ‘clear’ or ‘almost clear’ (0 or 1) response at week 12.

During the 12 week placebo-controlled period, the efficacy of both the low and the high dose of secukinumab was comparable for the co-primary endpoints. The odds ratio estimates in favour of both secukinumab doses were statistically significant for both the PASI 75 and IGA mod 2011 0 or 1 responses.

All patients were followed for efficacy and safety during the 52 weeks following the first dose. The proportion of patients achieving PASI 75 and IGA mod 2011 ‘clear’ or ‘almost clear’ (0 or 1) responses showed separation between secukinumab treatment groups and placebo at the first post-baseline visit at week 4, the difference becoming more prominent at week 12. The response was maintained throughout the 52 week time period (see Table 15). Improvement in PASI 50, 90, 100 responder rates and Children’s Dermatology Life Quality Index (CDLQI) scores of 0 or 1 were also maintained throughout the 52 week time period.

In addition, PASI 75, IGA 0 or 1, PASI 90 response rates at weeks 12 and 52 for both secukinumab low and high dose groups were higher than the rates for patients treated with etanercept (see Table 15).

Beyond week 12, efficacy of both the low and the high dose of secukinumab was comparable although the efficacy of the high dose was higher for patients ≥50 kg. The safety profiles of the low dose and the high dose were comparable and consistent with the safety profile in adults.

Table 15 Summary of clinical response in severe paediatric psoriasis at weeks 12 and 52 (paediatric psoriasis study 1)*

Response criterion	Treatment comparison 'test' vs. 'control'	'test' n**/m (%)	'control' n**/m (%)	odds ratio estimate (95% CI)	p-value
At week 12* **					
PASI 75	secukinumab low dose vs. placebo	32/40 (80.0)	6/41 (14.6)	25.78 (7.08, 114.66)	<0.0001
	secukinumab high dose vs. placebo	31/40 (77.5)	6/41 (14.6)	22.65 (6.31, 98.93)	<0.0001
	secukinumab low dose vs. etanercept	32/40 (80.0)	26/41 (63.4)	2.25 (0.73, 7.38)	
	secukinumab high dose vs. etanercept	31/40 (77.5)	26/41 (63.4)	1.92 (0.64, 6.07)	
IGA 0/1	secukinumab low dose vs. placebo	28/40 (70.0)	2/41 (4.9)	51.77 (10.02, 538.64)	<0.0001
	secukinumab high dose vs. placebo	24/40 (60.0)	2/41 (4.9)	32.52 (6.48, 329.52)	<0.0001
	secukinumab low dose vs. etanercept	28/40 (70.0)	14/41 (34.1)	4.49 (1.60, 13.42)	
	secukinumab high dose vs. etanercept	24/40 (60.0)	14/41 (34.1)	2.86 (1.05, 8.13)	
PASI 90	secukinumab low dose vs. placebo	29/40 (72.5)	1/41 (2.4)	133.67 (16.83, 6395.22)	<0.0001
	secukinumab high dose vs. placebo	27/40 (67.5)	1/41 (2.4)	102.86 (13.22, 4850.13)	<0.0001
	secukinumab low dose vs. etanercept	29/40 (72.5)	12/41 (29.3)	7.03 (2.34, 23.19)	
	secukinumab high dose vs. etanercept	27/40 (67.5)	12/41 (29.3)	5.32 (1.82, 16.75)	
At week 52					
PASI 75	secukinumab low dose vs. etanercept	35/40 (87.5)	28/41 (68.3)	3.12 (0.91, 12.52)	
	secukinumab high dose vs. etanercept	35/40 (87.5)	28/41 (68.3)	3.09 (0.90, 12.39)	
IGA 0/1	secukinumab low dose vs. etanercept	29/40 (72.5)	23/41 (56.1)	2.02 (0.73, 5.77)	
	secukinumab high dose vs. etanercept	30/40 (75.0)	23/41 (56.1)	2.26 (0.81, 6.62)	
PASI 90	secukinumab low dose vs. etanercept	30/40 (75.0)	21/41 (51.2)	2.85 (1.02, 8.38)	
	secukinumab high dose vs. etanercept	32/40 (80.0)	21/41 (51.2)	3.69 (1.27, 11.61)	

* non-responder imputation was used to handle missing values
** n is the number of responders, m = number of patients evaluable
*** extended visit window at week 12
Odds ratio, 95% confidence interval, and p-value are from an exact logistic regression model with treatment group, baseline body-weight category and age category as factors

A higher proportion of paediatric patients treated with secukinumab reported improvement in health-related quality of life as measured by a CDLQI score of 0 or 1 compared to placebo at week 12 (low dose 44.7%, high dose 50%, placebo 15%). Over time up to and including week 52 both secukinumab dose groups were numerically higher than the etanercept group (low dose 60.6%, high dose 66.7%, etanercept 44.4%).

Moderate to severe plaque psoriasis
Secukinumab was predicted to be effective for the treatment of paediatric patients with moderate plaque psoriasis based on the demonstrated efficacy and exposure response relationship in adult patients with moderate to severe plaque psoriasis, and the similarity of the disease course, pathophysiology, and drug effect in adult and paediatric patients at the same exposure levels.

Moreover, the safety and efficacy of secukinumab was assessed in an open-label, two-arm, parallel-group, multicentre phase III study in paediatric patients from 6 to <18 years of age with moderate to severe plaque psoriasis, as defined by a PASI score ≥12, an IGA mod 2011 score of ≥3, and BSA involvement of ≥10%, who were candidates for systemic therapy.

The paediatric psoriasis study 2 evaluated 84 patients who were randomised to receive low dose secukinumab (75 mg for body weight <50 kg or 150 mg for body weight ≥50 kg) or high dose secukinumab (75 mg for body weight <25 kg, 150 mg for body weight between ≥25 kg and <50 kg, or 300 mg for body weight ≥50 kg) at weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks. Patient distribution by weight and age at randomisation is described in Table 16.

Table 16 Patient distribution by weight and age for paediatric psoriasis study 2

Sub-groups	Description	Secukinumab low dose n=42	Secukinumab high dose n=42	Total N=84
Age	6-<12 years	17	16	33
	≥12-<18 years	25	26	51
Weight	<25 kg	4	4	8
	≥25-<50 kg	13	12	25
	≥50 kg	25	26	51

The co-primary endpoints were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 'clear' or 'almost clear' (0 or 1) response at week 12.

The efficacy of both the low and the high dose of secukinumab was comparable and showed statistically significant improvement compared to historical placebo for the co-primary endpoints. The estimated posterior probability of a positive treatment effect was 100%.

Patients were followed for efficacy over a 52 week period after first administration. Efficacy (defined as PASI 75 response and IGA mod 2011 'clear' or 'almost clear' [0 or 1]) was observed as early as the first post-baseline visit at week 2, and the proportion of patients who achieved a PASI 75 response and IGA mod 2011 'clear' or 'almost clear' (0 or 1) increased up to week 24 and were sustained until week 52. Improvement in PASI 90 and PASI 100 were also observed at week 12, increased up to week 24, and were sustained until week 52 (see Table 17).

The safety profiles of the low dose and the high dose were comparable and consistent with the safety profile in adults.

Table 17 Summary of clinical response in moderate to severe paediatric psoriasis at weeks 12 and 52 (paediatric psoriasis study 2)*

	Week 12		Week 52	
	Secukinumab low dose	Secukinumab high dose	Secukinumab low dose	Secukinumab high dose
Number of patients	42	42	42	42
PASI 75 response n (%)	39 (92.9%)	39 (92.9%)	37 (88.1%)	38 (90.5%)
IGA mod 2011 'clear' or 'almost clear' response n (%)	33 (78.6%)	35 (83.3%)	36 (85.7%)	35 (83.3%)
PASI 90 response n (%)	29 (69%)	32 (76.2%)	32 (76.2%)	35 (83.3%)
PASI 100 response n (%)	25 (59.5%)	23 (54.8%)	22 (52.4%)	29 (69.0%)
* non-responder imputation was used to handle missing values				

These outcomes in the paediatric moderate to severe plaque psoriasis population confirmed the predictive assumptions based on the efficacy and exposure response relationship in adult patients, mentioned above.

In the low dose group, 50% and 70.7% of patients achieved a CDLQI 0 or 1 score at weeks 12 and 52, respectively. In the high dose group, 61.9% and 70.3% achieved a CDLQI 0 or 1 score at weeks 12 and 52, respectively.

Juvenile idiopathic arthritis (JIA)

Enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA)
The efficacy and safety of secukinumab were assessed in 86 patients in a 3-part, double-blind, placebo-controlled, event-driven, randomised, phase III study in patients 2 to <18 years of age with active ERA or JPsA as diagnosed based on a modified International League of Associations for Rheumatology (ILAR) JIA classification criteria. The study consisted of an open-label portion (Part 1) where all patients received secukinumab until week 12. Patients demonstrating a JIA ACR 30 response at week 12 entered into the Part 2 double-blind phase and were randomised 1:1 to continue treatment with secukinumab or to begin treatment with placebo (randomised withdrawal) until week 104 or until a flare occured. Patients who flared then entered open-label secukinumab treatment until week 104 (Part 3).

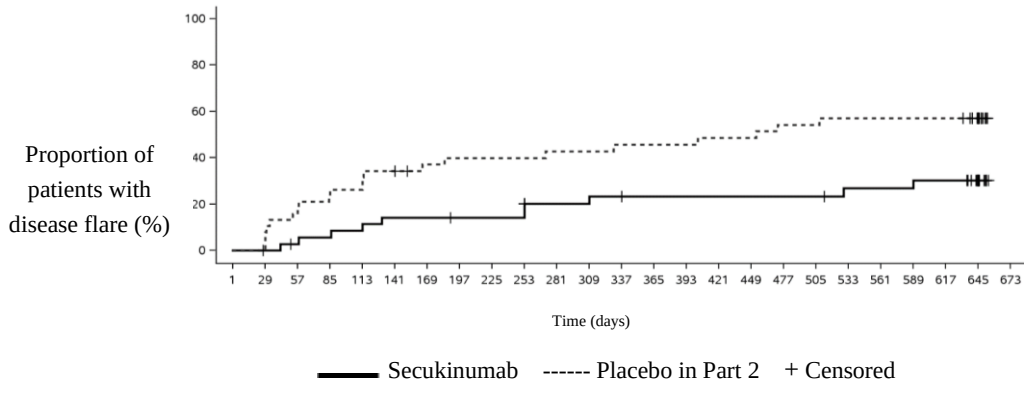
The JIA patient subtypes at study entry were: 60.5% ERA and 39.5% JPsA, who either had inadequate response or were intolerant to ≥1 disease-modifying antirheumatic drugs (DMARDs) and ≥1 non-steroidal anti-inflammatory drugs (NSAIDs). At baseline, MTX use was reported for 65.1% of patients; (63.5% [33/52] of ERA patients and 67.6% [23/34] of JPsA patients). There were 12 out of 52 ERA patients concomitantly treated with sulfasalazine (23.1%). Patients with a body weight at baseline <50 kg (n=30) were given a dose of 75 mg and patients with a body weight ≥50 kg (n=56) were given a dose of 150 mg. Age at baseline ranged from 2 to 17 years, with 3 patients between 2 to <6 years, 22 patients 6 to <12 years and 61 patients 12 to <18 years. At baseline the Juvenile Arthritis Disease Activity Score (JADAS)-27 was 15.1 (SD:7.1).

The primary endpoint was time to flare in the randomised withdrawal period (Part 2). Disease flare was defined as a ≥30% worsening in at least three of the six JIA ACR response criteria and ≥30% improvement in not more than one of the six JIA ACR response criteria and a minimum of two active joints.

At the end of Part 1, 75 out of 86 (87.2%) patients demonstrated a JIA ACR 30 response and entered into Part 2.

The study met its primary endpoint by demonstrating a statistically significant prolongation in the time to disease flare in patients treated with secukinumab compared to placebo in Part 2. The risk of flare was reduced by 72% for patients on secukinumab compared with patients on placebo in Part 2 (Hazard ratio=0.28, 95% CI: 0.13 to 0.63, p<0.001) (Figure 4 and Table 18). During Part 2, a total of 21 patients in the placebo group experienced a flare event (11 JPsA and 10 ERA) compared with 10 patients in the secukinumab group (4 JPsA and 6 ERA).

Figure 4 Kaplan-Meier estimates of the time to disease flare in Part 2



Number of patients at risk

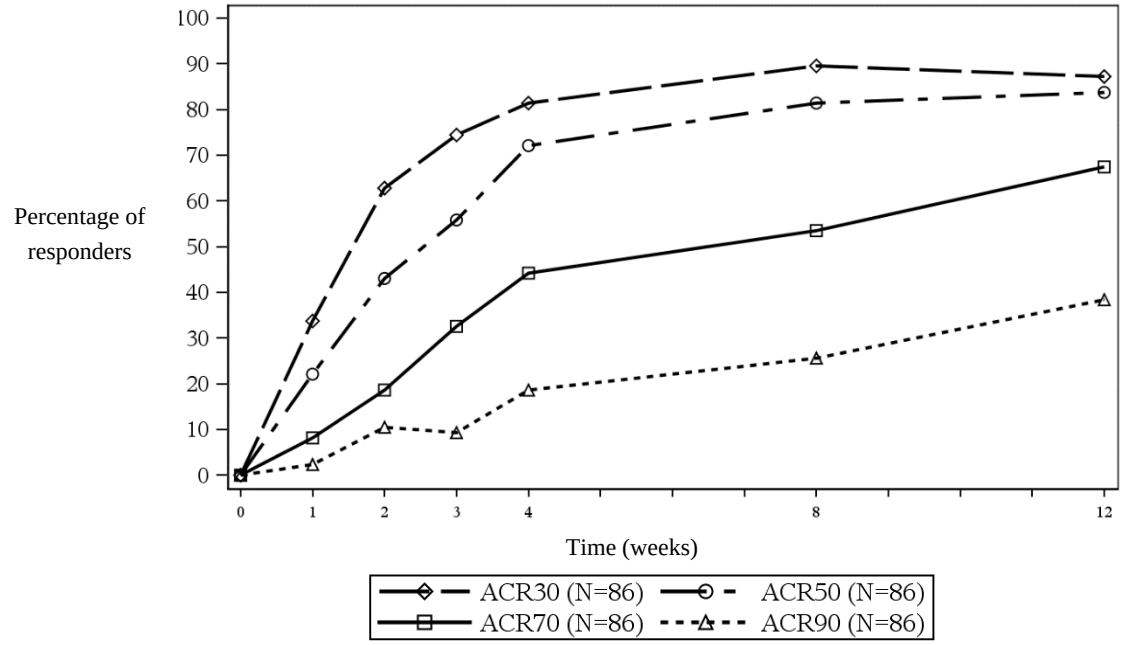
Secukinumab	37	36	34	33	32	30	30	29	29	29	25	25	24	23	23	23	23	23	23	21	21	21	20	14	0
Placebo in Part 2	38	38	32	29	28	25	22	21	21	21	20	20	19	19	19	18	18	16	16	15	15	15	15	10	0

Table 18 Survival analysis of time to disease flare – Part 2

	Secukinumab (N=37)	**Placebo in Part 2** (N=38)
Number of flare events at the end of Part 2, n (%)	10 (27.0)	21 (55.3)
Kaplan-Meier estimates:		
Median, in days (95% CI)	NC (NC, NC)	453.0 (114.0, NC)
Flare-free rate at 6 months (95% CI)	85.8 (69.2, 93.8)	60.1 (42.7, 73.7)
Flare-free rate at 12 months (95% CI)	76.7 (58.7, 87.6)	54.3 (37.1, 68.7)
Flare-free rate at 18 months (95% CI)	73.2 (54.6, 85.1)	42.9 (26.7, 58.1)
Hazard ratio to placebo: Estimate (95% CI)	0.28 (0.13, 0.63)	
Stratified log-rank test p-value	<0.001**	
Analysis was conducted on all randomised patients who received at least one dose of study drug in Part 2. Secukinumab: all patients who did not take any placebo. Placebo in Part 2: all patients who took placebo in Part 2 and secukinumab in other period/s. NC = Not calculable. ** = Statistically significant on one-sided significance level 0.025.		

In open-label Part 1, all patients received secukinumab until week 12. At week 12, 83.7%, 67.4%, and 38.4% of children were JIA ACR 50, 70 and 90 responders, respectively (Figure 5). The onset of action of secukinumab occurred as early as week 1. At week 12 the JADAS-27 score was 4.64 (SD:4.73) and the mean decrease from baseline in JADAS-27 was -10.487 (SD:7.23).

Figure 5 JIA ACR 30/50/70/90 response for subjects up to week 12 in Part 1*



*non-responder imputation was used to handle missing values

The data in the 2 to <6 age group were inconclusive due to the low number of patients below 6 years of age enrolled in the study.

The European Medicines Agency has waived the obligation to submit the results of studies with Cosentyx in plaque psoriasis in paediatric patients aged from birth to less than 6 years and in chronic idiopathic arthritis for paediatric patients aged from birth to less than 2 years (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Most pharmacokinetics properties observed in patients with plaque psoriasis, psoriatic arthritis and ankylosing spondylitis were similar.

Absorption

Following a single subcutaneous dose of 300 mg as a liquid formulation in healthy volunteers, secukinumab reached peak serum concentrations of 43.2±10.4 µg/ml between 2 and 14 days post dose.

Based on population pharmacokinetic analysis, following a single subcutaneous dose of either 150 mg or 300 mg in plaque psoriasis patients, secukinumab reached peak serum concentrations of 13.7±4.8 µg/ml or 27.3±9.5 µg/ml, respectively, between 5 and 6 days post dose.

After initial weekly dosing during the first month, time to reach the maximum concentration was between 31 and 34 days based on population pharmacokinetic analysis.

On the basis of simulated data, peak concentrations at steady-state ($C_{max,ss}$) following subcutaneous administration of 150 mg or 300 mg were 27.6 µg/ml and 55.2 µg/ml, respectively. Population pharmacokinetic analysis suggests that steady-state is reached after 20 weeks with monthly dosing regimens.

