Luveris

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
IA/0094	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	23/08/2022	n/a		
IB/0093	B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting	17/08/2022	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).

	material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method				
II/0091	Update of sections 4.1, 4.2, 5.1 and 5.2 of the SmPC in order to update details regarding the definition of severe LH and FSH deficiency, to clarify follicular development as the treatment target and selection of the most adequate Medically Assisted Reproduction procedure for healthcare providers and to clarify the pharmacokinetic and pharmacodynamic properties of the two gonadotropins, in alignment with the variation EMEA/H/C/000714/II/0075 for Pergoveris, based on a systematic literature search and review. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/06/2022		SmPC and PL	Based on literature review data and in alignment with Pergoveris EMEA/H/C/000714/II/0075, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC have been updated to remove LH threshold from the definition for severe LH and FSH deficiency, to add guidance to tailor treatment to individual patient's response, to clarify mechanism of action and to update pharmacodynamic and pharmacokinetic properties. Editorial amendments have also been performed. For more information, please refer to the Summary of Product Characteristics.
IB/0092	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	30/03/2022	n/a		
IA/0090/G	This was an application for a group of variations. B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new	05/07/2021	n/a		

	specification parameter to the specification with its corresponding test method 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.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits				
II/0089	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	06/05/2021	n/a		
IA/0088	B.II.f.1.e - Stability of FP - Change to an approved stability protocol	03/02/2021	n/a		
IB/0087	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	07/01/2021	31/01/2022	SmPC, Annex II, Labelling and PL	
PSUSA/1918/201911	Periodic Safety Update EU Single assessment - lutropin alfa	09/07/2020	n/a		PRAC Recommendation - maintenance

WS/1799/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.a.4.d - Change to in-process tests or limits applied during the manufacture of the AS - Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the AS B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer	18/06/2020	n/a		
IB/0086/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 B.II.b.3.a - Change in the manufacturing process of	02/06/2020	n/a		

	the finished or intermediate product - Minor change in the manufacturing process 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				
II/0082	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	28/11/2019	n/a		
IB/0083/G	This was an application for a group of variations. 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.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	08/11/2019	n/a		
IB/0079	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	11/07/2019	n/a		
IB/0080	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement	08/07/2019	n/a		

	or addition) for the AS or a starting material/intermediate				
IA/0081	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	14/06/2019	n/a		
IA/0078	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	13/02/2019	n/a		
T/0077	Transfer of Marketing Authorisation	30/07/2018	20/08/2018	SmPC, Labelling and PL	
IB/0076	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	21/02/2018	n/a		
IB/0075/G	This was an application for a group of variations. B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line) B.II.e.4.c - Change in shape or dimensions of the container or closure (immediate packaging) - Sterile medicinal products	09/02/2018	n/a		
IB/0074/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new/updated or	30/08/2017	n/a		

	deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material)				
N/0073	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/07/2017	20/08/2018	Labelling and PL	
PSUSA/1918/ 201611	Periodic Safety Update EU Single assessment - lutropin alfa	06/07/2017	n/a		PRAC Recommendation - maintenance
IB/0070	B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	17/11/2016	n/a		
IB/0071	To update the ultrafiltration 10kD membranes (Pall Omega C) used in steps I, II, V and VI of drug substance purification process with equivalent membranes (Pall Omega T) and to change the storage solution from 0.05M NaOH used for Pall Omega C to a 0.1M NaOH solution for Pall Omega T. In addition, MAH introduced editorial change to update the total surface area of the ultrafiltration membranes. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process	08/11/2016	n/a		

	of the AS				
IA/0069	B.II.e.3.b - Change in test procedure for the immediate packaging of the finished product - Other changes to a test procedure (including replacement or addition)	25/02/2016	n/a		
WS/0655	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Change in test procedure for AS and FP 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	20/11/2014	n/a		Change in test procedure for AS and FP
IB/0067	C.I.7.a - Deletion of - a pharmaceutical form	19/11/2014	24/04/2015	SmPC, Labelling and PL	
IG/0500	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	17/11/2014	n/a		
IA/0066	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	02/10/2014	n/a		

