ellaOne

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/0071	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	20/09/2024		Labelling and PL	
N/0069	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	10/06/2024		PL	

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

N/0068	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/01/2024		PL	
N/0067	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/09/2023		PL	
N/0066	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/06/2023		PL	
N/0065	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/04/2023		PL	
N/0064	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/01/2023		PL	
N/0063	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/11/2022	09/01/2023	PL	
N/0062	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/09/2022	09/01/2023	PL	
IA/0061	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	04/05/2022	n/a		
PSUSA/3074/ 202105	Periodic Safety Update EU Single assessment - ulipristal (female emergency contraceptive)	16/12/2021	16/02/2022	SmPC, Labelling and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/3074/202105.
IA/0060	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	14/02/2022	n/a		

	intermediate used in the manufacture of the AS or manufacturer of a novel excipient				
IB/0059	Update section 4.4 of the SmPC to align with the excipient guideline on Sodium and Lactose. The package leaflet has been updated accordingly. The MAH took the opportunity to update the package leaflet with revised contact details of the local representatives for Hungary, the Netherlands, and the United Kingdom (Northern Ireland). C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	18/01/2022	09/01/2023	SmPC and PL	
N/0057	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	31/03/2021	16/02/2022	PL	
N/0056	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/02/2021	16/02/2022	PL	
PSUSA/3074/ 202005	Periodic Safety Update EU Single assessment - ulipristal (female emergency contraceptive)	26/11/2020	n/a		PRAC Recommendation - maintenance
N/0054	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/05/2020	16/02/2022	PL	
N/0053	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/04/2020	16/02/2022	Labelling	
PSUSA/3074/ 201905	Periodic Safety Update EU Single assessment - ulipristal (female emergency contraceptive)	16/01/2020	n/a		PRAC Recommendation - maintenance

N/0052	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	05/09/2019	04/02/2020	PL	
IAIN/0050	A.1 - Administrative change - Change in the name and/or address of the MAH	31/01/2019	04/02/2020	SmPC, Labelling and PL	
PSUSA/3074/ 201805	Periodic Safety Update EU Single assessment - ulipristal (female emergency contraceptive)	29/11/2018	n/a		PRAC Recommendation - maintenance
N/0049	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/08/2018	04/02/2020	PL	
N/0047	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/02/2018	04/02/2020	Labelling and PL	
PSUSA/3074/ 201705	Periodic Safety Update EU Single assessment - ulipristal (female emergency contraceptive)	30/11/2017	n/a		PRAC Recommendation - maintenance
X/0045	Annex I_2.(d) Change or addition of a new pharmaceutical form	14/09/2017	10/11/2017	SmPC, Annex II, Labelling and PL	
IA/0044	B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms	30/01/2017	08/06/2017	SmPC, Labelling and PL	
IB/0043	C.I.1.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a Union referral procedure - The product is not covered by the defined scope of the procedure but the change(s) implements the outcome of the procedure and no	09/12/2016	08/06/2017	SmPC, Annex II, Labelling and PL	

	new additional data is required to be submitted by the MAH				
PSUSA/3074/ 201605	Periodic Safety Update EU Single assessment - ulipristal (female emergency contraceptive)	01/12/2016	n/a		PRAC Recommendation - maintenance
IAIN/0041	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	12/07/2016	08/06/2017	Annex II and PL	
IA/0040	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	22/02/2016	n/a		
PSUSA/3074/ 201505	Periodic Safety Update EU Single assessment - ulipristal (female emergency contraceptive)	03/12/2015	n/a		PRAC Recommendation - maintenance
IB/0038	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	13/08/2015	n/a		
II/0037	B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	23/04/2015	02/05/2016	SmPC and PL	
II/0033	Submission of the HRA 2914-012 final clinical study report to address CHMP request from the MEA007.5; the study HRA 2914-012 is a Prospective Multicenter Observational Study to Assess Clinical Follow-up and Outcomes of Pregnancies Exposed to ella/ellaOne. No changes to the product information are proposed. C.I.13 - Other variations not specifically covered	22/01/2015	n/a		

