

Medicinal product no longer authorised

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Eperzan 30 mg powder and solvent for solution for injection
Eperzan 50 mg powder and solvent for solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Eperzan 30 mg powder and solvent for solution for injection
Each pen delivers 30 mg albiglutide per 0.5 ml dose following reconstitution.

Eperzan 50 mg powder and solvent for solution for injection
Each pen delivers 50 mg albiglutide per 0.5 ml dose following reconstitution.

Albiglutide is a recombinant fusion protein consisting of two copies of a 30-amino acid sequence of modified human glucagon-like peptide 1 genetically fused in series to human albumin.

Albiglutide is produced in *Saccharomyces cerevisiae* cells by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.
Powder: lyophilised white to yellow powder.

Solvent: A clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Eperzan is indicated for the treatment of type 2 diabetes mellitus in adults to improve glycaemic control as:

Monotherapy

When diet and exercise alone do not provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate due to contraindications or intolerance.

Add-on combination therapy

In combination with other glucose-lowering medicinal products including basal insulin, when these, together with diet and exercise, do not provide adequate glycaemic control (see section 4.4 and 5.1 for available data on different combinations).

4.2 Posology and method of administration

Posology

The recommended dose of Eperzan is 30 mg once weekly, administered subcutaneously.

The dose may be increased to 50 mg once weekly based on individual glycaemic response.

When Eperzan is added to existing metformin therapy, the current metformin dose can be continued unchanged. It may be necessary to reduce the dose of concomitantly administered insulin secretagogues (such as sulphonylureas) or insulin to reduce the risk of hypoglycaemia when starting Eperzan (see sections 4.4 and 4.8).

The use of Eperzan does not require specific blood glucose self-monitoring. However, when used in combination with a sulphonylurea or a basal insulin, blood glucose self-monitoring may become necessary to adjust the dose of the sulphonylurea or the basal insulin.

Eperzan may be administered at any time of day without regard to meals.

Eperzan should be administered once a week on the same day each week. The day of weekly administration can be changed if necessary as long as the last dose was administered 4 or more days previously.

If a dose is missed, it should be administered as soon as possible within 3 days after the missed dose. Thereafter, patients can resume dosing on their usual day of administration. If it is more than 3 days after the missed dose, patients should wait and administer their next regularly scheduled weekly dose.

Elderly patients (≥ 65 years)

No dose adjustment is required based on age. The clinical experience in patients ≥ 75 years is very limited (see section 5.2).

Patients with renal impairment

No dose adjustment is necessary for patients with mild and moderate renal impairment (eGFR 60 to 89 and 30 to 59 ml/min/1.73m², respectively) (see sections 4.4, 4.8, 5.1, 5.2). Experience in patients with severe renal impairment (< 30 ml/min/1.73m²) or on dialysis is very limited and therefore Eperzan is not recommended in this population (see sections 4.4, 4.8, 5.1, 5.2).

Patients with hepatic impairment

No dose adjustment is recommended for patients with hepatic impairment. There have been no studies in patients with hepatic impairment (see section 5.2).

Paediatric population

The safety and efficacy of Eperzan in children and adolescents under 18 years have not been established (see section 5.2). No data are available.

Method of administration

Eperzan is intended for patient self-administration as a subcutaneous injection in the abdomen, thigh or upper arm region.

It must not be administered intravenously or intramuscularly.

Each pen injector should be used by one person only and is for single use.

The lyophilised powder contained within the pen must be reconstituted prior to administration. For full instructions on the reconstitution and administration of Eperzan see section 6.6 and the instructions for use included in the package leaflet.

When using Eperzan with insulin, each medicinal product must be administered as a separate injection. The two medicinal products should never be mixed. It is acceptable to inject Eperzan and insulin in the same body region but the injections should not be adjacent to each other.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

There is no therapeutic experience with Eperzan in patients with type 1 diabetes mellitus and it should not be used in these patients. Eperzan should not be used for treatment of diabetic ketoacidosis.

Acute pancreatitis

Use of GLP-1 receptor agonists has been associated with a risk of developing acute pancreatitis. In clinical trials, acute pancreatitis has been reported in association with Eperzan (see section 4.8).

Patients should be informed of the characteristic symptom of acute pancreatitis. If pancreatitis is suspected, Eperzan should be discontinued; if pancreatitis is confirmed, Eperzan should not be restarted. Caution should be exercised in patients with a history of pancreatitis.

Hypoglycaemia

The risk of hypoglycaemia is increased when Eperzan is used in combination with insulin secretagogues (such as sulphonylurea) or with insulin. Therefore, patients may require a lower dose of sulphonylurea or insulin to reduce the risk of hypoglycaemia (see sections 4.2, 4.8).

Severe gastrointestinal disease

Use of GLP-1 receptor agonists may be associated with gastrointestinal adverse reactions. Eperzan has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis, and therefore it is not recommended in these patients.

Renal impairment

Patients with severe renal impairment receiving Eperzan experienced a higher frequency of diarrhoea, nausea, and vomiting compared to patients with mild or moderate renal impairment. These types of gastrointestinal events may lead to dehydration, and worsen renal function.

Dehydration

Dehydration, sometimes leading to renal impairment and acute renal failure, has been reported in patients treated with albiglutide and has occurred in patients without gastrointestinal side effects. Patients treated with albiglutide should be advised of the potential risk of dehydration, and take precautions to avoid fluid depletion.

Discontinuation of treatment

After discontinuation, the effect of Eperzan may continue as plasma levels of albiglutide decline slowly over about 3 to 4 weeks. Choice of other medicinal products and dose selection should be considered accordingly, as adverse reactions may continue and efficacy may, at least partly, persist until albiglutide levels decline.

Populations not studied

There is no experience in patients with NYHA class III-IV cardiac failure. Eperzan has not been studied in combination with prandial insulin, dipeptidyl peptidase-4 (DPP-4) inhibitors, or sodium/glucose cotransporter 2 (SGLT2) inhibitors.

There is limited experience of albiglutide when combined with thiazolidinediones alone, sulphonylureas + thiazolidinediones, and metformin + sulphonylureas + thiazolidinediones.

Sodium content

This medicinal product contains less than 1 mmol sodium (23 mg) per 0.5 ml dose, i.e. essentially “sodium-free”.

4.5 Interaction with other medicinal products and other forms of interaction

Albiglutide delays gastric emptying, and has the potential to impact the absorption of concomitantly administered oral medicinal products. Albiglutide slowed gastric emptying compared with placebo for both solids and liquids when 100 mg was administered as a single dose in healthy subjects (see section 5.1). Caution should be exercised in patients receiving medicinal products with a narrow therapeutic index or medicinal products that require careful clinical monitoring.

Acarbose

Acarbose is contraindicated in patients with intestinal obstruction. Caution is advised if used concomitantly with albiglutide (see section 4.8).

Simvastatin

A single dose of simvastatin (80 mg) was administered with steady-state albiglutide (50 mg weekly). Simvastatin AUC was decreased by 40% and simvastatin C_{max} was increased by 18%. The AUC of simvastatin acid was increased by 36% and C_{max} was increased by approximately 100%. A decrease in half-life of simvastatin and simvastatin acid from ~7 hours to 3.5 hours was observed. Albiglutide showed no impact on the safety of simvastatin in clinical studies.

Digoxin

Albiglutide did not meaningfully alter the pharmacokinetics of a single-dose of digoxin (0.5 mg) when co-administered with steady-state albiglutide (50 mg weekly).

Warfarin

No clinically relevant effects on the pharmacokinetics of R- and S- enantiomers of warfarin were observed when a single dose of racemic warfarin (25 mg) was administered with steady-state albiglutide (50 mg weekly). In addition, albiglutide did not significantly alter the pharmacodynamic effects of warfarin as measured by the international normalized ratio.

Oral contraceptives

Albiglutide (50 mg weekly at steady-state) had no clinically relevant effects on the steady-state pharmacokinetics of a combination oral contraceptive containing norethindrone 0.5 mg and ethinyl estradiol 0.035 mg. In addition no clinically relevant effects on luteinizing hormone, follicle-stimulating hormone, or progesterone were observed when albiglutide and a combination oral contraceptive were co-administered.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of Eperzan in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). The potential risk for humans is unknown. Eperzan should not be used during pregnancy, and is not recommended in women of childbearing potential not using effective contraception.

Eperzan should be discontinued at least 1 month before a planned pregnancy due to the long washout period for albiglutide.

Breast-feeding

There are no adequate data to support the use of Eperzan during breast-feeding in humans. It is not known if albiglutide is excreted in human milk. Given that albiglutide is an albumin-based protein therapeutic agent, it is likely to be present in human milk. A decision should be made whether to discontinue breast-feeding or to discontinue therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the mother. Decreased body weight in offspring was observed in mice treated with albiglutide during gestation and lactation (see section 5.3).

Fertility

There are no data on the effects of Eperzan on human fertility. Studies in mice showed reduced oestrous cycling at maternally toxic doses, but did not indicate harmful effects with respect to fertility (see section 5.3). The potential risk for humans is unknown.

4.7 Effects on ability to drive and use machines

Eperzan has no or negligible influence on the ability to drive or use machines. When Eperzan is used in combination with insulin secretagogues (such as sulphonylureas) or insulin, patients should be advised to take precautions to avoid hypoglycaemia while driving and using machines (see section 4.4).

4.8 Undesirable effects

Summary of the safety profile

Over 2,300 patients have received Eperzan in 8 placebo- or active-controlled phase III studies.

Background therapies in these studies included diet and exercise, metformin, sulphonylurea, thiazolidinedione, insulin glargine, or a combination of antidiabetic medicinal products.

The duration of studies ranged from 32 weeks to up to 3 years. Frequency categories below reflect combined data for the 2 doses of Eperzan, 30 mg or 50 mg weekly subcutaneously.

The most serious adverse reaction in clinical trials was acute pancreatitis (see section 4.4).

The most frequent adverse reactions during clinical trials which occurred in $\geq 5\%$ of patients receiving Eperzan were diarrhoea, nausea, and injection site reactions including rash, erythema, or itching at the injection site.

Tabulated summary of adverse reactions

The table presents the adverse reactions that occurred more frequently among patients treated with Eperzan than patients treated with all comparators. Adverse reactions reported from a pooled analysis of seven placebo- and active-controlled phase III studies over the entire treatment period are presented in Table 1.

Patient frequencies are defined as: very common $\geq 1/10$; common $\geq 1/100$ to $< 1/10$; uncommon $\geq 1/1,000$ to $< 1/100$; rare: $\geq 1/10,000$ to $< 1/1,000$; very rare: $< 1/10,000$ and not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1. Adverse reactions from phase III studies during the entire treatment periods and postmarketing reports

System organ class	Very common	Common	Uncommon	Rare	Not known
Infections and infestations		Pneumonia			
Immune system disorders				Hypersensitivity reaction	
Metabolism and nutrition disorders	Hypoglycaemia (when Eperzan is used in combination with insulin or sulphonylurea)	Hypoglycaemia (when Eperzan is used as monotherapy or in combination with metformin or pioglitazone)			Decreased appetite
Cardiac disorders		Atrial fibrillation/flutter			
Gastrointestinal disorders	Diarrhoea, nausea	Vomiting, constipation, dyspepsia, gastroesophageal reflux disease	Pancreatitis, intestinal obstruction		
General disorders and administration site conditions	Injection site reactions				

Description of selected adverse reactions:

Allergic reactions

Possible hypersensitivity reactions including angioedema, erythema, generalised pruritus and rash with dyspnoea, have been reported with albiglutide.

Pancreatitis

The incidence of pancreatitis (adjudicated as likely to be related to therapy) in the clinical studies was 0.3% for Eperzan compared to 0% for placebo and 0.1% for comparators (i.e. liraglutide, pioglitazone, glimepiride, sitagliptin, and insulin glargine) with or without additional background antidiabetic therapy (e.g. metformin).

Gastrointestinal events

Gastrointestinal events occurred with a higher frequency for Eperzan compared to all comparators (38% versus 32%). Diarrhoea (13% versus 9%), nausea (12% versus 11%), vomiting (5% versus 4%), and constipation (5% versus 4%) were the most frequently reported, and the majority of events occurred within the first 6 months.

Gastrointestinal events with Eperzan occurred more frequently in patients with moderate to severe renal impairment (eGFR 15 to 59 ml/min/1.73 m²) than in those with mild renal impairment or normal renal function.

Injection site reactions

Injection site reactions (typically including rash, erythema, or itching at the injection site) occurred in 15% of patients treated with Eperzan compared to 7% with all comparators and led to discontinuation in 2% of all patients treated with Eperzan. Generally, injection site reactions were mild in intensity and did not require treatment.

Immunogenicity

The percentage of patients who developed antibodies to albiglutide on treatment was 4% (137/3,267). None of these antibodies were shown to neutralise the activity of albiglutide in an in vitro assay and antibody formation was generally transient and was not associated with reduced efficacy (HbA1c and FPG). Although most patients with injection site reactions were antibody negative (~85%), injection site reactions were reported more frequently for antibody positive (41%, N = 116) than antibody negative patients (14%, N = 1,927). These events were predominately mild and did not lead to discontinuation. Otherwise, the pattern of adverse events was generally similar for antibody positive and negative patients.