WS/0579/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.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other	24/07/2014	n/a		

	variation B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				
IG/0461	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	22/07/2014	n/a		
PSUV/0062	Periodic Safety Update	10/07/2014	n/a		PRAC Recommendation - maintenance
WS/0506	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Change to the manufacturing process of the active substance. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	20/03/2014	n/a		

IB/0061	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	18/03/2014	24/04/2015	SmPC, Labelling and PL	
IG/0395	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	20/12/2013	n/a		
N/0056	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/11/2013	18/12/2013	PL	
IG/0358	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	25/09/2013	n/a		
WS/0380	This was an application for a variation 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.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits	30/05/2013	n/a		
IB/0054	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/01/2013	18/12/2013	SmPC, Annex II, Labelling and PL	

IG/0224	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	11/10/2012	n/a		
WS/0275	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Change to the control of the finished product B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	19/07/2012	n/a		
IB/0046	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	21/10/2011	n/a	SmPC and PL	
WS/0174	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Change to the manufacturing process of lutropin alfa active substance 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	20/10/2011	20/10/2011		
WS/0148	This was an application for a variation following a	21/07/2011	21/07/2011		

	worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. New TSE certificate for a raw material used in the manufacture of the active substance. B.III.1.b.2 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer				
IG/0087	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	18/07/2011	n/a		
IG/0076/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV 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	01/07/2011	n/a		
II/0044/G	This was an application for a group of variations.	14/04/2011	23/05/2011	SmPC,	New pharmaceutical form: Luveris 450 IU solution for

	New pharmaceutical form: Luveris 450 IU solution for injection in a pre-filled pen. Additional sites for drug product manufacture. B.IV.1.c - Change of a measuring or administration device - Addition or replacement of a device which is an integrated part of the primary packaging B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for biological/immunological medicinal products. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site			Labelling and PL	injection in a pre-filled pen. Additional sites for drug product manufacture.
IG/0069	A.7 - Administrative change - Deletion of manufacturing sites	12/05/2011	n/a		
II/0045	Update of SPC and 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	17/02/2011	18/03/2011	SmPC, Labelling and PL	The MAH is updating the product information according to the company core safety data sheet. These changes include addition of a warning to include patients with porphyria, multiple pregnancy, recent thromboembolic disease and rewording of OHSS. In addition the product information will be amended according to the last QRD template, minor linguistic improvements and revised name and/or address of some local representatives of the Marketing Authorisation Holder.
WS/0016	This was an application for a variation following a worksharing procedure according to Article 20 of	24/06/2010	24/06/2010		

	Commission Regulation (EC) No 1234/2008. Change of reference standard 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				
II/0043	Update of DDPS (Pharmacovigilance)	22/04/2010	17/06/2010	Annex II	With this variation the MAH submitted a new version of the DDPS (core version 9.0) in accordance with the current Pharmacovigilance guideline. After assessing the documentation the CHMP concluded that the submitted DDPS contained all required elements. Consequently, Annex II has been updated with the new version number of the agreed DDPS.
IA/0042	IA_01_Change in the name and/or address of the marketing authorisation holder	09/07/2009	n/a	SmPC, Labelling and PL	
X/0037	Registration of an additional pharmaceutical form corresponding to a solution for injection in a cartridge (450 IU). This multidose formulation is intended to be used in the same clinical indication, posology and route of administration (subcutaneous injection) as the existing pharmaceutical form (powder and solvent for solution for injection -75 IU). Annex I_2.(d) Change or addition of a new	19/03/2009	26/05/2009	SmPC, Labelling and PL	

