Puregon

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
II/0130	B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS	19/09/2024	n/a		

[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).

PSUSA/1465/202305	Periodic Safety Update EU Single assessment - follitropin beta	25/01/2024	27/03/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1465/202305.
IB/0129	B.II.z - Quality change - Finished product - Other variation	13/02/2024	n/a		
IB/0126	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	28/03/2023	27/03/2024	SmPC and PL	
IA/0125	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	10/10/2022	n/a		
II/0124	B.II.e.1.a.3 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Sterile medicinal products and biological/immunological medicinal products	01/09/2022	n/a		
N/0123	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/10/2021	27/03/2024	PL	
II/0122	B.II.e.1.a.3 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Sterile medicinal products and biological/immunological medicinal products	30/09/2021	n/a		
IB/0121	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test	15/09/2021	n/a		

	procedure				
T/0120	Transfer of Marketing Authorisation	12/05/2021	04/06/2021	SmPC, Labelling and PL	
IB/0119/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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 B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place	23/04/2021	04/06/2021	Annex II	
IA/0118	B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter	22/03/2021	n/a		
IB/0116/G	This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change	15/02/2021	n/a		

	in the manufacturing process B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation				
II/0112/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 B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished	28/01/2021	n/a		

	product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - 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 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 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				
II/0111/G	This was an application for a group of variations. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a	28/01/2021	n/a		

	biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS				
N/0117	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/01/2021	04/06/2021	PL	
II/0113	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	14/01/2021	n/a		
PSUSA/1465/ 202005	Periodic Safety Update EU Single assessment - follitropin beta	14/01/2021	n/a		PRAC Recommendation - maintenance
N/0115	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/12/2020	04/06/2021	PL	
IA/0114/G	This was an application for a group of variations. B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier B.II.e.7.a - Change in supplier of packaging	23/11/2020	n/a		

	components or devices (when mentioned in the dossier) - Deletion of a supplier B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier				
IB/0110	C.I.7.a - Deletion of - a pharmaceutical form	29/09/2020	05/11/2020	SmPC, Labelling and PL	
IB/0107	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	13/08/2020	n/a		
IB/0108	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	01/07/2020	05/11/2020	SmPC, Annex II, Labelling and PL	
II/0106/G	This was an application for a group of variations. B.I.b.1.g - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Widening of the approved specs for starting mat./intermediates, which may have a significant effect on the quality of the AS and/or the FP B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test	05/06/2020	n/a		

	method or a method using a biological reagent for a biological AS				
IA/0105	B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised	21/02/2020	n/a		
WS/1702	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of section 4.4 of the SmPC in order to revise the safety information regarding Ovarian Hyperstimulation Syndrome (OHSS) to replace clinical advice describing specific interventions with the recommendation to follow current clinical practice for reducing the risk of OHSS during Assisted Reproductive Technology (ART), based on post-marketing data and literature review. The package Leaflet is updated accordingly. In addition, the worksharing applicant took the opportunity to update the list of local representatives in the Package Leaflet and made some editorial changes in the Product Information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	28/11/2019	05/11/2020	SmPC, Labelling and PL	Follow current clinical practice for reducing the risk of OHSS during Assisted Reproductive Technology (ART). Adherence to the recommended Fertavid dose and treatment regimen and careful monitoring of ovarian response is important to reduce the risk of OHSS.

IB/0103	B.II.z - Quality change - Finished product - Other variation	25/07/2019	n/a		
WS/1502	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol	16/05/2019	n/a		
IG/1062	A.7 - Administrative change - Deletion of manufacturing sites	11/02/2019	n/a		
WS/1457/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate	13/12/2018	n/a		
IG/0968	A.7 - Administrative change - Deletion of manufacturing sites	28/09/2018	04/10/2019	Annex II and	