Hypoglycaemia

Severe hypoglycaemia requiring the assistance of another person for treatment occurred uncommonly: 0.3% among patients receiving Eperzan and 0.4% among patients receiving a comparator. Most patients with severe hypoglycaemic events in clinical studies were receiving concurrent sulphonylurea or insulin and none required hospitalisation or led to withdrawal of treatment.

When Eperzan was used as monotherapy, the incidence of symptomatic hypoglycaemia (<3.9 mmol/l) was similar for Eperzan 30 mg (2%), Eperzan 50 mg (1%) and placebo (3%).

The rate of symptomatic hypoglycaemia was higher for Eperzan when used in combination with a sulphonylurea (15% to 22%) or with insulin (18%) compared to combinations not including a sulphonylurea or insulin (1% to 4%). Among patients randomised to other comparators, the incidence of symptomatic hypoglycaemia was 7% to 33% when used with a sulphonylurea or insulin and 2% to 4% in combinations without these medicinal products.

Pneumonia

Pneumonia occurred in 2% of patients receiving Eperzan compared to 0.8% of patients in the all comparators group. For Eperzan, these were single episodes of pneumonia in patients participating in studies with 32 weeks up to 3 years of observation.

Atrial fibrillation/flutter

Atrial fibrillation/flutter occurred in 1% of patients receiving Eperzan and 0.5% of patients in the all comparators group. In both the Eperzan and all comparator groups, patients with events were generally male, older, or had renal impairment.

Heart rate

In the Phase III studies in type 2 diabetes patients, small increases in heart rate (1 to 2 bpm) were observed with albiglutide. In a thorough QT study in healthy subjects, an increase in heart rate (6 to 8 bpm) was observed after repeat dosing with albiglutide 50 mg compared to baseline values.

Withdrawals

In clinical trials of at least 2 years duration, 8% of subjects in the Eperzan group discontinued active treatment because of an adverse event compared with 6% in the all comparators group. The most common events leading to discontinuation of Eperzan were reactions at the injection site and GI related events, each < 2%.

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

During clinical studies of patients with type 2 diabetes, the highest dose of Eperzan administered was 100 mg subcutaneously every four weeks for 12 weeks. This dose was associated with an increased frequency of nausea, vomiting, and headache.

There is no specific antidote for overdose with Eperzan. In the event of a suspected overdose, the appropriate supportive clinical care should be instituted, as dictated by the subject's clinical status. Anticipated symptoms of an overdose may be severe nausea, vomiting or headache. A prolonged period of observation and treatment for these symptoms may be necessary, taking into account the half-life of albiglutide (5 days).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in diabetes. Other blood glucose lowering drugs excl. insulins. Glucagon-like peptide-1 (GLP-1) analogues. ATC code: A10BJ04

Mechanism of action

Albiglutide is an agonist of the GLP-1 receptor and augments glucose-dependent insulin secretion. Albiglutide also slows gastric emptying.

Pharmacodynamic effects

Glucose control

Eperzan lowers fasting glucose and reduces postprandial glucose excursions. The majority of the observed reduction in fasting plasma glucose occurs after a single dose, consistent with the pharmacokinetic profile of albiglutide.

In patients with type 2 diabetes who received 2 doses of albiglutide 32 mg (Day 1 and 8), a statistically significant reduction (24%) in postprandial glucose $AUC_{(0.5-4.5\text{ h})}$ was observed compared to placebo following a standardised breakfast meal on Day 9.

A single dose of albiglutide 50 mg did not impair the glucagon, epinephrine, norepinephrine, cortisol or growth hormone counter-regulatory hormone response to hypoglycaemia.

Gastric motility

Albiglutide slowed gastric emptying compared with placebo for both solids and liquids when 100 mg was administered as a single dose in healthy subjects. For solids, gastric emptying $t_{1/2}$ increased from 1.14 h to 2.23 h ($p=0.0112$). For liquids, gastric emptying $t_{1/2}$ increased from 0.28 h to 0.69 h ($p=0.0018$).

Clinical efficacy and safety

A total of 2,365 patients with type 2 diabetes were treated with Eperzan and 2,530 received other study medications in 8 active and placebo-controlled phase III clinical trials. Studies evaluated the use of Eperzan 30 mg and 50 mg once weekly, allowing for optional titration of Eperzan from 30 mg to 50 mg once weekly in 5 of the 8 studies. Across the 8 clinical trials, and including subjects in all treatment groups, a total of 19% of patients ($N = 937$) were 65 years of age and older, and 2% ($N = 112$) were 75 years of age and older, 52%

were male, with a mean body mass index (BMI) of 33 kg/m². Sixty seven percent of patients were Caucasian, 15% African American/African heritage and 11% Asian; 26% of patients were Hispanic/Latino.

No overall differences in glycaemic effectiveness or body weight were observed across demographic subgroups (age, gender, race/ethnicity, duration of diabetes).

Monotherapy

The efficacy of Eperzan was evaluated in a 3-year randomised, double-blind, placebo-controlled, multicentre study (n = 296) in patients inadequately controlled on diet and exercise. Patients were randomised (1:1:1) to Eperzan 30 mg once weekly, Eperzan 30 mg once weekly uptitrated to 50 mg once weekly at week 12, or placebo. The primary endpoint was change in HbA_{1c} from baseline at 52 weeks. Compared to placebo, treatment with Eperzan 30 mg and 50 mg SC weekly resulted in statistically significant reductions in HbA_{1c} from baseline at Week 52. The change from baseline in HbA_{1c} at the 6 month timepoint was also statistically significant for the 30 mg (0.9%) and 50 mg (1.1%) weekly doses of Eperzan (see Table 2).

Table 2. Results at 52 weeks in a placebo-controlled study with two doses of Eperzan (30 vs. 50 mg SC weekly) as monotherapy

	Eperzan 30 mg weekly	Eperzan 50 mg weekly	Placebo
ITT^a (N)	N = 100	N = 97	N = 99
HbA_{1c} (%)			
Baseline (mean)	8.05	8.21	8.02
Change at Week 52 ^b	-0.70	-0.9	+0.2
Difference from placebo ^b (95% CI)	-0.8 (-1.1, -0.6) ^c	-1.0 (-1.3, -0.8) ^c	
Patients (%) Achieving HbA _{1c} <7%	49	40	21
Body Weight (kg)			
Baseline (mean)	96	97	96
Change at Week 52 ^b	-0.4	-0.9	-0.7
Difference from placebo ^b (95% CI)	0.3 (-0.9, 1.5)	-0.2 (-1.4, 1.0)	

^a Intent to treat population – last observation carried forward

^b Adjusted mean

^c P<0.05 for treatment difference

Combination Therapy

Add-on to metformin

The efficacy of Eperzan was evaluated in a 3-year, randomised, double-blind, multicentre study (n = 999). On background therapy of metformin ≥1,500 mg daily, Eperzan 30 mg SC weekly (with optional uptitration to 50 mg weekly after a minimum of 4 weeks) was compared to sitagliptin 100 mg daily, glimepiride 2 mg daily (with optional titration to 4 mg daily), or placebo. The primary endpoint was change in HbA_{1c} from baseline at 2 years compared to placebo. Results at 104 weeks are presented in Table 3. Eperzan demonstrated glycaemic lowering and was statistically superior in reduction in HbA_{1c} from baseline compared to placebo, sitagliptin, or glimepiride (see Table 3).

Table 3. Results at 104 weeks in a placebo-controlled study comparing Eperzan 30 mg SC weekly (with optional uptitration to 50 mg weekly) to sitagliptin 100 mg daily and glimepiride 2 to 4 mg daily as add-on therapy in patients inadequately controlled on metformin $\geq 1,500$ mg daily

	Eperzan 30 mg/50 mg Weekly + Metformin $\geq 1,500$ mg daily	Placebo + Metformin $\geq 1,500$ mg daily	Sitagliptin 100 mg daily + Metformin $\geq 1,500$ mg daily	Glimepiride 2 to 4 mg daily + Metformin $\geq 1,500$ mgd aily
ITT^a (N)	297	100	300	302
HbA_{1c} (%)				
Baseline (mean)	8.1	8.1	8.1	8.1
Change at Week 104 ^b	-0.6	+0.3	-0.3	-0.4
Difference from placebo + metformin ^b , (95% CI)	-0.9 (-1.2, -0.7) ^c			
Difference from sitagliptin + metformin ^b , (95% CI)	-0.4 (-0.5, -0.2) ^c			
Difference from glimepiride + metformin ^b , (95% CI)	-0.3 (-0.5, -0.1) ^c			
Proportion Achieving HbA _{1c} <7%	39	16	32	31
Body Weight (kg)				
Baseline (mean)	90	92	90	92
Change at Week 104 ^b	-1.2	-1.0	-0.9	+1.2
Difference from placebo + metformin ^b , (95% CI)	-0.2 (-1.1, 0.7)			
Difference from sitagliptin + metformin ^b , (95% CI)	-0.4 (-1.0, 0.3)			
Difference from glimepiride + metformin ^b , (95% CI)	-2.4 (-3.0, -1.7) ^c			

^a Intent to treat population – last observation carried forward

^b Adjusted mean

^c P<0.05 for treatment difference

Add-on to pioglitazone

The efficacy of Eperzan was evaluated in a 3-year, randomised, double-blind, multicentre study (n = 299). Eperzan 30 mg SC weekly was compared to placebo in patients inadequately controlled on pioglitazone ≥ 30 mg daily (with or without metformin $\geq 1,500$ mg daily).

Compared to placebo, treatment with Eperzan resulted in statistically significant reductions from baseline in HbA_{1c} (-0.8% for Eperzan versus -0.1% for placebo, p<0.05) and FPG (-1.3 mmol/l for Eperzan versus +0.4 mmol/l for placebo, p<0.05) at 52 weeks. The change from baseline in weight did not differ significantly between treatment groups (see Table 4).

Table 4. Results at 52 weeks in a placebo-controlled study comparing Eperzan 30 mg SC weekly as add-on therapy in patients inadequately controlled on pioglitazone ≥ 30 mg daily \pm metformin $\geq 1,500$ mg daily

	Eperzan 30 mg Weekly + Pioglitazone ≥ 30 mg daily (+/- Metformin $\geq 1,500$ mg daily)	Placebo + Pioglitazone ≥ 30 mg daily (+/- Metformin $\geq 1,500$ mg daily)
ITT^a (N)	N = 150	N = 149
HbA_{1c} (%)		
Baseline (mean)	8.1	8.1
Change at Week 52 ^b	-0.8	-0.05
Difference from placebo + pioglitazone ^b (95% CI)	-0.8 (-1.0, -0.6) ^c	
Proportion Achieving HbA _{1c} <7%	44	15
Body Weight (kg)		
Baseline (mean)	98	100
Change at Week 52 ^b	0.3	+0.5
Difference from placebo + pioglitazone ^b (95% CI)	-0.2 (-1.2, 0.8)	

^a Intent to treat population – last observation carried forward

^b Adjusted mean

^c P<0.05 for treatment difference

Add-on to metformin plus sulphonylurea

The efficacy of Eperzan was evaluated in a 3-year, randomised, double-blind, multicentre study (n = 657). On background therapy of metformin $\geq 1,500$ mg daily plus glimepiride 4 mg daily, Eperzan 30 mg SC weekly (with optional uptitration to 50 mg weekly after a minimum of 4 weeks) was compared to placebo or pioglitazone 30 mg daily (with optional titration to 45 mg/day). The primary endpoint was change in HbA_{1c} from baseline at 52 weeks compared to placebo. At 52 weeks, treatment with Eperzan resulted in statistically significant reductions from baseline in HbA_{1c} compared to placebo. Treatment with Eperzan did not meet the pre-specified noninferiority margin (0.3%) against pioglitazone for HbA_{1c}. The change from baseline in weight for Eperzan did not differ significantly from placebo but was significantly less compared to pioglitazone (see Table 5).

Table 5. Results at 52 weeks in a placebo-controlled study comparing Eperzan 30 mg SC weekly (with optional uptitration to 50 mg weekly) to pioglitazone 30 mg daily (with optional titration to 45 mg/day) as add-on therapy in patients inadequately controlled on metformin + sulphonylurea (glimepiride 4 mg daily)

	Eperzan 30 mg/50 mg Weekly + Metformin ≥1,500 mg daily + Glimepiride 4 mg daily	Placebo + Metformin ≥1,500 mg daily + Glimepiride 4 mg daily	Pioglitazone + Metformin ≥1,500 mg daily + Glimepiride 4 mg daily
ITT^a (N)	269	115	273
HbA_{1c} (%)			
Baseline (mean)	8.2	8.3	8.3
Change at Week 52 ^b	-0.6	+0.33	-0.80
Difference from placebo + met + glim ^b (95% CI)	-0.9 (-1.1, -0.7) ^c		
Difference from pioglitazone + met + glim ^b (95% CI)	0.3 (0.1, 0.4)		
Proportion Achieving HbA _{1c} <7%	30	9	35
Body Weight (kg)			
Baseline (mean)	91	90	91
Change at Week 52 ^b	-0.4	-0.4	+4.4
Difference from placebo + met + glim ^b (95% CI)	-0.03 (-0.9, 0.8)		
Difference from pioglitazone + met + glim ^b (95% CI)	-4.9 (-5.5, -4.2) ^c		

^a Intent to treat population – last observation carried forward

^b Adjusted mean

^c P<0.05 for treatment difference

Add-on to insulin glargine

The efficacy of Eperzan was evaluated in a 52 week, randomised, open-label, multicentre noninferiority study (n = 563). On background therapy of insulin glargine (started at 10 units and titrated to ≥ 20 units per day), Eperzan 30 mg SC once weekly (with uptitration to 50 mg if inadequately controlled after Week 8) was compared to prandial insulin lispro (administered daily at mealtimes, started according to standard of care and titrated to effect). The primary endpoint was change in HbA_{1c} from baseline at 26 weeks. At Week 26, the mean daily dose of insulin glargine was 53 IU for Eperzan and 51 IU for lispro. The mean daily dose of insulin lispro at Week 26 was 31 IU, and at Week 52, 69% of patients treated with Eperzan were on 50 mg weekly. At 26 weeks, the between-treatment difference in HbA_{1c} of 0.2% for Eperzan and insulin lispro met the pre-specified noninferiority margin (0.4%). Treatment with Eperzan resulted in a mean weight loss for Eperzan (-0.7 kg) compared to a mean weight gain for insulin lispro (+0.8 kg) and the difference between treatment groups was statistically significant (see Table 6).