	elsewhere in this Annex which involve the submission of studies to the competent authority				
II/0021	C.I.5.b - Change in the legal status of a medicinal product for centrally authorised products - All other legal status changes	20/11/2014	07/01/2015	SmPC, Annex II, Labelling and PL	Please refer to the assessment report: EMEA/H/C/001027/II/0021
PSUV/0032	Periodic Safety Update	04/12/2014	n/a		PRAC Recommendation - maintenance
IAIN/0036	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	02/12/2014	n/a		
II/0034	Update of section 4.5 and 5.2 of the SmPC in order to add information on interaction with BCRP transporters and update the information on interaction with P-gp substrates. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/10/2014	07/01/2015	SmPC	In vitro data indicate that ulipristal acetate may be an inhibitor of P-gp at clinically relevant concentrations. Results in vivo with the P-gp substrate fexofenadine were inconclusive. The effects of ulipristal acetate on the P-gp substrates are unlikely to have any clinical consequences. In vitro data indicate that ulipristal acetate may be an inhibitor of BCRP (Breast Cancer Resistance Protein) transporters at the intestinal level. The effects of ulipristal acetate on BCRP are unlikely to have any clinical consequences. Ulipristal acetate is not a substrate for either OATP1B1 or OATP1B3.
A31/0028	On 16 January 2014 the Swedish Agency initiated a review under Article 31 of directive 2001/83 EC regarding all emergency contraceptives containing LNG or UPA requesting the Committee for Medicinal Products for Human Use (CHMP) to give its opinion	24/07/2014	01/10/2014	SmPC and PL	For further information please refer to the Emergency contraceptives Article 31 referral - Assessment report.

	on whether the marketing authorisations should be maintained, varied, suspended or withdrawn. The CHMP was requested to assess whether the efficacy of emergency contraceptives is affected in relation to body weight and/or body mass index (BMI) of the women.				
IB/0031	B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF	30/07/2014	n/a		
IA/0030	B.II.d.2.b - Change in test procedure for the finished product - Deletion of a test procedure if an alternative method is already authorised	15/04/2014	n/a		
R/0025	Renewal of the marketing authorisation.	23/01/2014	21/03/2014	SmPC and PL	Based on the data retrieved during the 5 year renewal period since launch of EllaOne, the benefits of the product continue to outweigh the risks. The results of the study of Moreau (2012) (pooled Phase III studies of UPA) suggest a (non statistically significant) decrease of efficacy of UPA among women who have further unprotected intercourse in the same cycle, especially if they are morbidly obese. The impact of higher body weight/BMI on the efficacy of emergency contraceptives (levonorgestrel-containing medicinal products and ellaOne) will be further evaluated in a referral under Article 31 of Directive 2001/83/EC. The assessment of all data collected and any necessary follow-up affecting ellaOne in this respect, will be handled within the context of the Article 31 Referral EC (Procedure number: ellaOne

					EMEA/H/A-31/1391/C/001027/0028). The product information has been updated to reflect post-marketing data and pre-clinical data that have become available since initial marketing authorisation, and to bring it in line with the current Agency template. The risk-benefit balance for ellaOne remains positive; the CHMP recommends that the renewal of the marketing authorisation of ellaOne be granted with unlimited validity.
IB/0027	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	27/01/2014	01/10/2014	SmPC, Labelling and PL	
N/0026	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	20/11/2013	20/12/2013	PL	
N/0024	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	02/09/2013	20/12/2013	PL	
IB/0023	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	26/07/2013	n/a		
II/0020	Update of sections 4.4, 4.5 and 5.2 of the SmPC to update an existing warning and to add safety information based on a clinical Drug-drug interaction study with a CYP3A4 inducer (rifampicin). In addition, the MAH took the opportunity to update the list of contact details of local representatives in the Package Leaflet. Furthermore, the PI Annex II is being brought in line with the latest QRD template	30/05/2013	20/12/2013	SmPC, Annex II and PL	The MAH proposed to change the SmPC sections 4.4, 4.5 and 5.2 with respect to the interaction of rifampicin, a CYP3A4 inducer, based on the results of interaction study (Study HRA2914-551). The potential for interaction (as previously stated) has now been confirmed by the results from the DDI study. Results showed that the administration of ulipristal acetate with a CYP3A4 inducer such as rifampicin markedly decreases