				PL	
WS/1339/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation	12/07/2018	n/a		
T/0097	Transfer of Marketing Authorisation	13/06/2018	06/07/2018	SmPC, Labelling and PL	
PSUSA/1465/201705	Periodic Safety Update EU Single assessment - follitropin beta	30/11/2017	n/a		PRAC Recommendation - maintenance
WS/1186/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test	13/07/2017	n/a		

	method or a method using a biological reagent for a biological AS B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol				
WS/1124	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.4.e - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of an in-process test which may have a significant effect on the overall quality of the AS	21/04/2017	n/a		
N/0093	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	02/03/2017	28/04/2017	Labelling	
IG/0762	B.II.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Tightening of specification limits	26/01/2017	n/a		
IG/0730	B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information	10/10/2016	n/a		
WS/0975/G	This was an application for a group of variations following a worksharing procedure according to	15/09/2016	n/a		

	Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol				
IG/0703/G	This was an application for a group of variations. B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	18/07/2016	n/a		
IB/0087	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	24/05/2016	28/04/2017	SmPC, Annex II, Labelling and PL	
IG/0545/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name	27/04/2015	n/a		

	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 B.II.e.3.a - Change in test procedure for the immediate packaging of the finished product - Minor changes to an approved test procedure B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information				
WS/0691	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	26/03/2015	n/a		
PSUV/0082	Periodic Safety Update	04/12/2014	n/a		PRAC Recommendation - maintenance
WS/0627	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Addition of a site where batch control/testing takes place for the finished product 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	20/11/2014	n/a		

	control/testing takes place				
N/0084	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/11/2014	19/12/2014	PL	
WS/0571/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Changes in the test procedure 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 B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate	25/09/2014	n/a		Changes in the test procedure of the AS.
IG/0449/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	29/07/2014	n/a		

	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 manufacturer of a novel excipient B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer				
WS/0487/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Changes to the manufacturing process of the finished product. B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size	20/03/2014	n/a		

WS/0465	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of Product Information (PI) to address common medical knowledge concerning assisted reproduction technology regarding : monitoring of ovarian response (SmPC section 4.2) ; updates regarding infertility evaluation before starting treatment, multiple pregnancy, ectopic pregnancy, ovarian hyperstimulation syndrome, ovarian torsion, ovarian and other reproductive system neoplasms, vascular complications, other medical conditions (SmPC section 4.4). The Package leaflet is updated accordingly. The MAH is taking the opportunity to update the PI in line with QRD template version 9 and to make other editorial corrections. In addition, the details of the local representative of Croatia have been included in the German, Greek, Spanish and Italian PL. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	20/02/2014	19/12/2014	SmPC, Annex II, Labelling and PL	The Company has updated the product information, and has referred to published literature and the QRD template to justify changes in the wording of sections 4.2, 4.4 and 4.6 of the SmPC. The Company has revised wording of section 4.2 and 4.4 of the SPC to reflect current clinical practice in the management of fertility that recommends use of ultrasound images to guide management with the medicinal product by following follicular development and by detecting multi-fetal gestations. The Company has introduced information to section 4.4 of the SmPC on management of the ovarian hyper-stimulation syndrome. The revised wording is acceptable and is considered to enhance clinical safety of patients. Grammatical changes have been made to sections 4.4, 4.6, 4.8 and 5 of the SmPC to improve clarity of meaning on use of the medicinal product and to comply with the QRD template; furthermore minor editorial corrections were made throughout the SmPC. These changes are also acceptable. The PL has been updated in order to reflect the SmPC changes described above. Overall, the changes to the product information texts are considered to improve clinical safety and so the benefit / risk balance of the current product in the stated indications remains as positive.
IA/0078/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites	13/12/2013	19/12/2014	Annex II and PL	

