JEMPERLI

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/0023	Extension of indication to include in combination with carboplatin and paclitaxel the treatment of adult patients with mismatch repair deficient (dMMR)/ microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer (EC) and who are candidates for systemic therapy, based on results from study 213361 (RUBY) Part 1, listed as a	12/10/2023	07/12/2023	SmPC, Annex II and PL	Please refer to Scientific Discussion 'Jemperli-H-C-5204-II-0023'

[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).

	Specific Obligation in the Annex II; this is a phase 3, randomized, double-blind, multicenter study of dostarlimab (TSR-042) plus carboplatin-paclitaxel versus placebo plus carboplatin-paclitaxel in patients with recurrent or primary advanced endometrial cancer. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Annex II and Package Leaflet are updated in accordance. Version 3.2 of the RMP has also been submitted. This submission fulfils SOB002 thus supporting the switch from CMA to full MA. In addition, the marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to the PI. 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				
PSUSA/10931 /202304	Periodic Safety Update EU Single assessment - dostarlimab	30/11/2023	n/a		PRAC Recommendation - maintenance
IB/0028	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	28/11/2023	n/a		
IAIN/0027	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	20/10/2023	n/a		

IB/0025	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	07/08/2023	n/a		
PSUSA/10931 /202210	Periodic Safety Update EU Single assessment - dostarlimab	12/05/2023	n/a		PRAC Recommendation - maintenance
IB/0022	B.II.g.4.b - Changes to an approved change management protocol - Minor changes that do not change the strategy defined in the protocol	28/03/2023	n/a		
R/0017	Renewal of the marketing authorisation.	15/12/2022	15/02/2023		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional marketing authorisation for JEMPERLI, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
IB/0021/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.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	01/02/2023	n/a		
IB/0020/G	This was an application for a group of variations.	01/02/2023	n/a		

	B.II.d.2.a - Change in test procedure for the finished product - 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				
IB/0019/G	This was an application for a group of variations. B.II.d.2.a - Change in test procedure for the finished product - 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	01/02/2023	n/a		
II/0013	Update of section 5.1 of the SmPC in order to update efficacy and safety information based on interim results from study 4010-01-001 (GARNET) listed as a specific obligation (SOB) in the Annex II; This is a single-arm, open-label, phase I trial of intravenous dostarlimab in advanced solid tumours. Update of Annex II to remove the specific obligation. In addition, the MAH took the opportunity to update Annex II in line with the QRD template version 10.3. The RMP version 2.1 is approved. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	15/12/2022	15/02/2023	SmPC and Annex II	A total of 143 patients with dMMR/MSI H EC were evaluated for efficacy in the GARNET study. The overall median treatment duration in weeks was 34 (range 2 to 220). Twenty four percent of subjects who received any amount of dostarlimab received treatment >102 weeks (2 years). Dostarlimab treatment resulted in an Objective Response Rate (ORR) by response evaluation criteria in solid tumours (RECIST) v1.1 of 45.5% (95% CI: 37.1, 54.0) in patients with dMMR/MSI-H endometrial cancer. A complete response (CR) was reported in 23 (16.1%) dMMR/MSI-H patients. Median duration of response (DOR) was not reached at the time of data cutoff. The number of patients with duration of response ≥ 12 months and ≥ 24 months was 52 (80%) and 29 (44.6%) respectively. Disease control rate (DCR) was of 60.1% (n=86).

					For more information, please refer to the Summary of Product Characteristics.
PSUSA/10931 /202204	Periodic Safety Update EU Single assessment - dostarlimab	01/12/2022	n/a		PRAC Recommendation - maintenance
IB/0016	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	10/10/2022	15/02/2023	Annex II	To update Annex II in order to change the due date for the efficacy study 'RUBY' from ’31 December 2022’ to ’31 August 2023’.
II/0007	Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update dose modifications recommendations in immune related adverse reactions, amend existing warnings, and add further immune-related ADRs to the list of adverse drug reactions (ADRs), with different frequencies, based on data from company sponsored trials and literature. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor changes to sections 4.6 and 5.2 of the SmPC and to update the list of local representatives in the Package Leaflet. Changes are also made to the PI to bring it in line with the current QRD template version and excipients guideline. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	21/07/2022	13/09/2022	SmPC and PL	Recommended dose modifications have been added to section 4.2 of the SmPC for myocarditis and severe neurological toxicities (myasthenic syndrome/myasthenia gravis, Guillain-Barré syndrome, encephalitis, transverse myelitis). Furthermore, the table of recommended dose modifications has been amended to reflect a more precise terminology “Exfoliative dermatologic conditions (e.g. Stevens Johnson syndrom (SJS), toxic epidermal necrolysis (TEN), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS))” for immune-related cutaneous adverse effects. Section 4.4 of the SmPC has been updated in accordance. Based on available safety data, the following ADRs have also been included in the SmPC, section 4.8: encephalitis, myasthenia gravis, myasthenic syndrome, myocarditis, gastritis (including gastritis, immune-mediated gastritis and vasculitis gastrointestinal), oesophagitis, immune-mediated arthritis, polymyalgia rheumatica, myositis and systemic inflammatory response syndrome. In addition, immune-mediated enterocolitis and enteritis have been included as part of the composite term ‘colitis’. For more information, please refer to the Summary of

					Product Characteristics.
IB/0015	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	08/09/2022	n/a		
IB/0012	B.I.z - Quality change - Active substance - Other variation	16/06/2022	n/a		
PSUSA/10931 /202110	Periodic Safety Update EU Single assessment - dostarlimab	10/06/2022	n/a		PRAC Recommendation - maintenance
IB/0011/G	This was an application for a group of variations. 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) A.6 - Administrative change - Change in ATC Code/ATC Vet Code	08/06/2022	13/09/2022	SmPC and Labelling	
II/0009	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	28/04/2022	13/09/2022	SmPC and PL	
IA/0010/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	02/03/2022	n/a		

	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				
R/0004	Renewal of the marketing authorisation.	16/12/2021	16/02/2022		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for JEMPERLI, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
IB/0006	B.II.e.z - Change in container closure system of the Finished Product - Other variation	17/11/2021	n/a		
IB/0005	B.II.e.z - Change in container closure system of the Finished Product - Other variation	17/11/2021	n/a		
IA/0003/G	This was an application for a group of variations. B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier 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	17/09/2021	n/a		

	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure A.z - Administrative change - Other variation B.II.e.z - Change in container closure system of the Finished Product - 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/0002	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)	01/07/2021	16/02/2022	SmPC and PL	
IA/0001	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	20/05/2021	n/a		