Compared with exposure after a single dose, the population pharmacokinetic analysis showed that patients exhibited a 2-fold increase in peak serum concentrations and area under the curve (AUC) following repeated monthly dosing during maintenance.

Population pharmacokinetic analysis showed that secukinumab was absorbed with an average absolute bioavailability of 73% in patients with plaque psoriasis. Across studies, absolute bioavailabilities in the range between 60 and 77% were calculated.

The bioavailability of secukinumab in PsA patients was 85% on the basis of the population pharmacokinetic model.

Following subcutaneous administration of 300 mg at weeks 0, 1, 2, 3 and 4 followed by 300 mg every 2 weeks, the mean ± SD steady-state secukinumab trough concentration at week 16 was approximately 55.1±26.7 µg/ml and 58.1±30.1 µg/ml in HS study 1 and HS study 2, respectively.

Distribution

The mean volume of distribution during the terminal phase (V_z) following single intravenous administration ranged from 7.10 to 8.60 litres in plaque psoriasis patients, suggesting that secukinumab undergoes limited distribution to peripheral compartments.

Biotransformation

The majority of IgG elimination occurs via intracellular catabolism, following fluid-phase or receptor mediated endocytosis.

Elimination

Mean systemic clearance (CL) following a single intravenous administration to patients with plaque psoriasis ranged from 0.13 to 0.36 l/day. In a population pharmacokinetic analysis, the mean systemic clearance (CL) was 0.19 l/day in plaque psoriasis patients. The CL was not impacted by gender. Clearance was dose- and time-independent.

The mean elimination half-life, as estimated from population pharmacokinetic analysis, was 27 days in plaque psoriasis patients, ranging from 18 to 46 days across psoriasis studies with intravenous administration.

In a population pharmacokinetic analysis, the mean systemic CL following subcutaneous administration of 300 mg at weeks 0, 1, 2, 3, and 4 followed by 300 mg every 2 weeks to patients with hidradenitis suppurativa was 0.26 l/day.

The mean elimination half-life, as estimated from population pharmacokinetic analysis, was 23 days in hidradenitis suppurativa patients.

Linearity/non-linearity

The single and multiple dose pharmacokinetics of secukinumab in plaque psoriasis patients were determined in several studies with intravenous doses ranging from 1x 0.3 mg/kg to 3x 10 mg/kg and with subcutaneous doses ranging from 1x 25 mg to multiple doses of 300 mg. Exposure was dose proportional across all dosing regimens.

Special populations

Elderly patients
Based on population pharmacokinetic analysis with a limited number of elderly patients (n=71 for age ≥65 years and n=7 for age ≥75 years), clearance in elderly patients and patients less than 65 years of age was similar.

Patients with renal or hepatic impairment
No pharmacokinetic data are available in patients with renal or hepatic impairment. The renal elimination of intact secukinumab, an IgG monoclonal antibody, is expected to be low and of minor importance. IgGs are mainly eliminated via catabolism and hepatic impairment is not expected to influence clearance of secukinumab.

Effect of weight on pharmacokinetics
Secukinumab clearance and volume of distribution increase as body weight increases.

Paediatric population
Plaque psoriasis
In a pool of the two paediatric studies, patients with moderate to severe plaque psoriasis (6 to less than 18 years of age) were administered secukinumab at the recommended paediatric dosing regimen. At week 24, patients weighing ≥25 and <50 kg had a mean ± SD steady-state trough concentration of 19.8 ± 6.96 µg/ml (n=24) after 75 mg of secukinumab and patients weighing ≥50 kg had mean ±SD trough concentration of 27.3 ± 10.1 µg/ml (n=36) after 150 mg of secukinumab. The mean ± SD steady-state trough concentration in patients weighing <25 kg (n=8) was 32.6 ± 10.8 µg/ml at week 24 after 75 mg dose.

Juvenile idiopathic arthritis
In a paediatric study, ERA and JPsA patients (2 to less than 18 years of age) were administered secukinumab at the recommended paediatric dosing regimen. At week 24, patients weighing <50 kg, and weighing ≥50 kg had a mean ± SD steady-state trough concentration of 25.2±5.45 µg/ml (n=10) and 27.9±9.57 µg/ml (n=19), respectively.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans (adult or paediatric) based on conventional studies of safety pharmacology, repeated dose and reproductive toxicity, or tissue cross-reactivity.

Animal studies have not been conducted to evaluate the carcinogenic potential of secukinumab.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Histidine
Histidine hydrochloride monohydrate
Polysorbate 80

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

3 years

After reconstitution

Chemical and physical in-use stability has been demonstrated for 24 hours at 2ºC to 8ºC.
From a microbiological point of view, unless the method of reconstitution precludes the risk of microbial contamination, the product should be used immediately.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C).
For storage conditions after reconstitution of the medicinal product, see section 6.3

6.5 Nature and contents of container

Cosentyx is supplied in a colourless glass vial with a grey coated rubber stopper and aluminium cap with a white flip-off component containing 150 mg of secukinumab.

Cosentyx is available in packs containing one vial.

6.6 Special precautions for disposal and other handling

The single-use vial contains 150 mg secukinumab for reconstitution with sterile water for injections. The resulting solution should be clear and colourless to slightly yellow. Do not use if the lyophilised powder has not fully dissolved or if the liquid contains easily visible particles, is cloudy or is distinctly brown.

Reconstitution

Cosentyx 150 mg powder for solution for injection must be prepared by a healthcare professional. The preparation of the solution for subcutaneous injection must be done without interruption and ensuring that aseptic technique is used. The preparation time from piercing the stopper until end of reconstitution takes 20 minutes on average and should not exceed 90 minutes.

1. Bring the vial of powder to room temperature and ensure that the sterile water for injections is at room temperature.
2. Withdraw slightly more than 1.0 ml sterile water for injections into a 1 ml graduated disposable syringe and adjust to 1.0 ml.
3. Remove the plastic cap from the vial.
4. Insert the syringe needle into the vial containing the powder through the centre of the rubber stopper and reconstitute the powder by slowly injecting 1.0 ml of sterile water for injections into the vial. The stream of sterile water for injections should be directed onto the powder.
5. Tilt the vial to an angle of approx. 45° and gently rotate between the fingertips for approx. 1 minute. Do not shake or invert the vial.
6. Keep the vial standing at room temperature for a minimum of 10 minutes to allow for dissolution. Note that foaming of the solution may occur.
7. Tilt the vial to an angle of approx. 45° and gently rotate between the fingertips for approx. 1 minute. Do not shake or invert the vial.
8. Allow the vial to stand undisturbed at room temperature for approximately 5 minutes. The resulting solution should be clear. Its colour may vary from colourless to slightly yellow. Do not use if the lyophilised powder has not fully dissolved or if the liquid contains easily visible particles, is cloudy or is distinctly brown.
9. Prepare the required number of vials (2 vials for the 300 mg dose).

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Use in the paediatric population

For paediatric patients receiving the 75 mg dose from the single-use vial containing 150 mg secukinumab for reconstitution with sterile water for injections, slightly more than 0.5 ml of the reconstituted solution for subcutaneous injection have to be withdrawn and the rest of the solution must be discarded immediately. Detailed instructions for use are provided in the package leaflet.

7. MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15 January 2015
Date of latest renewal: 03 September 2019

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substance

Novartis Pharma S.A.S.
Centre de Biotechnologie
8, rue de l'Industrie
F-68330 Huningue
France

Novartis Pharmaceutical Manufacturing GmbH
Biochemiestrasse 10
6336 Langkampfen
Austria

Name and address of the manufacturer responsible for batch release

Powder for solution for injection

Lek Pharmaceuticals d.d.
Verovškova ulica 57
Ljubljana, 1526
Slovenia

Novartis Pharma GmbH
Roonstraße 25
90429 Nuremberg
Germany

Novartis Farmacéutica, S.A.
Gran Vía de les Corts Catalanes, 764
08013 Barcelona
Spain

Solution for injection in pre-filled syringe / Solution for injection in pre-filled pen
Novartis Pharma GmbH
Roonstraße 25
90429 Nuremberg
Germany

Sandoz GmbH
Biochemiestrasse 10
6336 Langkampfen
Austria

Novartis Pharmaceutical Manufacturing GmbH
Biochemiestrasse 10
6336 Langkampfen
Austria

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON OF UNIT PACK – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 75 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 75 mg secukinumab in 0.5 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.
Single use.

'QR code to be included'
www.cosentyx.eu

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/012 Pack containing 1 pre-filled syringe

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 75 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (INCLUDING BLUE BOX) – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 75 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 75 mg secukinumab in 0.5 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 3 (3 packs of 1) pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringes in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/013 Multipack containing 3 (3 x 1) pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 75 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX) – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 75 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 75 mg secukinumab in 0.5 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe. Component of a multipack. Not to be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.
Single use.

'QR code to be included'
www.cosentyx.eu

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/013 Multipack containing 3 (3 x 1) pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 75 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER OF PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 75 mg solution for injection in pre-filled syringe
secukinumab

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cosentyx 75 mg injection
secukinumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON OF UNIT PACK – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 150 mg secukinumab in 1 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe
2 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

'QR code to be included'
www.cosentyx.eu

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.
Keep the pre-filled syringes in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/002	Pack containing 1 pre-filled syringe
EU/1/14/980/003	Pack containing 2 pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (INCLUDING BLUE BOX) – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 150 mg secukinumab in 1 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 6 (3 packs of 2) pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringes in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/006 Multipack containing 6 (3 x 2) pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX) – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 150 mg secukinumab in 1 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

2 pre-filled syringes. Component of a multipack. Not to be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

'QR code to be included'
www.cosentyx.eu

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringes in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/006 Multipack containing 6 (3 x 2) pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER OF PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled syringe
secukinumab

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cosentyx 150 mg injection
secukinumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON OF UNIT PACK – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled pen
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 150 mg secukinumab in 1 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled SensoReady pen
2 pre-filled SensoReady pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

'QR code to be included'
www.cosentyx.eu

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pen in the outer carton in order to protect from light.
Keep the pre-filled pens in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/004	Pack containing 1 pre-filled pen
EU/1/14/980/005	Pack containing 2 pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (INCLUDING BLUE BOX) – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled pen
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 150 mg secukinumab in 1 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 6 (3 packs of 2) pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pens in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/007 Multipack containing 6 (3 x 2) pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX) – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled pen
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 150 mg secukinumab in 1 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

2 pre-filled pens. Component of a multipack. Not to be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

'QR code to be included'
www.cosentyx.eu

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pens in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/007 Multipack containing 6 (3 x 2) pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cosentyx 150 mg solution for injection in pre-filled pen
secukinumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

SensoReady pen

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON OF UNIT PACK – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 300 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 300 mg secukinumab in 2 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

'QR code to be included'
www.cosentyx.eu

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/008 Pack containing 1 pre-filled syringe

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 300 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (INCLUDING BLUE BOX) – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 300 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 300 mg secukinumab in 2 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 3 (3 packs of 1) pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringes in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/009 Multipack containing 3 (3 x 1) pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 300 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX) – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 300 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 300 mg secukinumab in 2 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe. Component of a multipack. Not to be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

'QR code to be included'
www.cosentyx.eu

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/009 Multipack containing 3 (3 x 1) pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 300 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER OF PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 300 mg solution for injection in pre-filled syringe
secukinumab

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cosentyx 300 mg injection
secukinumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON OF UNIT PACK – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 300 mg solution for injection in pre-filled pen
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 300 mg secukinumab in 2 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled UnoReady pen

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

'QR code to be included'
www.cosentyx.eu

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pen in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/010 Pack containing 1 pre-filled pen

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 300 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (INCLUDING BLUE BOX) – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 300 mg solution for injection in pre-filled pen
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 300 mg secukinumab in 2 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 3 (3 packs of 1) pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pens in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/011 Multipack containing 3 (3 x 1) pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 300 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX) – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 300 mg solution for injection in pre-filled pen
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 300 mg secukinumab in 2 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled pen. Component of a multipack. Not to be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

'QR code to be included'
www.cosentyx.eu

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pen in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/011 Multipack containing 3 (3 x 1) pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 300 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cosentyx 300 mg injection
secukinumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

UnoReady pen

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON – vial

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg powder for solution for injection
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 150 mg secukinumab. After reconstitution, 1 ml of solution contains 150 mg secukinumab.

3. LIST OF EXCIPIENTS

Also contains: Sucrose, histidine, histidine hydrochloride monohydrate, polysorbate 80.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for solution for injection

1 vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cosentyx 150 mg powder for solution for injection
secukinumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Cosentyx 75 mg solution for injection in pre-filled syringe

secukinumab

Read all of this leaflet carefully before you (or your child) start using this medicine because it contains important information.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you (or your child) only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours (or your child's).
- If you (or your child) get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cosentyx is and what it is used for
2. What you need to know before you (or your child) use Cosentyx
3. How to use Cosentyx
4. Possible side effects
5. How to store Cosentyx
6. Contents of the pack and other information

1. What Cosentyx is and what it is used for

Cosentyx contains the active substance secukinumab. Secukinumab is a monoclonal antibody which belongs to a group of medicines called interleukin (IL) inhibitors. This medicine works by neutralising the activity of a protein called IL-17A, which is present at increased levels in diseases such as psoriasis, psoriatic arthritis and axial spondyloarthritis.

Cosentyx is used for the treatment of the following inflammatory diseases:
- Paediatric plaque psoriasis
- Juvenile idiopathic arthritis, including enthesitis-related arthritis and juvenile psoriatic arthritis

Paediatric plaque psoriasis
Cosentyx is used to treat a skin condition called "plaque psoriasis", which causes inflammation affecting the skin. Cosentyx reduces the inflammation and other symptoms of the disease. Cosentyx is used in adolescents and children (6 years of age and older) with moderate to severe plaque psoriasis.

Using Cosentyx in plaque psoriasis will benefit you (or your child) by leading to improvements of skin clearance and reducing symptoms such as scaling, itching and pain.

Juvenile idiopathic arthritis, including enthesitis-related arthritis and juvenile psoriatic arthritis
Cosentyx is used in patients (6 years of age and older) to treat conditions of the juvenile idiopathic arthritis categories called "enthesitis-related arthritis" and "juvenile psoriatic arthritis". These conditions are inflammatory diseases affecting the joints and the places where tendons join the bone.

Using Cosentyx in enthesitis-related arthritis and juvenile psoriatic arthritis will benefit you (or your child) by reducing the symptoms and improving your (or your child's) physical function.

2. What you need to know before you (or your child) use Cosentyx

Do not use Cosentyx:
- **if you (or your child) are allergic** to secukinumab or any of the other ingredients of this medicine (listed in section 6).
  If you think you (or your child) may be allergic, ask your doctor for advice before using Cosentyx.
- **if you (or your child) have an active infection** which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, nurse or pharmacist before using Cosentyx:
- if you (or your child) currently have an infection.
- if you (or your child) have long-term or repeated infections.
- if you (or your child) have tuberculosis.
- if you (or your child) have ever had an allergic reaction to latex.
- if you (or your child) have an inflammatory disease affecting the gut called Crohn's disease.
- if you (or your child) have an inflammation of the large intestine called ulcerative colitis.
- if you (or your child) have recently had a vaccination or are due to have a vaccination during treatment with Cosentyx.
- if you (or your child) are receiving any other treatment for psoriasis, such as another immunosuppressant or phototherapy with ultraviolet (UV) light.

Inflammatory bowel disease (Crohn's disease or ulcerative colitis)
Stop using Cosentyx and tell your doctor or seek medical help immediately if you (or your child) notice abdominal cramps and pain, diarrhoea, weight loss, blood in the stool or any other signs of bowel problems.

Look out for infections and allergic reactions
Cosentyx can potentially cause serious side effects, including infections and allergic reactions. You must look out for signs of these conditions while you (or your child) are taking Cosentyx.

Stop using Cosentyx and tell your doctor or seek medical help immediately if you (or your child) notice any signs indicating a possible serious infection or an allergic reaction. Such signs are listed under "Serious side effects" in section 4.

Children and adolescents
Cosentyx is not recommended for children younger than 6 years of age with plaque psoriasis because it has not been studied in this age group.

Cosentyx is not recommended for children younger than 6 years of age with juvenile idiopathic arthritis (enthesitis-related arthritis and juvenile psoriatic arthritis).

Cosentyx is not recommended for children and adolescents (under 18 years of age) in other indications because it has not been studied in this age group.

Other medicines and Cosentyx
Tell your doctor or pharmacist:
- if you (or your child) are taking, have recently taken or might take any other medicines.
- if you (or your child) have recently had or are due to have a vaccination. You (or your child) should not be given certain types of vaccines (live vaccines) while using Cosentyx.

Pregnancy, breast-feeding and fertility

- It is preferable to avoid the use of Cosentyx in pregnancy. The effects of this medicine in pregnant women are not known. If you (or your child) are of childbearing potential, you (or your child) are advised to avoid becoming pregnant and must use adequate contraception while using Cosentyx and for at least 20 weeks after the last Cosentyx dose.
  Talk to your doctor if you (or your child) are pregnant, may be pregnant or are planning to have a baby.
- Talk to your doctor if you (or your child) are breast-feeding or are planning to breast-feed. You and your doctor should decide if you (or your child) will breast-feed or use Cosentyx. You (or your child) should not do both. After using Cosentyx you (or your child) should not breast-feed for at least 20 weeks after the last dose.

Driving and using machines

Cosentyx is unlikely to influence your ability to drive and use machines.

3. How to use Cosentyx

Always use this medicine exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

Cosentyx is given via injection under the skin (known as a subcutaneous injection). You and the doctor should decide if, after proper training, you should inject Cosentyx yourself or a caregiver should give the injection.

It is important not to try to inject Cosentyx before being trained by your doctor, nurse or pharmacist.

For detailed instructions on how to inject Cosentyx, see "Instructions for use of Cosentyx 75 mg pre-filled syringe" at the end of this leaflet.

