LIBTAYO

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
IAIN/0045/G	This was an application for a group of variations. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	21/06/2024		SmPC and 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).

II/0043	Update of section 4.8 of the SmPC in order to add 'uveitis' to the list of adverse drug reactions (ADRs) with frequency rare, based on a safety evaluation report. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor corrections to the efficacy data in section 5.1 of the SmPC based on an erratum for the interim report for study R2810-ONC-1620, as well as to introduce minor editorial and formatting changes to the PI and to update the list of local representatives in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	20/06/2024		SmPC and PL	
IB/0044/G	This was an application for a group of variations. 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 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	22/05/2024	n/a		
IB/0042	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	30/04/2024	n/a		

N/0039	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	10/01/2024		PL	
IB/0040	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	03/01/2024	n/a		
IB/0038/G	This was an application for a group of variations. 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 B.II.f.1.b.3 - Stability of FP - Extension of the shelf life of the finished product - After dilution or reconstitution (supported by real time data) 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	03/01/2024		SmPC and PL	
IA/0041/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.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation	27/11/2023	n/a		
IA/0037	B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of	01/08/2023	n/a		

	a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised				
PSUSA/10780 /202209	Periodic Safety Update EU Single assessment - cemiplimab	26/04/2023	26/06/2023	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10780/202209.
IA/0036	B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised	12/06/2023	n/a		
IB/0035/G	This was an application for a group of variations. B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits	19/04/2023	n/a		
II/0028	Extension of indication to include LIBTAYO in combination with platinum-based chemotherapy for the first-line treatment of adult patients with locally	23/02/2023	24/03/2023	SmPC and PL	

	advanced NSCLC who are not candidates for definitive chemoradiation or metastatic NSCLC with no EGFR, ALK or ROS1 aberrations; as a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.0 of the RMP has also been agreed. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IA/0034/G	This was an application for a group of variations. A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) 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 B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits 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.f.1.e - Stability of FP - Change to an approved stability protocol	21/03/2023	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 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.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol				
II/0026	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	13/10/2022	18/11/2022	SmPC, Annex II and PL	
II/0032	Update of sections 4.8 and 5.1 of the SmPC in order to update the list of adverse drug reactions (ADRs) and efficacy results for the BCC indication based on the primary analysis data from study R2810-ONC-1620 listed in the Annex II; this is a phase 2 study of cemiplimab in patients with advanced basal cell carcinoma who experienced progression of disease on hedgehog pathway inhibitor therapy or were intolerant of prior hedgehog pathway inhibitor therapy. 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	06/10/2022	18/11/2022	SmPC, Annex II and PL	SmPC new text The provided updated efficacy data from the primary analysis is consistent with previous results in the BCC indication with the clinical benefit in terms of ORR and DOR sustained. The updated safety data from Study 1620 are consistent with the data submitted previously. For more information, please refer to the Summary of Product Characteristics.

	data				
II/0031	Update of sections 4.8 and 5.1 of the SmPC in order to update the list of adverse drug reactions (ADRs) and efficacy information based on final results from study R2810-ONC-1540 in order to fulfil REC/005; this is a nonrandomized, multicenter, phase 2 study of cemiplimab in patients with advanced cutaneous squamous cell carcinoma; 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	06/10/2022	18/11/2022	SmPC and PL	SmPC new text The submitted results show consistent efficacy for both mCSCC and laCSCC patients and the additional safety data confirms the safety profile of cemiplimab described in the approved product information. In addition, cemiplimab exposure at steady-state in patients with solid tumours is similar at 350 mg Q3W and at 3 mg/kg Q2W. For more information, please refer to the Summary of Product Characteristics.
R/0029	Renewal of the marketing authorisation.	22/04/2022	01/07/2022	SmPC, Annex II and PL	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. Furthermore, the CHMP considered that, as all Specific Obligations have been fulfilled, there are no remaining grounds for the marketing authorisations to remain conditional and therefore recommends the granting of the MA no longer subject to Specific Obligations for LIBTAYO.
PSUSA/10780 /202109	Periodic Safety Update EU Single assessment - cemiplimab	05/05/2022	n/a		PRAC Recommendation - maintenance

