Bavencio

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/0051	Update of section 4.8 of the SmPC in order to add "neutropenia" to the list of adverse drug reactions (ADRs) with frequency "not known" based on post marketing data and literature. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the PI in accordance with the	13/03/2025		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).

	latest EMA excipients guideline. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
R/0050	Renewal of the marketing authorisation.	30/01/2025	12/03/2025	SmPC and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Bavencio in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
II/0046/G	This was an application for a group of variations. A grouped application consisting of: C.I.4: Update of sections 4.2, 4.4, 4.6 and 4.8 of the SmPC in order to add the immune-mediated adverse reactions sclerosing cholangitis, arthritis, polymyalgia rheumatica, and Sjogren's syndrome based on post-marketing data and literature. The Package Leaflet is updated accordingly. The RMP version 7.3 has also been submitted. C.I.4: Update of section 4.8 of the SmPC in order to update the immunogenicity information based on results from studies EMR100070-003, B9991003 and 100/B9991001. Study EMR100070-003 is a Phase 2, single-arm, open label, multicenter study to investigate the clinical activity and safety of avelumab in patients with mMCC. T. Study B9991003 is a Phase 3 multinational, multicenter, randomized (1:1), open-label, parallel 2 - arm study of avelumab	13/02/2025		SmPC and PL	SmPC new text Treatment emergent anti-drug antibodies (ADA) were detected in 8.5% of MCC patients (study EMR107000-003, 8.9% for Part A and 8.2% for Part B), 19% of UC patients (study B9991001) and 16% of RCC patients (study B9991003). The majority of the ADA were of neutralising character. No evidence of ADA or neutralising antibodies (nAb) impact on pharmacokinetics, efficacy or safety was observed. For more information, please refer to the Summary of Product Characteristics.

	in combination with axitinib versus sunitinib monotherapy in the 1L treatment of participants with aRCC. Study 100/B9991001 is a Phase 3, multicenter, multinational, randomized, open-label, parallel-arm efficacy and safety study of avelumab plus best supportive care (BSC) versus BSC alone as a maintenance treatment in adult participants with locally advanced or metastatic UC whose disease did not progress after completion of 1L platinum-containing chemotherapy. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0049/G	This was an application for a group of variations. B.I.b.z - Change in control of the AS - Other variation B.I.b.z - Change in control of the AS - Other variation B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	13/09/2024	n/a		
IB/0048	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement	28/08/2024	n/a		

	or addition) for the AS or a starting material/intermediate				
IA/0047/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.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)	18/07/2024	n/a		
II/0044/G	This was an application for a group of variations. Grouped application comprising four variations as follows: Type II (C.I.11.b): To update Annex II and the RMP version 7.1 for Bavencio to change the classification of "safety in patients with autoimmune disease" to the important identified risk "other immune mediated adverse reactions" along with removal of the patient information brochure from the educational material, following the PRAC assessment report PSUSA/00010635/202303. Type IA (A.6): To change ATC level name from Other antineoplastic agents, monoclonal antibodies to Antineoplastic agents, monoclonal antibodies, PD-1/PDL-1 (Programmed cell death protein 1/death ligand 1) inhibitors in Section 5.1 of the Summary of Product Characteristics (SmPC). The ATC code	11/07/2024	12/03/2025	SmPC, Annex II, Labelling and PL	

	remains unchanged. Type IA (C.I.z): To update the statement for "infusion-related reactions" in section 4.4 of the SmPC and to align terminology with the RMP for the term "immune-related" versus "immune-mediated". Type IAIN (C.I.12): To remove from the Product Information the black symbol and explanatory statements for medicinal products subject to additional monitoring. In addition, the MAH took this opportunity to introduce editorial changes and to bring the PI in line with the latest QRD template version 10.3. 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 C.I.12 - Inclusion or deletion of black symbol and explanatory statements for medicinal products in the list of medicinal products that are subject to additional monitoring C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation A.6 - Administrative change - Change in ATC Code/ATC Vet Code				
IAIN/0045/G	This was an application for a group of variations. C.I.1.a - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a Union	10/06/2024	12/03/2025	SmPC and PL	

	referral procedure - The product is not covered by the defined scope of the procedure C.I.1.a - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a Union referral procedure - The product is not covered by the defined scope of the procedure				
PSUSA/10635 /202303	Periodic Safety Update EU Single assessment - avelumab	09/11/2023	05/01/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10635/202303.
IA/0043/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	04/12/2023	n/a		
IB/0041	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	03/08/2023	n/a		
IA/0039/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	06/02/2023	n/a		