Table 6. Results at 26 weeks in a study comparing Eperzan 30 mg SC weekly (with optional uptitration to 50 mg weekly) to prandial insulin lispro as add-on therapy in patients inadequately controlled on insulin glargine alone

	Eperzan + Insulin glargine (≥ 20 units per day)	Insulin lispro + Insulin glargine (≥ 20 units per day)
ITT^a (N)	N = 282	N = 281
HbA_{1c} (%)		
Baseline (mean)	8.47	8.43
Change at Week 26 ^b	-0.8	-0.6
Difference from lispro insulin ^b (95% CI)	-0.2 (-0.3, 0.0)	
P value (noninferiority)	<0.0001	
Proportion Achieving HbA _{1c} <7%	30%	25%
Body Weight (kg)		
Baseline (mean)	93	92
Change at Week 26 ^b	-0.7	+0.8
Difference from lispro insulin ^b (95% CI)	-1.5 (-2.1, -1.0) ^c	

^a Intent to treat population – last observation carried forward

^b Adjusted mean

^c P<0.05 for treatment difference

In patients who completed the study (52 weeks), the adjusted mean change in baseline in HbA_{1c} was -1.0% for Eperzan (N = 121) and -0.9% for insulin lispro (N = 141). The adjusted mean change in body weight from baseline at 52 weeks was -1.0 kg for Eperzan (N = 122) and +1.7 kg for insulin lispro (N = 141). These data exclude the use of antidiabetic therapies permitted after the efficacy assessment if glycaemic thresholds were exceeded.

Active-controlled study versus insulin glargine as add-on to metformin \pm sulphonylurea

The efficacy of Eperzan was evaluated in a 3-year, randomised (2:1), open-label, insulin glargine-controlled noninferiority study (n = 735). On background therapy of metformin $\geq 1,500$ mg daily (with or without sulphonylurea), Eperzan 30 mg SC weekly (with optional uptitration to 50 mg weekly) was compared to insulin glargine (started at 10 units and titrated weekly per prescribing information). The primary endpoint was change in HbA_{1c} from baseline at 52 weeks. The starting total daily dose of insulin glargine ranged between 2 and 40 units (median daily dose of 10 units) and ranged between 3 and 230 units (median daily dose of 30 units) at Week 52. The median daily dose of insulin glargine used prior to hyperglycaemic rescue was 10 units (range 2 to 40 units) at study start and 30 units (range 3 to 230 units) at Week 52. At Week 156, 77% of patients treated with Eperzan were uptitrated to 50 mg SC weekly. The between-treatment difference in HbA_{1c} of 0.1% (-0.04, 0.27) from baseline at 52 weeks for Eperzan and insulin glargine met the pre-specified noninferiority margin (0.3%). A statistically significant decrease in body weight was observed for Eperzan compared to an increase in body weight for insulin glargine and the difference in weight change was statistically significant (see Table 7).

Table 7. Results at 52 weeks in an active-controlled study comparing Eperzan 30 mg SC weekly (with optional uptitration to 50 mg weekly) to insulin glargine (titrated weekly per prescribing information) as add-on therapy in patients inadequately controlled on metformin ± sulphonylurea

	Eperzan 30 mg/50 mg Weekly ± Metformin (with or without sulphonylurea)	Insulin glargine ± Metformin (with or without sulphonylurea)
ITT^a (N)	496	239
HbA_{1c} (%)		
Baseline (mean)	8.28	8.36
Change at Week 52 ^b	-0.7	-0.8
Difference from insulin glargine ^b (95% CI)	0.1 (-0.04, 0.3)	
P value (noninferiority)	<0.0086	
Proportion Achieving HbA _{1c} <7%	32	33
Body Weight (kg)		
Baseline (mean)	95	92
Change at Week 52 ^b	-1.1	1.6
Difference from insulin glargine ^b (95% CI)	-2.6 (-3.2, -2.0) ^c	

^a Intent to treat population – last observation carried forward

^b Adjusted mean

^c P<0.05 for treatment difference

In patients who were treated for at least 104 weeks, the adjusted mean change in baseline in HbA_{1c} was -0.97% for Eperzan (N = 182) and -1.04% for insulin glargine (N = 102). The adjusted mean change in body weight from baseline at 104 weeks was -2.6 kg for Eperzan (N = 184) and +1.4 kg for insulin glargine (N = 104). These data exclude the use of antidiabetic therapies permitted after the efficacy assessment if glycaemic thresholds were exceeded.

Active-controlled study versus liraglutide in combination with metformin, thiazolidinedione, or sulphonylurea (as monotherapy or dual therapy)

The efficacy of Eperzan was evaluated in a 32-week, randomised, open-label, liraglutide-controlled noninferiority study (N = 805). Eperzan 30 mg SC weekly (with uptitration to 50 mg weekly at Week 6) was compared to liraglutide 1.8 mg daily (titrated up from 0.6 mg at Week 1 and 1.2 mg at Week 1 to Week 2) in patients inadequately controlled on monotherapy or combination oral antidiabetic therapy (metformin, thiazolidinedione, or sulphonylureas). The primary endpoint was change in HbA_{1c} from baseline at 32 weeks. Treatment with Eperzan did not meet the pre-specified noninferiority margin (0.3%) against liraglutide for HbA_{1c} (see Table 8).

Table 8. Results of an active-controlled trial of Eperzan 30 mg SC weekly (with uptitration to 50 mg weekly) versus liraglutide 1.8 mg daily at 32 weeks^a

	Eperzan 30 mg/50 mg Weekly	Liraglutide 1.8 mg Daily
Intent to Treat Population (N)	402	403
HbA_{1c} (%)		
Baseline (mean)	8.2	8.2
Change at Week 32 ^b	-0.8	-1.0
Difference from liraglutide ^b (95% CI)	0.2 (0.1, 0.3)	
P value (noninferiority)	p = 0.0846	
Proportion Achieving HbA _{1c} <7%	42%	52%
Body Weight (kg)		
Baseline (mean)	92	93
Change at Week 32 ^b	-0.6	-2.2
Difference from liraglutide ^b (95% CI)	1.55 (1.05, 2.06) ^c	

^a Intent to treat population – last observation carried forward

^b Adjusted mean

^c P<0.05 for treatment difference

Active-controlled study versus sitagliptin in patients with type 2 diabetes and different degrees of renal impairment

The efficacy of Eperzan was evaluated in a randomised, double-blind, active-controlled 52-week study in 486 patients with mild, moderate, and severe renal impairment inadequately controlled on a current regimen of diet and exercise or other antidiabetic therapy. Eperzan 30 mg SC weekly (with uptitration to 50 mg weekly if needed) was compared to sitagliptin. Sitagliptin was dosed according to creatinine clearance estimated by Cockcroft-Gault formula (100 mg daily in mild, 50 mg daily in moderate, and 25 mg daily in severe renal impairment). The primary endpoint was change in HbA_{1c} from baseline at 26 weeks.

Treatment with Eperzan resulted in statistically significant reductions in HbA_{1c} from baseline at Week 26 compared to sitagliptin. The model-adjusted mean decrease in HbA_{1c} from baseline with Eperzan was -0.80 (n = 125), -0.83 (n = 98), and -1.08 (n = 19) in patients with mild (eGFR 60 to 89 ml/min/1.73m²), moderate (eGFR 30 to 59 ml/min/1.73m²), and severe (eGFR <30 ml/min/1.73m²) renal impairment, respectively (see Table 9).

Table 9. Results at 26 weeks in a study of Eperzan 30 mg SC weekly (with uptitration to 50 mg weekly if needed) versus sitagliptin (dosed according to renal function) in patients with different degrees of renal impairment

	Eperzan 30 mg/50 mg Weekly	Sitagliptin
Intent to Treat Population (N)	246 (125 mild, 98 moderate, 19 severe) ^a	240 (122 mild, 99 moderate, 15 severe) ^a
HbA_{1c} (%)		
Baseline (mean)	8.1	8.2
Change at Week 26 ^b	-0.8	-0.5
Difference from sitagliptin ^b (95% CI)	-0.3 (-0.5, -0.2) ^c	
Proportion Achieving HbA _{1c} <7%	43%	31%
Body Weight (kg)		
Baseline (mean)	84	83
Change at Week 26 ^b	-0.8	-0.19
Difference from sitagliptin ^b (95% CI)	-0.6 (-1.1, -0.1) ^c	

^a Intent to treat population – Last Observation Carried Forward (ITT-LOCF)

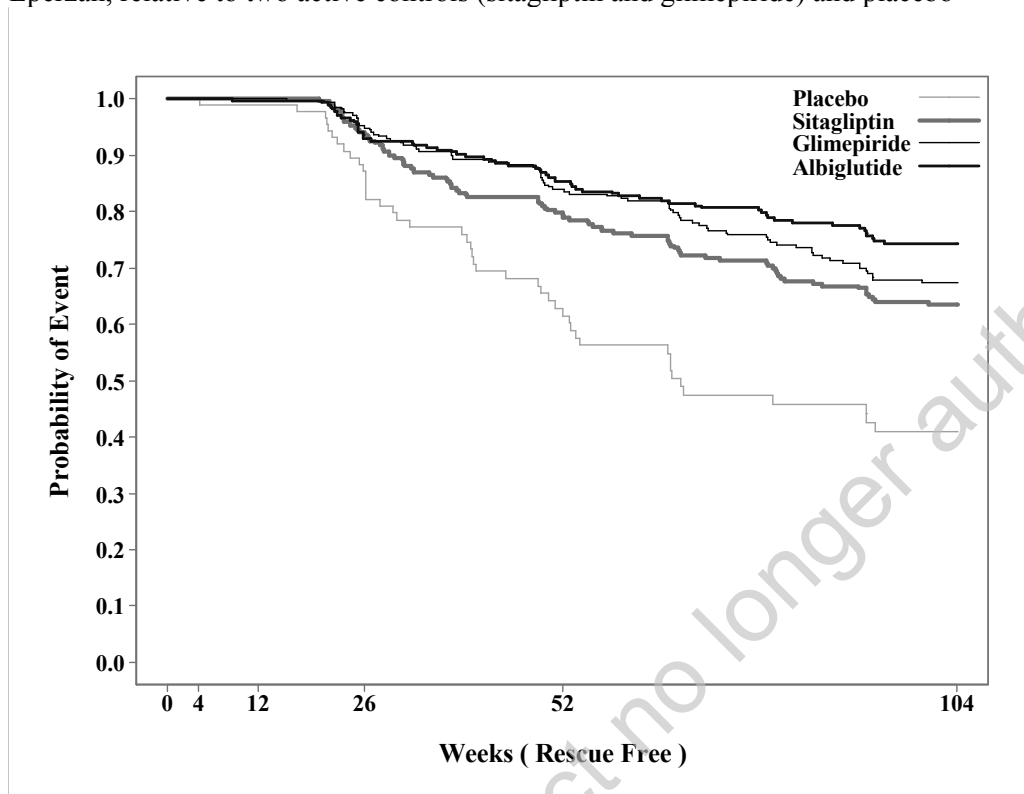
^b Adjusted mean

^c P<0.05 for treatment difference

Durability of glycaemic control

The durability of glycaemic control for Eperzan over time relative to other classes of type 2 antidiabetic agents and placebo is shown in Figure 1 as add-on to metformin.

Figure 1: Kaplan-Meier curve showing durability of glycaemic control (measured by time to rescue) for Eperzan, relative to two active controls (sitagliptin and glimepiride) and placebo



x axis; Weeks (Rescue free), y axis; Probability of event

Fasting plasma glucose

Treatment with Eperzan alone or in combination with one or two oral antidiabetic medicinal products resulted in a reduction in fasting plasma glucose from baseline as compared to placebo of 1.3 to 2.4 mmol/l. Most of this reduction was observed within the first two weeks of treatment.