Instructions for use can also be found via the following QR code and web site:
'QR code to be included'
www.cosentyx.eu

How much Cosentyx is given and for how long

Your doctor will decide how much Cosentyx you (or your child) need and for how long.

Paediatric plaque psoriasis (children aged 6 years and older)

- The recommended dose is based on body weight as follows:
  - Weight below 25 kg: 75 mg by subcutaneous injection.
  - Weight 25 kg or above and below 50 kg: 75 mg by subcutaneous injection.
  - Weight 50 kg or above: 150 mg by subcutaneous injection.
    Your doctor may increase the dose to 300 mg.
- Each 75 mg dose **is given as one injection of 75 mg**. Other dosage forms/strengths may be available for administration of the 150 mg and 300 mg doses.

After the first dose you (or your child) will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Juvenile idiopathic arthritis (enthesitis-related arthritis and juvenile psoriatic arthritis)

- The recommended dose is based on body weight as follows:
  - Weight below 50 kg: 75 mg by subcutaneous injection.
  - Weight 50 kg or above: 150 mg by subcutaneous injection.
- Each 75 mg dose is given as one injection of 75 mg. Other dosage forms/strengths may be available for administration of the 150 mg dose.

After the first dose you (or your child) will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Cosentyx is for long-term treatment. Your doctor will regularly monitor your (or your child's) condition to check that the treatment is having the desired effect.

If you use more Cosentyx than you should
If you (or your child) have received more Cosentyx than you (they) should or the dose has been administered sooner than according to your doctor's prescription, inform your doctor.

If you forget to use Cosentyx
If you have forgotten to inject a dose of Cosentyx, inject the next dose as soon as you (or your child) remember. Then talk to your doctor to discuss when you should inject the next dose.

If you (or your child) stop using Cosentyx
It is not dangerous to stop using Cosentyx. However, if you stop, your (or your child's) psoriasis symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Stop using Cosentyx and tell your doctor or seek medical help immediately if you (or you child) get any of the following side effects:

Possible serious infection - the signs may include:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters
- burning sensation when passing urine.

Serious allergic reaction - the signs may include:
- difficulty breathing or swallowing
- low blood pressure, which can cause dizziness or light-headedness
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps.

Your doctor will decide if and when you (or your child) may restart the treatment.

Other side effects
Most of the following side effects are mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Very common (may affect more than 1 in 10 people):
- upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis, rhinitis)

Common (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- runny nose (rhinorrhoea)
- headache
- nausea
- fatigue

Uncommon (may affect up to 1 in 100 people):
- oral thrush (oral candidiasis)
- signs of low levels of white blood cells, such as fever, sore throat or mouth ulcers due to infections (neutropenia)
- infection of the external ear (otitis externa)
- discharge from the eye with itching, redness and swelling (conjunctivitis)
- itchy rash (urticaria)
- lower respiratory tract infections
- abdominal cramps and pain, diarrhoea, weight loss or blood in the stool (signs of bowel problems)
- small, itchy blisters on the palms of hands, soles of feet and edges of the fingers and toes (dyshidrotic eczema)
- athlete's foot (tinea pedis)

Rare (may affect up to 1 in 1 000 people):
- severe allergic reaction with shock (anaphylactic reaction)
- redness and shedding of skin over a larger area of the body, which may be itchy or painful (exfoliative dermatitis)
- inflammation of small blood vessels, which can lead to a skin rash with small red or purple bumps (vasculitis)

Not known (frequency cannot be estimated from the available data):
- fungal infections of the skin and mucous membranes (including oesophageal candidiasis)
- painful swelling and skin ulceration (pyoderma gangrenosum)

Reporting of side effects
If you (or your child) get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cosentyx

Keep this medicine out of the sight and reach of children.

Do not use this medicine:
- after the expiry date which is stated on the outer box or the label on the syringe after "EXP".
- if the liquid contains easily visible particles, is cloudy or is distinctly brown.

Store the syringe sealed in its box to protect from light. Store in the refrigerator between 2°C and 8°C. Do not freeze. Do not shake.
If necessary, Cosentyx can be left out of the refrigerator for a single period of up to 4 days at room temperature, not above 30°C.

This medicine is for single use only.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Cosentyx contains
- The active substance is secukinumab. Each pre-filled syringe contains 75 mg secukinumab.
- The other ingredients are trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80 and water for injections.

What Cosentyx looks like and contents of the pack
Cosentyx solution for injection is a clear liquid. Its colour may vary from colourless to slightly yellow.
Cosentyx 75 mg solution for injection in pre-filled syringe is available in unit packs containing 1 pre-filled syringe and in multipacks containing 3 (3 packs of 1) pre-filled syringes.
Not all pack sizes may be marketed.

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Biochemiestrasse 10
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Austria

Novartis Pharmaceutical Manufacturing GmbH
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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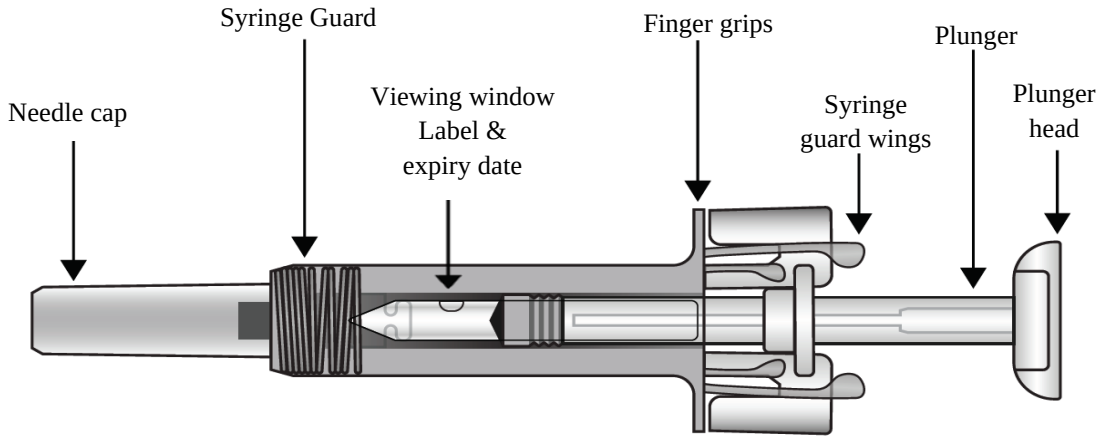
This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

Instructions for use of Cosentyx 75 mg pre-filled syringe

Read ALL the way through these instructions before injecting. It is important not to try to inject yourself or a person in your care until you have been trained by your doctor, nurse or pharmacist. The box contains one Cosentyx 75 mg pre-filled syringe individually sealed in a plastic blister.

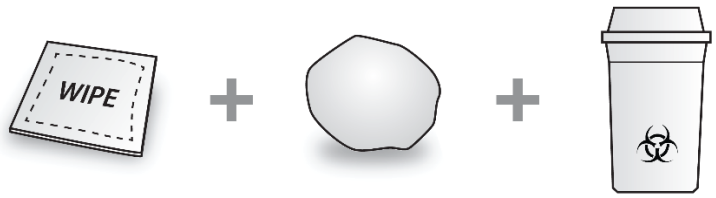
Your Cosentyx 75 mg pre-filled syringe



After the medicine has been injected the syringe guard will be activated to cover the needle. This is intended to aid in the protection of healthcare professionals, patients who self-inject doctor-prescribed medicines, and individuals who assist self-injecting patients from accidental needlestick injuries.

What you additionally need for your injection:

- Alcohol swab.
- Cotton ball or gauze.
- Sharps disposal container.



Important safety information

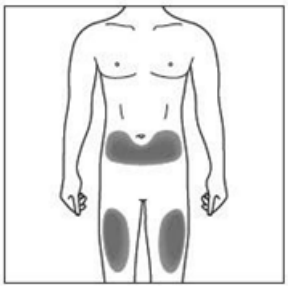
Caution: Keep the syringe out of the sight and reach of children.

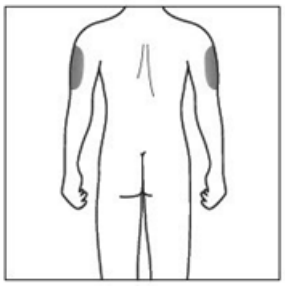
1. The needle cap of the syringe may contain dry rubber (latex), which should not be handled by persons sensitive to this substance.
2. Do not open the sealed outer box until you are ready to use this medicine.
3. Do not use this medicine if either the seal on the outer box or the seal of the blister is broken, as it may not be safe for you to use.
4. Do not use if the syringe has been dropped onto a hard surface or dropped after removing the needle cap.
5. Never leave the syringe lying around where others might tamper with it.
6. Do not shake the syringe.
7. Be careful not to touch the syringe guard wings before use. By touching them, the syringe guard may be activated too early.
8. Do not remove the needle cap until just before you give the injection.
9. The syringe cannot be re-used. Dispose of the used syringe immediately after use in a sharps container.

Storage of the Cosentyx 75 mg pre-filled syringe

1. Store this medicine sealed in its outer box to protect it from light. Store in the refrigerator between 2°C and 8°C. DO NOT FREEZE.
2. Remember to take the syringe out of the refrigerator and allow it to reach room temperature before preparing it for injection (15-30 minutes).
3. Do not use the syringe after the expiry date which is stated on the outer box or syringe label after "EXP". If it has expired, return the entire pack to the pharmacy.

The injection site





The injection site is the place on the body where you are going to use the syringe.

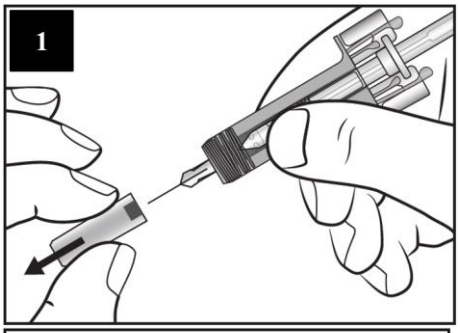
- The recommended site is the front of your thighs. You may also use the lower abdomen, but **not** the area 5 centimetres around the navel (belly button).
- Choose a different site each time you give yourself an injection.
- Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.

If a caregiver is giving you the injection, the outer upper arms may also be used.

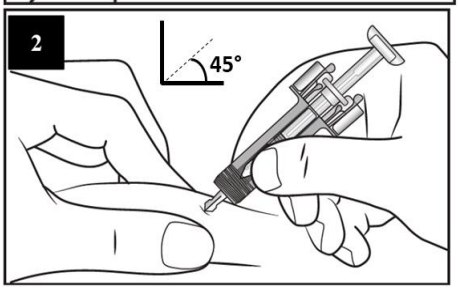
Preparing the Cosentyx 75 mg pre-filled syringe ready for use

1. Take the box containing the syringe out of the refrigerator and leave it **unopened** for about 15-30 minutes so that it reaches room temperature.
2. When you are ready to use the syringe, wash your hands thoroughly with soap and water.
3. Clean the injection site with an alcohol swab.
4. Remove the syringe from the outer box and take it out of the blister by holding the syringe guard body.
5. Inspect the syringe. The liquid should be clear. Its colour may vary from colourless to slightly yellow. You may see a small air bubble, which is normal. DO NOT USE if the liquid contains easily visible particles, is cloudy or is distinctly brown. DO NOT USE if the syringe is broken. In all these cases, return the entire product pack to the pharmacy.

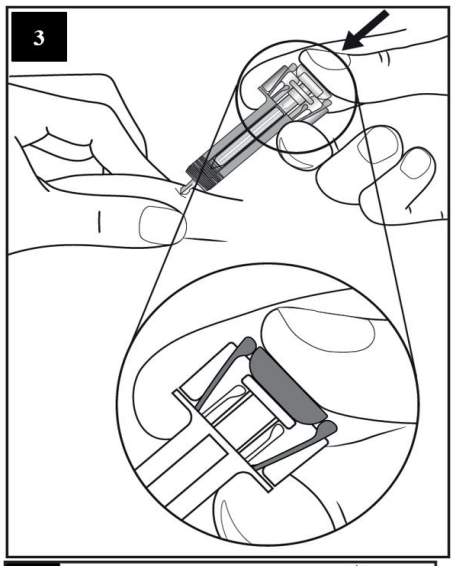
How to use the Cosentyx 75 mg pre-filled syringe



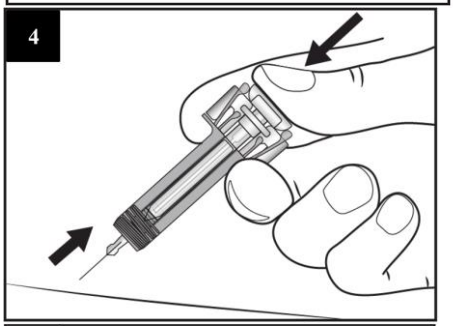
Carefully remove the needle cap from the syringe by holding the syringe guard body. Discard the needle cap. You may see a drop of liquid at the end of the needle. This is normal.



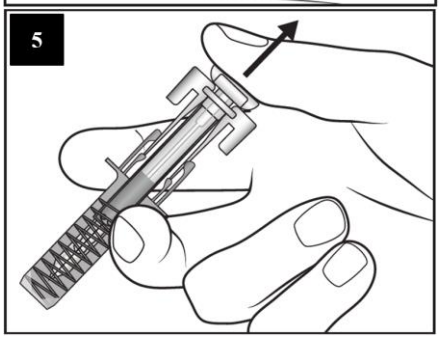
Gently pinch the skin at the injection site and insert the needle as shown. Push the needle all the way in at an angle of approximately 45 degrees to ensure that the medicine can be fully administered.



Hold the syringe as shown. **Slowly** depress the plunger **as far as it will go** so that the plunger head is completely between the syringe guard wings.
Keep the plunger pressed fully down while you hold the syringe in place for 5 seconds.



Keep the plunger fully depressed while you carefully lift the needle straight out from the injection site.



Slowly release the plunger and allow the syringe guard to automatically cover the exposed needle.

There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.

Disposal instructions

Dispose of the used syringe in a sharps container (closable, puncture resistant container). For the safety and health of you and others, needles and used syringes **must never** be re-used.

Package leaflet: Information for the user

Cosentyx 150 mg solution for injection in pre-filled syringe

secukinumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cosentyx is and what it is used for
2. What you need to know before you use Cosentyx
3. How to use Cosentyx
4. Possible side effects
5. How to store Cosentyx
6. Contents of the pack and other information

1. What Cosentyx is and what it is used for

Cosentyx contains the active substance secukinumab. Secukinumab is a monoclonal antibody which belongs to a group of medicines called interleukin (IL) inhibitors. This medicine works by neutralising the activity of a protein called IL-17A, which is present at increased levels in diseases such as psoriasis, hidradenitis suppurativa, psoriatic arthritis and axial spondyloarthritis.

Cosentyx is used for the treatment of the following inflammatory diseases:
- Plaque psoriasis
- Hidradenitis suppurativa
- Psoriatic arthritis
- Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis
- Juvenile idiopathic arthritis, including enthesitis-related arthritis and juvenile psoriatic arthritis

Plaque psoriasis
Cosentyx is used to treat a skin condition called “plaque psoriasis”, which causes inflammation affecting the skin. Cosentyx reduces the inflammation and other symptoms of the disease. Cosentyx is used in adults, adolescents and children (6 years of age and older) with moderate to severe plaque psoriasis.

Using Cosentyx in plaque psoriasis will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.

Hidradenitis suppurativa
Cosentyx is used to treat a condition called hidradenitis suppurativa, also sometimes called acne inversa or Verneuil’s disease. This condition is a chronic and painful inflammatory skin disease. Symptoms may include tender nodules (lumps) and abscesses (boils) that may leak pus. It commonly affects specific areas of the skin, such as under the breasts, the armpits, inner thighs, groin and buttocks. Scarring may also occur in affected areas.

Cosentyx can reduce the number of nodules and abscesses you have and the pain that is often associated with the disease. If you have hidradenitis suppurativa you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx.

Cosentyx is used in adults with hidradenitis suppurativa and can be used alone or with antibiotics.

Psoriatic arthritis
Cosentyx is used to treat a condition called "psoriatic arthritis". The condition is an inflammatory disease of the joints, often accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of active psoriatic arthritis, improve physical function and slow down the damage to the cartilage and bone of the joints involved in the disease.

Cosentyx is used in adults with active psoriatic arthritis and can be used alone or with another medicine called methotrexate.

Using Cosentyx in psoriatic arthritis will benefit you by reducing the signs and symptoms of the disease, slowing down the damage to the cartilage and bone of the joints and improving your ability to do normal daily activities.

Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis
Cosentyx is used to treat conditions called "ankylosing spondylitis" and "non-radiographic axial spondyloarthritis". These conditions are inflammatory diseases primarily affecting the spine which cause inflammation of the spinal joints. If you have ankylosing spondylitis or non-radiographic axial spondyloarthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of the disease, reduce inflammation and improve your physical function.

Cosentyx is used in adults with active ankylosing spondylitis and active non-radiographic axial spondyloarthritis.

Using Cosentyx in ankylosing spondylitis and non-radiographic axial spondyloarthritis will benefit you by reducing the signs and symptoms of your disease and improving your physical function.

Juvenile idiopathic arthritis, including enthesitis-related arthritis and juvenile psoriatic arthritis
Cosentyx is used in patients (6 years of age and older) to treat conditions of the juvenile idiopathic arthritis categories called "enthesitis-related arthritis" and "juvenile psoriatic arthritis". These conditions are inflammatory diseases affecting the joints and the places where tendons join the bone.

Using Cosentyx in enthesitis-related arthritis and juvenile psoriatic arthritis will benefit you (or your child) by reducing the symptoms and improving your (or your child's) physical function.