IB/0038	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)	15/12/2022	21/03/2023	SmPC	
II/0037/G	This was an application for a group of variations. 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 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 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.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS 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.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.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial	17/11/2022	n/a		

	change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS				
PSUSA/10635 /202203	Periodic Safety Update EU Single assessment - avelumab	27/10/2022	n/a		PRAC Recommendation - maintenance
II/0035	Update of sections 4.2, 5.1 and 5.2 of the SmPC based on final results from study MS100070-0306 following a P46 procedure (EMEA/H/C/004338/P46/009). This is a Phase I, multi-centre, open-label, international study to evaluate the dose, safety and tolerability, antitumor activity, pharmacokinetic and pharmacodynamics of avelumab in paediatric subjects 0 to less than 18	15/09/2022	21/03/2023	SmPC, Annex II and PL	Study MS100070-306 was a multi-centre, open-label, Phase I/II study to evaluate the dose, safety and tolerability, antitumour activity, pharmacokinetic, and pharmacodynamics of avelumab in paediatric patients from birth to less than 18 years of age with refractory or relapsed solid tumours including central nervous system (CNS) tumours and lymphoma for which no standard therapy is available or for which the patient was not eligible

	years of age with refractory or relapsed malignant solid tumours (including central nervous system tumours) and lymphoma for which no standard therapy is available or for which the subject is not eligible for the existing therapy. In addition, the MAH took the opportunity to update Annex II section D to be aligned with the EU Educational materials (EM) and the EU Risk Management Plan (RMP). Furthermore, the MAH took the opportunity to implement editorial changes. C.I.3.z - 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 - Other variation				for the existing therapy. The study enrolled 21 paediatric patients with an age ranged from 3 to 17 years receiving either 10 mg/kg or 20 mg/kg avelumab intravenously every 2 weeks until confirmed progression, death, or unacceptable toxicity. The paediatric PK parameters and the corresponding PK profiles for all patients were evaluated according to dosing and stratified by bodyweight. The exposure in paediatric patients receiving 20 mg/kg avelumab were similar or higher compared to those in adults receiving 10 mg/kg or 800 mg avelumab. In paediatric patients receiving 10 mg/kg avelumab the exposure was lower compared to those in adults. Based on currently available data of Bavencio, described in section 5.1, no recommendation on a posology in paediatric population can be made. For more information, please refer to the Summary of Product Characteristics.
IA/0034	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	21/04/2022	21/03/2023	SmPC	
IB/0032	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	09/02/2022	n/a		
PSUSA/10635 /202103	Periodic Safety Update EU Single assessment - avelumab	11/11/2021	06/01/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10635/202103.
IB/0033	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement	22/12/2021	n/a		

	or addition) for the AS or a starting material/intermediate				
IB/0031	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	06/12/2021	n/a		
II/0028	B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	14/10/2021	06/01/2022	SmPC	The SmPC section 3 has been updated as follows: The osmolality is between 285 and 350 mOsm/kg.
IAIN/0030	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	12/10/2021	06/01/2022	SmPC and PL	
IA/0029/G	This was an application for a group of variations. B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier 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)	11/08/2021	n/a		
IB/0026/G	This was an application for a group of variations. B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.II.d.1.a - Change in the specification parameters	04/05/2021	n/a		

	and/or limits of the finished product - Tightening of specification limits				
PSUSA/10635 /202009	Periodic Safety Update EU Single assessment - avelumab	09/04/2021	n/a		PRAC Recommendation - maintenance
II/0018	Extension of indication to include a new indication for Bavencio in the treatment as monotherapy for the first-line maintenance treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC) who are progression-free following platinum based chemotherapy; as a consequence, sections 4.1 , 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 5.0 of the RMP has also been submitted. The MAH took also the occasion to include some editorial changes in the PI. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	10/12/2020	21/01/2021	SmPC, Annex II and PL	Please refer to Scientific Discussion Bavencio-H-C-4338-II-0018.
IA/0024	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	21/12/2020	n/a		
IB/0022	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	21/12/2020	06/01/2022	SmPC	

IB/0023	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	04/12/2020	n/a		
PSUSA/10635 /202003	Periodic Safety Update EU Single assessment - avelumab	29/10/2020	n/a		PRAC Recommendation - maintenance
II/0015	Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to change posology recommendations, amend an existing warning and add new ADRs with frequency uncommon regarding myasthenia gravis and myasthenic syndrome. The update results from an update of the Company Core Data Sheet (CCDS) based on the review of cases of myasthenia gravis/myasthenic syndrome. The Package Leaflet is updated accordingly. The RMP version 2.2 has also been submitted to reclassify "Other immune-related events (myasthenic syndrome)" from an important potential risk to an important identified risk of "Other immune-related events (myasthenia gravis/myasthenic syndrome)". C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/07/2020	24/09/2020	SmPC and PL	Withholding or discontinuation guidance on use of Avelumab in case of myasthenia gravis, myasthenic syndrome is provided. Other clinically important immune related adverse reactions were reported in less than 1% of patients: myositis, hypopituitarism, uveitis, myasthenia gravis, myasthenic syndrome, and Guillain-Barré syndrome (see section 4.8). For more information, please refer to the Summary of Product Characteristics.
II/0020/G	This was an application for a group of variations. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a	03/09/2020	n/a		

	biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol				
II/0013	Update of section 5.1 of the SmPC in order to update efficacy information following results from study EMR100070-003 Part B listed as a specific obligation in the Annex II; this is a Phase II, open-label, multicenter trial to investigate the clinical activity and safety of avelumab (MSB0010718C) in subjects with Merkel cell carcinoma. With this submission the company is also taking the opportunity to update annex-II proposing deletion of the specific obligation and proposing the switch from conditional to full marketing authorisation. The package leaflet and the RMP (version 2.1) are updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	28/05/2020	19/08/2020	SmPC, Annex II and PL	Please refer to Scientific Discussion 'Bavencio-H-C-004338-II-13.
R/0017	Renewal of the marketing authorisation.	28/05/2020	23/07/2020		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. Furthermore, the CHMP confirmed the recommendation adopted in variation II/13 (EMEA/H/C/004338/II/0013) to grant for Bavencio Marketing Authorisation no longer subject to Specific Obligations.
IA/0021	A.7 - Administrative change - Deletion of manufacturing sites	06/07/2020	n/a		
PSUSA/10635 /201909	Periodic Safety Update EU Single assessment - avelumab	17/04/2020	n/a		PRAC Recommendation - maintenance
IA/0016/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 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	27/03/2020	n/a		

IB/0012	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	06/01/2020	n/a		
IB/0011	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	12/11/2019	n/a		
II/0009/G	This was an application for a group of variations. Extension of indication to include first-line combination treatment with avelumab and axitinib in adult patients with advanced renal cell carcinoma (aRCC) for Bavencio; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, section 4.2 of the SmPC is updated in order to introduce a switch of the avelumab dosing regimen from 10 mg/kg every two weeks (weight-based) to a flat dose of 800 mg every two weeks, both for the newly proposed indication aRCC and the already existing indication of Merkel cell carcinoma (MCC). The MAH also took the opportunity to implement some editorial changes in the Product information. An updated RMP version 2.0 has been agreed. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.6.a - Change(s) to therapeutic indication(s) -	19/09/2019	24/10/2019	SmPC, Annex II, Labelling and PL	Please refer to Scientific Discussion 'Bavencio-H-C-4338-II-09-G'.

	Addition of a new therapeutic indication or modification of an approved one				
PSUSA/10635 /201903	Periodic Safety Update EU Single assessment - avelumab	03/10/2019	n/a		PRAC Recommendation - maintenance
R/0008	Renewal of the marketing authorisation.	26/04/2019	20/06/2019	SmPC and Annex II	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 Bavencio, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion. Furthermore, section 5.1 of the SmPC has been updated based on data from interim analysis of the ongoing EMR100070-003 (Part A and B) study.
PSUSA/10635 /201809	Periodic Safety Update EU Single assessment - avelumab	26/04/2019	20/06/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10635/201809.
IB/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.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new	04/03/2019	n/a		

	specification parameter to the specification with its corresponding test method				
PSUSA/10635 /201803	Periodic Safety Update EU Single assessment - avelumab	04/10/2018	n/a		PRAC Recommendation - maintenance
R/0003	Renewal of the marketing authorisation.	28/06/2018	31/08/2018	SmPC	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 Bavencio, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
T/0004	Transfer of Marketing Authorisation	14/06/2018	02/07/2018	SmPC, Labelling and PL	
IB/0002	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	15/03/2018	n/a		
IA/0001	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	13/12/2017	02/07/2018	SmPC and PL	