IG/0366	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	08/11/2013	n/a		
T/0075	Transfer of Marketing Authorisation	23/08/2013	12/09/2013	SmPC, Labelling and PL	
IG/0225	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	26/02/2013	n/a		
WS/0228/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Change to the control of the active substance B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Change (replacement) to a biological/immunological/ immunochemical test method or a method using a biological reagent for a biological AS B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	19/04/2012	n/a		
IA/0071/G	This was an application for a group of variations. A.5.b - Administrative change - Change in the name	06/01/2012	26/03/2012	SmPC, Annex II, Labelling and PL	

	and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release) A.7 - Administrative change - Deletion of manufacturing sites B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer				
N/0072	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/12/2011	n/a	PL	
IB/0067/G	This was an application for a group of variations. 1. Type IB variation regarding a deletion of a complete pharmaceutical form; i.e. all strengths and presentations of the pharmaceutical form Powder and solvent for solution for injection [EU/1/96/008/001-016]. The deletion will require an update of Annex I, IIA, IIIA and IIIB of the Complete set of Annexes. 2. Type IB variation regarding a deletion of one of the strengths of the pharmaceutical form Solution for injection; i.e. 250 IU/0.5 ml Solution for Injection, all presentations [EU/1/96/008/035-037]. The deletion will require an update of Annex I, IIA, IIIA and IIIB of the Complete set of Annexes. Background of the changes:	12/08/2011	n/a	SmPC, Annex II, Labelling and PL	

	[1] Type IB - C.I.7.a Deletion of a pharmaceutical form; EU/1/96/008/001-016 - recFSH The Puregon Powder and solvent for solution for injection (Puregon Powder) pharmaceutical form was the first pharmaceutical form of Puregon as approved in the initial application in the EU in 1996. The Puregon Powder pharmaceutical form was approved in four strengths each with four presentations (including both ampoule-ampoule and ampoule-vial combinations). Since then, the pharmaceutical forms Solution for injection in vials and Solution for injection in cartridges (for use with Puregon Pen) have been approved and launched. The Puregon Powder presentations are the least user-friendly, and therefore the powder presentations have been taken off the market in the EU shortly after the launch of Puregon Solution for injection in vials. The last batch ever marketed in any country world-wide expired early 2010. [2] Type IB - C.I.7.b Deletion of a strength; EU/1/96/008/035-036 - recFSH In this submission the MAH applies for the deletion of one of the strengths of Puregon Solution for injection in vials (250 IU/0.5 ml). This strength is the highest strenght of the approved Puregon Solution for injections in vials, next to the stenghts of 50, 75 100, 150, 200 and 225 IU/0.5 ml. The strength 250 IU/0.5 ml in vials has never been on the market in				

	any EU C.I.7.a - Deletion of - a pharmaceutical form C.I.7.b - Deletion of - a strength				
N/0066	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/07/2011	n/a	PL	
WS/0112	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Changes to the manufacturing process of the drug product B.II.b.3.c - Change in the manufacturing process of the finished product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability	17/03/2011	17/03/2011		
WS/0072/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Changes to the active substance manufacturing process and control. B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	17/03/2011	17/03/2011		

	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological medicinal product and is not related to a protocol				
WS/0034	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	21/10/2010	29/11/2010	SmPC, Labelling and PL	This type II variation concerns a safety update of the SPC following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Following a re-analysis of safety data a separate warning regarding ovarian torsion is included in the SPC Section 4.4. OHSS, pregnancy, previous abdominal surgery, past history of ovarian torsion, previous or current ovarian cyst and polycystic ovaries have been identified as risk factors for ovarian torsion. Damage to the ovary due to reduced blood supply can be limited by early diagnosis and immediate detorsion. SPC Section 4.8 was amended by including the following adverse reactions in the table concerning treatment in females: abdominal discomfort, constipation, diarrhoea, metrorrhagia, ovarian cyst, ovarian torsion, uterine enlargement, vaginal haemorrhage (uncommon). Headache, rash and injection site pain (common) are included in the table concerning treatment in men. Minor changes in the labelling and other SPC sections (4.1; 4.2; 4.3; 4.6) and corrections of linguistic differences between the Puregon and Fertavid texts were also agreed. The PL is updated accordingly.
WS/0033	This was an application for a variation following a	23/09/2010	25/10/2010	SmPC	Section 5.1 of the SmPC was amended to support the

	worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				current information in Section 4.2. The information added to SmPC 5.1 shows a comparison to urinary FSH, including presentation of study data on (mean) total dosage and treatment period needed. A minor change was also made to the text of SmPC section 4.2.
II/0065	Change to the purification process of the drug substance Change(s) to the manufacturing process for the active substance	19/11/2009	08/12/2009		
II/0063	Update to the Summary of Product Characteristics (SPC), Labelling and Package Leaflet (PL) to comply with the SPC guideline and version 7.2 of the QRD template. Update to the Package Leaflet following the conduct of a Readability Testing. In addition, the Marketing Authorisation Holder took the opportunity to make some corrections in the SPC and in the Package Leaflet. The MAH also introduced some linguistic corrections in several languages versions of the Annexes. Update of Summary of Product Characteristics, Labelling and Package Leaflet	22/10/2009	23/11/2009	SmPC, Labelling and PL	The Puregon Product Information was updated to comply with the SPC guideline and version 7.2 of the QRD template by using short terms for the pharmaceutical form in section 3 of the SPC and in section 6 of the Package Leaflet, by using abbreviated terms for the administration route in the Labelling as well as by harmonising the prefixes used in the Labelling. Also the Package Leaflet has been updated following the conduct of a Readability Testing on the Puregon vials Package Leaflet.
IA/0064	IA_05_Change in the name and/or address of a manufacturer of the finished product	16/07/2009	n/a	Annex II and PL	

II/0062	Changes to a method for the control of the drug substance. Change(s) to the test method(s) and/or specifications for the active substance	19/03/2009	24/03/2009		
II/0061	Additional manufacturing site for Puregon solution for injection 833 IU/mL. Change(s) to the manufacturing process for the finished product	19/02/2009	10/03/2009		
IB/0060	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	14/11/2008	n/a		
II/0058	Additional site for the testing and final batch release of Puregon solution for injection in a cartridge. Change(s) to the test method(s) and/or specifications for the finished product	24/07/2008	05/09/2008	Annex II and PL	
II/0059	This procedure relates to an update of section 4.2 of the SPC requested by the CHMP further to assessment of FUM 010. Section 5.2 of Puregon solution for injection in cartridges (only) has been also updated. Update of Summary of Product Characteristics, Labelling and Package Leaflet	24/04/2008	20/06/2008	SmPC, Labelling and PL	As requested by the CHMP in their conclusion further to assessment of a Follow-Up Measure (FUM 010), section 4.2 of the SPC (Posology and method of administration) for Puregon was amended, as it made reference to a higher effectiveness of Puregon in comparison to urinary follicle-stimulating hormone (FSH). Reference to this has now been deleted. Section 5.2 of the SPC has been also updated for Puregon solution for injection in cartridges, only. Minor typographical amendments to the SPC and Labelling were also made. Finally, graphical amendments to pictures were

					implemented throughout the PL for all presentations.
II/0057	Change(s) to the manufacturing process for the active substance	20/09/2007	27/09/2007		
IA/0056	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	25/04/2007	n/a	SmPC, Annex II and PL	
II/0055	This variation relates to an update of section 4.8 of the Summary of Product Characteristics (SPC) and section 4 of the Package Leaflet (PL) in order to implement the results of the recoding from WHO ART to MedDRA and to the addition of warning on hepatotoxicity in association with ovarian hyperstimulation syndrome in section 4.4 of the SPC. In addition to this, the Marketing Authorisation Holder (MAH) updated the heading of the section 6.6 of the SPC according to the QRD template 7.1. Update of Summary of Product Characteristics and Package Leaflet	16/11/2006	09/01/2007	SmPC and PL	The MAH submitted a type II variation to update the section 4.8 of the SPC and section 4 of the PL in order to implement the results of the recoding from WHO ART to MedDRA and to the addition of warning on hepatotoxicity in association with ovarian hyperstimulation syndrome in section 4.4 of the SPC. In addition to this, the MAH updated the heading of the section 6.6 of the SPC according to the QRD template 7.1. The MAH stated, that cases of liver function abnormalities associated with Ovarian Hyperstimulation syndrome (OHSS) have been reported in the literature and clinical guidelines on OHSS include that liver enzymes may be elevated in serious cases of OHSS and should be monitored. The MAH proposed to include a warning in section 4.4 of the SPC that liver function test abnormalities have been observed in cases of severe or moderate OHSS. The following wording has been added: Transient liver function test abnormalities suggestive of hepatic dysfunction, which may be accompanied by morphologic changes on liver biopsy, have been reported in association with ovarian hyperstimulation syndrome. The MAH updated section 4.8 of SPC in order to reflect the

