EMA/638887/2020

Imlygic

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
R/0039	Renewal of the marketing authorisation.	17/09/2020	18/11/2020	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Imlygic in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.

[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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IB/0040	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	13/07/2020	n/a		
PSUSA/10459 /201910	Periodic Safety Update EU Single assessment - talimogene laherparepvec	14/05/2020	n/a		PRAC Recommendation - maintenance
II/0036	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	30/04/2020	n/a		
II/0037	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	27/02/2020	n/a		
II/0034	To update the RMP for Imlygic to version 7.0 in order to add 2 category 3 studies (Studies 20180062 and 20180099), as well as an internal evaluation of managed distribution process metrics, to evaluate the effectiveness of additional risk minimization measures (aRMM). 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	19/09/2019	n/a		

	where significant assessment is required				
IB/0035	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	22/07/2019	17/07/2020	Annex II	
PSUSA/10459 /201810	Periodic Safety Update EU Single assessment - talimogene laherparepvec	16/05/2019	n/a		PRAC Recommendation - maintenance
IA/0033	A.7 - Administrative change - Deletion of manufacturing sites	10/05/2019	n/a		
IB/0032	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	02/04/2019	n/a		
II/0029	Update of section 5.2 of the SmPC in order to update the pharmacokinetic properties information based on the final results from study 20120324, a phase 2, multicenter, single-arm trial to evaluate the biodistribution and shedding of talimogene laherparepvec in subjects with unresected, stage IIIB to IVM1c melanoma. This submission fulfils MEA 006.1. The RMP is updated accordingly (final consolidated version 6.0). In addition, the Marketing authorisation holder (MAH) took the opportunity to update Annex II as per the already assessed EMEA/H/C/002771/ANX/001 procedure. In addition, the MAH took the opportunity to update the details of local representatives for Ireland and Portugal in the package leaflet.	28/03/2019	06/06/2019	SmPC, Annex II and PL	The biodistribution and shedding of intralesionally administered talimogene laherparepvec were investigated in a clinical study that measured talimogene laherparepvec DNA in blood, urine, injection site, exterior of the occlusive dressings, oral mucosa, anogenital area, and suspected herpetic lesions. Sixty patients with melanoma received Imlygic intralesional injection and talimogene laherparepvec DNA was present in all sites during the study. No samples had detectable talimogene laherparepvec DNA 30 days after the end of treatment in blood, urine, oral mucosa, and anogenital area and no samples had detectable talimogene laherparepvec DNA 60 days after end of treatment in injected lesions. Overall 3 of 19 patients with lesions of suspected herpetic origin had talimogene laherparepvec DNA present at any time during the study. No viral activity was detected in samples of the

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				occlusive dressings, oral mucosa, anogenital area, and suspected herpetic lesions. Infectious talimogene laherparepvec virus was detected at the site of injection in 7 (11%) patients at multiple time points in the study; no samples were positive for viral infectivity after cycle 2 or after the end of treatment.
II/0028	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	28/03/2019	n/a		
IB/0031/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.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	06/02/2019	n/a		
II/0027	Update of section 4.8 of the SmPC in order to add granulomatous dermatitis as new adverse drug reaction with an uncommon frequency and to update the adverse reaction dyspnoea from dyspnoea exertional to dyspnoea. The package leaflet has been aligned accordingly.	13/12/2018	06/06/2019	SmPC and PL	

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
PSUSA/10459 /201804	Periodic Safety Update EU Single assessment - talimogene laherparepvec	29/11/2018	n/a		PRAC Recommendation - maintenance
II/0024	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	20/09/2018	n/a		
IA/0026	A.7 - Administrative change - Deletion of manufacturing sites	13/09/2018	n/a		
PSUSA/10459 /201710	Periodic Safety Update EU Single assessment - talimogene laherparepvec	31/05/2018	30/07/2018	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10459/201710.
IG/0946	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	04/06/2018	06/06/2019	PL	
II/0020	Update of section 4.8 of the SmPC in order to add the new ADR 'hypersensitivity' with a frequency allocation of 'unknown'. The Package Leaflet is updated accordingly. Further, the MAH is implementing a minor editorial change in section 3 of the SmPC in order to clarify that the current	31/05/2018	30/07/2018	SmPC and PL	N/A

	description of the liquid applies to both strengths, and minor changes in section 4.4 of the SmPC and the Package Leaflet regarding sorbitol and sodium subsequent to the revised Annex to the EC guideline on excipients in the labelling (EMA/CHMP/302620/2017). In addition, the MAH took the opportunity to update the contact details of the local representative in Slovenia in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0021/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 B.II.f.1.e - Stability of FP - Change to an approved stability protocol B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation	15/05/2018	30/07/2018	SmPC and PL	
IB/0019	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	02/02/2018	n/a		

PSUSA/10459 /201704	Periodic Safety Update EU Single assessment - talimogene laherparepvec	30/11/2017	n/a		PRAC Recommendation - maintenance
IB/0017	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	13/11/2017	n/a		
IG/0853	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	10/11/2017	30/07/2018	Annex II and PL	
IB/0014/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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	10/08/2017	n/a		
PSUSA/10459 /201610	Periodic Safety Update EU Single assessment - talimogene laherparepvec	05/05/2017	n/a		PRAC Recommendation - maintenance

IAIN/0013	B.II.e.6.a - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that affects the product information	26/04/2017	06/07/2017	SmPC and Labelling	
II/0008	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	21/04/2017	n/a		
IAIN/0012/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information	31/03/2017	n/a		
IB/0011	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	03/03/2017	n/a		
PSUSA/10459 /201604	Periodic Safety Update EU Single assessment - talimogene laherparepvec	01/12/2016	n/a		PRAC Recommendation - maintenance
IB/0007	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	07/10/2016	n/a		

IA/0006	A.7 - Administrative change - Deletion of manufacturing sites	06/09/2016	n/a		
IB/0001/G	This was an application for a group of variations. A.6 - Administrative change - Change in ATC Code/ATC Vet Code B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - 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 C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/07/2016	06/07/2017	SmPC and PL	
IB/0003	B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	15/06/2016	n/a		
IB/0002	B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	15/06/2016	n/a		