	pharmaceutical form				
IA/0041	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.) IA_05_Change in the name and/or address of a manufacturer of the finished product	26/02/2009	n/a	Annex II and PL	
IA/0040	IA_05_Change in the name and/or address of a manufacturer of the finished product	27/10/2008	n/a	Annex II and PL	
II/0038	Additional sites for the production of a raw material used in the manufacture of the active substance Change(s) to the manufacturing process for the active substance	25/09/2008	02/10/2008		
IB/0039	IB_31_a_Change to in-process tests/limits during manufacture - tightening of in-process limits	01/10/2008	n/a		
IA/0036	IA_05_Change in the name and/or address of a manufacturer of the finished product	20/02/2008	n/a		
N/0035	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	20/06/2007	n/a	PL	
R/0033	Renewal of the marketing authorisation.	15/09/2005	24/01/2006	SmPC, Annex II, Labelling and PL	Based on the CHMP review of the available information, the CHMP considered that the quality, the efficacy and the safety of this medicinal product continues to be adequately and sufficiently demonstrated and therefore considered by consensus that the benefit/risk profile of Luveris in the approved therapeutic indication remains favourable. The

					Committee for Medicinal Products for Human Use recommended therefore the renewal of the Marketing Authorisation for Luveris. The CHMP was of the opinion that no additional 5-year renewal is required. The renewal required amendments to the terms of the Community Marketing Authorisation. The following annexes have been amended: I, II, IIIA and IIIB. Future PSURs submission will take place in accordance to Article 24(3) of Regulation EC 726/2004.
IB/0032	IB_37_a_Change in the specification of the finished product - tightening of specification limits	10/06/2005	n/a		
IB/0031	IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening	10/06/2005	n/a		
IA/0030	IA_16_b_Submission of new TSE certificate relating to active substance - other substances	02/03/2005	n/a		
N/0028	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/11/2004	n/a	PL	
IA/0029	IA_05_Change in the name and/or address of a manufacturer of the finished product	28/10/2004	n/a		
II/0026	Change(s) to the test method(s) and/or specifications for the active substance	16/09/2004	22/09/2004		
N/0027	The Marketing Authorisation Holder applied for an update of the list of the local representatives in order to include the contact details of the Marketing	21/07/2004	n/a	Annex II and PL	

	Authorisations Holder in the new Member States. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)				
II/0025	Change in the manufacturing process of the finished product. Quality changes	23/06/2004	01/07/2004		
II/0024	Extension of the shelf life of the active substance. Change(s) to shelf-life or storage conditions	22/04/2004	27/04/2004		
IB/0023	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	15/01/2004	n/a	SmPC	
I/0021	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	08/10/2003	15/10/2003		
I/0022	31_Change in container shape	15/08/2003	22/09/2003	SmPC	
II/0020	Change(s) to the test method(s) and/or specifications for the active substance	26/06/2003	02/07/2003		
I/0019	20a_Extension of shelf-life or retest period of the active substance	08/05/2003	14/05/2003		
N/0018	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	10/02/2003	04/03/2003	PL	

I/0017	15a_Change in IPCs applied during the manufacture of the product	16/01/2003	22/01/2003		
I/0016	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	28/11/2002	04/12/2002		
I/0015	11b_Change in supplier of an intermediate compound used in manufacture of the active substance	21/08/2002	18/09/2002		
II/0006	Change in formulation	21/02/2002	15/05/2002	SmPC, Labelling and PL	
I/0012	20_Extension of shelf-life as foreseen at time of authorisation	10/11/2001	28/01/2002	SmPC	
I/0014	17_Change in specification of the medicinal product	14/01/2002	23/01/2002		
I/0009	24_Change in test procedure of active substance	19/10/2001	05/11/2001		
I/0008	25_Change in test procedures of the medicinal product	19/10/2001	05/11/2001		
I/0004	25_Change in test procedures of the medicinal product	19/10/2001	05/11/2001		
I/0011	12a_Change in specification of starting material/intermediate used in manuf. of the active substance	12/09/2001	n/a		

I/0007	24_Change in test procedure of active substance	20/08/2001	n/a		
I/0005	03_Change in the name and/or address of the marketing authorisation holder	20/07/2001	n/a	SmPC, Labelling and PL	
I/0001	20_Extension of shelf-life as foreseen at time of authorisation	11/02/2001	17/05/2001	SmPC	
I/0003	26_Changes to comply with supplements to pharmacopoeias	16/02/2001	n/a		