					change from WHO-ART to MedDRA terminology for reporting of adverse drug reactions (ADRs). The Package Leaflet has been amended accordingly.
II/0049	Change to the test procedure and/or specification of a raw material	21/09/2006	27/09/2006		
IB/0053	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	29/08/2006	n/a		
IB/0054	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	20/07/2006	n/a		
IB/0052	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	20/07/2006	n/a		
II/0050	Change(s) to the test method(s) and/or specifications for the active substance	01/06/2006	07/06/2006		
R/0048	Renewal of the marketing authorisation.	23/03/2006	29/05/2006	SmPC, Annex II, Labelling and PL	
II/0047	Change(s) to the test method(s) and/or specifications for the active substance	14/12/2005	21/12/2005		
N/0046	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	05/08/2005	n/a	Labelling	
IA/0045	IA_28_Change in any part of primary packaging material not in contact with finished product	19/07/2005	n/a		

IB/0044	IB_31_b_Change to in-process tests/limits during manufacture - addition of new tests/limits IB_38_c_Change in test procedure of finished product - other changes	07/12/2004	n/a		
II/0042	Change(s) to the test method(s) and/or specifications for the finished product	16/09/2004	20/10/2004	SmPC and Labelling	Decrease of the filling volume of the cartridge of Puregon 300 IU/0.36 ml and 600 IU/0.72 ml: 0.480 ml instead of 0.525 ml for the 300 IU presentation, 0.840 ml instead of 0.885 ml for the 600 IU presentation.
II/0041	Change(s) to container	23/06/2004	02/08/2004	SmPC	
II/0038	New presentation(s)	23/06/2004	02/08/2004	SmPC, Annex II, Labelling and PL	Addition of two new presentations of an already authorised strength (833 IU/ml) of Puregon solution for injection in cartridge: 150 IU/0.18 ml and 900 IU/ 1.08 ml.
IB/0039	IB_43_a_02_Add./replacement/del. of measuring or administration device - deletion	10/03/2004	n/a	SmPC and Labelling	
I/0036	24_Change in test procedure of active substance	25/09/2003	30/09/2003		
I/0037	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	18/09/2003	22/09/2003		
N/0035	Removal of text from Blister foil for presentations 038 and 039 (the text is the same appearing on the cartridge and the labelling information on the cartridge can be seen through the transparent blister foil) Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/07/2003	19/08/2003	Labelling	

II/0034	Change(s) to the test method(s) and/or specifications for the active substance	20/03/2003	31/03/2003		
II/0033	01_Change following modification(s) of the manufacturing authorisation(s) 24_Change in test procedure of active substance Change(s) to the test method(s) and/or specifications for the active substance Change(s) to the test method(s) and/or specifications for the finished product	25/07/2002	28/10/2002	SmPC and PL	As requested by the CPMP following the assessment of a pharmaceutical Follow-up Measure related to the manufacturing process, section 4.4 of the Summary of Product Characteristics (SPC) and section 2 of the Package Leaflet (PL) were updated. Information regarding the possibility of Puregon to contain traces of streptomycin and/or neomycin that may cause hypersensitivity reactions was included in these sections. In addition, section 4.8 of the SPC and section 4 of the PL were updated to include information regarding the occurrence of rash and erythema based on data from post-marketing experience and assessment of the 6th PSUR. Moreover, other minor changes were introduced in the SPC and PL.
I/0031	24_Change in test procedure of active substance	27/06/2002	02/07/2002		
I/0032	12_Minor change of manufacturing process of the active substance	30/05/2002	06/06/2002		
II/0030	Change(s) to the test method(s) and/or specifications for the active substance	30/05/2002	04/06/2002		
II/0029	Change(s) to the test method(s) and/or specifications for the active substance	21/02/2002	19/03/2002		
II/0026	Following the first 5-year renewal of the marketing authorisation, the Summary of product Characteristics and package leaflet. Sections 4.4 and 4.6 of the Summary of Product Characteristics (SPC)	27/06/2001	05/02/2002	SmPC and PL	Following the first 5-year renewal of the marketing authorisation, the Summary of product Characteristics and package leaflet. Sections 4.4 and 4.6 of the Summary of Product Characteristics (SPC) and section 2 of the Package