Cardiovascular Evaluation:

A meta-analysis of 9 clinical studies (8 major effectiveness studies and 1 phase II dose finding study) of up to 3 years duration was conducted to assess the cardiovascular safety of Eperzan (N=2,524) compared to all comparators (N=2,583) within these trials. An endpoint called MACE+ (major adverse cardiac events plus) included hospitalisation for unstable angina in addition to the MACE endpoints (acute myocardial infarction, stroke, and CV death). The hazard ratio for Eperzan versus comparators for MACE+ was 1.0 (95% CI 0.68, 1.49). The incidence rates observed for first MACE+ were 1.2 and 1.1 events per 100 person-years for Eperzan versus all comparators, respectively.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Eperzan in one or more subsets of the paediatric population in the treatment of type 2 diabetes mellitus (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

Following SC administration of a single 30 mg dose to subjects with type 2 diabetes, maximum concentrations were reached 3 to 5 days post dose with mean peak albiglutide concentration (C_{max}) of 1.74 mcg/ml and mean area under the time-concentration curve (AUC) of 465 mcg.h/ml. The average weekly steady state concentrations following SC administration of 30 mg or 50 mg albiglutide estimated in the population PK analyses from phase III patient studies were approximately 2.6 mcg/ml and 4.4 mcg/ml, respectively. Steady-state exposures are achieved following 3-5 weeks of once-weekly administration. Exposures at the 30 mg and 50 mg dose levels were consistent with a dose-proportional increase. However, in healthy volunteers following 50 mg the steady state concentration was 7.39 µg/ml at day 36, thus higher than population PK analyses from phase III patient studies predicted. Similar exposure is achieved with SC administration of albiglutide in the abdomen, thigh, or upper arm.

Distribution

The mean estimate of apparent volume of distribution of albiglutide following SC administration is 11 litres. As albiglutide is an albumin fusion molecule, plasma protein binding has not been assessed.

Biotransformation

Albiglutide is a protein for which the expected metabolic pathway is degradation to small peptides and individual amino acids by ubiquitous proteolytic enzymes.

Elimination

The mean apparent clearance of albiglutide is 67 ml/h with an elimination half-life of approximately 5 days based on estimations from the population PK analyses from phase III patient studies and measured values.

Special populations

Patients with renal impairment

In a population pharmacokinetic analysis including a phase III trial in patients with mild, moderate and severe renal impairment, exposures were increased by approximately 30 to 40% in severe renal impairment compared to those observed in type 2 diabetic patients with normal renal function. In addition, a clinical pharmacology study showed a similar increased exposure for patients with moderate or severe renal impairment or those on haemodialysis relative to patients without renal impairment. These differences were not considered clinically relevant (see section 4.2).

Patients with hepatic insufficiency

No clinical studies were conducted to examine the effects of hepatic impairment on the pharmacokinetics of Eperzan. Therapeutic proteins such as albiglutide are catabolised by widely distributed proteolytic enzymes, which are not restricted to hepatic tissue; therefore, changes in hepatic function are unlikely to have any effect on the elimination of Eperzan (see section 4.2).

Gender

Based on the results of population pharmacokinetic analyses, there is no clinically relevant effect of gender on clearance.

Race and ethnicity

Based on the results of population pharmacokinetic analyses that included Caucasian, African American/African, Asian and Hispanic/Non-Hispanic patients, race and ethnicity had no clinically meaningful effect on the pharmacokinetics of Eperzan clearance.

Japanese patients showed approximately 30 to 40% higher exposures than Caucasians, likely attributable to lower body weight. This effect was not considered clinically relevant.

Elderly patients (≥ 65 years)

Age had no clinically relevant effect on the pharmacokinetics of albiglutide based on a population pharmacokinetic analysis of subjects aged 24-83 years (see section 4.2).

Body weight

Body weight has no clinically relevant effect on albiglutide AUC over the range 44 to 158 kg. A 20% increase in body weight resulted in an approximate 18.5% increase in clearance.

Paediatric population:

No pharmacokinetic data are available in paediatric patients.

5.3 Preclinical safety data

Non-clinical data reveal no special hazards for humans based on studies of safety pharmacology or repeat-dose toxicity. As albiglutide is a recombinant protein, no genotoxicity studies have been conducted.

In a 52-week monkey study, there was a small increase in pancreas tissue weight at 50 mg/kg/week (75 times clinical exposure based on AUC) associated with acinar cell hypertrophy. A small increase in islet cell number was also observed. The pancreas changes were not associated with histomorphologic abnormalities or evidence of increased proliferation.

No carcinogenicity studies have been performed with albiglutide due to immunogenicity in rodents. Thyroid C-cell tumours were observed in 2 year rodent carcinogenicity studies with other GLP-1 receptor agonists. Increased serum calcitonin levels have been associated with the thyroid C-cell hyperplasia and tumours observed in rodent studies with these other agents. Albiglutide also produced dose-dependent increases in serum calcitonin levels in a 21-day study in mice, suggesting that thyroid tumours in rodents are a theoretical possibility for albiglutide as well. There were no albiglutide related findings in thyroids of monkeys given up to 50 mg/kg/week for up to 52 weeks (75 times clinical exposure based on AUC). The clinical relevance of the observed thyroid C-cell tumours in rodents is unknown.

In reproductive toxicology studies with albiglutide in mice, there were no effects on mating or fertility at doses up to 50 mg/kg/day (at low multiple of clinical exposure). Reductions in oestrous cycles were observed at 50 mg/kg/day, a dose associated with maternal toxicity (body weight loss and reduced food consumption). Effects on embryo-foetal development (embryo-foetal lethality and skeletal variations) were observed at 50 mg/kg/day (at low multiple of clinical exposure). Offspring of mice dosed with 50 mg/kg/day during organogenesis had reduced weight during the pre-weaning period (which recovered after weaning), dehydration and coldness, and a delay in balanopreputial separation. No effects were seen at 5 mg/kg/day (at exposures similar to clinical exposure).

In pre- and postnatal development studies in mice administered albiglutide during pregnancy or while nursing, reduced pre-weaning body weight of F1 offspring was observed at ≥ 1 mg/kg/day (at exposures below clinical exposure). Reduced F1 body weight reversed post-weaning with the exception of F1 females from dams treated perinatally (end of gestation to 10 days postpartum) at ≥ 5 mg/kg/day with no other effects on development. Trace levels of albiglutide were detected in plasma of offspring. It is unknown whether the reduced offspring body weight was caused by a direct albiglutide effect on the offspring or secondary to effects on the dam.

Increased mortality and morbidity were seen at all doses (≥ 1 mg/kg/day) in lactating females in mouse pre- and postnatal development studies. Mortalities have not been observed in previous toxicology studies in non-lactating or non-pregnant mice, nor in pregnant mice. These findings are consistent with lactational ileus syndrome which has been previously reported in mice. Since the relative stress of lactation energy demands is much lower in humans than mice and humans have large energy reserves, the mortalities observed in lactating mice are considered not relevant to humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder for solution for injection:

Sodium dihydrogen phosphate monohydrate

Disodium phosphate, anhydrous

Trehalose dihydrate

Mannitol (E421)

Polysorbate 80

Solvent:

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

3 years.

After reconstitution, the pen should be used within 8 hours. Use the pen immediately after the needle is attached otherwise the solution can dry inside the needle and block it.

6.4 Special precautions for storage

Store refrigerated at 2°C to 8°C. Do not freeze.

Patients may store the pens at room temperature, not exceeding 30°C, for no more than a total of 4 weeks prior to use. At the end of this period the pen should be used or discarded.

For shelf life of the reconstituted product, see section 6.3.

6.5 Nature and contents of container

Dual Chamber Cartridge (DCC) composed of a Type 1 glass barrel sealed with bromobutyl rubber stoppers and a bromobutyl rubber closure disc encased in a polypropylene snap on cap. Each cartridge is assembled into a disposable single use plastic pen injector (pen).

Each pen delivers a single 30 mg or 50 mg dose of Eperzan in a volume of 0.5 ml.

Pack sizes:

Carton of 4 single-dose pens and 4 pen needles.

Multipack containing 12 single-dose pens and 12 pen needles (3 packs of 4 pens and 4 needles).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Disposal

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

Instructions for use

Eperzan that has been frozen must not be used.

Inspect the pen to ensure that the number '1' is visible in the number window. Do not use the pen if the number '1' is not showing.

Reconstitution and administration by the patient

Full instructions for reconstitution and administration to be used by the patient are provided in the Instructions for Use section of the Package Leaflet.

Instruct the patient to read the full Instructions for Use (IFU) including the Questions and Answers before starting the therapy and refer back to the IFU each time before injecting the dose.

Alternate method of reconstitution (healthcare professional use only):

The Instructions for Use included in the Package Leaflet provide directions for the patient to wait 15 minutes for the 30 mg pen and 30 minutes for the 50 mg pen after the lyophilised powder and diluent are mixed to ensure reconstitution. Healthcare professionals may utilise the following alternate method of reconstitution that allows for more rapid dissolution. Because this method relies on appropriate swirling and visual inspection of the solution, it is intended only for healthcare professionals.

Inspect the pen for '1' in the number window and expiration date. Follow instructions to twist the cartridge until '2' appears in the number window and a "click" is heard. This mixes the diluent in the rear chamber of the cartridge with the lyophilised powder in the front chamber. With the clear cartridge pointing up, gently swirl the pen for one minute. Avoid shaking as this can result in foaming. Inspect, and continue to swirl the pen until all the powder is dissolved. Complete dissolution for the 30 mg pen usually occurs within 2 minutes but may take up to 5 minutes, as confirmed by visual inspection for a clear solution free of particles. Complete dissolution for the 50 mg pen usually occurs within 7 minutes but may take up to 10 minutes. A small amount of foam on top of the solution at the end of the reconstitution is normal. After reconstitution, continue to follow the steps in the instructions for use to attach the needle, prime the pen injector and administer the injection.

Use Eperzan only if it is a clear yellow solution and contains no particles.

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Trading Services Limited,
Currabinny,
Carrigaline,
County Cork,
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/908/001
EU/1/13/908/002
EU/1/13/908/003
EU/1/13/908/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21 March 2014

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>.

Medicinal product no longer authorised

ANNEX II

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

Name and address of the manufacturer of the biological active substance

GlaxoSmithKline LLC
Building 40
893 River Road
Conshohocken, PA 19428
USA

Name and address of the manufacturer responsible for batch release

Glaxo Operations UK Limited (Trading as Glaxo Wellcome Operations)
Harmire Road
Barnard Castle
Durham, DL12 8DT
United Kingdom

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

• **Periodic Safety Update Reports**

The requirements for submission of periodic safety update reports 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 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.

Medicinal product no longer authorised

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

Medicinal product no longer authorised

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON – 4 pen pack

1. NAME OF THE MEDICINAL PRODUCT

Eperzan 30 mg powder and solvent for solution for injection.
albiglutide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each dose contains 30 mg per 0.5 ml following reconstitution.

3. LIST OF EXCIPIENTS

Also contains: Sodium dihydrogen phosphate monohydrate, disodium phosphate, anhydrous, trehalose dihydrate, mannitol (E421), polysorbate 80, water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

4 pens
4 pen needles

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read package leaflet.
Subcutaneous use
Once weekly.

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

Single use only.
Discard pen after use.
Read package leaflet
After mixing, wait 15 minutes before injection

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store refrigerated at 2°C to 8°C.
Do not freeze.

Pens may be stored at room temperature, not exceeding 30°C, for no more than a total of 4 weeks prior to use.

Use within 8 hours of reconstitution.
Use immediately after needle is attached.

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**

GlaxoSmithKline Trading Services Limited
Currabinny
Carrigaline
County Cork
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/908/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE**16. INFORMATION IN BRAILLE**

eperzan 30

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:
SN:
NN:

Medicinal product no longer authorised

PARTICULARS TO APPEAR ON INTERMEDIATE PACKAGING

CARTON – Multipack containing 12 single-dose pens and 12 pen needles (3 packs of 4 pens and 4 needles) – without blue box

1. NAME OF THE MEDICINAL PRODUCT

Eperzan 30 mg powder and solvent for solution for injection.
Albiglutide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each dose contains 30 mg per 0.5 ml following reconstitution.

3. LIST OF EXCIPIENTS

Also contains: Sodium dihydrogen phosphate monohydrate, disodium phosphate, anhydrous, trehalose dihydrate, mannitol (E421), polysorbate 80, water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

Component of a multipack comprising 3 packs, each containing 4 pens and 4 pen needles.
Do not sell separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read package leaflet.
Subcutaneous use
Once weekly.

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Single use only.
Discard pen after use.
Read package leaflet
After mixing, wait 15 minutes before injection

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store refrigerated at 2°C to 8°C.
Do not freeze.

A single carton of 4 pens and 4 needles may be stored at room temperature, not exceeding 30°C, for no more than a total of 4 weeks prior to use. Remaining cartons must be stored at 2°C to 8°C until required.

Use within 8 hours of reconstitution.
Use immediately after needle is attached.

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

GlaxoSmithKline Trading Services Limited
Currabinny
Carrigaline
County Cork
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/908/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

eperzan 30

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

Medicinal product no longer authorised

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER LABEL – Multipack containing 12 single-dose pens and 12 pen needles (3 packs of 4 pens and 4 needles) –with blue box

1. NAME OF THE MEDICINAL PRODUCT

Eperzan 30 mg powder and solvent for solution for injection.
albiglutide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each dose contains 30 mg per 0.5 ml following reconstitution.

3. LIST OF EXCIPIENTS

Also contains: Sodium dihydrogen phosphate monohydrate, disodium phosphate, anhydrous, trehalose dihydrate, mannitol (E421), polysorbate 80, water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

Multipack: 12 pens (3 cartons of 4 pens/4 needles)
Do not sell separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet.
Subcutaneous use
Once weekly.