	version 9. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				Cmax and AUC of ulipristal acetate by 90% or more and decreases ulipristal acetate half-life by 2.2-fold corresponding to an approximately 10-fold decrease of ulipristal acetate exposure. Concomitant use of ellaOne with CYP3A4 inducers may result in a decreased efficacy of ellaOne and is therefore not recommended. During the procedure the CHMP requested additional amendments to the Product Information in addition to the changes proposed by the MAH: the text on interactions (including newly proposed text) is moved from SmPC section 5.2 to section 4.5 as the new data submitted concern in vivo studies; this interaction is cross-referred in section 4.4, not only with rifampicin, but an exhaustive list of inducers is mentioned in the SmPC sections 4.4 and 4.5 (including efavirenz, fosphenytoine, nevirapine, oxcarbazepine, primidone, rifabutine). The package leaflet text section 2 is updated in accordance with the SmPC. Updates to the list of contact details of local representatives in the Package Leaflet (Denmark, Estonia, Finland, Latvia, Lithuania, Norway and Sweden) and the PI Annex II alignment with the latest QRD template version 9 were also agreed by the CHMP.
IB/0022/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.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.e - Replacement or addition of a	22/04/2013	20/12/2013	Annex II and PL	

	manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products B.II.b.2.b.2 - Change to batch release arrangements and quality control testing of the FP - Including batch control/testing B.II.b.3.a - Change in the manufacturing process of the finished product - Minor change in the manufacturing process of an immediate release solid oral dosage form or oral solutions B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier				
II/0018	Update of SmPC section 4.4, 4.6 and 5.2 in order to update the safety information following completion of a PK study HRA2914-514 in lactating women (FUM 004). The Package Leaflet and Labelling are updated accordingly. Furthermore, the PI is being brought in line with the latest QRD template version 8 Rev.1. The requested variation proposed amendments to the Update of Summary of Product Characteristics, 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	15/11/2012	20/12/2013	SmPC, Annex II, Labelling and PL	This variation concerns an update of the product information following completion of a PK study HRA2914-514 in lactating women (requested as FUM 004). Study HRA2914-514 was designed to investigate the pharmacokinetics of ulipristal acetate in healthy breastfeeding women who take 30 mg and the amount of drug transferred into human milk. The PL is updated accordingly Study HRA2914-514 was a pharmacokinetic study consisting of a single dose of 30 mg ulipristal acetate followed by a blood and milk sampling period of 120 hours in lactating women. The concentrations in breast milk for UPA and monodemethylated-UPA over time followed the same profile as those in plasma but were lower than the plasma concentrations. After a 48-72 hour period after dosing the total amount excreted ulipristal in milk was less than 0.004% of the total administered dose. At 120 hours

					after UPA administration, both UPA and its main active metabolite were still detectable in both biological media in all subjects. The benefit-risk for ellaOne in the indication Emergency contraception within 120 hours of unprotected sexual intercourse or contraceptive failure remains unchanged.
II/0017	Update of sections 4.4 , 4.5 and 5.2 of the SmPC in order to update the safety information based on four clinical studies conducted to assess potential drug-drug interactions with erythromycin, ketoconazole, esomeprazole and fexofenadine. The Package Leaflet section 2 is updated accordingly. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	15/11/2012	20/12/2013	SmPC and PL	Following completion of four clinical studies conducted to assess potential drug-drug interactions with erythromycin, ketoconazole, esomeprazole and fexofenadine, the applicant proposed to adapt the SmPC and PL based on the results of the submitted studies (SmPC section 4.4, 4.5, and 5.2). As the interaction with CYP3A4 inhibitors and P-gp substrates is shown to be of no clinical relevance, it was agreed to omit this information in SmPC 4.4 and 4.5; the in vivo interaction results are shortly mentioned in section 5. With regard to the interaction with esomeprazole, as the clinical implications of a 65% decrease in ellaOne Cmax are unknown, no specific recommendations can be given in the SmPC. Therefore some information on esomeprazole should remain in the SmPC in section 4.5, but can be omitted in section 4.4. The benefit-risk for ellaOne in the indication of Emergency contraception within 120 hours of unprotected sexual intercourse or contraceptive failure remains unchanged.
N/0019	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/11/2012		PL	
IAIN/0016/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	02/07/2012	n/a		