	and section 2 of the Package Leaflet (PL) were updated to include wording on potential multiple births and congenital malformations. Moreover, other minor changes were introduced in the SPC and PL. Update of Summary of Product Characteristics and Package Leaflet				Leaflet (PL) were updated to include wording on potential multiple births and congenital malformations. Moreover, other minor changes were introduced in the SPC and PL.
N/0028	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	31/10/2001	08/03/2002	Labelling	
I/0027	20_Extension of shelf-life as foreseen at time of authorisation	13/07/2001	18/10/2001	SmPC	
R/0024	Renewal of the marketing authorisation.	28/03/2000	26/07/2001	SmPC, Annex II, Labelling and PL	
II/0023	Extension of Indication	14/12/2000	10/04/2001	SmPC and PL	
II/0020	01_Change following modification(s) of the manufacturing authorisation(s) Change(s) to the test method(s) and/or specifications for the active substance	28/08/2000	19/01/2001		
I/0022	01_Change following modification(s) of the manufacturing authorisation(s)	10/10/2000	15/01/2001		
II/0018	Change(s) to shelf-life or storage conditions	29/06/2000	08/12/2000	SmPC, Labelling and PL	

II/0016	Update of Summary of Product Characteristics, Labelling and Package Leaflet	29/06/2000	08/12/2000	SmPC, Labelling and PL	
I/0021	15a_Change in IPCs applied during the manufacture of the product	22/09/2000	n/a		
I/0019	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	25/07/2000	28/08/2000		
N/0017	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/04/2000	11/07/2000	Labelling and PL	
II/0011	Update of Summary of Product Characteristics, Labelling and Package Leaflet	23/09/1999	21/02/2000	SmPC, Annex II, Labelling and PL	
X/0010	X-3-iii_Addition of new strength	23/09/1999	10/02/2000	SmPC, Annex II, Labelling and PL	
II/0013	Change(s) to the test method(s) and/or specifications for the active substance	23/09/1999	22/12/1999		
I/0015	24_Change in test procedure of active substance	14/12/1999	22/12/1999		
N/0014	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/10/1999	21/02/2000	Labelling and PL	
N/0012	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	28/05/1999	08/07/1999	Labelling	
X/0009	X-3-iv_Change or addition of a new pharmaceutical	19/11/1998	26/04/1999	SmPC, Annex	

	form			II, Labelling and PL	
II/0008	Update of Summary of Product Characteristics and Package Leaflet	22/04/1998	05/10/1998	SmPC and PL	
I/0007	01_Change following modification(s) of the manufacturing authorisation(s)	17/01/1997	03/04/1997	Annex II and PL	
I/0006	01_Change following modification(s) of the manufacturing authorisation(s)	17/01/1997	03/04/1997	Annex II and PL	
I/0005	01_Change following modification(s) of the manufacturing authorisation(s)	17/01/1997	03/04/1997	Annex II and PL	
T/0004	Transfer of Marketing Authorisation	04/09/1996	20/01/1997	SmPC, Labelling and PL	
I/0003	24_Change in test procedure of active substance	12/09/1996	28/11/1996		
I/0002	13_Batch size of active substance	12/09/1996	28/11/1996		
I/0001	11_Change in or addition of manufacturer(s) of active substance	12/09/1996	28/11/1996	Annex II	