Zyclara

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
N/0032	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/02/2024		PL	
PSUSA/1729/ 202301	Periodic Safety Update EU Single assessment - imiquimod	28/09/2023	n/a		PRAC Recommendation - maintenance

[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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IA/0030	A.7 - Administrative change - Deletion of manufacturing sites	05/07/2023		Annex II and PL	
T/0028	Transfer of Marketing Authorisation	28/10/2022	02/12/2022	SmPC and PL	
N/0027	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/12/2021	28/03/2022	PL	
IB/0026	B.II.f.1.a.1 - Stability of FP - Reduction of the shelf life of the finished product - As packaged for sale	13/07/2021	28/03/2022	SmPC	To reduce the shelf-life of the finished product as packaged for sale, from 30 months to 18 months.
IA/0025/G	This was an application for a group of variations. B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) 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.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)	16/04/2021	n/a		
IA/0024	A.7 - Administrative change - Deletion of manufacturing sites	10/03/2021	28/03/2022	Annex II, Labelling and PL	

IB/0023	B.II.d.2.z - Change in test procedure for the finished product - Other variation	11/01/2021	n/a		
PSUSA/1729/ 202001	Periodic Safety Update EU Single assessment - imiquimod	15/10/2020	14/12/2020	PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1729/202001.
IB/0021/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.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products	25/06/2020	14/12/2020	Annex II and PL	

	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 B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Tightening of specification limits				
IA/0020/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	14/08/2019	n/a		
IAIN/0018/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a	21/11/2018	n/a		

	manufacturing site for the FP - Secondary packaging site 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				
N/0017	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/08/2018	25/02/2019	PL	
IB/0016	C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH	16/02/2018	25/02/2019	SmPC and PL	
II/0013	Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to add information from study X-03016-3284 (LEIDA 2) and from a meta-analysis of studies X-03016-3271 and X-03016-3284, two open-label randomized, controlled studies investigating the long-term effects of imiquimod 5% (and not with this 3.75% product) in comparison to topical diclofenac (3% gel). The MAH took the opportunity to update the details of local representatives in the PL. C.I.2.b - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference	09/11/2017	11/12/2017	SmPC and PL	One additional 2-week treatment of Zyclara may be considered in case lesions do not respond completely to treatment at 8 weeks after the second treatment cycle. A different therapy is recommended if the treated lesions show insufficient response to Zyclara. Also, that actinic keratosis (AK) lesions that have cleared after two Zyclara treatment cycles of 2 weeks and subsequently recur can be re-treated with one or two further Zyclara treatment cycles of 2 weeks following an at least 12 weeks treatment pause. Two open-label randomized, controlled studies investigated the long-term effects of imiquimod 5% (and not with this 3.75% product) in comparison to topical diclofenac (3% gel). These studies showed that imiquimod was better than

	product - Change(s) require to be further substantiated by new additional data to be submitted by the MAH				topical diclofenac in preventing the histological progression of AK lesions to in-situ or invasive squamous cell carcinoma (SCC). In addition, these studies supported the use of up to two additional treatment cycles of imiquimod when the AK lesions are not completely cleared or if the AK lesions recurred after successful initial treatment with imiquimod.
PSUSA/1729/201701	Periodic Safety Update EU Single assessment - imiquimod	28/09/2017	n/a		PRAC Recommendation - maintenance
IA/0014	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	11/05/2017	n/a		
R/0012	Renewal of the marketing authorisation.	26/01/2017	22/03/2017	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 Zyclara in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
N/0011	Update of the package leaflet with revised contact details of the local representatives for Italy, Spain and France. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/06/2016	22/03/2017	PL	
N/0010	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/09/2015	02/12/2015	PL	

IA/0009	B.II.d.2.e - Change in test procedure for the finished product - Update of the test procedure to comply with the updated general monograph in the Ph. Eur.	27/04/2015	n/a		
IB/0008	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	16/12/2014	02/12/2015	SmPC, Annex II, Labelling and PL	
PSUSA/1729/201401	Periodic Safety Update EU Single assessment - imiquimod	11/09/2014	n/a		PRAC Recommendation - maintenance
IB/0007	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	24/06/2014	n/a		
N/0005	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/09/2013	02/12/2015	PL	
IG/0277	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	26/03/2013	n/a		
IB/0002	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate	21/01/2013	n/a		
IB/0003/G	This was an application for a group of variations. B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.d - Change in test procedure for an excipient	14/12/2012	n/a		

	- Other changes to a test procedure (including replacement or addition) B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition) B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure				
IB/0001	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate	07/12/2012	n/a		