Xaluprine

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
IB/0042/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	10/01/2025	10/02/2025	SmPC, Labelling 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).

	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 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 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				
IB/0041/G	This was an application for a group of variations. B.II.e.z - Change in container closure system of the Finished Product - Other variation B.II.e.z - Change in container closure system of the Finished Product - Other variation	10/07/2024	n/a		
PSUSA/1988/202309	Periodic Safety Update EU Single assessment - mercaptopurine	25/04/2024	20/06/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1988/202309.
IAIN/0040	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is	08/12/2023	n/a		

	not an integrated part of the primary packaging - Device with CE marking				
IAIN/0038/G	This was an application for a group of variations. B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	17/05/2023	15/11/2023	SmPC and PL	
IA/0037/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites	09/11/2022	15/11/2023	Annex II and PL	
PSUSA/1988/202109	Periodic Safety Update EU Single assessment - mercaptopurine	22/04/2022	21/06/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1988/202109.

IB/0035	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	28/04/2022	n/a		
IA/0036/G	This was an application for a group of variations. B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products 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 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	21/04/2022	n/a		
IB/0033/G	This was an application for a group of variations. B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data) B.II.f.1.e - Stability of FP - Change to an approved stability protocol	12/01/2022	21/06/2022	SmPC	
IB/0032/G	This was an application for a group of variations. 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.d - Change in the specification parameters	02/07/2021	n/a		

	and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation				
IA/0031	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	19/05/2021	n/a		
IA/0030	A.7 - Administrative change - Deletion of manufacturing sites	03/03/2021	16/04/2021	Annex II and PL	
IAIN/0029	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	02/02/2021	16/04/2021	Annex II and PL	
IA/0028	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	09/12/2020	n/a		
IA/0027	B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-	30/10/2020	n/a		

	sterile medicinal products				
IA/0026/G	This was an application for a group of variations. B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method 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) B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State	05/08/2020	n/a		
II/0022	Update of section 4.8 of the SmPC to add Portal hypertension, nodular regenerative hyperplasia and sinusoidal obstruction syndrome. The MAH took the opportunity to implement minor editorial changes to the SmPC, Annex II and PIL. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	30/04/2020	16/04/2021	SmPC, Annex II and PL	The SmPC has been updated to include the adverse drug reactions: Portal hypertension, nodular regenerative hyperplasia and sinusoidal obstruction syndrome, with a frequency uncknown.

IB/0025	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	15/04/2020	n/a		
IA/0024	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	11/12/2019	n/a		
IAIN/0023/G	This was an application for a group of variations. B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	05/09/2019	n/a		
IAIN/0021/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP -	24/04/2019	08/04/2020	Annex II and PL	

	Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing 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				
T/0020	Transfer of Marketing Authorisation	20/12/2018	31/01/2019	SmPC, Labelling and PL	
IB/0019/G	This was an application for a group of variations. 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.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) 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.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	30/01/2019	n/a		
IA/0018	B.III.1.a.2 - Submission of a new/updated or	26/11/2018	n/a		

	deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer				
N/0017	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	14/11/2018	31/01/2019	Labelling	
IB/0016/G	This was an application for a group of variations. B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data) B.II.f.1.e - Stability of FP - Change to an approved stability protocol	23/10/2018	31/01/2019	SmPC	
IA/0015	B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products	18/08/2017	n/a		
PSUSA/1988/201609	Periodic Safety Update EU Single assessment - mercaptopurine	18/05/2017	13/07/2017	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1988/201609.
R/0012	Renewal of the marketing authorisation.	15/09/2016	18/11/2016	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 Xaluprine in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IAIN/0013	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	09/06/2016	18/11/2016	SmPC and PL	

IAIN/0011	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	29/07/2015	n/a		
PSUV/0008	Periodic Safety Update	25/09/2014	19/11/2014	SmPC and PL	Please refer to Xaluprine (EMEA/H/C/2022/PSUV/0008) EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
IAIN/0010	C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV and/or QPPV contact details and/or back-up procedure	17/10/2014	n/a		
IAIN/0009	C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV and/or QPPV contact details and/or back-up procedure	16/06/2014	n/a		
IAIN/0007	C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV and/or QPPV contact details and/or back-up procedure	21/03/2014	n/a		
PSUV/0006	Periodic Safety Update	24/10/2013	20/12/2013	SmPC and PL	Update of Sections 4.4 and 4.8 of the SmPC to add a warning on hepatosplenic T cell lymphoma and lymphoproliferative disorders and to add the adverse reaction hepatosplenic T cell lymphoma and lymphoproliferative disorders with a frequency unknown. The Package leaflet is to be updated accordingly. Please refer to: Xaluprine-H-C-2022-PSUV-0006 EPAR -

					Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
IB/0004	B.II.f.1.b.2 - Stability of FP - Extension of the shelf life of the finished product - After first opening (supported by real time data)	11/03/2013	20/12/2013	SmPC, Labelling and PL	
IAIN/0005	B.III.1.a.1 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from an already approved manufacturer	05/03/2013	n/a		
II/0002/G	This was an application for a group of variations. The preservative system of the finished product Xaluprine has been revised: changes involve deletion of propyl parahydroxybenzoate and replacement with ethyl parahydroxybenzoate, sodium salt and potassium sorbate, sodium salt of methyl parahydroxybenzoate. In addition revision to the manufacturing process and the test procedures have been performed with the new formulation. B.II.a.3.b.2 - Changes in the composition (excipients) of the finished product - Other excipients - Qualitative or quantitative changes in one or more excipients that may have a significant impact on the safety, quality or efficacy of the product B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation B.II.d.2.d - Change in test procedure for the finished	20/09/2012	15/11/2012	SmPC, Labelling and PL	

	product - Other changes to a test procedure (including replacement or addition) B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation				
IAIN/0003	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	15/08/2012	n/a		
IAIN/0001	A.2.a - Administrative change - Change in the (invented) name of the medicinal product for CAPs	11/05/2012	15/11/2012	SmPC, Labelling and PL	