2. What you need to know before you use Cosentyx

Do not use Cosentyx:
- **if you are allergic** to secukinumab or any of the other ingredients of this medicine (listed in section 6).
  If you think you may be allergic, ask your doctor for advice before using Cosentyx.
- **if you have an active infection** which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, nurse or pharmacist before using Cosentyx:
- if you currently have an infection.
- if you have long-term or repeated infections.
- if you have tuberculosis.
- if you have ever had an allergic reaction to latex.
- if you have an inflammatory disease affecting your gut called Crohn's disease.
- if you have an inflammation of your large intestine called ulcerative colitis.
- if you have recently had a vaccination or if you are due to have a vaccination during treatment with Cosentyx.
- if you are receiving any other treatment for psoriasis, such as another immunosuppressant or phototherapy with ultraviolet (UV) light.

Inflammatory bowel disease (Crohn's disease or ulcerative colitis)
Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice abdominal cramps and pain, diarrhoea, weight loss, blood in the stool or any other signs of bowel problems.

Look out for infections and allergic reactions
Cosentyx can potentially cause serious side effects, including infections and allergic reactions. You must look out for signs of these conditions while you are taking Cosentyx.

Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice any signs indicating a possible serious infection or an allergic reaction. Such signs are listed under "Serious side effects" in section 4.

Children and adolescents
Cosentyx is not recommended for children younger than 6 years of age with plaque psoriasis because it has not been studied in this age group.

Cosentyx is not recommended for children younger than 6 years of age with juvenile idiopathic arthritis (enthesitis related arthritis and juvenile psoriatic arthritis).

Cosentyx is not recommended for children and adolescents (under 18 years of age) in other indications because it has not been studied in this age group.

Other medicines and Cosentyx
Tell your doctor or pharmacist:
- if you are taking, have recently taken or might take any other medicines.
- if you have recently had or are due to have a vaccination. You should not be given certain types of vaccines (live vaccines) while using Cosentyx.

Pregnancy, breast-feeding and fertility
- It is preferable to avoid the use of Cosentyx in pregnancy. The effects of this medicine in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and must use adequate contraception while using Cosentyx and for at least 20 weeks after the last Cosentyx dose.
  Talk to your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.
- Talk to your doctor if you are breast-feeding or are planning to breast-feed. You and your doctor should decide if you will breast-feed or use Cosentyx. You should not do both. After using Cosentyx you should not breast-feed for at least 20 weeks after the last dose.

Driving and using machines
Cosentyx is unlikely to influence your ability to drive and use machines.

3. How to use Cosentyx

Always use this medicine exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

Cosentyx is given via injection under your skin (known as a subcutaneous injection). You and your doctor should decide if you should inject Cosentyx yourself.

It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist. A caregiver may also give you your Cosentyx injection after proper training.

For detailed instructions on how to inject Cosentyx, see "Instructions for use of Cosentyx 150 mg pre-filled syringe" at the end of this leaflet.

Instructions for use can also be found via the following QR code and web site:
'QR code to be included'
www.cosentyx.eu

How much Cosentyx is given and for how long
Your doctor will decide how much Cosentyx you need and for how long.

Plaque psoriasis
Adult
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. Based on your response, further adjustments to your dose may be recommended by your doctor. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

Children aged 6 years and older
- The recommended dose is based on body weight as follows:
  - Weight below 25 kg: 75 mg by subcutaneous injection.
  - Weight 25 kg or above and below 50 kg: 75 mg by subcutaneous injection.
  - Weight 50 kg or above: 150 mg by subcutaneous injection.
    Your doctor may increase the dose to 300 mg.
- Each 150 mg dose **is given as one injection of 150 mg**. Other dosage forms/strengths may be available for administration of the 75 mg and 300 mg doses.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Hidradenitis suppurativa
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg.**

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. Based on your response, further adjustments to your dose may be recommended by your doctor.

Psoriatic arthritis
If you have both psoriatic arthritis and also moderate to severe plaque psoriasis, your doctor may adjust the dose recommendation as needed.

For patients who did not respond well to medicines called tumour necrosis factor (TNF) blockers:
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

For other psoriatic arthritis patients:

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg.

Ankylosing spondylitis (Radiographic axial spondyloarthritis)

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg. Each 300 mg dose is given as two injections of 150 mg.

Non-radiographic axial spondyloarthritis

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Juvenile idiopathic arthritis (enthesitis-related arthritis and juvenile psoriatic arthritis)

- The recommended dose is based on body weight as follows:
  - Weight below 50 kg: 75 mg by subcutaneous injection.
  - Weight 50 kg or above: 150 mg by subcutaneous injection.
- Each 150 mg dose **is given as one injection of 150 mg**. Other dosage forms/strengths may be available for administration of the 75 mg dose.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Cosentyx is for long-term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you use more Cosentyx than you should
If you have received more Cosentyx than you should or the dose has been administered sooner than according to your doctor's prescription, inform your doctor.

If you forget to use Cosentyx
If you have forgotten to inject a dose of Cosentyx, inject the next dose as soon as you remember. Then talk to your doctor to discuss when you should inject the next dose.

If you stop using Cosentyx
It is not dangerous to stop using Cosentyx. However, if you stop, your psoriasis, psoriatic arthritis or axial spondyloarthritis symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Stop using Cosentyx and tell your doctor or seek medical help immediately if you get any of the following side effects:

Possible serious infection - the signs may include:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters
- burning sensation when passing urine.

Serious allergic reaction - the signs may include:
- difficulty breathing or swallowing
- low blood pressure, which can cause dizziness or light-headedness
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps.

Your doctor will decide if and when you may restart the treatment.

Other side effects
Most of the following side effects are mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Very common (may affect more than 1 in 10 people):
- upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis, rhinitis)

Common (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- runny nose (rhinorrhoea)
- headache
- nausea
- fatigue

Uncommon (may affect up to 1 in 100 people):
- oral thrush (oral candidiasis)
- signs of low levels of white blood cells, such as fever, sore throat or mouth ulcers due to infections (neutropenia)
- infection of the external ear (otitis externa)
- discharge from the eye with itching, redness and swelling (conjunctivitis)
- itchy rash (urticaria)
- lower respiratory tract infections
- abdominal cramps and pain, diarrhoea, weight loss or blood in the stool (signs of bowel problems)
- small, itchy blisters on the palms of hands, soles of feet and edges of the fingers and toes (dyshidrotic eczema)
- athlete’s foot (tinea pedis)

Rare (may affect up to 1 in 1 000 people):
- severe allergic reaction with shock (anaphylactic reaction)
- redness and shedding of skin over a larger area of the body, which may be itchy or painful (exfoliative dermatitis)
- inflammation of small blood vessels, which can lead to a skin rash with small red or purple bumps (vasculitis)

Not known (frequency cannot be estimated from the available data):
- fungal infections of the skin and mucous membranes (including oesophageal candidiasis)
- painful swelling and skin ulceration (pyoderma gangrenosum)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cosentyx

Keep this medicine out of the sight and reach of children.

Do not use this medicine:
- after the expiry date which is stated on the outer box or the label on the syringe after "EXP".
- if the liquid contains easily visible particles, is cloudy or is distinctly brown.

Store the syringe sealed in its box to protect from light. Store in the refrigerator between 2°C and 8°C. Do not freeze. Do not shake.
If necessary, Cosentyx can be left out of the refrigerator for a single period of up to 4 days at room temperature, not above 30°C.

This medicine is for single use only.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Cosentyx contains
- The active substance is secukinumab. Each pre-filled syringe contains 150 mg secukinumab.
- The other ingredients are trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80 and water for injections.

What Cosentyx looks like and contents of the pack
Cosentyx solution for injection is a clear liquid. Its colour may vary from colourless to slightly yellow.
Cosentyx 150 mg solution for injection in pre-filled syringe is available in unit packs containing 1 or 2 pre-filled syringe(s) and in multipacks containing 6 (3 packs of 2) pre-filled syringes.
Not all pack sizes may be marketed.

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Vista Building
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Manufacturer
Novartis Pharma GmbH
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Biochemiestrasse 10
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Austria

Novartis Pharmaceutical Manufacturing GmbH
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Austria

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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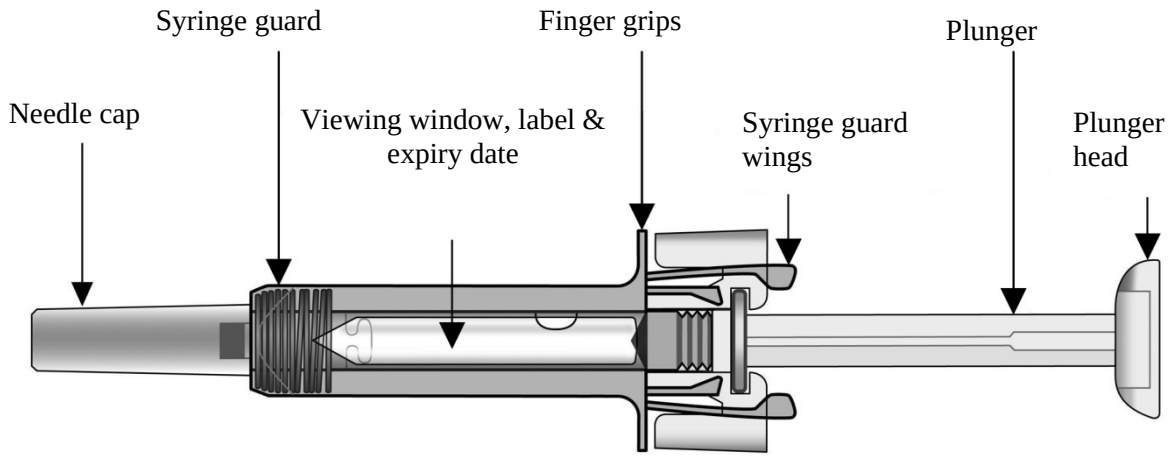
This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

Instructions for use of Cosentyx 150 mg pre-filled syringe

Read ALL the way through these instructions before injecting. It is important not to try to inject yourself or a person in your care until you have been trained by your doctor, nurse or pharmacist. The box contains Cosentyx 150 mg pre-filled syringe(s) individually sealed in a plastic blister.

Your Cosentyx 150 mg pre-filled syringe



After the medicine has been injected the syringe guard will be activated to cover the needle. This is intended to aid in the protection of healthcare professionals, patients who self-inject doctor-prescribed medicines, and individuals who assist self-injecting patients from accidental needlestick injuries.

What you additionally need for your injection:

- Alcohol swab.
- Cotton ball or gauze.
- Sharps disposal container.

Important safety information

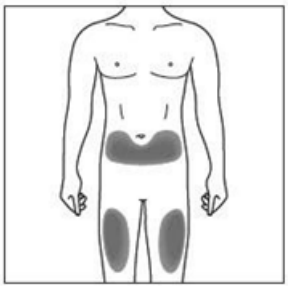
Caution: Keep the syringe out of the sight and reach of children.

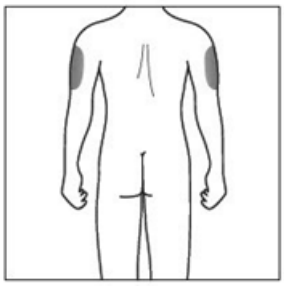
1. The needle cap of the syringe may contain dry rubber (latex), which should not be handled by persons sensitive to this substance.
2. Do not open the sealed outer box until you are ready to use this medicine.
3. Do not use this medicine if either the seal on the outer box or the seal of the blister is broken, as it may not be safe for you to use.
4. Do not use if the syringe has been dropped onto a hard surface or dropped after removing the needle cap.
5. Never leave the syringe lying around where others might tamper with it.
6. Do not shake the syringe.
7. Be careful not to touch the syringe guard wings before use. By touching them, the syringe guard may be activated too early.
8. Do not remove the needle cap until just before you give the injection.
9. The syringe cannot be re-used. Dispose of the used syringe immediately after use in a sharps container.

Storage of the Cosentyx 150 mg pre-filled syringe

1. Store this medicine sealed in its outer box to protect it from light. Store in the refrigerator between 2°C and 8°C. DO NOT FREEZE.
2. Remember to take the syringe out of the refrigerator and allow it to reach room temperature before preparing it for injection (15-30 minutes).
3. Do not use the syringe after the expiry date which is stated on the outer box or syringe label after "EXP". If it has expired, return the entire pack to the pharmacy.

The injection site





The injection site is the place on the body where you are going to use the syringe.

- The recommended site is the front of your thighs. You may also use the lower abdomen, but **not** the area 5 centimetres around the navel (belly button).
- Choose a different site each time you give yourself an injection.
- Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.

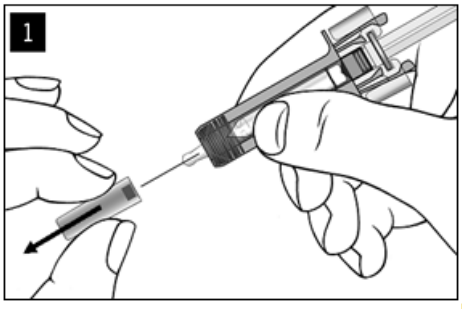
If a caregiver is giving you the injection, the outer upper arms may also be used.

Preparing the Cosentyx 150 mg pre-filled syringe ready for use

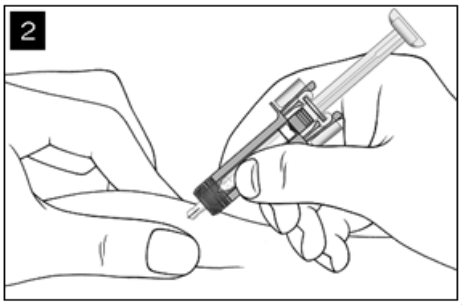
Note: For a 150 mg dose, prepare 1 pre-filled syringe and inject the content. For a 300 mg dose, prepare 2 pre-filled syringes and inject the contents of both.

1. Take the box containing the syringe out of the refrigerator and leave it **unopened** for about 15-30 minutes so that it reaches room temperature.
2. When you are ready to use the syringe, wash your hands thoroughly with soap and water.
3. Clean the injection site with an alcohol swab.
4. Remove the syringe from the outer box and take it out of the blister by holding the syringe guard body.
5. Inspect the syringe. The liquid should be clear. Its colour may vary from colourless to slightly yellow. You may see a small air bubble, which is normal. DO NOT USE if the liquid contains easily visible particles, is cloudy or is distinctly brown. DO NOT USE if the syringe is broken. In all these cases, return the entire product pack to the pharmacy.

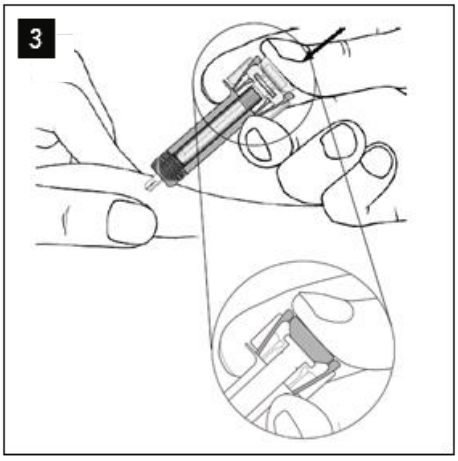
How to use the Cosentyx 150 mg pre-filled syringe



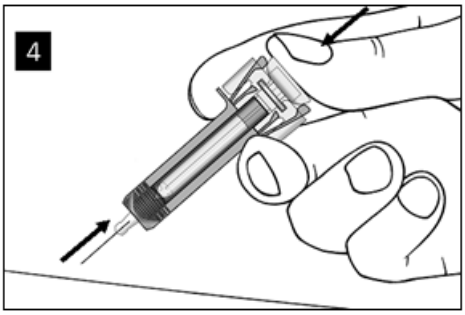
Carefully remove the needle cap from the syringe by holding the syringe guard body. Discard the needle cap. You may see a drop of liquid at the end of the needle. This is normal.



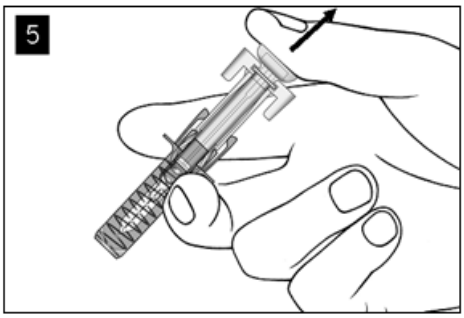
Gently pinch the skin at the injection site and insert the needle as shown. Push the needle all the way in to ensure that the medicine can be fully administered.



Hold the syringe as shown. **Slowly** depress the plunger **as far as it will go** so that the plunger head is completely between the syringe guard wings.
Keep the plunger pressed fully down while you hold the syringe in place for 5 seconds.



Keep the plunger fully depressed while you carefully lift the needle straight out from the injection site.



Slowly release the plunger and allow the syringe guard to automatically cover the exposed needle.

There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.

Disposal instructions

Dispose of the used syringe in a sharps container (closable, puncture resistant container). For the safety and health of you and others, needles and used syringes **must never** be re-used.

Package leaflet: Information for the user

Cosentyx 150 mg solution for injection in pre-filled pen

secukinumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cosentyx is and what it is used for
2. What you need to know before you use Cosentyx
3. How to use Cosentyx
4. Possible side effects
5. How to store Cosentyx
6. Contents of the pack and other information

1. What Cosentyx is and what it is used for

Cosentyx contains the active substance secukinumab. Secukinumab is a monoclonal antibody which belongs to a group of medicines called interleukin (IL) inhibitors. This medicine works by neutralising the activity of a protein called IL-17A, which is present at increased levels in diseases such as psoriasis, hidradenitis suppurativa, psoriatic arthritis and axial spondyloarthritis.

Cosentyx is used for the treatment of the following inflammatory diseases:
- Plaque psoriasis
- Hidradenitis suppurativa
- Psoriatic arthritis
- Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis
- Juvenile idiopathic arthritis, including enthesitis-related arthritis and juvenile psoriatic arthritis

Plaque psoriasis
Cosentyx is used to treat a skin condition called “plaque psoriasis”, which causes inflammation affecting the skin. Cosentyx reduces the inflammation and other symptoms of the disease. Cosentyx is used in adults, adolescents and children (6 years of age and older) with moderate to severe plaque psoriasis.

Using Cosentyx in plaque psoriasis will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.

