Elonva

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
N/0065	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	20/03/2023		PL	
IB/0064/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of	12/08/2022	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).

	the AS - Minor change in the manufacturing process of the AS 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				
II/0061	Extension of indication to include treatment of adolescent males (14 years and older) with hypogonadotropic hypogonadism, in combination with human Chorionic Gonadotropin (hCG) for Elonva, based on final results of the paediatric study P043. Study P043 was an open-label, non-comparative, multi-center safety and efficacy study of corifollitropin in association with hCG in male adolescents with hypogonadotropic hypogonadism, part of the paediatric investigation plan; as a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 10 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement some minor editorial and formatting changes throughout the PI. The variation leads to amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP). C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or	22/04/2022	21/06/2022	SmPC and PL	A multi-centre, open-label, single-group paediatric study was performed that evaluated the treatment of corifollitropin alfa (CFA) in combination with human Chorionic Gonadotropin (hCG) to induce and/or restore puberty and induce and/or restore spermatogenesis with a total maximum duration of 73 weeks in 17 adolescent males aged 14 years and older with hypogonadotropic hypogonadism. The applied regimen of 12 weeks of pre-treatment with CFA and subsequently 52 weeks of CFA combined with hCG showed adequate induction of testicular development (measured by increase in testicular volume from prepubertal to mid pubertal size) in adolescent males with HH. Important findings on development of secondary sexual characteristics at week 64 included increased testosterone levels, growth velocity and progression of puberty (Tanner III, IV and V) indicated appropriate responses to hCG. Decreasing anti-Mullerian hormone levels and increases in Inhibin B levels were suggestive of initiation of spermatogenesis. The use of CFA appeared to be well-tolerated with an acceptable safety profile and without unexpected safety signals over a treatment period of 64 weeks.

	modification of an approved one				Update of sections 4.2, 4.4, 4.6, 4.8, 4.9, 5.1 and 5.2 of the SmPC were implemented to reflect a new indication and recommendations of use for the treatment of adolescent males (14 years and older) with hypogonadotropic hypogonadism, in combination with human Chorionic Gonadotropin (hCG) and to include the final study results of the paediatric study.
II/0062	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	24/02/2022	n/a		
N/0063	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/10/2021	21/06/2022	PL	
T/0060	Transfer of Marketing Authorisation	12/05/2021	14/06/2021	SmPC, Labelling and PL	
IB/0059/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.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch	11/05/2021	14/06/2021	Annex II	

	control/testing takes place 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				
II/0057	B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation	06/05/2021	n/a		
II/0055	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	06/05/2021	n/a		
II/0058/G	This was an application for a group of variations. B.II.d.2.z - Change in test procedure for the finished product - Other variation B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation	15/04/2021	n/a		
II/0056/G	This was an application for a group of variations. B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	25/03/2021	n/a		

PSUSA/875/202007	Periodic Safety Update EU Single assessment - corifollitropin alfa	11/03/2021	n/a		PRAC Recommendation - maintenance
IB/0053/G	This was an application for a group of variations. B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation	29/01/2021	n/a		
N/0054	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/01/2021	14/06/2021	PL	
N/0052	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/12/2020	14/06/2021	PL	
IA/0050	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)	22/05/2020	n/a		
IB/0049	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	20/04/2020	09/10/2020	SmPC, Annex II, Labelling and PL	
IB/0047	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	20/09/2019	n/a		

II/0046	Update of sections 4.3, 4.4 and 4.9 of the SmPC in order to revise the current text regarding Ovarian Hyperstimulation Syndrome (OHSS) to add clarity and remove clinical advice describing specific clinical interventions for reducing OHSS that have become outdated, based on post-marketing data and literature review. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder included some editorial changes in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	12/09/2019	09/10/2020	SmPC and PL	
IB/0048	B.II.z - Quality change - Finished product - Other variation	27/08/2019	n/a		
IG/1062	A.7 - Administrative change - Deletion of manufacturing sites	11/02/2019	n/a		
IA/0044	B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits	11/02/2019	n/a		
II/0043	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	17/01/2019	n/a		

	where significant assessment is required				
IG/0968	A.7 - Administrative change - Deletion of manufacturing sites	28/09/2018	16/09/2019	Annex II and PL	
IB/0041/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)	22/06/2018	n/a		
T/0040	Transfer of Marketing Authorisation	20/04/2018	08/05/2018	SmPC, Labelling and PL	
PSUSA/875/201707	Periodic Safety Update EU Single assessment - corifollitropin alfa	08/03/2018	n/a		PRAC Recommendation - maintenance
II/0037/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.II.d.2.c - Change in test procedure for the finished	14/12/2017	n/a		