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

Single use only.
Discard pen after use.
Read package leaflet
After mixing, wait 15 minutes before injection

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store refrigerated at 2°C to 8°C.
Do not freeze.

A single carton of 4 pens and 4 needles may be stored at room temperature, not exceeding 30°C, for no more than a total of 4 weeks prior to use. Remaining cartons must be stored at 2°C to 8°C until required.

Use within 8 hours of reconstitution.
Use immediately after needle is attached.

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

GlaxoSmithKline Trading Services Limited
Currabinny
Carrigaline
County Cork
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/908/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

eperzan 30

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:
SN:
NN:

Medicinal product no longer authorised

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON – 4 pen pack

1. NAME OF THE MEDICINAL PRODUCT

Eperzan 50 mg powder and solvent for solution for injection.
Albiglutide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each dose contains 50 mg per 0.5 ml following reconstitution.

3. LIST OF EXCIPIENTS

Also contains: Sodium dihydrogen phosphate monohydrate, disodium phosphate, anhydrous, trehalose dihydrate, mannitol (E421), polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

4 pens
4 pen needles

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read package leaflet.
Subcutaneous use
Once weekly.

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

Single use only.
Discard pen after use.
Read package leaflet
Reconstitution time
After mixing, wait 30 minutes before injection

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store refrigerated at 2°C to 8°C.

Do not freeze.

Pens may be stored at room temperature, not exceeding 30°C, for no more than a total of 4 weeks prior to use.

Use within 8 hours of reconstitution.

Use immediately after needle is attached.

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**

GlaxoSmithKline Trading Services Limited
Currabinny
Carrigaline
County Cork
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/908/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE**16. INFORMATION IN BRAILLE**

eperzan 50

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:

SN:

NN:

Medicinal product no longer authorised

PARTICULARS TO APPEAR ON INTERMEDIATE PACKAGING

CARTON - Multipack containing 12 single-dose pens and 12 pen needles (3 packs of 4 pens and 4 needles) – without blue box

1. NAME OF THE MEDICINAL PRODUCT

Eperzan 50 mg powder and solvent for solution for injection.
albiglutide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each dose contains 50 mg per 0.5 ml following reconstitution.

3. LIST OF EXCIPIENTS

Also contains: Sodium dihydrogen phosphate monohydrate, disodium phosphate, anhydrous, trehalose dihydrate, mannitol (E421), polysorbate 80, water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

Component of a multipack comprising 3 packs, each containing 4 pens and 4 pen needles
Do not sell separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read package leaflet.
Subcutaneous use
Once weekly.

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Single use only.
Discard pen after use.
Read package leaflet
Reconstitution time
After mixing, wait 30 minutes before injection

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store refrigerated at 2°C to 8°C.
Do not freeze.

A single carton of 4 pens and 4 needles may be stored at room temperature, not exceeding 30°C, for no more than a total of 4 weeks prior to use. Remaining cartons must be stored at 2°C to 8°C until required.

Use within 8 hours of reconstitution.
Use immediately after needle is attached.

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

GlaxoSmithKline Trading Services Limited
Currabinny
Carrigaline
County Cork
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/908/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

eperzan 50

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

Medicinal product no longer authorised

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER LABEL – Multipack containing 12 single-dose pens and 12 pen needles (3 packs of 4 pens and 4 needles) –with blue box

1. NAME OF THE MEDICINAL PRODUCT

Eperzan 50 mg powder and solvent for solution for injection.
albiglutide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each dose contains 50 mg per 0.5 ml following reconstitution.

3. LIST OF EXCIPIENTS

Also contains: Sodium dihydrogen phosphate monohydrate, disodium phosphate, anhydrous, trehalose dihydrate, mannitol (E421), polysorbate 80, water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

Multipack: 12 pens (3 cartons of 4 pens/4 needles)
Do not sell separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet.
Subcutaneous use
Once weekly.

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

Single use only.
Discard pen after use.
Read package leaflet
Reconstitution time
After mixing, wait 30 minutes before injection

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store refrigerated at 2°C to 8°C.
Do not freeze.

A single carton of 4 pens and 4 needles may be stored at room temperature, not exceeding 30°C, for no more than a total of 4 weeks prior to use. Remaining cartons must be stored at 2°C to 8°C until required.

Use within 8 hours of reconstitution.
Use immediately after needle is attached.

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**

GlaxoSmithKline Trading Services Limited
Currabinny
Carrigaline
County Cork
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/908/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE**16. INFORMATION IN BRAILLE**

eperzan 50

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:

SN:

NN:

Medicinal product no longer authorised

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

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

Eperzan 30 mg powder and solvent for solution for injection
albiglutide
Subcutaneous use
Once weekly

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

30 mg

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

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

Eperzan 50 mg powder and solvent for solution for injection
albiglutide
Subcutaneous use
Once weekly

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

50 mg

6. OTHER

Medicinal product no longer authorised

Medicinal product no longer authorised

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Eperzan 30 mg powder and solvent for solution for injection

Albiglutide

- ▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking 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 or pharmacist.
- 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, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

- 1. What Eperzan is and what it is used for**
- 2. What you need to know before you take Eperzan**
- 3. How to take Eperzan**
- 4. Possible side effects**
- 5. How to store Eperzan**
- 6. Contents of the pack and other information**
Instructions for use of the pre-filled pen (*overleaf*)
Questions and answers about the instructions for use of the pre-filled pen

Read both sides of this leaflet

1. What Eperzan is and what it is used for

Eperzan contains the active ingredient albiglutide which belongs to a group of medicines called GLP-1 receptor agonists that are used to lower blood sugar (glucose) in adults with Type 2 diabetes.

You have Type 2 diabetes either:

- because your body does not make enough insulin to control the level of sugar in your blood
- or
- because your body is not able to use the insulin properly.

Eperzan helps your body to increase the production of insulin when your blood sugar is high.

Eperzan is used to help control your blood sugar, either:

- on its own if your blood sugar is not properly controlled by diet and exercise alone, and you can't take metformin (another diabetes medicine)
- or
- in combination with other diabetes medicines that are taken by mouth (such as metformin, or medicines known as sulphonylureas or thiazolidinediones), or with insulin.

It is very important that you continue to follow any diet and lifestyle advice from your doctor while taking Eperzan.

2. What you need to know before you use Eperzan

Don't use Eperzan:

- if you are **allergic** to albiglutide or any of the other ingredients of this medicine (listed in section 6).

If you think this applies to you, **don't use Eperzan** until you have checked with your doctor, nurse or pharmacist.

Warnings and precautions

Talk to your doctor, nurse or pharmacist before using Eperzan:

- if you have **Type 1** (insulin-dependent) **diabetes** or **ketoacidosis** (a very serious complication of diabetes which happens when your body is not able to break down glucose because there is not enough insulin), this medicine will not be right for you. Speak to your doctor about how to recognise the symptoms of ketoacidosis and **seek urgent medical treatment** if they occur.
- if you have ever had **pancreatitis** (inflammation of the pancreas). Your doctor will decide if you can use Eperzan, and will explain the symptoms of pancreatitis (see 'Conditions you need to look out for' in section 4).
- if you are taking a **sulphonylurea** or **insulin** for your diabetes, as low blood sugar (hypoglycaemia) can occur. Your doctor may need to change your dose of these other medicines to reduce this risk. (See 'Very common side effects' in section 4 for signs of low blood sugar).
- if you have a serious problem with emptying your stomach (gastroparesis) or if you have **severe bowel disease** (severe gastrointestinal disease). Eperzan is not recommended if you have these conditions.
- When initiating treatment with albiglutide, you may experience fluid loss from vomiting, nausea, diarrhoea or dehydration. It is important to avoid dehydration by drinking plenty of fluids.

Check with your doctor, nurse or pharmacist before you use Eperzan if you think any of these apply to you.

Children and adolescents

It is not known if Eperzan is safe and effective in people under 18 years of age. Eperzan is not recommended for children and adolescents.

Other medicines and Eperzan

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, (see also earlier in section 2 'Warnings and precautions').

You should not take acarbose if you suffer from bowel obstruction.

Talk to your doctor if you are taking acarbose and Eperzan at the same time.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, if you think you may be pregnant, or are planning to have a baby, ask your doctor, nurse or pharmacist for advice before using this medicine. If there is a possibility that you could become pregnant, you must use effective contraception while using this medicine.

Pregnancy

Tell your doctor, nurse or pharmacist immediately if you become pregnant during treatment with Eperzan.

There is no information about the safety of Eperzan in pregnant women. Eperzan should not be used while you're pregnant.

If you are planning to have a baby, your doctor may decide to stop your treatment with Eperzan at least one month before you try to get pregnant. This is because it takes time for Eperzan to clear from your body.

Breast-feeding

If you are breast-feeding you must check with your doctor before you use Eperzan. It is not known if Eperzan passes into your breast milk. You and your doctor should decide whether you will use Eperzan or breast-feed. You should not do both.

Fertility

For both men and women, it is not known if Eperzan could affect your fertility.

Driving and using machines

Eperzan has no or negligible influence on your ability to drive or use machines. However, if you take Eperzan with sulphonylurea or insulin, you may get low blood sugar (hypoglycaemia). This can make it difficult to concentrate and make you dizzy or sleepy. If this happens, don't drive or use machines.

Sodium content

This medicine contains less than 1 mmol sodium (23 mg) per 0.5 ml dose, so is essentially 'sodium free'.

3. How to use Eperzan

Always use this medicine exactly as your doctor, nurse or pharmacist has told you. Check with your doctor, nurse or pharmacist if you are not sure.

The recommended dose is 30 mg once a week, injected on the same day each week. Your doctor may increase your dose to 50 mg once weekly if your blood sugar is not controlled by the 30 mg dose. If necessary you can change the day of the week on which you use Eperzan, as long as it is at least 4 days since your last dose.

You can use Eperzan at any time of day, with or without meals.

Eperzan comes in a pen injector that you can inject yourself. Talk to your doctor, nurse or pharmacist about how to inject Eperzan the right way. You inject Eperzan under your skin in your stomach area, upper leg (thigh) or in the back of your upper arm. You can inject the same area of your body each week, but don't inject in exactly the same place every time.

Eperzan must not be injected into a vein (intravenously) or into a muscle (intramuscularly).

The pen injector contains powder and water which you need to mix before you can use it. After section 6 of this leaflet there are **Instructions For Use** giving you step-by-step instructions on how to mix your medicine and how to inject it. If you have questions or do not understand how to use your pen, talk to your doctor, nurse or pharmacist.

Never mix insulin and Eperzan together. If you need to give yourself both at the same time, use two separate injections. You may give both injections in the same body area (for example, your stomach area), but you should not give the injections very close together.

If you use more Eperzan than you should

If you use too much Eperzan, contact a doctor or pharmacist for advice. If possible show them the pack, or this leaflet. You may feel very sick (severe nausea), be sick (vomit), or get a headache.

If you forget to use Eperzan

If you miss a dose, inject the next dose as soon as possible within 3 days after the missed dose. After that, you can go back to having your injection on the usual day. If it is more than 3 days since you missed your dose, wait until your usually scheduled day for your next injection. Do not inject a double dose to make up for a forgotten dose.

If you stop using Eperzan

Use Eperzan for as long as your doctor recommends. If you stop using Eperzan, your blood sugar levels may be affected. Don't stop unless your doctor advises you to.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Conditions you need to look out for:

Risk of acute pancreatitis (an inflamed pancreas)

Pancreatitis has been reported as an uncommon side effect. It may affect up to 1 in 100 people. Pancreatitis can be severe and life-threatening.

If you get:

- **severe stomach (abdominal) pain that does not go away**, this can be a symptom of pancreatitis. The pain may happen with or without you being sick (vomiting). You may feel the pain going from your front (abdomen) through to your back.

Stop taking Eperzan and talk to your doctor straight away

Severe allergic reactions

These are rare in people taking Eperzan (may affect up to 1 in 1000 people).

Signs include:

- raised and itchy rashes,
- swelling, sometimes of the face, mouth or throat, causing difficulty in breathing.

Get medical help immediately if you get these symptoms. **Stop taking Eperzan.**

Other side effects reported with Eperzan

Very common: may affect **more than 1 in 10 people:**

- low blood sugar (hypoglycaemia) when you use Eperzan in combination with insulin or sulphonylurea. The warning signs of low blood sugar may include cold sweat, cool pale skin, headache, feeling drowsy, weakness, dizziness, feeling confused or irritable, feeling hungry, fast heart beat and feeling jittery. Your doctor will tell you what to do if you get low blood sugar.
- diarrhoea
- feeling sick (nausea)
- rash, redness or itching of the skin where you have injected Eperzan

Common: may affect **up to 1 in 10 people:**

- chest infection (pneumonia)
- low blood sugar (hypoglycaemia) if you use Eperzan on its own or in combination with metformin or pioglitazone
- irregular heartbeat

- being sick (vomiting)
- constipation
- indigestion
- heartburn (gastro-oesophageal reflux)

Uncommon: may affect **up to 1 in 100 people**:

- bowel obstruction

Rare: may affect **up to 1 in 1000 people**:

- allergic reaction (hypersensitivity); this includes symptoms such as local or widespread rash, redness or itching of the skin and difficulty breathing (also see ‘Conditions you need to look out for’ at the beginning of this section)

In addition some other side effects have been reported (frequency not known, cannot be estimated from the available data):

- reduced appetite

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 Eperzan

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 pen and the carton after ‘EXP’. The expiry date refers to the last day of that month.