Hidradenitis suppurativa
Cosentyx is used to treat a condition called hidradenitis suppurativa, also sometimes called acne inversa or Verneuil’s disease. This condition is a chronic and painful inflammatory skin disease. Symptoms may include tender nodules (lumps) and abscesses (boils) that may leak pus. It commonly affects specific areas of the skin, such as under the breasts, the armpits, inner thighs, groin and buttocks. Scarring may also occur in affected areas.

Cosentyx can reduce the number of nodules and abscesses you have and the pain that is often associated with the disease. If you have hidradenitis suppurativa you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx.

Cosentyx is used in adults with hidradenitis suppurativa and can be used alone or with antibiotics.

Psoriatic arthritis
Cosentyx is used to treat a condition called "psoriatic arthritis". The condition is an inflammatory disease of the joints, often accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of active psoriatic arthritis, improve physical function and slow down the damage to the cartilage and bone of the joints involved in the disease.

Cosentyx is used in adults with active psoriatic arthritis and can be used alone or with another medicine called methotrexate.

Using Cosentyx in psoriatic arthritis will benefit you by reducing the signs and symptoms of the disease, slowing down the damage to the cartilage and bone of the joints and improving your ability to do normal daily activities.

Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis
Cosentyx is used to treat conditions called "ankylosing spondylitis" and "non-radiographic axial spondyloarthritis". These conditions are inflammatory diseases primarily affecting the spine which cause inflammation of the spinal joints. If you have ankylosing spondylitis or non-radiographic axial spondyloarthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of the disease, reduce inflammation and improve your physical function.

Cosentyx is used in adults with active ankylosing spondylitis and active non-radiographic axial spondyloarthritis.

Using Cosentyx in ankylosing spondylitis and non-radiographic axial spondyloarthritis will benefit you by reducing the signs and symptoms of your disease and improving your physical function.

Juvenile idiopathic arthritis, including enthesitis-related arthritis and juvenile psoriatic arthritis
Cosentyx is used in patients (6 years of age and older) to treat conditions of the juvenile idiopathic arthritis categories called "enthesitis-related arthritis" and "juvenile psoriatic arthritis". These conditions are inflammatory diseases affecting the joints and the places where tendons join the bone.

Using Cosentyx in enthesitis-related arthritis and juvenile psoriatic arthritis will benefit you (or your child) by reducing the symptoms and improving your (or your child's) physical function.

2. What you need to know before you use Cosentyx

Do not use Cosentyx:
- **if you are allergic** to secukinumab or any of the other ingredients of this medicine (listed in section 6).
  If you think you may be allergic, ask your doctor for advice before using Cosentyx.
- **if you have an active infection** which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, nurse or pharmacist before using Cosentyx:
- if you currently have an infection.
- if you have long-term or repeated infections.
- if you have tuberculosis.
- if you have ever had an allergic reaction to latex.
- if you have an inflammatory disease affecting your gut called Crohn's disease.
- if you have an inflammation of your large intestine called ulcerative colitis.
- if you have recently had a vaccination or if you are due to have a vaccination during treatment with Cosentyx.
- if you are receiving any other treatment for psoriasis, such as another immunosuppressant or phototherapy with ultraviolet (UV) light.

Inflammatory bowel disease (Crohn's disease or ulcerative colitis)
Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice abdominal cramps and pain, diarrhoea, weight loss, blood in the stool or any other signs of bowel problems.

Look out for infections and allergic reactions
Cosentyx can potentially cause serious side effects, including infections and allergic reactions. You must look out for signs of these conditions while you are taking Cosentyx.

Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice any signs indicating a possible serious infection or an allergic reaction. Such signs are listed under "Serious side effects" in section 4.

Children and adolescents
Cosentyx is not recommended for children younger than 6 years of age with plaque psoriasis because it has not been studied in this age group.

Cosentyx is not recommended for children younger than 6 years of age with juvenile idiopathic arthritis (enthesitis-related arthritis and juvenile psoriatic arthritis).

Cosentyx is not recommended for children and adolescents (under 18 years of age) in other indications because it has not been studied in this age group.

Other medicines and Cosentyx
Tell your doctor or pharmacist:
- if you are taking, have recently taken or might take any other medicines.
- if you have recently had or are due to have a vaccination. You should not be given certain types of vaccines (live vaccines) while using Cosentyx.

Pregnancy, breast-feeding and fertility
- It is preferable to avoid the use of Cosentyx in pregnancy. The effects of this medicine in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and must use adequate contraception while using Cosentyx and for at least 20 weeks after the last Cosentyx dose.
  Talk to your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.
- Talk to your doctor if you are breast-feeding or are planning to breast-feed. You and your doctor should decide if you will breast-feed or use Cosentyx. You should not do both. After using Cosentyx you should not breast-feed for at least 20 weeks after the last dose.

Driving and using machines
Cosentyx is unlikely to influence your ability to drive and use machines.

3. How to use Cosentyx

Always use this medicine exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

Cosentyx is given via injection under your skin (known as a subcutaneous injection). You and your doctor should decide if you should inject Cosentyx yourself.

It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist. A caregiver may also give you your Cosentyx injection after proper training.

For detailed instructions on how to inject Cosentyx, see "Instructions for use of the Cosentyx 150 mg SensoReady pen" at the end of this leaflet.

Instructions for use can also be found via the following QR code and web site:
'QR code to be included'
www.cosentyx.eu

How much Cosentyx is given and for how long
Your doctor will decide how much Cosentyx you need and for how long.

Plaque psoriasis
Adult
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. Based on your response, further adjustments to your dose may be recommended by your doctor. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

Children aged 6 years and older
- The recommended dose is based on body weight as follows:
  - Weight below 25 kg: 75 mg by subcutaneous injection.
  - Weight 25 kg or above and below 50 kg: 75 mg by subcutaneous injection.
  - Weight 50 kg or above: 150 mg by subcutaneous injection.
    Your doctor may increase the dose to 300 mg.
- Each 150 mg dose **is given as one injection of 150 mg**. Other dosage forms/strengths may be available for administration of the 75 mg and 300 mg doses.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Hidradenitis suppurativa
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg.**

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. Based on your response, further adjustments to your dose may be recommended by your doctor.

Psoriatic arthritis
If you have both psoriatic arthritis and also moderate to severe plaque psoriasis, your doctor may adjust the dose recommendation as needed.

For patients who did not respond well to medicines called tumour necrosis factor (TNF) blockers:
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

For other psoriatic arthritis patients:

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg.

Ankylosing spondylitis (Radiographic axial spondyloarthritis)

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg. Each 300 mg dose is given as two injections of 150 mg.

Non-radiographic axial spondyloarthritis

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Juvenile idiopathic arthritis (enthesitis-related arthritis and juvenile psoriatic arthritis)

- The recommended dose is based on body weight as follows:
  - Weight below 50 kg: 75 mg by subcutaneous injection.
  - Weight 50 kg or above: 150 mg by subcutaneous injection.
- Each 150 mg dose **is given as one injection of 150 mg**. Other dosage forms/strengths may be available for administration of the 75 mg dose.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Cosentyx is for long-term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you use more Cosentyx than you should
If you have received more Cosentyx than you should or the dose has been administered sooner than according to your doctor's prescription, inform your doctor.

If you forget to use Cosentyx
If you have forgotten to inject a dose of Cosentyx, inject the next dose as soon as you remember. Then talk to your doctor to discuss when you should inject the next dose.

If you stop using Cosentyx
It is not dangerous to stop using Cosentyx. However, if you stop, your psoriasis, psoriatic arthritis or axial spondyloarthritis symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Stop using Cosentyx and tell your doctor or seek medical help immediately if you get any of the following side effects:

Possible serious infection - the signs may include:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters
- burning sensation when passing urine.

Serious allergic reaction - the signs may include:
- difficulty breathing or swallowing
- low blood pressure, which can cause dizziness or light-headedness
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps.

Your doctor will decide if and when you may restart the treatment.

Other side effects
Most of the following side effects are mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Very common (may affect more than 1 in 10 people):
- upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis, rhinitis)

Common (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- runny nose (rhinorrhoea)
- headache
- nausea
- fatigue

Uncommon (may affect up to 1 in 100 people):
- oral thrush (oral candidiasis)
- signs of low levels of white blood cells, such as fever, sore throat or mouth ulcers due to infections (neutropenia)
- infection of the external ear (otitis externa)
- discharge from the eye with itching, redness and swelling (conjunctivitis)
- itchy rash (urticaria)
- lower respiratory tract infections
- abdominal cramps and pain, diarrhoea, weight loss or blood in the stool (signs of bowel problems)
- small, itchy blisters on the palms of hands, soles of feet and edges of the fingers and toes (dyshidrotic eczema)
- athlete’s foot (tinea pedis)

Rare (may affect up to 1 in 1 000 people):
- severe allergic reaction with shock (anaphylactic reaction)
- redness and shedding of skin over a larger area of the body, which may be itchy or painful (exfoliative dermatitis)
- inflammation of small blood vessels, which can lead to a skin rash with small red or purple bumps (vasculitis)

Not known (frequency cannot be estimated from the available data):
- fungal infections of the skin and mucous membranes (including oesophageal candidiasis)
- painful swelling and skin ulceration (pyoderma gangrenosum)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cosentyx

Keep this medicine out of the sight and reach of children.

Do not use this medicine:
- after the expiry date which is stated on the outer box or the label on the pen after "EXP".
- if the liquid contains easily visible particles, is cloudy or is distinctly brown.

Store the pen sealed in its box to protect from light. Store in the refrigerator between 2°C and 8°C. Do not freeze. Do not shake.
If necessary, Cosentyx can be left out of the refrigerator for a single period of up to 4 days at room temperature, not above 30°C.

This medicine is for single use only.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Cosentyx contains
- The active substance is secukinumab. Each pre-filled pen contains 150 mg secukinumab.
- The other ingredients are trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80 and water for injections.

What Cosentyx looks like and contents of the pack
Cosentyx solution for injection is a clear liquid. Its colour may vary from colourless to slightly yellow.
Cosentyx 150 mg solution for injection in pre-filled pen is available in unit packs containing 1 or 2 pre-filled pen(s) and in multipacks containing 6 (3 packs of 2) pre-filled pens.
Not all pack sizes may be marketed.

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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

Instructions for use of the Cosentyx 150 mg SensoReady pen

Cosentyx 150 mg SensoReady pen

Solution for injection in a pre-filled pen

Secukinumab

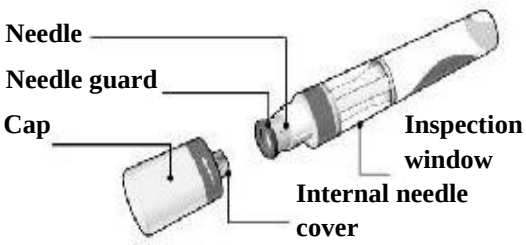
Patient Instructions for Use

Read ALL the way through these instructions before injecting.

These instructions are to help you to inject correctly using the Cosentyx SensoReady pen.

It is important not to try to inject yourself or the person in your care until you have been trained by your doctor, nurse or pharmacist.

Your Cosentyx 150 mg SensoReady pen:



Cosentyx 150 mg SensoReady pen shown with the cap removed. **Do not** remove the cap until you are ready to inject.

Store your boxed pen in a **refrigerator** between 2°C and 8°C and **out of the reach of children**.

- **Do not freeze** the pen.
- **Do not shake** the pen.
- Do not use the pen if it has been **dropped** with the cap removed.

For a more comfortable injection, take the pen out of the refrigerator **15-30 minutes before injecting** to allow it to reach room temperature.

What you need for your injection:

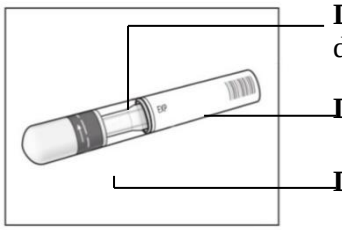
Included in the carton:

A new and unused Cosentyx 150 mg SensoReady pen (1 pen is needed for a 150 mg dose and 2 pens are needed for a 300 mg dose).

Not included in the carton:

- Alcohol swab.
- Cotton ball or gauze.
- Sharps disposal container.

Before your injection:



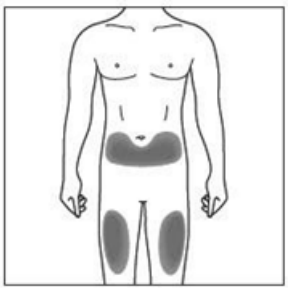
1. Important safety checks before you inject:
The liquid should be clear. Its colour may vary from colourless to slightly yellow.

Do not use if the liquid contains easily visible particles, is cloudy or is distinctly brown. You may see a small air bubble, which is normal.

Do not use the pen if the **expiry date** has passed.

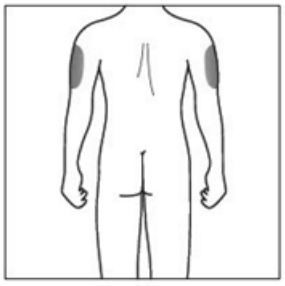
Do not use if the **safety seal** has been broken.

Contact your pharmacist if the pen fails any of these checks.



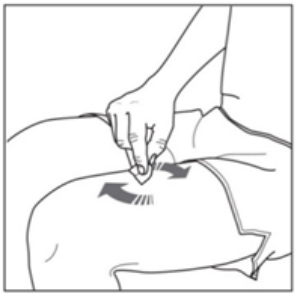
2a. Choose your injection site:

- The recommended site is the front of the thighs. You may also use the lower abdomen, but **not** the area 5 centimetres around the navel (belly button).
- Choose a different site each time you give yourself an injection.
- Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.



2b. Caregivers and healthcare professionals only:

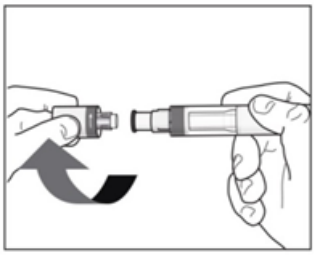
- If a **caregiver** or **healthcare professional** is giving you your injection, they may also inject into your outer upper arm.



3. Cleaning your injection site:

- Wash your hands with soap and hot water.
- Using a circular motion, clean the injection site with the alcohol swab. Leave it to dry before injecting.
- Do not touch the cleaned area again before injecting.

Your injection:

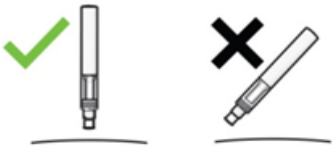


4. Removing the cap:

- Only remove the cap when you are ready to use the pen.
- Twist off the cap in the direction of the arrows.
- Once removed, throw away the cap. **Do not try to re-attach the cap.**
- Use the pen within 5 minutes of removing the cap.

5. Holding your pen:

- Hold the pen at 90 degrees to the cleaned injection site.



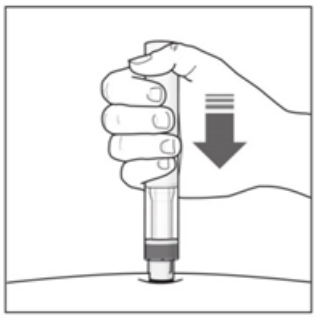
Correct **Incorrect**

YOU MUST READ THIS BEFORE INJECTING.

During the injection you will hear **2 loud clicks**.

The **1st click** indicates that the injection has started. Several seconds later a **2nd click** will indicate that the injection is **almost** finished.

You must keep holding the pen firmly against your skin until you see a **green indicator** fill the window and stop moving.



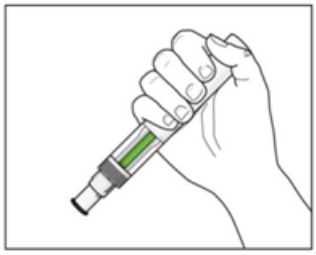
6. Starting your injection:

- Press the pen firmly against the skin to start the injection.
- The **1st click** indicates the injection has started.
- **Keep holding** the pen firmly against your skin.
- The **green indicator** shows the progress of the injection.

7. Completing your injection:

- Listen for the **2nd click**. This indicates the injection is **almost** complete.
- Check the **green indicator** fills the window and has stopped moving.
- The pen can now be removed.

After your injection:



8. Check the green indicator fills the window:

- This means the medicine has been delivered. Contact your doctor if the green indicator is not visible.
- There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.

9. Disposing of your Cosentyx SensoReady pen:

- Dispose of the used pen in a sharps disposal container (i.e. a puncture-resistant closable container, or similar).
- Never try to reuse your pen.

Package leaflet: Information for the user

Cosentyx 300 mg solution for injection in pre-filled syringe

secukinumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cosentyx is and what it is used for
2. What you need to know before you use Cosentyx
3. How to use Cosentyx
4. Possible side effects
5. How to store Cosentyx
6. Contents of the pack and other information

1. What Cosentyx is and what it is used for

Cosentyx contains the active substance secukinumab. Secukinumab is a monoclonal antibody which belongs to a group of medicines called interleukin (IL) inhibitors. This medicine works by neutralising the activity of a protein called IL-17A, which is present at increased levels in diseases such as psoriasis, hidradenitis suppurativa, psoriatic arthritis and axial spondyloarthritis.

Cosentyx is used for the treatment of the following inflammatory diseases:
- Plaque psoriasis
- Hidradenitis suppurativa
- Psoriatic arthritis
- Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis

Plaque psoriasis
Cosentyx is used to treat a skin condition called “plaque psoriasis”, which causes inflammation affecting the skin. Cosentyx reduces the inflammation and other symptoms of the disease. Cosentyx is used in adults, adolescents and children (6 years of age and older) with moderate to severe plaque psoriasis.

Using Cosentyx in plaque psoriasis will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.

Hidradenitis suppurativa
Cosentyx is used to treat a condition called hidradenitis suppurativa, also sometimes called acne inversa or Verneuil’s disease. This condition is a chronic and painful inflammatory skin disease. Symptoms may include tender nodules (lumps) and abscesses (boils) that may leak pus. It commonly affects specific areas of the skin, such as under the breasts, the armpits, inner thighs, groin and buttocks. Scarring may also occur in affected areas.

