Verzenios

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/0033	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	04/07/2024		SmPC	
PSUSA/10724 /202309	Periodic Safety Update EU Single assessment - abemaciclib	25/04/2024	17/06/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for

[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).

					PSUSA/10724/202309.
IAIN/0035	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	13/06/2024		SmPC and PL	
IAIN/0034	B.II.g.5.a - Implementation of changes foreseen in an approved change management protocol - Requires no further supporting data	26/02/2024	n/a		
IB/0031/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.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	10/01/2024	n/a		
IB/0030/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	29/11/2023	n/a		

	B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS B.I.b.z - Change in control of the AS - Other variation				
II/0028	Update of section 4.4 of the SmPC in order to add a new warning on "arterial thromboembolic events", based on a safety review. The Package Leaflet is updated accordingly. In addition the MAH took the opportunity to update section 9 of the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	09/11/2023	17/06/2024	SmPC and PL	A potential increased risk for serious arterial thromboembolic events (ATEs), including ischemic stroke and myocardial infarction, has been observed in metastatic breast cancer studies when abemaciclib was administered in combination with endocrine therapies. The benefits and risks of continuing abemaciclib in patients who experience a serious ATE should be considered.
IG/1620	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	01/08/2023	n/a		
IAIN/0027	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	11/07/2023	n/a		
R/0025	Renewal of the marketing authorisation.	26/04/2023	23/06/2023	SmPC, Annex II, Labelling	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Verzenios in the approved indication remains favourable

				and PL	and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10724 /202209	Periodic Safety Update EU Single assessment - abemaciclib	14/04/2023	n/a		PRAC Recommendation - maintenance
II/0024	Update of section 5.1 of the SmPC in order to include overall survival data based on final results from study MONARCH 2; this is a randomized, double-blind, placebo-controlled, phase 3 study of fulvestrant with or without abemaciclib, a CDK4/6 Inhibitor, for women with hormone receptor-positive, HER2-negative locally advanced or metastatic breast cancer. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/01/2023	23/06/2023	SmPC	At the pre specified final OS analysis of study MONARCH 2 (18 March 2022 cut off), 440 events were observed across the 2 arms. The improvement in OS previously observed at the interim OS analysis (20 June 2019 cut off) was maintained in the abemaciclib plus fulvestrant arm compared to the placebo plus fulvestrant arm, with a HR of 0.784 (95 % CI: 0.644, 0.955). Median OS was 45.8 months in the abemaciclib plus fulvestrant arm and 37.25 months in the placebo plus fulvestrant arm. For more information, please refer to the Summary of Product Characteristics.
PSUSA/10724 /202109	Periodic Safety Update EU Single assessment - abemaciclib	05/05/2022	n/a		PRAC Recommendation - maintenance
IA/0023	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	11/04/2022	n/a		
II/0013	Extension of indication to include Verzenios in combination with endocrine therapy for adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive early breast cancer at high risk of recurrence; as a consequence, section	24/02/2022	01/04/2022	SmPC and PL	Please refer to Scientific Discussion 'Verzenios-II-0013'

	4.1, 4.2, 4.4, 4.6, 4.8, 5.1 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
II/0021	Update of section 5.1 of the SmPC in order to include second OS interim results from study MONARCH 3; this is a randomised, double blind, placebo-controlled phase 3 study of Nonsteroidal Aromatase Inhibitors (Anastrozole or Letrozole) plus LY2835219, a CDK4/6 Inhibitor, or Placebo in Postmenopausal Women with Hormone Receptor-Positive, HER2-Negative Locoregionally Recurrent or Metastatic Breast Cancer with No Prior Systemic Therapy in this Disease Setting. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	27/01/2022	01/04/2022	SmPC	SmPC new text In study MONARCH 3, at the second OS interim analysis, 255 events were observed across the two arms. Median OS was 67.1 months in the abemaciclib plus AI arm and 54.5 months in the placebo plus AI arm. As the observed HR of 0.754 (95% CI: 0.584, 0.974) did not reach statistical significance, the study continues to fully characterise overall survival. For more information, please refer to the Summary of Product Characteristics.
IAIN/0020	B.II.e.6.a - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that affects the product information	05/08/2021	01/04/2022	SmPC and Labelling	
IB/0019	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	16/07/2021	n/a		

IB/0017/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.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	25/05/2021	n/a		
II/0016/G	This was an application for a group of variations. Update of section 5.1 of the SmPC in order to include OS interim results from MONARCH 3 study, a randomised, double blind, placebo controlled phase 3 study in women with HR positive, HER2 negative locally advanced or metastatic breast cancer who had not received prior systemic therapy in this disease setting. In addition, the MAH is updating the ATC code in the SmPC. The MAH is also taking the opportunity to update the list of local representatives in the Package Leaflet in line with the QRD template 10.2. A.6 - Administrative change - Change in ATC Code/ATC Vet Code C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	20/05/2021	01/04/2022	SmPC and PL	In study MONARCH 3, at the first OS interim analysis, 197 events were observed across the two arms. As the observed HR of 0.786 (95% CI: 0.589, 1.049) did not reach statistical significance, the study continues to fully characterise overall survival.