N/0030	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/02/2022	29/06/2022	PL	
IB/0025/G	This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.e.z - Change in container closure system of the Finished Product - Other variation	11/01/2022	n/a		
PSUSA/10780 /202103	Periodic Safety Update EU Single assessment - cemiplimab	11/11/2021	07/01/2022	PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10780/202103.
IB/0024	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	12/10/2021	07/01/2022	SmPC and PL	
II/0020/G	This was an application for a group of variations. B.I.a.4.d - Change to in-process tests or limits applied during the manufacture of the AS - Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the AS B.I.a.4.e - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of an in-process test which may have a significant effect on the overall quality of the AS	02/09/2021	n/a		
IB/0022	B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including	28/07/2021	n/a		

	replacement or addition)				
II/0012	Extension of indication to include : LIBTAYO as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic basal cell carcinoma (laBCC or mBCC) who have progressed on or are intolerant to a hedgehog pathway inhibitor (HHI).SmPC sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 have been revised. The PL has been updated accordingly. Version 2.0 of the RMP has been submitted. Annex IID has been revised. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	20/05/2021	21/06/2021	SmPC, Annex II and PL	Please refer to Scientific Discussion Libtayo-H-C-4844-II-12
II/0011	Extension of indication for LIBTAYO as monotherapy indicated for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) expressing PD-L1 (in ≥ 50% tumour cells), with no EGFR, ALK or ROS1 aberrations based on the results of study R2810-ONC-1624 comparing cemiplimab monotherapy to platinum doublet chemotherapy. The PL is revised accordingly. RMP version 2.0 has been agreed. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	20/05/2021	21/06/2021	SmPC and PL	Please refer to Scientific Discussion 'Libtayo-H-C-4844-II-11
R/0017	Renewal of the marketing authorisation.	25/03/2021	10/05/2021		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 LIBTAYO, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
PSUSA/10780 /202009	Periodic Safety Update EU Single assessment - cemiplimab	06/05/2021	n/a		PRAC Recommendation - maintenance
IB/0019/G	This was an application for a group of variations. 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 A.1 - Administrative change - Change in the name and/or address of the MAH	08/03/2021	10/05/2021	SmPC, Labelling and PL	
IB/0018	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	24/02/2021	n/a		
IB/0016/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	19/01/2021	n/a		

	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.b.z - Change in control of the AS - Other variation				
IB/0015/G	This was an application for a group of variations. 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) B.I.b.z - Change in control of the AS - Other variation	07/01/2021	n/a		
N/0013	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	25/11/2020	10/05/2021	PL	
PSUSA/10780 /202003	Periodic Safety Update EU Single assessment - cemiplimab	29/10/2020	n/a		PRAC Recommendation - maintenance
II/0010/G	This was an application for a group of variations. 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 B.I.a.1.e - Change in the manufacturer of AS or of a	10/09/2020	10/05/2021	Annex II	

	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.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				
II/0007	Update of sections 4.2, 4.4, 4.8 of the SmPC to amend an existing warning and add new ADRs with frequency uncommon, regarding new safety	11/06/2020	31/07/2020	SmPC and PL	

	information in the post marketing setting on the terms "Transplant rejection", "Graft Versus Host Disease (GVHD)" and "Myositis" and amended relevant recommendations for treatment modification. The MAH took the opportunity to update Section 5.1, based on minor corrections to the efficacy data in the SmPC from study R2810-ONC-1540 (primary analysis for group 2 and 3 dated 09 Jul 2019), considering errors that were revealed in two patient's data following the completion of the MA. The pharmacokinetic properties (section 5.2 of the SmPC) has been updated with population predicted and observed cemiplimab exposure at 350 mg Q3W from the group 3 primary analysis. The Package Leaflet is updated accordingly. The MAH also took the opportunity to introduce editorial changes in the PI across sections 4.2, 4.9, 6.3 and 6.6. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
PSUSA/10780 /201909	Periodic Safety Update EU Single assessment - cemiplimab	30/04/2020	26/06/2020	SmPC and PL	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 LIBTAYO, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.

R/0006	Renewal of the marketing authorisation.	26/03/2020	20/05/2020		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 LIBTAYO, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
IAIN/0008	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	15/05/2020	31/07/2020	SmPC	
II/0003	B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes	28/11/2019	n/a		
IB/0004/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	07/11/2019	n/a		

	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation				
II/0002/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.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.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation 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 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 B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP -	17/10/2019	n/a		

	Replacement/addition of a site where batch control/testing takes place B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation				
IB/0001/G	This was an application for a group of variations. A.1 - Administrative change - Change in the name and/or address of the MAH 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 A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release 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	06/09/2019	20/05/2020	SmPC, Annex II, Labelling and PL	