Cosentyx can reduce the number of nodules and abscesses you have and the pain that is often associated with the disease. If you have hidradenitis suppurativa you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx.

Cosentyx isused in adults with hidradenitis suppurativa and can be used alone or with antibiotics.

Psoriatic arthritis
Cosentyx is used to treat a condition called "psoriatic arthritis". The condition is an inflammatory disease of the joints, often accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of active psoriatic arthritis, improve physical function and slow down the damage to the cartilage and bone of the joints involved in the disease.

Cosentyx is used in adults with active psoriatic arthritis and can be used alone or with another medicine called methotrexate.

Using Cosentyx in psoriatic arthritis will benefit you by reducing the signs and symptoms of the disease, slowing down the damage to the cartilage and bone of the joints and improving your ability to do normal daily activities.

Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis
Cosentyx is used to treat conditions called "ankylosing spondylitis" and "non-radiographic axial spondyloarthritis". These conditions are inflammatory diseases primarily affecting the spine which cause inflammation of the spinal joints. If you have ankylosing spondylitis or non-radiographic axial spondyloarthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of the disease, reduce inflammation and improve your physical function.

Cosentyx is used in adults with active ankylosing spondylitis and active non-radiographic axial spondyloarthritis.

Using Cosentyx in ankylosing spondylitis and non-radiographic axial spondyloarthritis will benefit you by reducing the signs and symptoms of your disease and improving your physical function.

2. What you need to know before you use Cosentyx

Do not use Cosentyx:
- **if you are allergic** to secukinumab or any of the other ingredients of this medicine (listed in section 6).
  If you think you may be allergic, ask your doctor for advice before using Cosentyx.
- **if you have an active infection** which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, nurse or pharmacist before using Cosentyx:
- if you currently have an infection.
- if you have long-term or repeated infections.
- if you have tuberculosis.
- if you have an inflammatory disease affecting your gut called Crohn's disease.
- if you have an inflammation of your large intestine called ulcerative colitis.
- if you have recently had a vaccination or if you are due to have a vaccination during treatment with Cosentyx.
- if you are receiving any other treatment for psoriasis, such as another immunosuppressant or phototherapy with ultraviolet (UV) light.

Inflammatory bowel disease (Crohn's disease or ulcerative colitis)
Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice abdominal cramps and pain, diarrhoea, weight loss, blood in the stool or any other signs of bowel problems.

Look out for infections and allergic reactions
Cosentyx can potentially cause serious side effects, including infections and allergic reactions. You must look out for signs of these conditions while you are taking Cosentyx.

Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice any signs indicating a possible serious infection or an allergic reaction. Such signs are listed under "Serious side effects" in section 4.

Children and adolescents
Cosentyx is not recommended for children younger than 6 years of age with plaque psoriasis because it has not been studied in this age group.

Cosentyx is not recommended for children and adolescents (under 18 years of age) in other indications because it has not been studied in this age group.

Other medicines and Cosentyx
Tell your doctor or pharmacist:
- if you are taking, have recently taken or might take any other medicines.
- if you have recently had or are due to have a vaccination. You should not be given certain types of vaccines (live vaccines) while using Cosentyx.

Pregnancy, breast-feeding and fertility
- It is preferable to avoid the use of Cosentyx in pregnancy. The effects of this medicine in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and must use adequate contraception while using Cosentyx and for at least 20 weeks after the last Cosentyx dose.
  Talk to your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.
- Talk to your doctor if you are breast-feeding or are planning to breast-feed. You and your doctor should decide if you will breast-feed or use Cosentyx. You should not do both. After using Cosentyx you should not breast-feed for at least 20 weeks after the last dose.

Driving and using machines
Cosentyx is unlikely to influence your ability to drive and use machines.

3. How to use Cosentyx

Always use this medicine exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

Cosentyx is given via injection under your skin (known as a subcutaneous injection). You and your doctor should decide if you should inject Cosentyx yourself.

It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist. A caregiver may also give you your Cosentyx injection after proper training.

For detailed instructions on how to inject Cosentyx, see "Instructions for use of Cosentyx 300 mg pre-filled syringe" at the end of this leaflet.

Instructions for use can also be found via the following QR code and web site:
'QR code to be included'
www.cosentyx.eu

How much Cosentyx is given and for how long
Your doctor will decide how much Cosentyx you need and for how long.

Plaque psoriasis
Adult
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as one injection of 300 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. Based on your response, further adjustments to your dose may be recommended by your doctor. At each timepoint you will receive a 300 mg dose given as one injection of 300 mg.

Children aged 6 years and older
- The recommended dose is based on body weight as follows:
  - Weight below 25 kg: 75 mg by subcutaneous injection.
  - Weight 25 kg or above and below 50 kg: 75 mg by subcutaneous injection.
  - Weight 50 kg or above: 150 mg by subcutaneous injection.
    Your doctor may increase the dose to 300 mg.
- Each 300 mg dose **is given as one injection of 300 mg or as two injections of 150 mg**. Other dosage forms/strengths may be available for administration of the 75 mg and 150 mg doses.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Hidradenitis suppurativa
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as one injection of 300 mg.**

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. Based on your response, further adjustments to your dose may be recommended by your doctor.

Psoriatic arthritis
If you have both psoriatic arthritis and also moderate to severe plaque psoriasis, your doctor may adjust the dose recommendation as needed.

For patients who did not respond well to medicines called tumour necrosis factor (TNF) blockers:
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as one injection of 300 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as one injection of 300 mg.

For other psoriatic arthritis patients:
- The recommended dose is 150 mg by subcutaneous injection. Other dosage forms/strengths are available for the 150 mg dose.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg.

Ankylosing spondylitis (Radiographic axial spondyloarthritis)

- The recommended dose is 150 mg by subcutaneous injection. Other dosage forms/strengths are available for the 150 mg dose.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg. Each 300 mg dose is given as one injection of 300 mg.

Non-radiographic axial spondyloarthritis

- The recommended dose is 150 mg by subcutaneous injection. Other dosage forms/strengths are available for the 150 mg dose.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Cosentyx is for long-term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you use more Cosentyx than you should
If you have received more Cosentyx than you should or the dose has been administered sooner than according to your doctor's prescription, inform your doctor.

If you forget to use Cosentyx
If you have forgotten to inject a dose of Cosentyx, inject the next dose as soon as you remember. Then talk to your doctor to discuss when you should inject the next dose.

If you stop using Cosentyx
It is not dangerous to stop using Cosentyx. However, if you stop, your psoriasis, psoriatic arthritis or axial spondyloarthritis symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Stop using Cosentyx and tell your doctor or seek medical help immediately if you get any of the following side effects:

Possible serious infection - the signs may include:

- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters
- burning sensation when passing urine.

Serious allergic reaction - the signs may include:

- difficulty breathing or swallowing
- low blood pressure, which can cause dizziness or light-headedness
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps.

Your doctor will decide if and when you may restart the treatment.

Other side effects
Most of the following side effects are mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Very common (may affect more than 1 in 10 people):
- upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis, rhinitis)

Common (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- runny nose (rhinorrhoea)
- headache
- nausea
- fatigue

Uncommon (may affect up to 1 in 100 people):
- oral thrush (oral candidiasis)
- signs of low levels of white blood cells, such as fever, sore throat or mouth ulcers due to infections (neutropenia)
- infection of the external ear (otitis externa)
- discharge from the eye with itching, redness and swelling (conjunctivitis)
- itchy rash (urticaria)
- lower respiratory tract infections
- abdominal cramps and pain, diarrhoea, weight loss or blood in the stool (signs of bowel problems)
- small, itchy blisters on the palms of hands, soles of feet and edges of the fingers and toes (dyshidrotic eczema)
- athlete's foot (tinea pedis)

Rare (may affect up to 1 in 1 000 people):
- severe allergic reaction with shock (anaphylactic reaction)
- redness and shedding of skin over a larger area of the body, which may be itchy or painful (exfoliative dermatitis)
- inflammation of small blood vessels, which can lead to a skin rash with small red or purple bumps (vasculitis)

Not known (frequency cannot be estimated from the available data):
- fungal infections of the skin and mucous membranes (including oesophageal candidiasis)
- painful swelling and skin ulceration (pyoderma gangrenosum)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cosentyx

Keep this medicine out of the sight and reach of children.

Do not use this medicine:
- after the expiry date which is stated on the outer box or the label on the syringe after "EXP".
- if the liquid contains easily visible particles, is cloudy or is distinctly brown.

Store the syringe sealed in its box to protect from light. Store in the refrigerator between 2°C and 8°C. Do not freeze. Do not shake.
If necessary, Cosentyx can be left out of the refrigerator for a single period of up to 4 days at room temperature, not above 30°C.

This medicine is for single use only.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Cosentyx contains
- The active substance is secukinumab. Each pre-filled syringe contains 300 mg secukinumab.
- The other ingredients are trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80 and water for injections.

What Cosentyx looks like and contents of the pack
Cosentyx solution for injection is a clear liquid. Its colour may vary from colourless to slightly yellow.
Cosentyx 300 mg solution for injection in pre-filled syringe is available in a pack containing 1 pre-filled syringe and in multipacks containing 3 (3 packs of 1) pre-filled syringes.
Not all pack sizes may be marketed.

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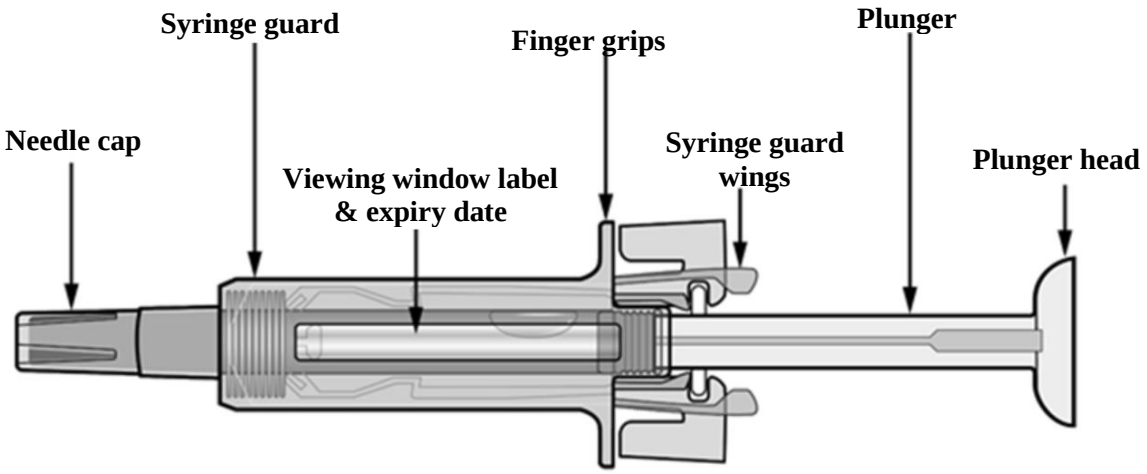
This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

Instructions for use of Cosentyx 300 mg pre-filled syringe

Read ALL the way through these instructions before injecting. It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist. The box contains the Cosentyx 300 mg pre-filled syringe individually sealed in a plastic blister.

Your Cosentyx 300 mg pre-filled syringe



After the medicine has been injected the syringe guard will be activated to cover the needle. This is intended to aid in the protection of healthcare professionals, patients who self-inject doctor-prescribed medicines, and individuals who assist self-injecting patients from accidental needlestick injuries.

What you additionally need for your injection:

- Alcohol swab.
- Cotton ball or gauze.
- Sharps disposal container.

Important safety information

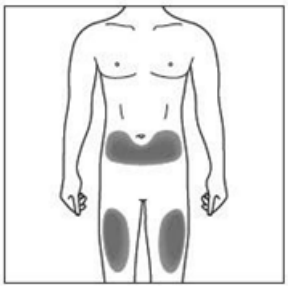
Caution: Keep the syringe out of the sight and reach of children.

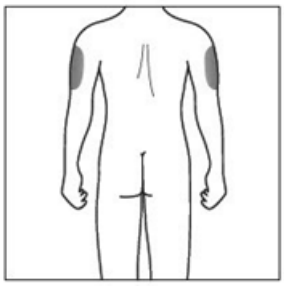
1. Do not open the sealed outer box until you are ready to use this medicine.
2. Do not use this medicine if either the seal on the outer box or the seal of the blister is broken, as it may not be safe for you to use.
3. Do not use if the syringe has been dropped onto a hard surface or dropped after removing the needle cap.
4. Never leave the syringe lying around where others might tamper with it.
5. Do not shake the syringe.
6. Be careful not to touch the syringe guard wings before use. By touching them, the syringe guard may be activated too early.
7. Do not remove the needle cap until just before you give the injection.
8. The syringe cannot be re-used. Dispose of the used syringe immediately after use in a sharps container.

Storage of the Cosentyx 300 mg pre-filled syringe

1. Store this medicine sealed in its outer box to protect it from light. Store in the refrigerator between 2°C and 8°C. DO NOT FREEZE.
2. Remember to take the syringe out of the refrigerator and allow it to reach room temperature before preparing it for injection (30-45 minutes).
3. Do not use the syringe after the expiry date which is stated on the outer box or syringe label after "EXP". If it has expired, return the entire pack to the pharmacy.

The injection site





The injection site is the place on the body where you are going to use the syringe.

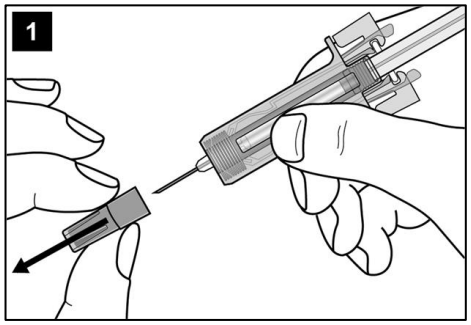
- The recommended site is the front of your thighs. You may also use the lower abdomen, but **not** the area 5 centimetres around the navel (belly button).
- Choose a different site each time you give yourself an injection.
- Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.

If a caregiver is giving you the injection, the outer upper arms may also be used.

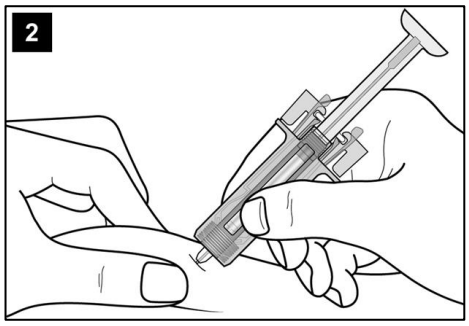
Preparing the Cosentyx 300 mg pre-filled syringe ready for use

1. Take the box containing the syringe out of the refrigerator and leave it **unopened** for about 30-45 minutes so that it reaches room temperature.
2. When you are ready to use the syringe, wash your hands thoroughly with soap and water.
3. Clean the injection site with an alcohol swab.
4. Remove the syringe from the outer box and take it out of the blister by holding the syringe guard body.
5. Inspect the syringe. The liquid should be clear. Its colour may vary from colourless to slightly yellow. You may see a small air bubble, which is normal. DO NOT USE if the liquid contains easily visible particles, is cloudy or is distinctly brown. DO NOT USE if the syringe is broken. In all these cases, return the entire product pack to the pharmacy.

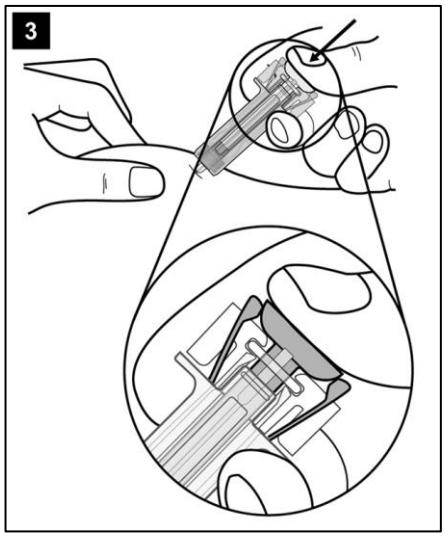
How to use the Cosentyx 300 mg pre-filled syringe



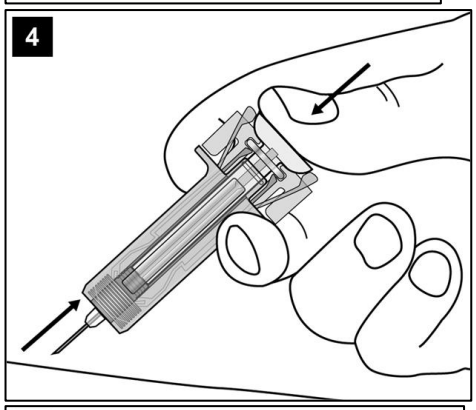
Carefully remove the needle cap from the syringe by holding the syringe guard body. Discard the needle cap. You may see a drop of liquid at the end of the needle. This is normal.



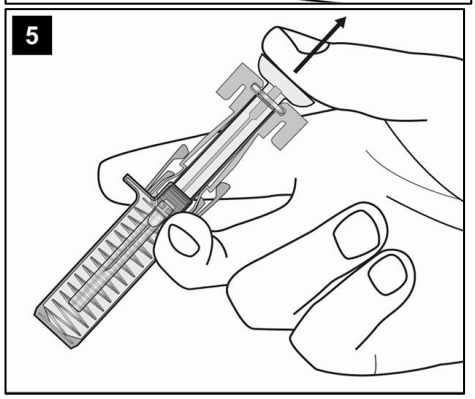
Gently pinch the skin at the injection site and insert the needle as shown. Push the needle all the way in to ensure that the medicine can be fully administered.



Hold the syringe as shown. **Slowly** depress the plunger **as far as it will go** so that the plunger head is completely between the syringe guard wings.
Keep the plunger pressed fully down while you hold the syringe in place for 5 seconds.



