Firmagon

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification[1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
IAIN/0041	A.1 - Administrative change - Change in the name and/or address of the MAH	30/03/2022		SmPC, Annex II, Labelling and PL	
N/0040	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/02/2022		Labelling and PL	

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

II/0039/G	This was an application for a group of variations. Extension of indications to include: • Extension of indication to include treatment of high-risk localized and locally advanced hormone dependent prostate cancer in combination with radiotherapy. As a consequence, sections 4.1, 4.2, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. • Extension of indication to include treatment as neo-adjuvant prior to radiotherapy in patients with high-risk localised or locally advanced hormone dependent prostate cancer. As a consequence, sections 4.1, 4.2, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	16/09/2021	19/10/2021	SmPC and PL	Please refer to Scientific Discussion Firmagon-H-C-000986-II-0039G
II/0037	C.I.11.b update of Annex II to revise risk minimisation measures based on previous and a newly submitted study. As a consequence, the RMP is updated accordingly. The MAH took the occasion to transfer to GVP V revision 2 of the RMP, to align the	09/07/2020	21/06/2021	SmPC, Annex II, Labelling and PL	The amendments to the SmPC proposed by the MAH to be in accordance with the QRD template (V10.1) are consistent with the QRD recommendations, as well as the proposal to combine SmPC for different strengths of the same pharmaceutical form when SmPCs are completely

	PI to QRD template v.10.1 and propose combination of different strengths. C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required				identical, except for the few strength-specific details. Indeed, the SmPC of the starting dose (240mg) and the maintenance dose (80mg) are well combined into the same SmPC and are introduced into the section 1, 2, 4.2, 5.1, 6.5, 6.6 and 8 of the degarelix SmPC. Moreover, instructions for reconstitution and administration are well described for each dosage into the section 6.6 of the same degarelix SmPC.
II/0035	Submission of the FE 200486 CS39 Post Authorisation Safety Study (PASS) report; this was a Prospective Observational Safety Study in Patients with Advanced Prostate Cancer Treated with FIRMAGON (Degarelix) or a GnRH Agonist. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	13/02/2020	n/a		
IA/0036/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or	17/01/2020	n/a		

	manufacturer of a novel excipient A.7 - Administrative change - Deletion of manufacturing sites B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State				
PSUSA/944/201902	Periodic Safety Update EU Single assessment - degarelix	17/10/2019	16/12/2019		Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/944/201902.
N/0033	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	25/07/2018	16/12/2019	Labelling	
IA/0032	A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)	19/04/2018	n/a		
N/0031	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/04/2017	16/12/2019	PL	
IAIN/0030	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	15/09/2016	n/a		

PSUSA/944/201602	Periodic Safety Update EU Single assessment - degarelix	02/09/2016	n/a		PRAC Recommendation - maintenance
II/0028/G	This was an application for a group of variations. B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products B.II.b.3.b - Change in the manufacturing process of the finished or intermediate product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product	01/04/2016	n/a		
II/0026/G	This was an application for a group of variations. B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products B.II.b.3.b - Change in the manufacturing process of the finished or intermediate product - Substantial	29/10/2015	n/a		

	changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product				
PSUSA/944/201502	Periodic Safety Update EU Single assessment - degarelix	10/09/2015	n/a		PRAC Recommendation - maintenance
IA/0027	B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits	20/07/2015	n/a		
II/0022/G	This was an application for a group of variations. B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient	22/01/2015	n/a		
PSUV/0023	Periodic Safety Update	25/09/2014	21/11/2014	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUV/0023.
IAIN/0024	C.I.3.a - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Implementation of	01/07/2014	21/11/2014	SmPC and PL	

	wording agreed by the competent authority				
N/0021	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/01/2014	21/11/2014	PL	
PSUV/0020	Periodic Safety Update	19/09/2013	13/11/2013	SmPC and PL	"Please refer to Firmagon-H-C-986-PSUV-020 - Scientific conclusion and grounds recommending the variation to the terms of the marketing authorisation."
R/0018	Renewal of the marketing authorisation.	19/09/2013	13/11/2013	PL	Based on the CHMP review of data on quality, safety and efficacy, including all variations introduced since the marketing authorisation was granted, the CHMP considers by consensus that the risk-benefit balance of Firmagon in the treatment of adult male patients with advanced hormone-dependent prostate cancer remains favourable and therefore recommends the renewal of the marketing authorisation with unlimited validity.
IB/0019/G	This was an application for a group of variations. B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place	23/10/2013	n/a		

II/0015	Update of section 5.1 of the SmPC based on the results from studies CS21/CS21A, CS30, CS31 and CS37. Furthermore, the MAH took the opportunity to add the local representative for Croatia in the Package Leaflet. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	25/07/2013	13/11/2013	SmPC and PL	Study CS37 was an open-label, randomised, parallel-arm trial with subcutaneous injections of degarelix one-month depot or intramuscular injections of leuprolide one- and three-month depot in patients with advanced prostatic carcinoma and with rising serum PSA levels after curative intent. Patients were administered Firmagon for seven months followed by a seven months monitoring period. In this study, the median time to testosterone >0.5 ng/mL (above castrate level) after discontinuation of treatment was 112 days and the median time to testosterone >1.5 ng/mL (above lower limit of normal range) was 168 days. Results from two randomised, active controlled studies (CS30 and CS31) showed that three months therapy with degarelix (240/80 mg dose regimen) resulted in a 37% reduction in prostate volume as measured by trans-rectal ultrasound scan (TRUS) in patients requiring hormonal therapy prior to radiotherapy and in patients who were candidates for medical castration. The prostate volume reduction was similar to that attained with goserelin plus anti-androgen protection. Study CS21 provided immunogenicity data for up to 5.5 years. In this study, anti-degarelix antibody development was observed in 29% of patients after treatment with Firmagon after up to 5.5 years. Data obtained from these studies have been adequately reflected in section 5.1 of the SmPC.
IAIN/0017	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	07/05/2013	n/a		

