Padcev

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/0021/G	This was an application for a group of variations. B.I.a.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant	05/12/2024		SmPC	

[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).

	update to the relevant AS section in the dossier B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol				
II/0020	Update of section 4.8 of the SmPC in order to add skin hyperpigmentation, skin discoloration, pigmentation disorder with frequency 'not known' based on available clinical, post marketing, and preclinical data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	28/11/2024		SmPC, Annex II and PL	
IB/0022/G	This was an application for a group of variations. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	22/11/2024	n/a		

	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation 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				
IB/0019/G	This was an application for a group of variations. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	30/09/2024	n/a		
PSUSA/10989 /202312	Periodic Safety Update EU Single assessment - enfortumab vedotin	25/07/2024	27/09/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10989/202312.
II/0016	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	05/09/2024		SmPC and PL	Update of sections 4.4 and 4.6 of the SmPC in order to update information on contraception for males and females in line with the SWP/NcWP (EMA/CHMP/SW P/74077/2020 rev. 1) recommendations on the duration of contraception following the end of treatment with a genotoxic drug. The Package Leaflet is updated accordingly.
II/0013	Extension of indication to include PADCEV in combination with pembrolizumab, the first-line treatment of adult patients with locally advanced or metastatic urothelial cancer who are eligible for	25/07/2024	26/08/2024	SmPC and PL	Please refer to Scientific Discussion of PADCEV-EMEA/H/C/005392/II/0013.

	platinum-containing chemotherapy, based on the final results from study KEYNOTE-A39/EV-302. This was an open label, randomized, controlled phase 3 study of enfortumab vedotin in combination with pembrolizumab versus chemotherapy alone in previously untreated locally advanced (LA) or metastatic urothelial cancer (mUC)". As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.1 of the RMP has also been submitted. As part of the application the MAH is requesting a 1-year extension of the market protection. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IA/0018/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	16/07/2024	n/a		

IB/0015	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	24/04/2024	n/a		
IB/0012	B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation	05/02/2024	n/a		
PSUSA/10989 /202306	Periodic Safety Update EU Single assessment - enfortumab vedotin	11/01/2024	n/a		PRAC Recommendation - maintenance
N/0011	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/11/2023	26/08/2024	PL	
PSUSA/10989 /202212	Periodic Safety Update EU Single assessment - enfortumab vedotin	06/07/2023	n/a		PRAC Recommendation - maintenance
IB/0009	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	15/05/2023	n/a		
II/0007	Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to introduce new posology recommendations in case of pneumonitis/interstitial lung disease (ILD), add a new warning on 'pneumonitis/ILD' and add it to the list of adverse drug reactions (ADRs). The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to	30/03/2023	26/04/2023	SmPC and PL	Based on a comprehensive review of the safety data relevant to pneumonitis/Interstitial lung disease (ILD) the following information have been added to the SmPC: Severe, life-threatening or fatal pneumonitis/ILD have occurred in patients treated with enfortumab vedotin. Monitor patients for signs and symptoms indicative of pneumonitis/ILD such as hypoxia, cough, dyspnea or interstitial infiltrates on radiologic exams. Corticosteroids should be administered for Grade ≥ 2 events (e.g., initial dose of 1-2 mg/kg/day prednisone or equivalent followed

	new quality, preclinical, clinical or pharmacovigilance data				by a taper). Withhold Padcev for Grade 2 pneumonitis/ILD and consider dose reduction. Permanently discontinue Padcev for Grade ≥3 pneumonitis/ILD.
II/0005/G	This was an application for a group of variations. B.I.a.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant update to the relevant AS section in the dossier 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.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.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	23/03/2023	n/a		
II/0006/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 -	26/01/2023	n/a		

	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.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product 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.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product				
PSUSA/10989 /202206	Periodic Safety Update EU Single assessment - enfortumab vedotin	12/01/2023	n/a		PRAC Recommendation - maintenance
II/0002	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	22/09/2022	n/a		

IA/0003	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	29/07/2022	n/a		
II/0001	B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol	21/07/2022	n/a		