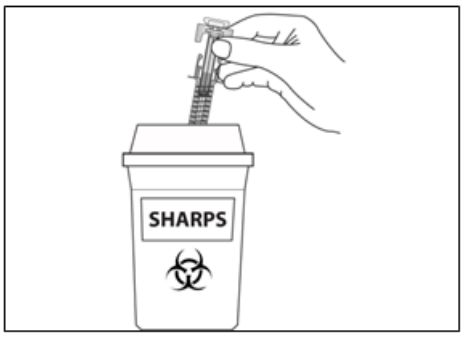
Keep the plunger fully depressed while you carefully lift the needle straight out from the injection site.



Slowly release the plunger and allow the syringe guard to automatically cover the exposed needle.

There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.

Disposal instructions



Dispose of the used syringe in a sharps container (closable, puncture resistant container). For the safety and health of you and others, needles and used syringes **must never** be re-used.

Package leaflet: Information for the user

Cosentyx 300 mg solution for injection in pre-filled pen
secukinumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cosentyx is and what it is used for
2. What you need to know before you use Cosentyx
3. How to use Cosentyx
4. Possible side effects
5. How to store Cosentyx
6. Contents of the pack and other information

1. What Cosentyx is and what it is used for

Cosentyx contains the active substance secukinumab. Secukinumab is a monoclonal antibody which belongs to a group of medicines called interleukin (IL) inhibitors. This medicine works by neutralising the activity of a protein called IL-17A, which is present at increased levels in diseases such as psoriasis, hidradenitis suppurativa, psoriatic arthritis and axial spondyloarthritis.

Cosentyx is used for the treatment of the following inflammatory diseases:
- Plaque psoriasis
- Hidradenitis suppurativa
- Psoriatic arthritis
- Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis

Plaque psoriasis
Cosentyx is used to treat a skin condition called “plaque psoriasis”, which causes inflammation affecting the skin. Cosentyx reduces the inflammation and other symptoms of the disease. Cosentyx is used in adults, adolescents and children (6 years of age and older) with moderate to severe plaque psoriasis.

Using Cosentyx in plaque psoriasis will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.

Hidradenitis suppurativa
Cosentyx is used to treat a condition called hidradenitis suppurativa, also sometimes called acne inversa or Verneuil’s disease. This condition is a chronic and painful inflammatory skin disease. Symptoms may include tender nodules (lumps) and abscesses (boils) that may leak pus. It commonly affects specific areas of the skin, such as under the breasts, the armpits, inner thighs, groin and buttocks. Scarring may also occur in affected areas.

Cosentyx can reduce the number of nodules and abscesses you have and the pain that is often associated with the disease. If you have hidradenitis suppurativa you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx.

Cosentyx isused in adults with hidradenitis suppurativa and can be used alone or with antibiotics.

Psoriatic arthritis
Cosentyx is used to treat a condition called “psoriatic arthritis”. The condition is an inflammatory disease of the joints, often accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of active psoriatic arthritis, improve physical function and slow down the damage to the cartilage and bone of the joints involved in the disease.

Cosentyx is used in adults with active psoriatic arthritis and can be used alone or with another medicine called methotrexate.

Using Cosentyx in psoriatic arthritis will benefit you by reducing the signs and symptoms of the disease, slowing down the damage to the cartilage and bone of the joints and improving your ability to do normal daily activities.

Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis
Cosentyx is used to treat conditions called “ankylosing spondylitis” and “non-radiographic axial spondyloarthritis”. These conditions are inflammatory diseases primarily affecting the spine which cause inflammation of the spinal joints. If you have ankylosing spondylitis or non-radiographic axial spondyloarthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of the disease, reduce inflammation and improve your physical function.

Cosentyx is used in adults with active ankylosing spondylitis and active non-radiographic axial spondyloarthritis.

Using Cosentyx in ankylosing spondylitis and non-radiographic axial spondyloarthritis will benefit you by reducing the signs and symptoms of your disease and improving your physical function.

2. What you need to know before you use Cosentyx

Do not use Cosentyx:
- **if you are allergic** to secukinumab or any of the other ingredients of this medicine (listed in section 6).
  If you think you may be allergic, ask your doctor for advice before using Cosentyx.
- **if you have an active infection** which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, nurse or pharmacist before using Cosentyx:
- if you currently have an infection.
- if you have long-term or repeated infections.
- if you have tuberculosis.
- if you have an inflammatory disease affecting your gut called Crohn’s disease.
- if you have an inflammation of your large intestine called ulcerative colitis.
- if you have recently had a vaccination or if you are due to have a vaccination during treatment with Cosentyx.
- if you are receiving any other treatment for psoriasis, such as another immunosuppressant or phototherapy with ultraviolet (UV) light.

Inflammatory bowel disease (Crohn’s disease or ulcerative colitis)
Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice abdominal cramps and pain, diarrhoea, weight loss, blood in the stool or any other signs of bowel problems.

Look out for infections and allergic reactions
Cosentyx can potentially cause serious side effects, including infections and allergic reactions. You must look out for signs of these conditions while you are taking Cosentyx.

Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice any signs indicating a possible serious infection or an allergic reaction. Such signs are listed under "Serious side effects" in section 4.

Children and adolescents
Cosentyx is not recommended for children younger than 6 years of age with plaque psoriasis because it has not been studied in this age group.

Cosentyx is not recommended for children and adolescents (under 18 years of age) in other indications because it has not been studied in this age group.

Other medicines and Cosentyx
Tell your doctor or pharmacist:
- if you are taking, have recently taken or might take any other medicines.
- if you have recently had or are due to have a vaccination. You should not be given certain types of vaccines (live vaccines) while using Cosentyx.

Pregnancy, breast-feeding and fertility
- It is preferable to avoid the use of Cosentyx in pregnancy. The effects of this medicine in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and must use adequate contraception while using Cosentyx and for at least 20 weeks after the last Cosentyx dose.
  Talk to your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.
- Talk to your doctor if you are breast-feeding or are planning to breast-feed. You and your doctor should decide if you will breast-feed or use Cosentyx. You should not do both. After using Cosentyx you should not breast-feed for at least 20 weeks after the last dose.

Driving and using machines
Cosentyx is unlikely to influence your ability to drive and use machines.

3. How to use Cosentyx

Always use this medicine exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

Cosentyx is given via injection under your skin (known as a subcutaneous injection). You and your doctor should decide if you should inject Cosentyx yourself.

It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist. A caregiver may also give you your Cosentyx injection after proper training.

For detailed instructions on how to inject Cosentyx, see "Instructions for use of the Cosentyx 300 mg UnoReady pen" at the end of this leaflet.

Instructions for use can also be found via the following QR code and web site:
'QR code to be included'
www.cosentyx.eu

How much Cosentyx is given and for how long
Your doctor will decide how much Cosentyx you need and for how long.

Plaque psoriasis
Adult
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as one injection of 300 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. Based on your response, further adjustments to your dose may be recommended by your doctor. At each timepoint you will receive a 300 mg dose given as one injection of 300 mg.

Children aged 6 years and older
- The recommended dose is based on body weight as follows:
  - Weight below 25 kg: 75 mg by subcutaneous injection.
  - Weight 25 kg or above and below 50 kg: 75 mg by subcutaneous injection.
  - Weight 50 kg or above: 150 mg by subcutaneous injection.
    Your doctor may increase the dose to 300 mg.
- Each 300 mg dose **is given as one injection of 300 mg or as two injections of 150 mg**. Other dosage forms/strengths may be available for administration of the 75 mg and 150 mg doses.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Hidradenitis suppurativa
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as one injection of 300 mg.**

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. Based on your response, further adjustments to your dose may be recommended by your doctor.

Psoriatic arthritis
If you have both psoriatic arthritis and also moderate to severe plaque psoriasis, your doctor may adjust the dose recommendation as needed.

For patients who did not respond well to medicines called tumour necrosis factor (TNF) blockers:
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as one injection of 300 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as one injection of 300 mg.

For other psoriatic arthritis patients:
- The recommended dose is 150 mg by subcutaneous injection. Other dosage forms/strengths are available for the 150 mg dose.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg.

Ankylosing spondylitis (Radiographic axial spondyloarthritis)

- The recommended dose is 150 mg by subcutaneous injection. Other dosage forms/strengths are available for the 150 mg dose.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg. Each 300 mg dose is given as one injection of 300 mg.

Non-radiographic axial spondyloarthritis

- The recommended dose is 150 mg by subcutaneous injection. Other dosage forms/strengths are available for the 150 mg dose.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Cosentyx is for long-term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you use more Cosentyx than you should
If you have received more Cosentyx than you should or the dose has been administered sooner than according to your doctor's prescription, inform your doctor.

If you forget to use Cosentyx
If you have forgotten to inject a dose of Cosentyx, inject the next dose as soon as you remember. Then talk to your doctor to discuss when you should inject the next dose.

If you stop using Cosentyx
It is not dangerous to stop using Cosentyx. However, if you stop, your psoriasis, psoriatic arthritis or axial spondyloarthritis symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Stop using Cosentyx and tell your doctor or seek medical help immediately if you get any of the following side effects:

Possible serious infection - the signs may include:

- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters
- burning sensation when passing urine.

Serious allergic reaction - the signs may include:

- difficulty breathing or swallowing
- low blood pressure, which can cause dizziness or light-headedness
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps.

Your doctor will decide if and when you may restart the treatment.

Other side effects
Most of the following side effects are mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Very common (may affect more than 1 in 10 people):
- upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis, rhinitis)

Common (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- runny nose (rhinorrhoea)
- headache
- nausea
- fatigue

Uncommon (may affect up to 1 in 100 people):
- oral thrush (oral candidiasis)
- signs of low levels of white blood cells, such as fever, sore throat or mouth ulcers due to infections (neutropenia)
- infection of the external ear (otitis externa)
- discharge from the eye with itching, redness and swelling (conjunctivitis)
- itchy rash (urticaria)
- lower respiratory tract infections
- abdominal cramps and pain, diarrhoea, weight loss or blood in the stool (signs of bowel problems)
- small, itchy blisters on the palms of hands, soles of feet and edges of the fingers and toes (dyshidrotic eczema)
- athlete's foot (tinea pedis)

Rare (may affect up to 1 in 1 000 people):
- severe allergic reaction with shock (anaphylactic reaction)
- redness and shedding of skin over a larger area of the body, which may be itchy or painful (exfoliative dermatitis)
- inflammation of small blood vessels, which can lead to a skin rash with small red or purple bumps (vasculitis)

Not known (frequency cannot be estimated from the available data):
- fungal infections of the skin and mucous membranes (including oesophageal candidiasis)
- painful swelling and skin ulceration (pyoderma gangrenosum)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cosentyx

Keep this medicine out of the sight and reach of children.

Do not use this medicine:
- after the expiry date which is stated on the outer box or the label on the pen after "EXP".
- if the liquid contains easily visible particles, is cloudy or is distinctly brown.

Store the pen sealed in its box to protect from light. Store in the refrigerator between 2°C and 8°C. Do not freeze. Do not shake.
If necessary, Cosentyx can be left out of the refrigerator for a single period of up to 4 days at room temperature, not above 30°C.

This medicine is for single use only.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Cosentyx contains
- The active substance is secukinumab. Each pre-filled pen contains 300 mg secukinumab.
- The other ingredients are trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80 and water for injections.

What Cosentyx looks like and contents of the pack
Cosentyx solution for injection is a clear liquid. Its colour may vary from colourless to slightly yellow.
Cosentyx 300 mg solution for injection in pre-filled pen is available in a pack containing 1 pre-filled pen and in multipacks containing 3 (3 packs of 1) pre-filled pens.
Not all pack sizes may be marketed.

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This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

Instructions for use of Cosentyx 300 mg UnoReady pen

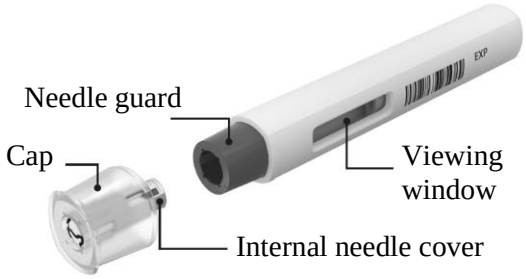
secukinumab

Read ALL the way through these instructions before injecting.

These instructions are to help you to inject correctly using the Cosentyx UnoReady pen.

It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist.

Your Cosentyx 300 mg UnoReady pen:



Cosentyx 300 mg UnoReady pen is shown above with the cap removed. **Do not** remove the cap until you are ready to inject.

Do not use the Cosentyx UnoReady pen if the seal on the outer carton is broken.

Keep the Cosentyx UnoReady pen in the sealed outer carton until you are ready to use it to protect it from light.

Store your Cosentyx UnoReady pen in a **refrigerator** between 2°C and 8°C and **out of the reach of children**.

- **Do not freeze** the pen.
- **Do not shake** the pen.
- Do not use the pen if it has been **dropped** with the cap removed.

The needle is covered by the needle guard and the needle will not be seen. Do not touch or push the needle guard because you could get a needle stick injury.

What you need for your injection:

Included in the carton:

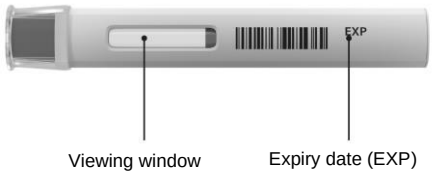
A new and unused Cosentyx 300 mg UnoReady pen.

Not included in the carton:

- Alcohol swab.
- Cotton ball or gauze.
- Sharps disposal container.

Before your injection:

Take the Cosentyx 300 mg UnoReady pen out of the refrigerator **30 to 45 minutes before injecting** to allow it to reach room temperature.



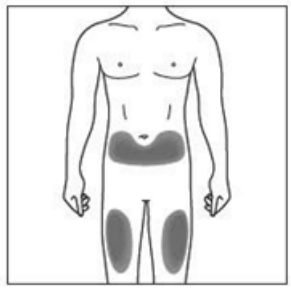
1. Important safety checks before you inject:

For the "Viewing window":
The liquid should be clear. Its colour may vary from colourless to slightly yellow.
Do not use if the liquid contains easily visible particles, is cloudy or is distinctly brown. You may see a small air bubble, which is normal.

For the "Expiry date":
Look at the expiry date (EXP) on your Cosentyx UnoReady pen. **Do not use** the pen if the **expiry date** has passed.

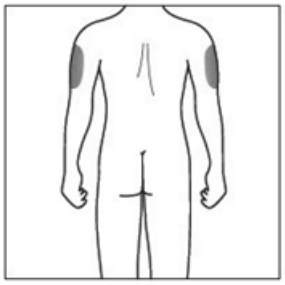
Check that your pen contains the correct medicine and dose.

Contact your pharmacist if the pen fails any of these checks.



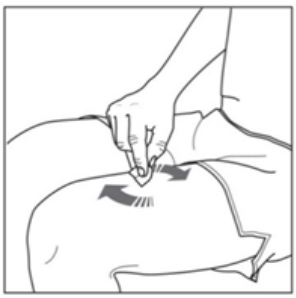
2a. Choose your injection site:

- The recommended site is the front of the thighs. You may also use the lower abdomen, but **not** the area 5 centimetres around the navel (belly button).
- Choose a different site each time you give yourself an injection.
- Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.



2b. Caregivers and healthcare professionals only:

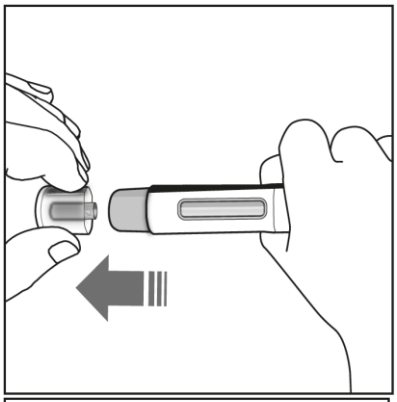
- If a **caregiver** or **healthcare professional** is giving you your injection, they may also inject into your outer upper arm.



3. Cleaning your injection site:

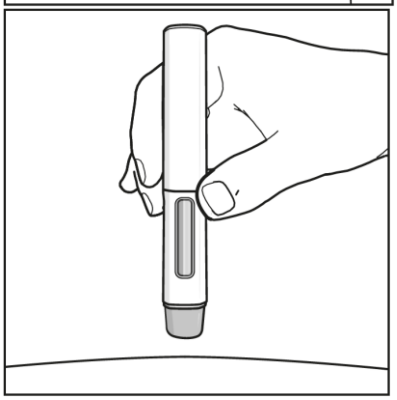
- Wash your hands with soap and hot water.
- Using a circular motion, clean the injection site with the alcohol swab. Leave it to dry before injecting.
- Do not touch the cleaned area again before injecting.

Your injection:



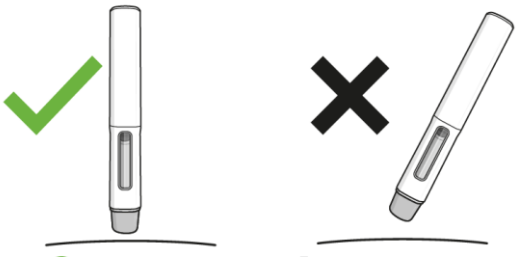
4. Removing the cap:

- Only remove the cap when you are ready to use the pen.
- Pull the cap straight off in the direction of the arrow that is shown in the figure on the left.
- Once removed, throw away the cap. Do not try to re-attach the cap.
- Use the pen within 5 minutes of removing the cap.



5. Holding your pen:

- Hold the pen at 90 degrees to the cleaned injection site.



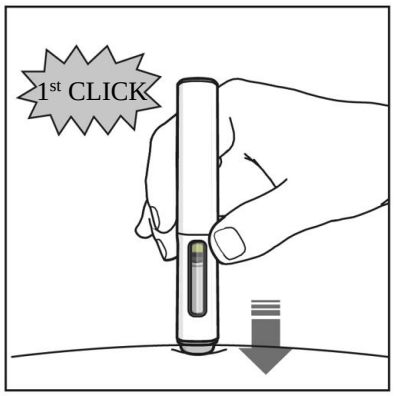
Correct **Incorrect**

YOU MUST READ THIS BEFORE INJECTING.