	QPPV 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.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD 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				
II/0014	B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	21/06/2012	21/06/2012		
N/0015	Update in the contact details for Bulgaria, Ireland, Netherland, Slovakia and UK. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/02/2012	28/06/2012	PL	
IAIN/0012	A.5.a - Administrative change - Change in the name and/or address of a manufacturer responsible for batch release	19/12/2011	28/06/2012	Annex II and PL	
IAIN/0013		16/12/2011	n/a	Annex II and PL	

II/0011/G	This was an application for a group of variations. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data A.6 - Administrative change - Change in ATC Code/ATC Vet Code	22/09/2011	10/11/2011	SmPC, Annex II and PL	This was an application for a group of variations to update SPC section 4.5 and 5.1. In SPC 4.5 an inconsistency was corrected regarding CYP3A4 interaction and ritonavir, and new information from 3 preclinical studies was added to SPC 4.5 and 5.2. Studies HRA2914-476 and HRA2914-477 describe the effects of ulipristal acetate on CYP3A4 activity and study HRA2914-479 characterises the interaction of ulipristal acetate with the P-gp transporter. SPC section 4.4 was revised accordingly. In addition in SPC section 4.8 an inconsistency in frequencies of adverse reactions was corrected. SPC section 5.1 was updated following granting of the ATC code (G03AD02) by WHO. The PL is amended accordingly; in addition details of local representatives in the PL were updated for France and Ireland and Annex II was updated in line with QRD wording on the RMP.
IB/0010	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	26/11/2010	n/a		
IA/0009	B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the currently approved batch size	15/10/2010	n/a		
IB/0008	Deletion of specifications of the active substance. B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting	02/09/2010	n/a		

	material/intermediate/reagent - Other variation				
II/0002	Update of SPC further to FUM 005 with data from clinical studies; the update affects SPC sections 4.2; 4.4; 4.8; 5.1. The package leaflet was amended accordingly. In addition changes in contact details of the local representatives, and a correction of spelling of the invented name (in SPC, labelling and package leaflet). Update of Summary of Product Characteristics, Labelling and Package Leaflet	20/05/2010	02/07/2010	SmPC, Labelling and PL	Update of the SPC with data from clinical studies. The MAH submitted study HRA2914-511 (a mechanism of action study) and the final study report of study HRA2914-513, as well as a meta-analysis of studies HRA2914-513 and HRA2914-507. Results from study HRA2914-511 show that ellaOne is able to postpone follicular rupture in some women even when taken immediately before ovulation is scheduled to occur. Study HRA2914-513 is a prospective, randomized, single blind, multicenter comparative study of the efficacy, safety and tolerability of ulipristal acetate versus levonorgestrel as emergency contraception. The SPC sections 4.4 and 4.8 were updated with results from this study and the meta-analysis. As a limited number of patients under 18 years were included in this study, this is also mentioned in SPC section 4.2. The package leaflet was amended accordingly. In addition changes in contact details of the local representatives, and a correction of spelling of the invented name (in SPC, labelling and package leaflet) in line with spelling in the approved mock-ups.
II/0006/G	This was an application for a group of variations. Changes in the manufacturing process of the finished product in the new added manufacturing site. B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-	22/04/2010	10/06/2010	Annex II and PL	

	release, batch control, primary and secondary packaging, for non-sterile medicinal products B.II.b.3.b - Change in the manufacturing process of the finished product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product 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 currently approved batch size B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.2.b.2 - Change to batch release arrangements and quality control testing of the FP - Including batch control/testing B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter				
IA/0004	C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV	19/03/2010	n/a	Annex II	

IA/0005	Change in the name of the finished product manufacturer responsible for batch release from 'Cardinal Health France S.A.S.' to 'Osny Pharma S.A.S.' The address (17, Rue de Pontoise, FR-95520 Osny, France) is unchanged. A.5.a - Administrative change - Change in the name and/or address of a manufacturer responsible for batch release	12/02/2010	n/a	Annex II and PL	
II/0001	Update of the DDPS. Update of DDPS (Pharmacovigilance)	24/09/2009	23/10/2009	Annex II	Update of Detailed Descritption of the Pharmacovigilance System (DDPS). The MAH has submitted the version 4 of the DDPS as requested by the CHMP at the time of the granting of the Marketing Authorisation and the CHMP concluded that the updated DDPS addresses the outstanding issues and fulfills the requirements. The Annex II of the Product Information was updated accordingly.