Store pens and needles in the original carton until use.

Store in a refrigerator (between 2°C and 8°C). Do not freeze. The medicine can be stored at room temperature (less than 30°C) for no more than a total of 4 weeks before use. After this time, pens should be used or thrown away.

- After the powder and liquid are mixed within the pen, the pen should be used within 8 hours.
- Use the pen immediately after you have attached and primed the needle otherwise the solution can dry up inside the needle and block it.

Use each pen only once.

After you have used the pen, do not remove the needle. Dispose of the pen as instructed by your doctor, pharmacist or nurse.

Do not throw away any medicines via wastewater or household waste. 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 Eperzan contains

- The active substance is albiglutide.
Each 30 mg pen delivers 30 mg albiglutide in a volume of 0.5 ml.
- The solvent is water for injections.
- The other ingredients are: sodium dihydrogen phosphate monohydrate and disodium phosphate, anhydrous (see section 2 under 'Sodium content'), trehalose dihydrate, mannitol, polysorbate 80.

What Eperzan looks like and contents of the pack

Eperzan is supplied as a pen for self injection. Each pen contains a white to yellow powder and a colourless solvent in separate compartments. A needle is provided with each pen.

Pens are supplied in packs of 4 pens and 4 needles and multipacks comprising 3 packs, each containing 4 pens and 4 needles.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

GlaxoSmithKline Trading Services Limited, Currabinny, Carrigaline, County Cork, Ireland

Name and address of the manufacturer responsible for batch release:

Glaxo Operations UK Limited (Trading as Glaxo Wellcome Operations)
Harmire Road
Barnard Castle
Durham
DL12 8DT
United Kingdom

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Luxembourg/Luxemburg

GlaxoSmithKline Pharmaceuticals s.a./n.v.
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customercontactuk@gsk.com

Lietuva

GlaxoSmithKline Lietuva UAB

Tel: + 370 5 264 90 00

info.lt@gsk.com

This leaflet was last revised in <{MM/YYYY}>

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:

<http://www.ema.europa.eu>

Medicinal product no longer authorised

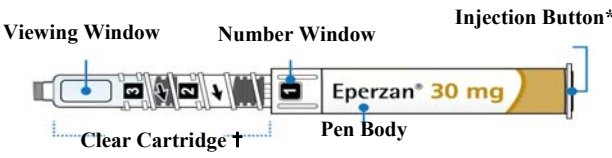
INSTRUCTIONS FOR USE

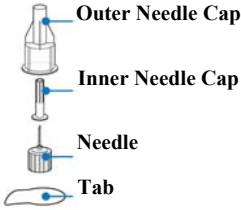


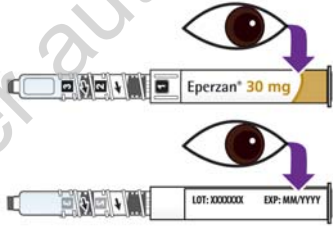
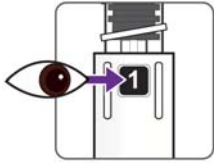
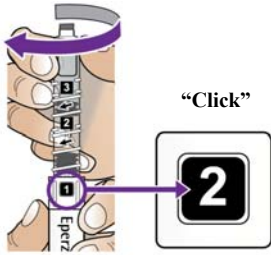
Once weekly Eperzan pen 30 mg




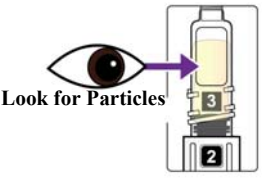
Read all of this leaflet carefully before you start taking this medicine, as well as all the instructions including the Pen Storage and Important Warnings.

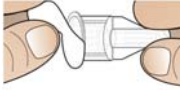
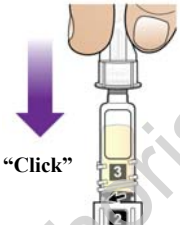

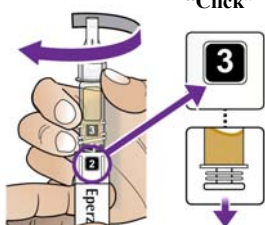
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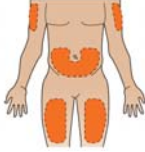
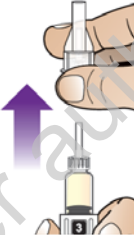
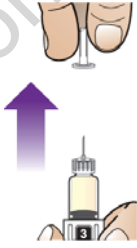

This medicine is injected once a week. The pen has the medicine powder in one compartment and the water in another compartment. You will mix them together by twisting the pen. Each pen is used to deliver one dose. A pen cannot be re-used.

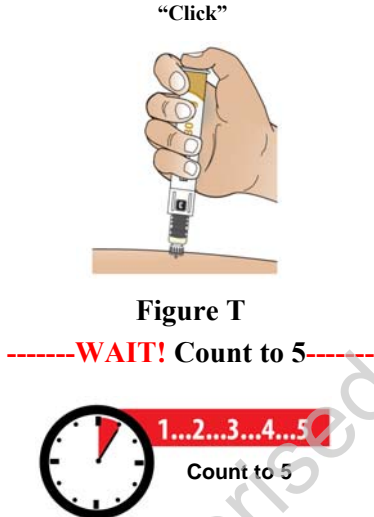
Pen storage	
<ul style="list-style-type: none"> • Store your pens at room temperature, not to exceed 30°C, for up to 4 weeks. Always store in the box. • If a box of pens will be stored for more than 4 weeks, keep them refrigerated (2°C to 8°C). • If stored in the refrigerator, allow the pen to sit at room temperature for 15 minutes before starting Step 1. • DO NOT allow the pen to freeze. Throw away the pen if frozen. 	
Important warnings	
<ul style="list-style-type: none"> • DO NOT attach needle until instructed in Step 5. • DO NOT reuse needles, recap needles, or remove used needles from the pen. Throw out the pen in a container for pen disposal right away after injecting, as shown in Step 9. • Throw away the pen if leaking or jammed. • Keep your pen out of the sight and reach of children 	
<p>For each injection, gather the following items:</p> <ul style="list-style-type: none"> • A new pen (Figure A). • A new needle (Figure B). • A clean empty cup (Figure C). • A clock or timer (Figure C). • A container for pen disposal. <p><i>The cup, timer and container are not provided in the pack.</i></p>	<p style="text-align: center;">Pen</p>  <p style="text-align: center;">Figure A</p> <p>* Injection Button is inside the pen until the pen is ready for injection.</p> <p>† The numbers on the clear cartridge represent stages of preparation for your medicine.</p>

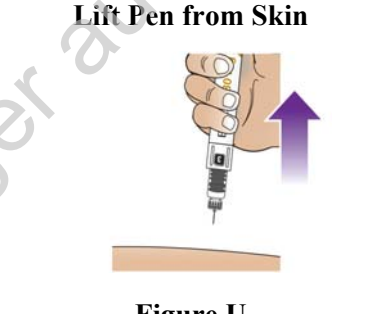
<p style="text-align: center;">Pen Needle</p>  <p style="text-align: center;">Figure B</p>	<p style="text-align: center;">Other Supplies Needed</p> <p style="text-align: center;">Clean Empty Cup Clock/Timer</p>  <p style="text-align: center;">Figure C</p>
<p>Step 1 Check Pen</p>	
<p>1a Wash your hands (Figure D).</p>	<p style="text-align: center;">Wash Hands and Check Pen</p>  <p style="text-align: center;">Figure D</p>
<p>1b Check dosage and expiration date on pen (Figure E).</p> <p>DO NOT use if the pen is expired or shows the incorrect dose.</p>	 <p style="text-align: center;">Figure E</p>
<p>1c Check that the pen has a [1] in the number window (Figure F).</p> <p>DO NOT use if the [1] is not showing.</p>	 <p style="text-align: center;">Figure F</p>
<p>Step 2 Mix Medicine</p>	
<p>2a Hold pen body with clear cartridge pointing up so that you can see the [1] in the window.</p> <p>Twist clear cartridge several times in the direction of the arrow until you feel/hear the pen “click” into place. You should see the [2] in the number window (Figure G). This will mix the medicine powder and liquid.</p>	<p style="text-align: center;">Hold Upright & Twist to 2</p> <p style="text-align: center;">Twist Pen to Mix Medicine</p>  <p style="text-align: center;">Figure G</p>

<p>2b Slowly and gently rock the pen side-to-side 5 times (like a windscreen wiper) (Figure H). This will help mix the medicine.</p> <p>DO NOT shake the pen to avoid foaming, which may affect your dose.</p>	<p style="text-align: center;">Rock Pen</p> <p style="text-align: center;">5 Times</p>  <p style="text-align: center;">Figure H</p>
<p>Step 3 Wait 15 minutes</p>	
<p>3 Place pen into cup with clear cartridge pointing up (Figure I).</p> <p>Set a timer for 15 minutes. You must wait 15 minutes for the medicine to dissolve before continuing.</p>	<p style="text-align: center;">Wait 15 Minutes</p>  <p style="text-align: center;">Figure I</p>
<p>IMPORTANT: Make sure you have waited 15 minutes before continuing onto step 4. This is to make sure the medicine has dissolved.</p>	
<p>Step 4 Rock Pen and Check Medicine</p>	
<p>4a Again, slowly and gently rock the pen side-to-side side 5 times (like a windscreen wiper) (Figure J).</p> <p>DO NOT shake the pen to avoid foaming, which may affect your dose.</p>	<p style="text-align: center;">Rock Pen Again</p> <p style="text-align: center;">5 Times</p>  <p style="text-align: center;">Figure J</p>
<p>4b Check medicine through the viewing window. It should be yellow and see-through, without any particles (Figure K).</p> <p>DO NOT use pen if there are still particles in the liquid.</p> <p>It is okay to have large air bubbles on top of the liquid. These are removed in step 6.</p>	<p style="text-align: center;">Check Medicine</p>  <p style="text-align: center;">Figure K</p>
<p>IMPORTANT: Make sure you do not twist the pen to [3] until you have attached the needle in step 5. The needle must be attached to allow air to escape while turning the cartridge from [2] to [3] in the number window.</p>	

Step 5 Attach needle	
<p>5a Peel tab from outer needle cap (Figure L).</p> <p>Hold the pen upright before attaching the needle.</p>	<p>Peel Off Tab</p>  <p>Figure L</p>
<p>5b Push needle straight down onto the clear cartridge until you hear a “click” and feel the needle “snap” into place. This means the needle is attached (Figure M).</p> <p>DO NOT attach at an angle. DO NOT attach by screwing the needle on</p>	<p>Attach Needle</p> <p>Push Straight Down</p>  <p>Figure M</p>
<p>IMPORTANT: After the needle has been securely attached, make sure to complete the remaining steps of the injection procedure right away. Waiting may result in a blocked or clogged needle.</p>	
Step 6 Remove Air from Cartridge	
<p>6a With needle pointing up, gently tap the clear cartridge 2-3 times to bring large air bubbles to the top (Figure N). Small air bubbles are okay and do not need to rise to the top.</p>	<p>Tap Pen Cartridge</p>  <p>Figure N</p>
<p>6b Hold pen upright, slowly twist the clear cartridge several times in the direction of the arrow until you feel/hear the pen “click” and you see the [3] in the number window (Figure O). This removes the large air bubbles.</p> <p>The white injection button will also pop out from the bottom of the pen.</p> <p>DO NOT use the pen if the injection button does not pop out.</p>	<p>Hold Upright and Twist to 3</p> <p>Twist Pen to Prime the Needle</p> <p>“Click”</p>  <p>Figure O</p>
<p>IMPORTANT: You may hear a “click” when you first start twisting the cartridge from [2] to [3]. Keep twisting until you see [3] in the window.</p>	

Step 7 Prepare for injection	
<p>7a Choose your injection site (Figure P). You can use your abdomen, thigh, or upper arm.</p>	<p>Choose Injection Site</p>  <p>Figure P</p>
IMPORTANT: There are two needle caps, an outer and inner needle cap.	
<p>7b While holding the pen in the air, remove outer needle cap (Figure Q) and inner needle cap (Figure R). A few drops of liquid may come out of the needle. This is normal.</p> <p>DO NOT rest the back of the device (where the injection button is exposed) on a flat surface while removing needle caps.</p> <p>7c Place both needle caps into a container for pen disposal.</p>	<p>Pull off Needle Caps and Discard</p> <p>Step 1 Remove Outer Needle Cap</p>  <p>Figure Q</p> <p>Step 2 Remove Inner Needle Cap</p>  <p>Figure R</p>
Step 8 Deliver injection	
<p>8a Insert needle straight into the injection site.</p> <p>8b Press the injection button down slowly and steadily until you hear a “click” (Figure S).</p> <p>The slower you press, the easier the injection will feel.</p>	<p>Insert, Push Button, & Wait</p> <p>Push Down Slowly</p>  <p>Figure S</p>

<p>8c After hearing the “click,” continue holding down the injection button and slowly count to 5 to deliver the full dose of medicine (Figure T).</p>	<p style="text-align: center;">“Click”</p>  <p style="text-align: center;">Figure T</p> <p style="text-align: center;">-----WAIT! Count to 5-----</p> <p style="text-align: center;">Count to 5</p>
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<p>Step 9 Dispose pen</p>	
<p>9a Pull the needle out of your skin (Figure U). DO NOT recap the needle or take the needle off the pen.</p> <p>9b Immediately put the pen (with needle attached) in a container for pen disposal. Do not dispose of the used pen in the household waste. Dispose of it as your doctor or pharmacist has instructed.</p>	<p style="text-align: center;">Lift Pen from Skin</p>  <p style="text-align: center;">Figure U</p>

<p>QUESTIONS AND ANSWERS</p>
<p>MIXING YOUR MEDICINE AND WAITING 15 MINUTES (STEPS 2-3)</p>
<p>➤ What if I do not wait 15 minutes after turning the pen to the Number 2? If you do not wait the full 15 minutes the medicine may not be mixed with the water the right way. This can result in particles floating in the clear cartridge, not getting your full dose, or a blocked needle. Waiting the full 15 minutes ensures that the medicine powder and water are mixed the right way, even though it may look like it is mixed sooner.</p>
<p>➤ What if I leave my pen for more than 15 minutes after turning the pen to the Number 2 (Step 2)? As long as the needle has not been attached, the pen can be used for up to 8 hours from the time Step 2 was started. If it has been more than 8 hours since the medicine was mixed in Step 2, throw away the pen and use another pen. If you have attached the needle, EPERZAN should be used right away.</p>

ATTACHING NEEDLE, REMOVING AIR FROM CARTRIDGE, AND PREPARING PEN FOR INJECTION (STEPS 5-7)

- **What if I leave my pen with the needle attached (Step 5), and then come back to finish the next step much later?**

This can cause your needle to block, you should continue from **Step 5** to **Step 6** right away.