II/0016	Update of section 5.2 of the SmPC with PK data based on the results of CS38 trial. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	25/04/2013	13/11/2013	SmPC	Based on the results of the PK study CS38, Cmax Degarelix plasma concentration decreases in a biphasic fashion, with a mean median terminal half-life (t½) of 29 days for the maintenance dose. The SmPC has been updated to reflect these data.
II/0014/G	This was an application for a group of variations. Update of sections 4.4 and 4.8 of the SmPC with data on effect of degarelix on QT/QTc supported by the results of the study CS22 (FUM 030). In addition, section 4.4 of the SmPC has been updated to delete the statement that data available on degarelix is limited to one year based on the results of the long term studies CS12A, CS14A and CS21A. Furthermore, section 4.8 of the SmPC has been updated to include anaphylaxis reactions further to the request of the CHMP during the assessment of the 4th PSUR. The package leaflet has been updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the MAH took this opportunity to bring the PI in line with the latest QRD template version 9.0. Finally the MAH made minor changes in sections 4.2, 4.6 and 5.1 of the SmPC and in the PL. C.I.4 - Variations related to significant modifications	25/04/2013	13/11/2013	SmPC, Annex II and PL	Based on the results of study CS22 (FUM030), the lack of intrinsic effect of degarelix on cardiac epolarisation (QTcF), heart rate, AV conduction, cardiac depolarisation, or T or U wave morphology was confirmed in healthy subjects (N=80) receiving an i.v. infusion of degarelix over 60 minutes, reaching a mean Cmax of 222 ng/mL, approximately 3-4-fold the Cmax obtained during prostate cancer treatment. Sections 4.4 and 4.8 of the SmPC have been updated to reflect these results. In addition, section 4.8 of the SmPC has been updated in order to include that rare reports of anaphylactic reactions have been received from post-marketing use of firmagon. Finally the statement ''the data available on efficacy and safety experience with degarelix is limited to a one year treatment'' has been removed from section 4.4 of the SmPC since long-term (up to >5 years) efficacy and safety data are available based on the results from studies CS12A, CS14A and CS21A.

	of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data C.I.3.a - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46, or amendments to reflect a Core SPC - Changes with NO new additional data are submitted by the MAH				
IA/0013/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	19/11/2012	n/a		
II/0011	Change in the intermediate container closure system for the solvent (water for injections), to replace glass vials with glass pre-filled syringes. In addition the applicant took an opportunity to align the Product Information with the current QRD template. B.II.e.1.b.2 - Change in immediate packaging of the finished product - Type of container - Sterile medicinal products and biological/immunological medicinal products	24/05/2012	28/06/2012	SmPC, Labelling and PL	
II/0012	Deletion of a parameter from the specification for the	21/06/2012	21/06/2012		

	finished product B.II.d.1.f - Change in the specification parameters and/or limits of the finished product - Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product				
IA/0010/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system	22/12/2011	n/a		
IA/0009/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	11/05/2011	n/a		

	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State				
IB/0008/G	This was an application for a group of variations. C.I.9.z - Changes to an existing pharmacovigilance system as described in the DDPS - Other variation C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system C.I.9.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database	25/11/2010	n/a		
IA/0006/G	This was an application for a group of variations. B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	18/06/2010	n/a	SmPC, Labelling and PL	

	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking				
IB/0005	To add a new in-process test during the manufacture of the active substance B.I.a.4.f - Change to in-process tests or limits applied during the manufacture of the AS - Addition or replacement of an in-process test as a result of a safety or quality issue	14/06/2010	n/a		
IB/0003	IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	09/02/2010	09/02/2010	SmPC, Labelling and PL	
IB/0004	IB_13_b_Change in test proc. for active substance - other changes (replacement/addition) IB_12_b_02_Change in spec. of active subst./agent in manuf. of active subst. - test parameter	21/01/2010	n/a		
IB/0002	IB_13_b_Change in test proc. for active substance - other changes (replacement/addition) IB_12_b_02_Change in spec. of active subst./agent in manuf. of active subst. - test parameter	21/01/2010	n/a		
II/0001	Update of SPC section 4.8 to include numerous adverse drug reactions (ADRs) from Phase 2 and 3 trials following a request by the CHMP at the time of the original marketing authorisation. The Package Leaflet has been updated accordingly. In addition,	25/06/2009	24/07/2009	SmPC, Labelling and PL	The SPC section 4.8 has been updated based on all adverse drug reactions (ADRs) reported with any degarelix 1 month dosing regimen. These studies included 1259 patients treated for a total of 1,781 patient years compared to the previously included information which derived from 409

	the MAH took the opportunity to add the MA date and numbers in the SPC and Labelling as well as to update the List of Local Representatives for Bulgaria in the English Package Leaflet. Update of Summary of Product Characteristics, Labelling and Package Leaflet				patients of the confirmatory phase III study. The Package Leaflet has been updated accordingly.