During the injection you will hear **2 clicks**.

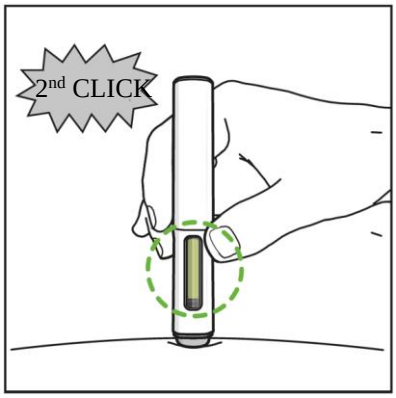
The **1st click** indicates that the injection has started. Several seconds later a **2nd click** will indicate that the injection is **almost** finished.

You must keep holding the pen firmly against your skin until you see a **green indicator with a grey tip** fill the window and stop moving.



6. Starting your injection:

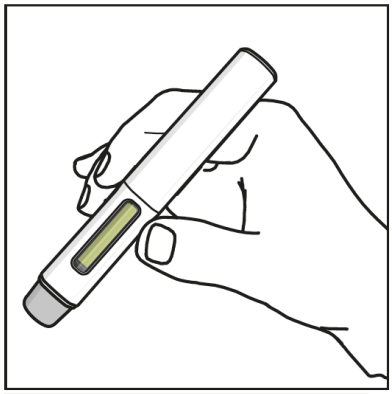
- Press the pen firmly against the skin to start the injection.
- The **1st click** indicates the injection has started.
- **Keep holding** the pen firmly against your skin.
  The **green indicator with the grey tip** shows the progress of the injection.



7. Completing your injection:

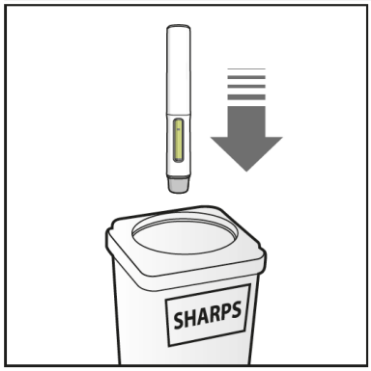
- Listen for the **2nd click**. This indicates the injection is **almost** complete.
- Check the **green indicator with the grey tip** fills the window and has stopped moving.
- The pen can now be removed.

After your injection:



8. Check the green indicator fills the window:

- This means the medicine has been delivered. Contact your doctor if the green indicator is not visible.
- There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.



9. Disposing of your Cosentyx 300 mg UnoReady pen:

- Dispose of the used pen in a sharps disposal container (i.e. a puncture-resistant closable container, or similar).
- Never try to reuse your pen.

Package leaflet: Information for the user

Cosentyx 150 mg powder for solution for injection

secukinumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cosentyx is and what it is used for
2. What you need to know before you use Cosentyx
3. How to use Cosentyx
4. Possible side effects
5. How to store Cosentyx
6. Contents of the pack and other information

1. What Cosentyx is and what it is used for

Cosentyx contains the active substance secukinumab. Secukinumab is a monoclonal antibody which belongs to a group of medicines called interleukin (IL) inhibitors. This medicine works by neutralising the activity of a protein called IL-17A, which is present at increased levels in diseases such as psoriasis, hidradenitis suppurativa, psoriatic arthritis and axial spondyloarthritis.

Cosentyx is used for the treatment of the following inflammatory diseases:
- Plaque psoriasis
- Hidradenitis suppurativa
- Psoriatic arthritis
- Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis
- Juvenile idiopathic arthritis, including enthesitis-related arthritis and juvenile psoriatic arthritis

Plaque psoriasis
Cosentyx is used to treat a skin condition called “plaque psoriasis”, which causes inflammation affecting the skin. Cosentyx reduces the inflammation and other symptoms of the disease. Cosentyx is used in adults, adolescents and children (6 years of age and older) with moderate to severe plaque psoriasis.

Using Cosentyx in plaque psoriasis will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.

Hidradenitis suppurativa
Cosentyx is used to treat a condition called hidradenitis suppurativa, also sometimes called acne inversa or Verneuil’s disease. This condition is a chronic and painful inflammatory skin disease. Symptoms may include tender nodules (lumps) and abscesses (boils) that may leak pus. It commonly affects specific areas of the skin, such as under the breasts, the armpits, inner thighs, groin and buttocks. Scarring may also occur in affected areas.

Cosentyx can reduce the number of nodules and abscesses you have and the pain that is often associated with the disease. If you have hidradenitis suppurativa you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx.

Cosentyx isused in adults with hidradenitis suppurativa and can be used alone or with antibiotics.

Psoriatic arthritis
Cosentyx is used to treat a condition called "psoriatic arthritis". The condition is an inflammatory disease of the joints, often accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of active psoriatic arthritis, improve physical function and slow down the damage to the cartilage and bone of the joints involved in the disease.

Cosentyx is used in adults with active psoriatic arthritis and can be used alone or with another medicine called methotrexate.

Using Cosentyx in psoriatic arthritis will benefit you by reducing the signs and symptoms of the disease, slowing down the damage to the cartilage and bone of the joints and improving your ability to do normal daily activities.

Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis
Cosentyx is used to treat conditions called "ankylosing spondylitis" and "non-radiographic axial spondyloarthritis". These conditions are inflammatory diseases primarily affecting the spine which cause inflammation of the spinal joints. If you have ankylosing spondylitis or non-radiographic axial spondyloarthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of the disease, reduce inflammation and improve your physical function.

Cosentyx is used in adults with active ankylosing spondylitis and active non-radiographic axial spondyloarthritis.

Using Cosentyx in ankylosing spondylitis and non-radiographic axial spondyloarthritis will benefit you by reducing the signs and symptoms of your disease and improving your physical function.

Juvenile idiopathic arthritis, including enthesitis-related arthritis and juvenile psoriatic arthritis
Cosentyx is used in patients (6 years of age and older) to treat conditions of the juvenile idiopathic arthritis categories called "enthesitis-related arthritis" and "juvenile psoriatic arthritis". These conditions are inflammatory diseases affecting the joints and the places where tendons join the bone.

Using Cosentyx in enthesitis-related arthritis and juvenile psoriatic arthritis will benefit you (or your child) by reducing the symptoms and improving your (or your child's) physical function.

2. What you need to know before you use Cosentyx

Do not use Cosentyx:
- **if you are allergic** to secukinumab or any of the other ingredients of this medicine (listed in section 6).
  If you think you may be allergic, ask your doctor for advice before using Cosentyx.
- **if you have an active infection** which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, nurse or pharmacist before using Cosentyx:
- if you currently have an infection.
- if you have long-term or repeated infections.
- if you have tuberculosis.
- if you have an inflammatory disease affecting your gut called Crohn's disease.
- if you have an inflammation of your large intestine called ulcerative colitis.
- if you have recently had a vaccination or if you are due to have a vaccination during treatment with Cosentyx.
- if you are receiving any other treatment for psoriasis, such as another immunosuppressant or phototherapy with ultraviolet (UV) light.

Inflammatory bowel disease (Crohn's disease or ulcerative colitis)
Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice abdominal cramps and pain, diarrhoea, weight loss, blood in the stool or any other signs of bowel problems.

Look out for infections and allergic reactions
Cosentyx can potentially cause serious side effects, including infections and allergic reactions. You must look out for signs of these conditions while you are taking Cosentyx.

Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice any signs indicating a possible serious infection or an allergic reaction. Such signs are listed under "Serious side effects" in section 4.

Children and adolescents
Cosentyx is not recommended for children younger than 6 years of age with plaque psoriasis because it has not been studied in this age group.

Cosentyx is not recommended for children younger than 6 years of age with juvenile idiopathic arthritis (enthesitis-related arthritis and juvenile psoriatic arthritis).

Cosentyx is not recommended for children and adolescents (under 18 years of age) in other indications because it has not been studied in this age group.

Other medicines and Cosentyx
Tell your doctor or pharmacist:
- if you are taking, have recently taken or might take any other medicines.
- if you have recently had or are due to have a vaccination. You should not be given certain types of vaccines (live vaccines) while using Cosentyx.

Pregnancy, breast-feeding and fertility
- It is preferable to avoid the use of Cosentyx in pregnancy. The effects of this medicine in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and must use adequate contraception while using Cosentyx and for at least 20 weeks after the last Cosentyx dose.
  Talk to your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.
- Talk to your doctor if you are breast-feeding or are planning to breast-feed. You and your doctor should decide if you will breast-feed or use Cosentyx. You should not do both. After using Cosentyx you should not breast-feed for at least 20 weeks after the last dose.

Driving and using machines
Cosentyx is unlikely to influence your ability to drive and use machines.

3. How to use Cosentyx

Cosentyx is given via injection under your skin (known as a subcutaneous injection) by a healthcare professional.

Make sure you discuss with your doctor when you will have your injections and your follow-up appointments.

How much Cosentyx is given and for how long
Your doctor will decide how much Cosentyx you need and for how long.

Plaque psoriasis
Adult
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. Based on your response, further adjustments to your dose may be recommended by your doctor. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

Children aged 6 years and older
- The recommended dose is based on body weight as follows:
  - Weight below 25 kg: 75 mg by subcutaneous injection.
  - Weight 25 kg or above and below 50 kg: 75 mg by subcutaneous injection.
  - Weight 50 kg or above: 150 mg by subcutaneous injection.
    Your doctor may increase the dose to 300 mg.
- Each 150 mg dose **is given as one injection of 150 mg**. Other dosage forms/strengths may be available for administration of the 75 mg and 300 mg doses.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Hidradenitis suppurativa
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg.**

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. Based on your response, further adjustments to your dose may be recommended by your doctor.

Psoriatic arthritis
If you have both psoriatic arthritis and also moderate to severe plaque psoriasis, your doctor may adjust the dose recommendation as needed.

For patients who did not respond well to medicines called tumour necrosis factor (TNF) blockers:
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

For other psoriatic arthritis patients:

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg.

Ankylosing spondylitis (Radiographic axial spondyloarthritis)

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg. Each 300 mg dose is given as two injections of 150 mg.

Non-radiographic axial spondyloarthritis

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Juvenile idiopathic arthritis (enthesitis-related arthritis and juvenile psoriatic arthritis)

- The recommended dose is based on body weight as follows:
  - Weight below 50 kg: 75 mg by subcutaneous injection.
  - Weight 50 kg or above: 150 mg by subcutaneous injection.
- Each 150 mg dose **is given as one injection of 150 mg**. Other dosage forms/strengths may be available for administration of the 75 mg dose.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Cosentyx is for long-term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you use more Cosentyx than you should
If you have received more Cosentyx than you should or the dose has been administered sooner than according to your doctor's prescription, inform your doctor.

If you forget to use Cosentyx
If you have missed a Cosentyx injection, talk to your doctor.

If you stop using Cosentyx
It is not dangerous to stop using Cosentyx. However, if you stop, your psoriasis, psoriatic arthritis or axial spondyloarthritis symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Stop using Cosentyx and tell your doctor or seek medical help immediately if you get any of the following side effects:

Possible serious infection - the signs may include:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters
- burning sensation when passing urine.

Serious allergic reaction - the signs may include:
- difficulty breathing or swallowing
- low blood pressure, which can cause dizziness or light-headedness
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps.

Your doctor will decide if and when you may restart the treatment.

Other side effects
Most of the following side effects are mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Very common (may affect more than 1 in 10 people):
- upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis, rhinitis)

Common (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- runny nose (rhinorrhoea)
- headache
- nausea
- fatigue

Uncommon (may affect up to 1 in 100 people):
- oral thrush (oral candidiasis)
- signs of low levels of white blood cells, such as fever, sore throat or mouth ulcers due to infections (neutropenia)
- infection of the external ear (otitis externa)
- discharge from the eye with itching, redness and swelling (conjunctivitis)
- itchy rash (urticaria)
- lower respiratory tract infections
- abdominal cramps and pain, diarrhoea, weight loss or blood in the stool (signs of bowel problems)
- small, itchy blisters on the palms of hands, soles of feet and edges of the fingers and toes (dyshidrotic eczema)
- athlete’s foot (tinea pedis)

Rare (may affect up to 1 in 1 000 people):
- severe allergic reaction with shock (anaphylactic reaction)
- redness and shedding of skin over a larger area of the body, which may be itchy or painful (exfoliative dermatitis)
- inflammation of small blood vessels, which can lead to a skin rash with small red or purple bumps (vasculitis)

Not known (frequency cannot be estimated from the available data):
- fungal infections of the skin and mucous membranes (including oesophageal candidiasis)
- painful swelling and skin ulceration (pyoderma gangrenosum)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cosentyx

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the outer box or vial after "EXP".

Before reconstitution: Store the vial in the refrigerator between 2°C and 8°C.

After reconstitution: The solution can be used immediately or can be stored at 2°C to 8°C for up to 24 hours. Do not freeze. The solution should be administered within one hour after removal from 2°C to 8°C storage.

Do not use this medicine if you notice that the powder has not fully dissolved or if the liquid contains easily visible particles, is cloudy or is distinctly brown.

This medicine is for single use only.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Cosentyx contains
- The active substance is secukinumab. Each vial of powder for solution for injection contains 150 mg secukinumab. After reconstitution, 1 ml of solution contains 150 mg secukinumab.
- The other ingredients are sucrose, histidine, histidine hydrochloride monohydrate and polysorbate 80.

What Cosentyx looks like and contents of the pack
Cosentyx powder for solution for injection is a white solid powder in a glass vial.
Cosentyx is supplied in a pack containing one vial.

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Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

Instructions for use of Cosentyx powder for solution for injection

The following information is intended for medical or healthcare professionals only.

The preparation of the solution for subcutaneous injection must be done without interruption and ensuring that aseptic technique is used. The preparation time from piercing the stopper until end of reconstitution takes 20 minutes on average and should not exceed 90 minutes.

To prepare Cosentyx 150 mg powder for solution for injection, please adhere to the following instructions:

Instructions for reconstitution of Cosentyx 150 mg powder for solution for injection:

1. Bring the vial of powder to room temperature and ensure that the sterile water for injections is at room temperature.
2. Withdraw slightly more than 1.0 ml sterile water for injections into a 1 ml graduated disposable syringe and adjust to 1.0 ml.
3. Remove the plastic cap from the vial.
4. Insert the syringe needle into the vial containing the powder through the centre of the rubber stopper and reconstitute the powder by slowly injecting 1.0 ml of sterile water for injections into the vial. The stream of sterile water for injections should be directed onto the powder.

5. Tilt the vial to an angle of approx. 45° and gently rotate between the fingertips for approx. 1 minute. Do not shake or invert the vial.

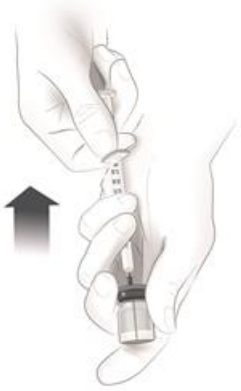
6. Keep the vial standing at room temperature for a minimum of 10 minutes to allow for dissolution. Note that foaming of the solution may occur.
7. Tilt the vial to an angle of approx. 45° and gently rotate between the fingertips for approx. 1 minute. Do not shake or invert the vial.

8. Allow the vial to stand undisturbed at room temperature for approximately 5 minutes. The resulting solution should be clear. Its colour may vary from colourless to slightly yellow. Do not use if the lyophilised powder has not fully dissolved or if the liquid contains easily visible particles, is cloudy or is distinctly brown.
9. Prepare the required number of vials (1 vial for the 75 mg dose, 1 vial for the 150 mg dose, 2 vials for the 300 mg dose).

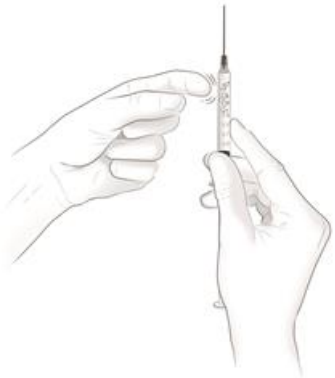
After storage at 2°C to 8°C, the solution should be allowed to come to room temperature for approximately 20 minutes before administration.

Instructions for administration of Cosentyx solution

1. Tilt the vial to an angle of approximately 45° and position the needle tip at the very bottom of the solution in the vial when drawing the solution into the syringe. DO NOT invert the vial.



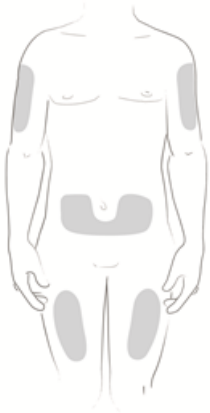
2. For the 150 mg and 300 mg doses, carefully withdraw slightly more than 1.0 ml of the solution for subcutaneous injection from the vial into a 1 ml graduated disposable syringe using a suitable needle (e.g. 21G x 2″). This needle will only be used for withdrawing Cosentyx into the disposable syringe. Prepare the required number of syringes (2 syringes for the 300 mg dose). For a child receiving the 75 mg dose, carefully withdraw slightly more than 0.5 ml of the solution for subcutaneous injection and discard the rest immediately.
3. With the needle pointing upward, gently tap the syringe to move any air bubbles to the top.



4. Replace the attached needle with a 27G x ½″ needle.

5. Expel the air bubbles and advance the plunger to the 1.0 ml mark for the 150 mg dose. Expel the air bubbles and advance the plunger to the 0.5 ml mark for the 75 mg dose.
6. Clean the injection site with an alcohol swab.

7. Inject the Cosentyx solution subcutaneously into the front of thighs, lower abdomen (but not the area 5 centimetres around the navel) or outer upper arms. Choose a different site each time an injection is administered. Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.



8. Any remaining solution in the vial must not be used and should be discarded in accordance with local requirements. Vials are for single use only. Dispose of the used syringe in a sharps container (closable, puncture-resistant container). For the safety and health of you and others, needles and used syringes must never be re-used.