	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				
II/0038	Update of section 5.1 of the SmPC to include updated information regarding congenital malformations reported in infants born after a frozen-thawed embryo transfer (FTET) cycle. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	02/11/2017	26/04/2018	SmPC	Following use of Elonva, 61 infants were born after an FTET cycle in the PURSUE study follow-up, and 607 infants were born after fresh ART cycles in the ENSURE, ENGAGE and PURSUE studies combined. The rates for congenital malformations (major and minor combined) reported for infants born after an FTET cycle in the PURSUE study follow-up (16.4%) were similar to those reported for infants born after fresh ART cycles in the ENSURE, ENGAGE and PURSUE studies combined (16.8%).
II/0034	Update of section 4.5 of the SmPC to add information pertaining to potential hCG cross-reactivity resulting in a false positive pregnancy test. The Package Leaflet has been updated accordingly. In addition, the MAH is taking the opportunity to implement changes in the annexes in line with the QRD templates (versions 9.1 and 10) and to propose combined versions of the SmPCs and Package Leaflets for the different strengths. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/09/2017	26/04/2018	SmPC, Annex II, Labelling and PL	Elonva may cause a false positive hCG pregnancy test if the test is administered during the ovarian stimulation portion of the ART cycle. This may be due to cross-reactivity of some hCG pregnancy tests with the carboxy-terminal peptide of the beta subunit of Elonva.
II/0036/G	This was an application for a group of variations.	20/07/2017	n/a		

	B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test 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				
II/0033	Update of section 4.8 of the SmPC to add the new ADR 'hypersensitivity reactions (both local and generalized, including rash)', identified through post-marketing surveillance, with frequency 'unknown' under the system organ class of 'immune system disorders'. The Package Leaflet has been updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	18/05/2017	26/04/2018	SmPC and PL	n/a
IB/0035	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	10/04/2017	n/a		
IAIN/0032/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	14/09/2016	n/a		

	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release				
IB/0031	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	17/08/2016	n/a		
IB/0030/G	This was an application for a group of variations. B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation B.II.d.2.z - Change in test procedure for the finished product - Other variation	04/05/2016	n/a		
IB/0029/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.2.z - Change to importer, batch release arrangements and quality control testing of the FP - Other variation 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	06/01/2016	n/a		
II/0026	Update of section 5.1 of the SmPC in order to update the Elonva Product Information with the results of	24/09/2015	21/11/2016	SmPC, Annex II and PL	

	Trials 38831 and P06031. Both studies assess the outcome and safety of the FTET (frozen-thawed embryo transfer) cycles of the two largest Phase III trials conducted with Elonva. In addition, the Marketing authorisation holder (MAH) took the opportunity to include editorial changes in section 9 of the SmPC and Annex II as agreed with the authorities. Furthermore, the MAH took the occasion to update the contact information of the local representative for Luxembourg in the PL. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IA/0028	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	24/08/2015	n/a		
IA/0027/G	This was an application for a group of variations. 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) 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) A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites	16/06/2015	n/a		

	(excluding manufacturer for batch release)				
IA/0025/G	This was an application for a group of variations. 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 components or devices (when mentioned in the dossier) - Deletion of a supplier	20/03/2015	n/a		
IB/0024	To update the RMP with the already agreed and approved changes to the labeling text from variation EMEA/H/C/1106/II/015/G. In this variation the results of the PURSUE and TRUST studies where submitted. Also, some updates were made to the RMP to reflect to current status with respect to clinical trials (inclusion of the most recent CSR of the PURSUE study (also submitted as part of II/15/G), study end of the FTET trial (P06031), and, updated exposure for the HH males trial). C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	05/03/2015	n/a		
PSUSA/875/201407	Periodic Safety Update EU Single assessment - corifollitropin alfa	12/02/2015	n/a		PRAC Recommendation - maintenance
IB/0023	B.I.a.1.z - Change in the manufacturer of AS or of a	15/01/2015	n/a		