- **What if I do not attach the needle at Step 5?**

If the needle is attached **before Step 5**, some of the medicine may be lost during mixing.

DO NOT attach the needle before **Step 5**.

DO NOT turn the cartridge to **[3]** (Step 6b) before attaching the needle (Step 5).

The needle must be attached to allow air to escape while turning the cartridge from **[2]** to **[3]** in the number window.

- **What if I do not attach the needle as instructed?**

If you do not push the needle on completely, the pen may jam or leak.

If the pen is jammed or leaking, throw it away and use another pen.

- **What if I do not hear the “click” when the [2] or when the [3] is moved into the Number Window?**

If you do not hear a “click” when the **[2]** or when the **[3]** is moved into the number window, you may not have the number fully centered in the window. **Twist the clear cartridge** slightly in the direction of the arrows (clockwise) to complete the “click” and center the number in the window.

If you are unable to turn to position **[3]**, throw it away and use another pen.

REMOVING BOTH NEEDLE CAPS AND INJECTING YOUR MEDICINE (STEPS 7-8)

- **After I turn the pen to Number 3 (Step 6), there are still some small air bubbles remaining. Can I still use the pen?**

Seeing small air bubbles remaining is normal and you can still use the pen.

- **After I give my medicine, there is some liquid still seen in the clear cartridge.**

This is normal. If you have heard and felt the injection button “click” and slowly counted to **5** before pulling the needle out of your skin, you should have received the full dose of your medicine.

Package leaflet: Information for the patient

Eperzan 50 mg powder and solvent for solution for injection

Albiglutide

- ▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking 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 or pharmacist.
- 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, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Eperzan is and what it is used for
 2. What you need to know before you take Eperzan
 3. How to take Eperzan
 4. Possible side effects
 5. How to store Eperzan
 6. Contents of the pack and other information
- Instructions for use of the pre-filled pen (*overleaf*)
Questions and answers about the instructions for use of the pre-filled pen

Read both sides of this leaflet

1. What Eperzan is and what it is used for

Eperzan contains the active ingredient albiglutide which belongs to a group of medicines called GLP-1 receptor agonists that are used to lower blood sugar (glucose) in adults with Type 2 diabetes.

You have Type 2 diabetes either:

- because your body does not make enough insulin to control the level of sugar in your blood
- or
- because your body is not able to use the insulin properly.

Eperzan helps your body to increase the production of insulin when your blood sugar is high.

Eperzan is used to help control your blood sugar, either:

- on its own if your blood sugar is not properly controlled by diet and exercise alone, and you can't take metformin (another diabetes medicine)

or

- in combination with other diabetes medicines that are taken by mouth (such as metformin, or medicines known as sulphonylureas or thiazolidinediones), or with insulin.

It is very important that you continue to follow any diet and lifestyle advice from your doctor while taking Eperzan.

2. What you need to know before you use Eperzan

Don't use Eperzan:

- if you are **allergic** to albiglutide or any of the other ingredients of this medicine (listed in section 6).

If you think this applies to you, **don't use Eperzan** until you have checked with your doctor, nurse or pharmacist.

Warnings and precautions

Talk to your doctor, nurse or pharmacist before using Eperzan:

- if you have **Type 1** (insulin-dependent) **diabetes** or **ketoacidosis** (a very serious complication of diabetes which happens when your body is not able to break down glucose because there is not enough insulin), this medicine will not be right for you. Speak to your doctor about how to recognise the symptoms of ketoacidosis and **seek urgent medical treatment** if they occur.
- if you have ever had **pancreatitis** (inflammation of the pancreas). Your doctor will decide if you can use Eperzan, and will explain the symptoms of pancreatitis (see 'Conditions you need to look out for' in section 4).
- if you are taking a **sulphonylurea** or **insulin** for your diabetes, as low blood sugar (hypoglycaemia) can occur. Your doctor may need to change your dose of these other medicines to reduce this risk. (See 'Very common side effects' in section 4 for signs of low blood sugar).
- if you have a serious problem with emptying your stomach (gastroparesis) or if you have **severe bowel disease** (severe gastrointestinal disease). Eperzan is not recommended if you have these conditions.
- When initiating treatment with albiglutide, you may experience fluid loss from vomiting, nausea, diarrhoea or dehydration. It is important to avoid dehydration by drinking plenty of fluids.

Check with your doctor, nurse or pharmacist before you use Eperzan if you think any of these apply to you.

Children and adolescents

It is not known if Eperzan is safe and effective in people under 18 years of age. Eperzan is not recommended for children and adolescents.

Other medicines and Eperzan

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, (see also earlier in section 2 'Warnings and precautions').

You should not take acarbose if you suffer from bowel obstruction.

Talk to your doctor if you are taking acarbose and Eperzan at the same time.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, if you think you may be pregnant, or are planning to have a baby, ask your doctor, nurse or pharmacist for advice before using this medicine. If there is a possibility that you could become pregnant, you must use effective contraception while using this medicine.

Pregnancy

Tell your doctor, nurse or pharmacist immediately if you become pregnant during treatment with Eperzan.

There is no information about the safety of Eperzan in pregnant women. Eperzan should not be used while you're pregnant.

If you are planning to have a baby, your doctor may decide to stop your treatment with Eperzan at least one month before you try to get pregnant. This is because it takes time for Eperzan to clear from your body.

Breast-feeding

If you are breast-feeding you must check with your doctor before you use Eperzan. It is not known if Eperzan passes into your breast milk. You and your doctor should decide whether you will use Eperzan or breast-feed. You should not do both.

Fertility

For both men and women, it is not known if Eperzan could affect your fertility.

Driving and using machines

Eperzan has no or negligible influence on your ability to drive or use machines. However, if you take Eperzan with sulphonylurea or insulin, you may get low blood sugar (hypoglycaemia). This can make it difficult to concentrate and make you dizzy or sleepy. If this happens, don't drive or use machines.

Sodium content

This medicine contains less than 1 mmol sodium (23 mg) per 0.5 ml dose, so is essentially 'sodium free'.

3. How to use Eperzan

Always use this medicine exactly as your doctor, nurse or pharmacist has told you. Check with your doctor, nurse or pharmacist if you are not sure.

The recommended dose is 30 mg once a week, injected on the same day each week. Your doctor may increase your dose to 50 mg once weekly if your blood sugar is not controlled by the 30 mg dose. If necessary you can change the day of the week on which you use Eperzan, as long as it is at least 4 days since your last dose.

You can use Eperzan at any time of day, with or without meals.

Eperzan comes in a pen injector that you can inject yourself. Talk to your doctor, nurse or pharmacist about how to inject Eperzan the right way. You inject Eperzan under your skin in your stomach area, upper leg (thigh) or in the back of your upper arm. You can inject the same area of your body each week, but don't inject in exactly the same place every time.

Eperzan must not be injected into a vein (intravenously) or into a muscle (intramuscularly).

The pen injector contains powder and water which you need to mix before you can use it. After section 6 of this leaflet there are **Instructions For Use** giving you step-by-step instructions on how to mix your medicine and how to inject it. If you have questions or do not understand how to use your pen, talk to your doctor, nurse or pharmacist.

Never mix insulin and Eperzan together. If you need to give yourself both at the same time, use two separate injections. You may give both injections in the same body area (for example, your stomach area), but you should not give the injections very close together.

If you use more Eperzan than you should

If you use too much Eperzan, contact a doctor or pharmacist for advice. If possible show them the pack, or this leaflet. You may feel very sick (severe nausea), be sick (vomit), or get a headache.

If you forget to use Eperzan

If you miss a dose, inject the next dose as soon as possible within 3 days after the missed dose. After that, you can go back to having your injection on the usual day. If it is more than 3 days since you missed your dose, wait until your usually scheduled day for your next injection. Do not inject a double dose to make up for a forgotten dose.

If you stop using Eperzan

Use Eperzan for as long as your doctor recommends. If you stop using Eperzan, your blood sugar levels may be affected. Don't stop unless your doctor advises you to.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Conditions you need to look out for:

Risk of acute pancreatitis (an inflamed pancreas)

Pancreatitis has been reported as an uncommon side effect. It may affect up to 1 in 100 people. Pancreatitis can be severe and life-threatening.

If you get:

- **severe stomach (abdominal) pain that does not go away**, this can be a symptom of pancreatitis. The pain may happen with or without you being sick (vomiting). You may feel the pain going from your front (abdomen) through to your back.

Stop taking Eperzan and talk to your doctor straight away

Severe allergic reactions

These are rare in people taking Eperzan (may affect up to 1 in 1000 people).

Signs include:

- raised and itchy rashes,
- swelling, sometimes of the face, mouth or throat, causing difficulty in breathing.

Get medical help immediately if you get these symptoms. Stop taking Eperzan.

Other side effects reported with Eperzan

Very common: may affect **more than 1 in 10 people:**

- low blood sugar (hypoglycaemia) when you use Eperzan in combination with insulin or sulphonylurea. The warning signs of low blood sugar may include cold sweat, cool pale skin, headache, feeling drowsy, weakness, dizziness, feeling confused or irritable, feeling hungry, fast heart beat and feeling jittery. Your doctor will tell you what to do if you get low blood sugar.
- diarrhoea
- feeling sick (nausea)
- rash, redness or itching of the skin where you have injected Eperzan

Common: may affect **up to 1 in 10 people:**

- chest infection (pneumonia)
- low blood sugar (hypoglycaemia) if you use Eperzan on its own or in combination with metformin or pioglitazone
- irregular heartbeat
- being sick (vomiting)
- constipation
- indigestion
- heartburn (gastro-oesophageal reflux)

Uncommon: may affect **up to 1 in 100 people:**

- bowel obstruction

Rare: may affect **up to 1 in 1000 people:**

- allergic reaction (hypersensitivity) ; this includes symptoms such as local or widespread rash, redness or itching of the skin and difficulty breathing (also see ‘Conditions you need to look out for’ at the beginning of this section)

In addition some other side effects have been reported (frequency not known, cannot be estimated from the available data):

- reduced appetite

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 Eperzan

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 pen and the carton after ‘EXP’. The expiry date refers to the last day of that month.

Store pens and needles in the original carton until use.

Store in a refrigerator (between 2°C and 8°C). Do not freeze. The medicine can be stored at room temperature (less than 30°C) for no more than a total of 4 weeks before use. After this time, pens should be used or thrown away.

- After the powder and liquid are mixed within the pen, the pen should be used within 8 hours.
- Use the pen immediately after you have attached and primed the needle otherwise the solution can dry up inside the needle and block it.

Use each pen only once.

After you have used the pen, do not remove the needle. Dispose of the pen as instructed by your doctor, pharmacist or nurse.

Do not throw away any medicines via wastewater or household waste. 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 Eperzan contains

- The active substance is albiglutide.
Each 50 mg pen delivers 50 mg albiglutide in a volume of 0.5 ml.
- The solvent is water for injections.
- The other ingredients are: sodium dihydrogen phosphate monohydrate and disodium phosphate, anhydrous (see section 2 under 'Sodium content'), trehalose dihydrate, mannitol, polysorbate 80.

What Eperzan looks like and contents of the pack

Eperzan is supplied as a pen for self injection. Each pen contains a white to yellow powder and a colourless solvent in separate compartments. A needle is provided with each pen.

Pens are supplied in packs of 4 pens and 4 needles and multipacks comprising 3 packs, each containing 4 pens and 4 needles.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

GlaxoSmithKline Trading Services Limited, Currabinny, Carrigaline, County Cork, Ireland

Name and address of the manufacturer responsible for batch release:

Glaxo Operations UK Limited (Trading as Glaxo Wellcome Operations)
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Durham
DL12 8DT
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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 <{MM/YYYY}>

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:

<http://www.ema.europa.eu>.

