Duavive

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
IB/0040	B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF	19/11/2024	n/a		
IA/0039	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process	01/10/2024	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).

	of the AS				
IA/0038	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	01/10/2024	n/a		
II/0036	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	02/05/2024	24/07/2024	SmPC and PL	
IA/0037	B.III.2.a.2 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material	04/12/2023	n/a		
IB/0035	B.II.e.1.b.1 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Solid, semi-solid and non-sterile liquid pharmaceutical forms	19/06/2023	24/07/2024	SmPC and PL	
II/0032	Submission of an updated RMP version 3.4 in order to reflect the updated study milestones and completion of the post authorisation safety study of CE/BZA in the United States (US PASS, Study B2311060) previously assessed as part of II/0030 (MEA002.15), as well as to update the post marketing data with the data lock point of 31 October 2021 and the final sign off date 03.03.2023. C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing	12/05/2023	n/a		

	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				
PSUSA/10321 /202204	Periodic Safety Update EU Single assessment - oestrogens conjugated / bazedoxifene	01/12/2022	n/a		PRAC Recommendation - maintenance
IB/0033/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.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.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)	19/07/2022	n/a		
II/0030	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	02/12/2021	16/12/2022	SmPC and PL	The aim of this PASS study was to estimate the incidence and to compare some risks (i.e. endometrial hyperplasia, endometrial cancer) among postmenopausal women initiating either CE/BZA or E+P HRT. The results of the study show that the risk of breast cancern and stroke might be in the same range as among users of estrogen-progestin

					combination hormone therapy. The corresponding incidence rates are stated in the SmPC section 5.1.
N/0031	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	01/10/2021	16/12/2022	PL	
N/0029	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/12/2020	10/05/2021	PL	
II/0025	Submission of the final clinical study report (CSR) for the Duavive Non-Interventional EU Drug Utilisation Study (DUS) - Study B2311061. This final CSR relates to the Post-Authorisation Measure MEA 003. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	03/09/2020	n/a		
II/0024	Update of the Risk Management Plan (RMP) to version 3.1, to include amended study milestones and to revise the RMP document format in line with latest Good Pharmacovigilance Practices Guidance Module V, revision 2 guidelines, as requested during the assessment of the renewal. 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	03/09/2020	n/a		

IB/0028	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	26/08/2020	10/05/2021	SmPC and PL	
IA/0027	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	10/06/2020	n/a		
IB/0026	B.II.e.1.z - Change in immediate packaging of the finished product - Other variation	14/05/2020	10/05/2021	SmPC and PL	
R/0021	Renewal of the marketing authorisation.	19/09/2019	11/11/2019	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Duavive in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10321 /201904	Periodic Safety Update EU Single assessment - oestrogens conjugated / bazedoxifene	31/10/2019	n/a		PRAC Recommendation - maintenance
N/0022	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/04/2019	11/11/2019	PL	
IA/0020	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	07/02/2019	n/a		
IA/0019	B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP -	17/12/2018	n/a		

	Replacement/addition of a site where batch control/testing takes place				
PSUSA/10321 /201804	Periodic Safety Update EU Single assessment - oestrogens conjugated / bazedoxifene	31/10/2018	n/a		PRAC Recommendation - maintenance
T/0018	Transfer of Marketing Authorisation	11/07/2018	02/08/2018	SmPC, Labelling and PL	
PSUSA/10321 /201704	Periodic Safety Update EU Single assessment - oestrogens conjugated / bazedoxifene	26/10/2017	n/a		PRAC Recommendation - maintenance
N/0016	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	10/10/2017	24/01/2018	Labelling and PL	
IB/0014	C.I.3.a - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Implementation of wording agreed by the competent authority	21/02/2017	24/01/2018	SmPC and PL	
N/0013	Update of the package leaflet with revised contact details of the local representative for Germany. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	28/10/2016	24/01/2018	PL	
PSUSA/10321 /201604	Periodic Safety Update EU Single assessment - oestrogens conjugated / bazedoxifene	27/10/2016	n/a		PRAC Recommendation - maintenance
IAIN/0011	C.I.z - Changes (Safety/Efficacy) of Human and	19/04/2016	08/09/2016	SmPC and PL	

	Veterinary Medicinal Products - Other variation				
PSUSA/10321 /201510	Periodic Safety Update EU Single assessment - oestrogens conjugated / bazedoxifene	14/04/2016	n/a		PRAC Recommendation - maintenance
N/0010	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	31/03/2016	08/09/2016	PL	
N/0009	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/02/2016	08/09/2016	PL	
IB/0008	B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF	02/02/2016	n/a		
IAIN/0007/G	This was an application for a group of variations. B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer 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	11/01/2016	n/a		
II/0002	Update of sections 4.5 and 5.2 of the SmPC based on clinical drug-drug interaction study B2311065 undertaken to evaluate the effects of the strong CYP3A4 inhibitor, itraconazole, on the	19/11/2015	08/09/2016	SmPC	In vitro and in vivo studies have shown that oestrogens are partially metabolized by cytochrome P450 enzymes, including CYP3A4. However, in a clinical drug drug interaction study, repeat administration of 200 mg

	pharmacokinetics of CE 0.45 mg/BZA 20 mg. The provision of the study report addresses the post-authorisation measure MEA 001. In addition, the MAH took the opportunity to update section 5.1 of the SmPC with the assigned pharmacotherapeutic group and ATC code. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				itraconazole, a strong CYP3A4 inhibitor, had minimal impact on the pharmacokinetics of CE (as measured by estrone and equilin) and bazedoxifene when administered with a single dose of CE 0.45 mg/bazedoxifene 20 mg. In a pharmacokinetic study (n=24) BMI appeared to have little impact on systemic exposure to CE and bazedoxifene.
IB/0005	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	16/11/2015	n/a		
PSUSA/10321 /201504	Periodic Safety Update EU Single assessment - oestrogens conjugated / bazedoxifene	06/11/2015	n/a		PRAC Recommendation - maintenance
II/0004	Update of section 4.8 of the Smpc to include revised frequency categories of a number of ADRs for the bazedoxifene monotherapy component. 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	17/09/2015	08/09/2016	SmPC and PL	The frequency categories have changed as follows: Retinal vein thrombosis from 'rare' to 'uncommon'; rash, pruritus from 'not known' to 'common'; oedema peripheral from 'common' to 'very common'.
N/0001	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/06/2015	08/09/2016	PL	