Orgalutran

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/0043	Update of sections 4.4 and 4.8 of the SmPC to include anaphylaxis (including anaphylactic shock), angioedema, and urticaria under hypersensitivity reactions. In addition, the MAH took the opportunity to include minor editorial corrections in the SmPC and to update the list of local representatives (PT and NL) in the Package Leaflet.	26/04/2019		SmPC and PL	The SmPC section 4.4 was updated to include under "Hypersensitivity reaction": Cases of hypersensitivity reactions (both generalised and local), have been reported with Orgalutran, as early as with the first dose, during post marketing surveillance. These events have included anaphylaxis (including anaphylactic shock), angioedema and urticaria. (See section 4.8.) If a hypersensitivity reaction is suspected, Orgalutran should be discontinued and appropriate treatment administered.

[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).

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				The SmPC section 4.8 was updated to include the adverse reaction anaphylaxis (including anaphylactic shock), angioedema and urticaria) with frequency “very rare”. The PL has been updated accordingly.
IB/0044/G	This was an application for a group of variations. 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 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 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	10/04/2019	n/a		
II/0041	Update of sections 4.4 and 6.5 of the SmPC to clarify that this product is in contact with dry natural rubber/latex, which may cause allergic reactions. The labelling and Package Leaflet have been updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representative in Belgium in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	31/01/2019		SmPC, Labelling and PL	Each pre filled syringe is affixed with a needle closed by a needle cover. The needle cover contains dry natural rubber/latex which comes into contact with the needle and may cause allergic reactions.

	data				
IA/0042	A.7 - Administrative change - Deletion of manufacturing sites	28/09/2018		Annex II and PL	
T/0040	Transfer of Marketing Authorisation	20/04/2018	29/06/2018	SmPC, Labelling and PL	
PSUSA/1517/ 201702	Periodic Safety Update EU Single assessment - ganirelix	28/09/2017	n/a		PRAC Recommendation - maintenance
N/0037	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	05/01/2017	11/04/2017	Labelling and PL	
IB/0035	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	28/04/2016	11/04/2017	SmPC, Annex II, Labelling and PL	
IA/0036/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.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	19/04/2016	n/a		
IB/0034/G	This was an application for a group of variations. B.I.b.2.e - Change in test procedure for AS or starting	27/11/2015	n/a		

	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)				
IA/0033	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	24/03/2015	n/a		
N/0032	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/11/2014	11/04/2017	PL	
IB/0031	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	19/09/2014	n/a		
IG/0404	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	14/02/2014	n/a		
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/0027	Transfer of Marketing Authorisation	09/08/2013	19/09/2013	SmPC, Labelling and	

				PL	
N/0028	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/08/2013	11/04/2017	PL	
II/0025	Update of sections 4.4, 4.8 and 6.5 of the SmPC with safety information concerning allergic reactions that may be caused by the natural rubber latex in the packaging of Orgalutran. Updates of the labelling (section 7) and Package leaflet (sections 2, 4 and 6) are proposed accordingly. In addition updates of the Product Information according to the QRD template (version 8) and the SmPC Guideline (rev2). Furthermore the applicant takes the opportunity to update the list of local representatives (Netherlands, Iceland, Lithuania). The requested variation proposed amendments to the SmPC, Annex II, Labelling 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	19/07/2012	10/09/2012	SmPC, Annex II, Labelling and PL	In this variation sections 4.4, 4.8 and 6.5 of the SmPC were updated with safety information (derived from postmarketing data) concerning allergic reactions that may be caused by the natural rubber latex in the packaging of Orgalutran. The labelling (section 7) and Package leaflet (sections 2, 4 and 6) are updated accordingly. Especially the information that the needle shield is made of natural rubber latex is important to warn the subjects with history of latex allergy. It is also clarified in the SmPC that the rubber piston (in pre-filled syringes) does not contain latex. The updates of the Product Information according to the QRD template (version 8) and the SmPC Guideline (rev2) and to the list of local representatives (Netherlands, Iceland, Lithuania) were accepted.
IG/0184	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	21/08/2012	n/a		
N/0024	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/12/2011	10/09/2012	PL	
IG/0117/G	This was an application for a group of variations.	18/11/2011	18/11/2011	Annex II	