Medicinal product no longer authorised

INSTRUCTIONS FOR USE

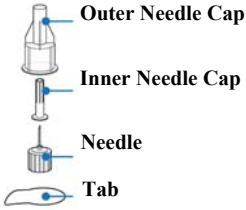


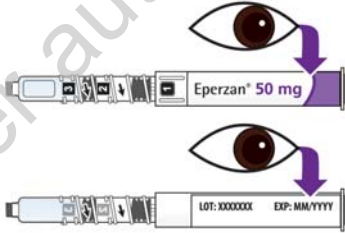
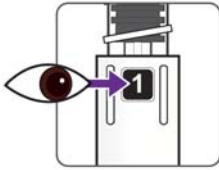
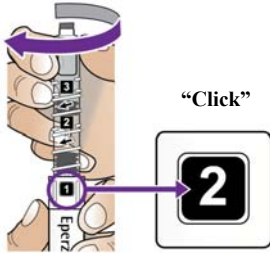
Once weekly Eperzan pen 50 mg




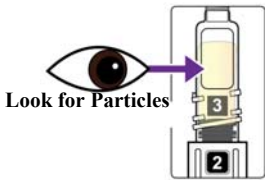
Read all of this leaflet carefully before you start taking this medicine, as well as all the instructions including the Pen Storage and Important Warnings.

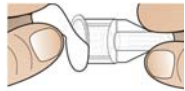


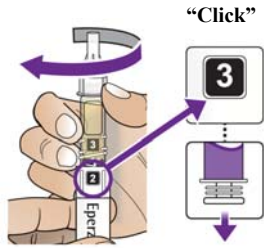
Follow the steps below in the exact order they are presented.

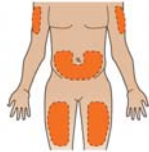
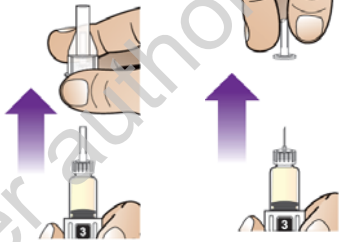

This medicine is injected once a week. The pen has the medicine powder in one compartment and the water in another compartment. You will mix them together by twisting the pen. Each pen is used to deliver one dose. A pen cannot be re-used.

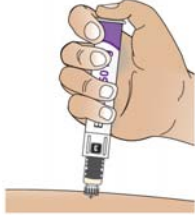

Pen storage	
<ul style="list-style-type: none"> • Store your pens at room temperature, not to exceed 30°C, for up to 4 weeks. Always store in the box. • If a box of pens will be stored for more than 4 weeks, keep them refrigerated (2°C to 8°C). • If stored in the refrigerator, allow the pen to sit at room temperature for 15 minutes before starting Step 1. • DO NOT allow the pen to freeze. Throw away the pen if frozen. 	
Important warnings	
<ul style="list-style-type: none"> • DO NOT attach needle until instructed in Step 5. • DO NOT reuse needles, recap needles, or remove used needles from the pen. Throw out the pen in a container for pen disposal right away after injecting, as shown in Step 9. • Throw away the pen if leaking or jammed. • Keep your pen out of the sight and reach of children 	
<p>For each injection, gather the following items:</p> <ul style="list-style-type: none"> • A new pen (Figure A). • A new needle (Figure B). • A clean empty cup (Figure C). • A clock or timer (Figure C). • A container for pen disposal. <p><i>The cup, timer and container are not provided in the pack.</i></p>	<div style="text-align: center;"> <p>Pen</p> <p>Viewing Window Number Window Injection Button*</p> <p>Clear Cartridge † Pen Body</p> <p>Figure A</p> <p>* Injection Button is inside the pen until the pen is ready for injection.</p> <p>† The numbers on the clear cartridge represent stages of preparation for your medicine.</p> </div>

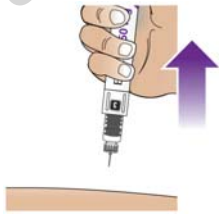
<p style="text-align: center;">Pen Needle</p>  <p style="text-align: center;">Figure B</p>	<p style="text-align: center;">Other Supplies Needed</p> <p style="text-align: center;">Clean Empty Cup Clock/Timer</p>  <p style="text-align: center;">Figure C</p>
<p>Step 1 Check pen</p>	
<p>1a Wash your hands (Figure D).</p>	<p style="text-align: center;">Wash Hands and Check Pen</p>  <p style="text-align: center;">Figure D</p>
<p>1b Check dosage and expiration date on pen (Figure E).</p> <p>DO NOT use if the pen is expired or shows the incorrect dose.</p>	 <p style="text-align: center;">Figure E</p>
<p>1c Check that the pen has a [1] in the number window (Figure F).</p> <p>DO NOT use if the [1] is not showing.</p>	 <p style="text-align: center;">Figure F</p>
<p>Step 2 Mix Medicine</p>	
<p>2a Hold pen body with clear cartridge pointing up so that you can see the [1] in the window.</p> <p>Twist clear cartridge several times in the direction of the arrow until you feel/hear the pen “click” into place. You should see the [2] in the number window (Figure G). This will mix the medicine powder and liquid.</p>	<p style="text-align: center;">Hold Upright & Twist to 2</p> <p style="text-align: center;">Twist Pen to Mix Medicine</p>  <p style="text-align: center;">Figure G</p>

<p>2b Slowly and gently rock the pen side-to-side 5 times (like a windscreen wiper) (Figure H). This will help mix the medicine.</p> <p>DO NOT shake the pen to avoid foaming, which may affect your dose.</p>	<p style="text-align: center;">Rock Pen</p> <p style="text-align: center;">5 Times</p>  <p style="text-align: center;">Figure H</p>
<p>Step 3 Wait 30 minutes</p>	
<p>3 Place pen into cup with clear cartridge pointing up (Figure I).</p> <p>Set a timer for 30 minutes. You must wait 30 minutes for the medicine to dissolve before continuing.</p>	<p style="text-align: center;">Wait 30 Minutes</p>  <p style="text-align: center;">Figure I</p>
<p>IMPORTANT: Make sure you have waited 30 minutes before continuing onto step 4. This is to make sure the medicine has dissolved.</p>	
<p>Step 4 Rock pen and check medicine</p>	
<p>4a Again, slowly and gently rock the pen side-to-side side 5 times (like a windscreen wiper) (Figure J).</p> <p>DO NOT shake the pen to avoid foaming, which may affect your dose.</p>	<p style="text-align: center;">Rock Pen Again</p> <p style="text-align: center;">5 Times</p>  <p style="text-align: center;">Figure J</p>
<p>4b Check medicine through the viewing window. It should be yellow and see-through, without any particles (Figure K).</p> <p>DO NOT use pen if there are still particles in the liquid.</p> <p>It is okay to have large air bubbles on top of the liquid. These are removed in step 6.</p>	<p style="text-align: center;">Check Medicine</p>  <p style="text-align: center;">Figure K</p>
<p>IMPORTANT: Make sure you do not twist the pen to [3] until you have attached the needle in step 5. The needle must be attached to allow air to escape while turning the cartridge from [2] to [3] in the number window.</p>	

Step 5 Attach needle	
<p>5a Peel tab from outer needle cap (Figure L).</p> <p>Hold the pen upright before attaching the needle.</p>	<p>Peel Off Tab</p>  <p>Figure L</p>
<p>5b Push needle straight down onto the clear cartridge until you hear a “click” and feel the needle “snap” into place. This means the needle is attached (Figure M).</p> <p>DO NOT attach at an angle. DO NOT attach by screwing the needle on</p>	<p>Attach Needle</p> <p>Push Straight Down</p>  <p>Figure M</p>
<p>IMPORTANT: After the needle has been securely attached, make sure to complete the remaining steps of the injection procedure right away. Waiting may result in a blocked or clogged needle.</p>	
Step 6 Remove air from cartridge	
<p>6a With needle pointing up, gently tap the clear cartridge 2-3 times to bring large air bubbles to the top (Figure N). Small air bubbles are okay and do not need to rise to the top.</p>	<p>Tap Pen Cartridge</p>  <p>Figure N</p>
<p>6b Hold pen upright, slowly twist the clear cartridge several times in the direction of the arrow until you feel/hear the pen “click” and you see the [3] in the number window (Figure O). This removes the large air bubbles.</p> <p>The white injection button will also pop out from the bottom of the pen.</p> <p>DO NOT use the pen if the injection button does not pop out.</p>	<p>Hold Upright and Twist to 3</p> <p>Twist Pen to Prime the Needle</p>  <p>Figure O</p>
<p>IMPORTANT: You may hear a “click” when you first start twisting the cartridge from [2] to [3]. Keep twisting until you see [3] in the window.</p>	

Step 7 Prepare for injection	
<p>7a Choose your injection site (Figure P). You can use your abdomen, thigh, or upper arm.</p>	<p>Choose Injection Site</p>  <p>Figure P</p>
<p>IMPORTANT: There are two needle caps, an outer and inner needle cap.</p>	
<p>7b While holding the pen in the air, remove outer needle cap (Figure Q) and inner needle cap (Figure R). A few drops of liquid may come out of the needle. This is normal.</p> <p>DO NOT rest the back of the device (where the injection button is exposed) on a flat surface while removing needle caps.</p> <p>7c Place both needle caps into a container for pen disposal.</p>	<p>Pull off Needle Caps and Discard</p> <p>Step 1 Remove Outer Needle Cap</p> <p>Step 2 Remove Inner Needle Cap</p>  <p>Figure Q Figure R</p>
Step 8 Deliver injection	
<p>8a Insert needle straight into the injection site.</p> <p>8b Press the injection button down slowly and steadily until you hear a “click” (Figure S).</p> <p>The slower you press, the easier the injection will feel.</p>	<p>Insert, Push Button, & Wait</p> <p>Push Down Slowly</p>  <p>Figure S</p>

<p>8c After hearing the “click,” continue holding down the injection button and slowly count to 5 to deliver the full dose of medicine (Figure T).</p>	<p style="text-align: center;">“Click”</p>  <p style="text-align: center;">Figure T</p> <p style="text-align: center;">-----WAIT! Count to 5-----</p> 
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<p>Step 9 Dispose pen</p>	
<p>9a Pull the needle out of your skin (Figure U). DO NOT recap the needle or take the needle off the pen.</p> <p>9b Immediately put the pen (with needle attached) in a container for pen disposal. Do not dispose of the used pen in the household waste. Dispose of it as your doctor or pharmacist has instructed.</p>	<p style="text-align: center;">Lift Pen from Skin</p>  <p style="text-align: center;">Figure U</p>

<p>QUESTIONS AND ANSWERS</p>
<p>MIXING YOUR MEDICINE AND WAITING 30 MINUTES (STEPS 2-3)</p>
<p>➤ What if I do not wait 30 minutes after turning the pen to the Number 2? If you do not wait the full 30 minutes the medicine may not be mixed with the water the right way. This can result in particles floating in the clear cartridge, not getting your full dose, or a blocked needle. Waiting the full 30 minutes ensures that the medicine powder and water are mixed the right way, even though it may look like it is mixed sooner.</p>
<p>➤ What if I leave my pen for more than 30 minutes after turning the pen to the Number 2 (Step 2)? As long as the needle has not been attached, the pen can be used for up to 8 hours from the time Step 2 was started. If it has been more than 8 hours since the medicine was mixed in Step 2, throw away the pen and use another pen. If you have attached the needle, EPERZAN should be used right away.</p>

ATTACHING NEEDLE, REMOVING AIR FROM CARTRIDGE, AND PREPARING PEN FOR INJECTION (STEPS 5-7)

- **What if I leave my pen with the needle attached (Step 5), and then come back to finish the next step much later?**

This can cause your needle to block, you should continue from **Step 5** to **Step 6** right away.

- **What if I do not attach the needle at Step 5?**

If the needle is attached **before Step 5**, some of the medicine may be lost during mixing.

DO NOT attach the needle before **Step 5**.

DO NOT turn the cartridge to **[3]** (Step 6b) before attaching the needle (Step 5).

The needle must be attached to allow air to escape while turning the cartridge from **[2]** to **[3]** in the number window.

- **What if I do not attach the needle as instructed?**

If you do not push the needle on completely, the pen may jam or leak.

If the pen is jammed or leaking, throw it away and use another pen.

- **What if I do not hear the “click” when the [2] or when the [3] is moved into the Number Window?**

If you do not hear a “click” when the **[2]** or when the **[3]** is moved into the number window, you may not have the number fully centered in the window. **Twist the clear cartridge** slightly in the direction of the arrows (clockwise) to complete the “click” and center the number in the window.

If you are unable to turn to position **[3]**, throw it away and use another pen.

REMOVING BOTH NEEDLE CAPS AND INJECTING YOUR MEDICINE (STEPS 7-8)

- **After I turn the pen to Number 3 (Step 6), there are still some small air bubbles remaining. Can I still use the pen?**

Seeing small air bubbles remaining is normal and you can still use the pen.

- **After I give my medicine, there is some liquid still seen in the clear cartridge.**

This is normal. If you have heard and felt the injection button “click” and slowly counted to **5** before pulling the needle out of your skin, you should have received the full dose of your medicine.