PSUSA/10724 /202009	Periodic Safety Update EU Single assessment - abemaciclib	06/05/2021	n/a		PRAC Recommendation - maintenance
IAIN/0015	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	26/01/2021	n/a		
PSUSA/10724 /202003	Periodic Safety Update EU Single assessment - abemaciclib	29/10/2020	n/a		PRAC Recommendation - maintenance
II/0012/G	This was an application for a group of variations. B.I.a.1.c - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer uses a substantially different route of synthesis or manufacturing conditions B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol	15/10/2020	n/a		
PSUSA/10724 /201909	Periodic Safety Update EU Single assessment - abemaciclib	17/04/2020	n/a		PRAC Recommendation - maintenance
II/0006	Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add interstitial lung disease (ILD)-like events (including pneumonitis) as new adverse drug reactions together with a related warning and dose adjustments recommendations. The Package Leaflet	12/12/2019	17/01/2020	SmPC, Annex II, Labelling and PL	Interstitial lung disease (ILD)/pneumonitis was reported in patients receiving abemaciclib. Patients should be monitored for pulmonary symptoms indicative of ILD/pneumonitis and treated as medically appropriate. Based on the grade of ILD/pneumonitis, abemaciclib may

	is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1 and make few corrections to the PL to bring it in line with the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				require dose modification. Abemaciclib should be permanently discontinued in patients with Grade 3 or 4 ILD/pneumonitis.
II/0008	Update of section 5.1 of the SmPC to include the results of the interim OS analysis from study MONARCH 2, a randomised, double-blind, placebo-controlled, phase 3 study of fulvestrant with or without abemaciclib, for women with hormone receptor positive, HER2 negative locally advanced or metastatic breast cancer. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	16/01/2020	17/12/2020	SmPC	Overall survival (OS) analysis in the ITT population in study MONARCH 2 showed a statistically significant improvement in patients receiving Verzenios plus fulvestrant compared with those receiving placebo plus fulvestrant. The median OS was 46.7 months in the Verzenios plus fulvestrant arm versus 37.3 months in the placebo plus fulvestrant arm (HR=0.757 (95% CI (0.606, 0.945), p-value=0.0137). Analyses for OS by stratification factors showed OS HR of 0.675 (95 % CI: 0.511, 0.891) in patients with visceral disease, and 0.686 (95 % CI: 0.451, 1.043) in patients with primary endocrine resistance.
IB/0009	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)	13/12/2019	17/12/2020	SmPC	
PSUSA/10724 /201903	Periodic Safety Update EU Single assessment - abemaciclib	31/10/2019	n/a		PRAC Recommendation - maintenance
II/0003	Update of section 4.2 of the SmPC in order to add a criterion for discontinuing abemaciclib in the event of specific hepatic changes based on available safety	19/09/2019	21/10/2019	SmPC	Patients should discontinue abemaciclib in case of elevation in AST and/or ALT >3 x ULN with total bilirubin >2 x ULN in the absence of cholestasis.

	data. Furthermore, section 4.5 of the SmPC is updated in order to update the information on contraceptive methods. In addition, the Marketing authorisation holder (MAH) took the opportunity to make editorial changes to section 5.1 of the SmPC and to the list of local representatives in the PL. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation				Moreover, the recommendation for use of an additional barrier contraceptive method for women receiving systematically acting hormonal contraceptives was removed, as women treated with abemaciclib for breast cancer should not be using exogenous oestrogen and progestins.
II/0005	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	12/09/2019	n/a		
IA/0007	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	14/08/2019	n/a		
IAIN/0002/G	This was an application for a group of variations. B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes	26/11/2018	21/10/2019	SmPC, Labelling and PL	

	B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes				
IAIN/0001/G	This was an application for a group of variations. B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished	12/10/2018	21/10/2019	SmPC, Labelling and PL	

	product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes				