EMA/77300/2021

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/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	10/12/2020	21/01/2021	SmPC, Annex II and PL	Please refer to Scientific Discussion Bavencio-H-C-4338-II-0018.

[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).

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	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				
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		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)	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

	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				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 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	03/09/2020	n/a		
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,	28/05/2020	19/08/2020	SmPC, Annex II and PL	Please refer to Scientific Discussion 'Bavencio-H-C-004338-II-13.

	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				
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.	27/03/2020	n/a		

	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				
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	19/09/2019	24/10/2019	SmPC, Annex II, Labelling and PL	Please refer to Scientific Discussion 'Bavencio-H-C-4338-II-09-G'.

	(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) - 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 specification parameter to the specification with its corresponding test method	04/03/2019	n/a		
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	