	starting material/reagent/intermediate for AS - Other variation				
IA/0022	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	07/11/2014	n/a		
II/0015/G	This was an application for a group of variations. Grouping of 2 type II variations in order to update sections 4.2, 4.8, 5.1 and 5.2 of the SmPC with data from the final CSR of the TRUST study (study 38825) and with responses to the conclusions of the CHMP on FUM EMEA/H/C/001106/MEA 015. The Package Leaflet is updated accordingly. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/09/2014	30/10/2014	SmPC, Labelling and PL	In the treatment of women of reproductive age, the dose of Elonva is based on weight and age. A single 100 microgram dose is recommended in women who weigh less than or equal to 60 kilograms and who are 36 years of age or younger. A single 150 microgram dose is recommended in women who weigh more than 60 kilograms, regardless of age, and women who weigh 50 kilograms or more and who are older than 36 years of age. Women older than 36 years of age who weighed less than 50 kilograms were not studied. The integrated safety, efficacy and pharmacokinetic information from an integrated analysis of the phase III studies PURSUE, ENSURE, ENGAGE and TRUST has been updated in sections 4.8, 5.1 and 5.2 of the Elonva SmPC, respectively. With regard to immunogenicity, of the 2,511 women treated with Elonva who were evaluated for the formation of post-treatment antibodies, four (0.16%) had evidence of antibody formation, including three who had been exposed once to Elonva and one who had been exposed twice to Elonva. In each case, these antibodies were non-neutralizing and did not interfere with the response to

					stimulation or the normal physiologic responses of the Hypothalamic-Pituitary-Ovarian (HPO) axis. Two of these four women became pregnant during the same treatment cycle in which antibodies were detected, suggesting that the presence of non-neutralizing antibodies after stimulation with Elonva is not clinically relevant.
R/0018	Renewal of the marketing authorisation.	26/06/2014	22/08/2014		
IB/0020	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	03/06/2014	n/a		
IB/0019	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	16/05/2014	n/a		
II/0014	Update to SmPC sections 4.2 Posology, 4.3 Contraindication, 4.4 Special warnings and precautions for use, 4.6 Pregnancy and lactation, 4.8 Undesirable Effects, 4.9 Overdose, 5.1 Pharmacologic properties, 5.2 Pharmacokinetic properties, and 5.3 Preclinical safety data in order to reflect recent medical information relevant to safety and efficacy, which has evolved, or to provide more clarity. The package leaflet was proposed to be updated accordingly. Furthermore, the MAH proposed this opportunity to bring the PI in line with the latest QRD template version 9.0.	20/02/2014	21/03/2014	SmPC, Annex II, Labelling and PL	Based on data from literature and the company`s safety database, the product information in SmPC 4.2, 4.3 and 4.4 has been updated to better reflect current medical knowledge regarding Ovarian hyperstimulation syndrome (OHSS), Polycystic Ovarian Syndrome (PCOS) and the measuring of oestradiol levels. Some of the existing text in the remaining SmPC sections and the package leaflet has been clarified, and brought in line with the Agency`s latest template. With this variation PCOS was upgraded by adding it as a contraindication in SmPC section 4.3 (instead of a warning in section 4.4). It is unknown whether patients with PCOS without polycystic ovaries will have a higher follicular response. As Elonva consists of one single injection for one

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				week, which cannot be adjusted in case of a higher follicular response, it is safer to treat these patients with daily injections of FSH to reduce the risk of OHSS.
II/0013	New syringe tip cap 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	20/02/2014	n/a		
PSUV/0016	Periodic Safety Update	06/02/2014	n/a		PRAC Recommendation - maintenance
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/0012	Transfer of Marketing Authorisation	15/08/2013	19/09/2013	SmPC, Labelling and PL	
II/0009	Change to the control of the active substance and finished product 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	25/07/2013	n/a		

N/0011	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	03/07/2013	19/09/2013	PL	
IA/0010	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)	12/04/2013	n/a		
IB/0008	B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation	01/10/2012	n/a		
II/0006	Change to the manufacturing process of the active substance B.I.e.2 - Design Space - Introduction of a post approval change management protocol related to the AS	20/09/2012	n/a		
IG/0184	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	21/08/2012	n/a		
IG/0117/G	This was an application for a group of variations. 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	18/11/2011	17/02/2012	Annex II	

	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/0004	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/09/2011	n/a	PL	
IB/0003	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol	23/08/2010	n/a	SmPC	
IA/0002/G	This was an application for a group of variations. Additional site for the manufacture of the drug product B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier 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)	26/05/2010	n/a		
IA/0001	C.I.9.i - Changes to an existing pharmacovigilance system as described in the DDPS - Change(s) to a	24/03/2010	n/a	Annex II	

	DDPS following the assessment of the same DDPS in relation to another medicinal product of the same MAH				