	C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site undertaking pharmacovigilance activities C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in 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				
N/0022	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/07/2011	n/a	PL	
IA/0021	A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release)	17/06/2011	n/a		
II/0019	C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH	16/12/2010	27/01/2011	SmPC, Annex II and PL	SmPC section 4.8 of the SmPC has been updated further to assessment of FUM 25. Following the assessment of variation II-16 (change in posology) a safety report was submitted (FUM25), showing a similar safety profile for Orgalutran, whether started on day 5 or day 6 of an ovarian stimulation protocol for assisted reproduction techniques. In addition changes to SmPC sections 4.1 ; 4.2 ; 5.1 to add reference to corifollitropin alfa (Elonva). The PL was amended accordingly.
IB/0020	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life	11/11/2010	n/a	SmPC	

	of the finished product - As packaged for sale (supported by real time data)				
R/0018	Renewal of the marketing authorisation.	18/02/2010	10/05/2010	SmPC, Labelling and PL	Based on the CHMP review of the available information and on the basis of a re-evaluation of the benefit risk balance, the CHMP is of the opinion that the quality, safety and efficacy of this medicinal product continues to be adequately and sufficiently demonstrated and therefore considered that the benefit risk profile of Orgalutran continues to be favourable. The CHMP is also of the opinion that the renewal can be granted with unlimited validity.
II/0016	Update of the section 4.2, 4.8 and 5.1 of the Summary of Product Characteristics and section 3 of Package Leaflet. Update of Summary of Product Characteristics and Package Leaflet	17/12/2009	22/01/2010	SmPC and PL	Update of the SmPC (section 4.2) to update the start day (day 5 or day 6) of treatment with Orgalutran for Controlled Ovarian Stimulation during ART, depending on the ovarian response. Consequently changes are also introduced in section 4.8 and 5.1 of the SPC. The Package leaflet is amended accordingly (section 3).
IA/0017	IA_09_Deletion of manufacturing site	21/08/2009	n/a		
II/0015	To change the manufacturing process of the active substance. Change(s) to the manufacturing process for the active substance	25/06/2009	02/07/2009		
II/0014	Update of section 4.4 "Special warnings and precautions for use" of the SPC further to the assessment of the PSUR 009 in order to include a	13/12/2007	18/01/2008	SmPC and PL	Further to the assessment of PSUR 009, the MAH updated section 4.4 "Special warnings and precautions for use" of the SPC to include the following warning on tubal abnormalities

	sentence regarding tubal abnormalities and the risk of ectopic pregnancies. The PL was amended accordingly. Update of Summary of Product Characteristics and Package Leaflet				and the incidence of ectopic pregnancies: 'Since infertile women undergoing assisted reproduction and particularly IVF, often have tubal abnormalities the incidence of ectopic pregnancies might be increased. Early Ultrasound confirmation that a pregnancy is intrauterine is therefore important.' Section 2 "Before you use Orgalutran" of the PL was amended accordingly.
II/0012	Update of section 4.4 of the Summary of Product Characteristics (SPC) further to the Assessment of the FUM 009 (prospective follow-up study on pregnancies) in order to include a statement on congenital malformations in children after Orgalutran treatment of their mothers. In addition, the Product Information has been updated in accordance to the QRD template version 7.2. Update of Summary of Product Characteristics, Labelling and Package Leaflet	26/04/2007	04/06/2007	SmPC, Annex II, Labelling and PL	Further to the assessment of the FUM 009 (prospective follow-up study on pregnancies) the MAH updated the section 4.4 of the SPC in order to include the incidence of congenital malformations in children after Orgalutran treatment of their mothers in comparison with GnRH agonist treatment as follows: ''In clinical trials investigating more than 1000 newborns it has been demonstrated that the incidence of congenital malformations in children born after COH treatment using Orgalutran is comparable with that reported after COH treatment using GnRH agonist''. The Package leaflet was amended accordingly. In addition the Product Information updated in accordance to the latest version of QRD template.
IA/0013	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	13/04/2007	n/a		
II/0011	Update of Summary of Product Characteristics and Package Leaflet	15/09/2005	25/10/2005	SmPC and PL	
R/0010	Renewal of the marketing authorisation.	16/12/2004	03/03/2005	SmPC, Annex II, Labelling and PL	

N/0009	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/08/2004	n/a	Labelling and PL	
N/0008	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	01/07/2003	18/07/2003	Labelling	
I/0007	24_Change in test procedure of active substance	28/03/2003	02/04/2003		
I/0006	14_Change in specifications of active substance	28/03/2003	02/04/2003		
II/0005	Change(s) to container	18/12/2002	09/01/2003		Replacement of the soft needle shield by a rigid needle shield.
II/0004	Update of Summary of Product Characteristics	17/01/2002	18/04/2002	SmPC	
I/0002	20_Extension of shelf-life as foreseen at time of authorisation	16/07/2001	n/a	SmPC, Labelling and PL	
I/0001	24_Change in test procedure of active substance	07/03/2001	13/03/2001		