



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Nordimet

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/0030	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	30/03/2023		SmPC and PL	
N/0028	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/03/2023		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).



N/0029	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	02/03/2023		PL	
IAIN/0026/G	This was an application for a group of variations. B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	23/08/2022	28/11/2022	Annex II and PL	
PSUSA/2014/202110	Periodic Safety Update EU Single assessment - methotrexate	10/06/2022	n/a		PRAC Recommendation - maintenance
IB/0024	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	24/02/2022	28/11/2022	SmPC and PL	Update of Section 4.4 of the SmPC with revised wording on liver function tests
IB/0022	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	13/01/2022	28/11/2022	SmPC, Labelling and PL	
IAIN/0023	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	02/12/2021	28/11/2022	SmPC and PL	
R/0018	Renewal of the marketing authorisation.	22/04/2021	21/06/2021	SmPC, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Nordimet in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity. Section 4.5 of the SmPC has been updated based on

					literature reference data to add information on the concomitant use of methotrexate and cyclosporin: "Cyclosporine may potentiate methotrexate efficacy and toxicity. There is an increased risk of renal dysfunction. In addition, there is a biological plausibility of excessive immunosuppression and its associated complications."
IB/0019/G	<p>This was an application for a group of variations.</p> <p>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier</p> <p>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</p> <p>B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation</p> <p>B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation</p> <p>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</p> <p>B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation</p>	27/01/2021	n/a		
II/0016	Extension of Indication to include the new indication "Induction of remission in moderate steroid-dependent Crohn's disease in adult patients, in combination with corticosteroids and for maintenance	10/12/2020	21/01/2021	SmPC and PL	Please refer to the Scientific Discussion Nordimet EMA/H/C/003983/II/0016

	<p>of remission, as monotherapy, in patients who have responded to methotrexate” for Nordimet; as a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 5.3 has been adopted. The MAH took the opportunity to update the RMP with changes related to GVP V version 2 template and the outcome of MTX referral.</p> <p>C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one</p>				
PSUSA/2014/201910	Periodic Safety Update EU Single assessment - methotrexate	28/05/2020	23/07/2020	SmPC and PL	Please refer to Jylamvo - Nordimet EMEA/H/C/PSUSA/00002014/201910 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation.
IAIN/0015/G	<p>This was an application for a group of variations.</p> <p>A.1 - Administrative change - Change in the name and/or address of the MAH</p> <p>B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation</p> <p>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</p>	11/12/2019	23/07/2020	SmPC, Labelling and PL	
IA/0014	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	13/11/2019	n/a		

	from an already approved manufacturer				
A31/0006	<p>Pursuant to Article 31 of Directive 2001/83/EC, Spain requested on 22 March 2018 the opinion of the European Medicines Agency further to serious cases of overdose, sometimes fatal, having been reported in patients inadvertently receiving the product daily instead of weekly for indications that require weekly dosing despite additional risk minimisation measures having been put in place by several Member States. The CHMP was requested to assess the impact thereof on the benefit-risk balance of methotrexate-containing medicinal products and to give its recommendation whether the marketing authorisation of these products should be maintained, varied, suspended or revoked. As the request results from the evaluation of data resulting from pharmacovigilance activities, the CHMP opinion should be adopted on the basis of a recommendation of the Pharmacovigilance Risk Assessment Committee (PRAC).</p>	22/08/2019	17/10/2019	SmPC, Annex II and Labelling	Please refer to the assessment report: Jylamvo EMEA/H/A-31/1463/C/3756/0002 Nordimet EMEA/H/A-31/1463/C/3983/0006
IB/0013	B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation	17/09/2019	n/a		
PSUSA/2014/201810	Periodic Safety Update EU Single assessment - methotrexate	27/06/2019	23/08/2019	SmPC and PL	Please refer to Jylamvo - Nordimet EMEA/H/C/PSUSA/00002014/201810 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation

IB/0012/G	<p>This was an application for a group of variations.</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p>	17/04/2019	23/08/2019	SmPC, Labelling and PL	
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IB/0010/G	<p>This was an application for a group of variations.</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p>	18/12/2018	25/03/2019	SmPC, Labelling and PL	

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IA/0009	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	13/11/2018	n/a		
IB/0008	B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size	23/05/2018	n/a		
PSUSA/2014/201706	Periodic Safety Update EU Single assessment - methotrexate	22/03/2018	16/05/2018	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2014/201706.
IAIN/0007	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	24/04/2018	25/03/2019	SmPC and PL	
IB/0005	B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation	12/12/2017	n/a		
IB/0003/G	This was an application for a group of variations. B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes	16/09/2017	16/05/2018	SmPC, Labelling and PL	

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IB/0002/G	<p>This was an application for a group of variations.</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p>	11/10/2016	07/08/2017	SmPC, Labelling and PL	
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IAIN/0001/G	<p>This was an application for a group of variations.</p> <p>B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site</p> <p>B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing</p>	15/09/2016	07/08/2017	Annex II and PL	