Leflunomide ratiopharm

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
IA/0027	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	09/07/2024		SmPC and PL	
IB/0026	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	13/05/2022	05/05/2023	SmPC 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).

	product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH				
IAIN/0025/G	This was an application for a group of variations. B.III.1.a.3 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition) 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	04/08/2021	n/a		
N/0024	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/07/2021	05/05/2023	PL	
IB/0023	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	20/08/2020	28/07/2021	SmPC, Annex II, Labelling and PL	
IAIN/0022	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	21/12/2017	26/11/2018	SmPC, Labelling and PL	
IAIN/0020	C.I.3.a - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the	15/12/2015	22/09/2016	SmPC and PL	

	assessment done under A 45/46 - Implementation of wording agreed by the competent authority				
IB/0019/G	This was an application for a group of variations. B.II.z - Quality change - Finished product - Other variation B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation 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)	13/11/2015	22/09/2016	SmPC	
IAIN/0018	C.I.3.a - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Implementation of wording agreed by the competent authority	24/09/2015	22/09/2016	SmPC and PL	
R/0015	Renewal of the marketing authorisation.	23/04/2015	19/06/2015	SmPC and PL	
IB/0017/G	This was an application for a group of variations. 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	23/04/2015	13/05/2015	SmPC and PL	

	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 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				

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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 from an already approved manufacturer	20/10/2014	n/a		
IB/0013	Update of sections 4.4 and 4.8 of the SmPC following the same changes for the reference product Arava. Sections 2 and 4 of the Package Leaflet have been updated accordingly. Additionally, some minor	14/08/2014	06/02/2015	SmPC and PL	

	linguistic corrections have been performed in the following languages: DA, DE, ES, FR, HR, IS, LT, NL, NO, PL, RO and SK to align the texts to the originator's. 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				
PSUSA/1837/ 201309	Periodic Safety Update EU Single assessment - leflunomide	10/04/2014	n/a		PRAC Recommendation - maintenance
IB/0012	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	06/02/2014	06/02/2015	SmPC and PL	Introduction of an additional statement on the reporting of ADRs in the Product Information. Furthermore, the Croatian annexes have been included together with the Croatian affiliate in the list of local representatives. Additionally minor editorial changes in local representatives of Hungary, Croatia, Iceland and United Kingdom have been made.
IAIN/0010	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	20/06/2013	n/a		
IB/0009	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 are submitted by the MAH	06/02/2013	22/01/2014	SmPC and PL	

IB/0008	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 are submitted by the MAH	06/06/2012	20/09/2012	SmPC, Annex II, Labelling and PL	Implementation of changes approved in reference product – update of section 4.4 to add a warning for peripheral neuropathy and the frequency of this event has been changed to 'common' in section 4.8 as requested by CHMP. The PIL has been updated accordingly. Further updates concern the implementation of the latest QRD template.
IA/0007	B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	04/04/2012	n/a		
IB/0006	Update of section 4.4 of the SmPC regarding the risk of leflunomide use in combination with biologicals following the CHMP assessment of the COLEBI study (FU2 038.1) as implemented in the originator product Arava II-49. 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 are submitted by the MAH	09/01/2012	20/09/2012	SmPC	Update of section 4.4 of the SmPC regarding the risk of leflunomide use in combination with biologicals following the CHMP assessment of the COLEBI study (FU2 038.1) as implemented in the originator product Arava II-49.
IA/0005	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	26/10/2011	n/a		
IB/0004	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	06/09/2011	n/a	SmPC and PL	Update of sections 4.2 and 5.1 of the SmPC to reflect the outcome of the clinical study R01143 (LEADER) regarding the use of a loading dose, as requested by CHMP. The MAH also took the opportunity to make minor linguistic

	new additional data are submitted by the MAH				corrections to align with the reference product and made changes to the contact details of the local representatives in the package leaflets.
IB/0003	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 are submitted by the MAH	04/08/2011	n/a	SmPC and PL	Implementation of changes approved in reference product - update of section 4.4 to amend the warning for interstitial lung disease (ILD) as requested by CHMP. The PIL was revised accordingly. In addition the description of the risk of teratogenicity in the PIL was strengthened. Further updates concern the implementation of the latest QRD template. In addition, the MAH made linguistic corrections in the bg, cs, de, el, fi, fr, hu, it, lv, mt, nl, ro, sl and sv language PI.
II/0002	Introduction of a new Pharmacovigilance system which has not been assessed by the relevant national competent authority/EMEA for another product of the same MAH. C.I.8.a - Introduction of a new Pharmacovigilance system - which has not been assessed by the relevant NCA/EMA for another product of the same MAH	23/06/2011	23/06/2011		Following the acquisition of ratiopharm GmbH by the TEVA Group, the MAH has submitted this Type II variation to introduce a new Pharmacovigilance System (TEVA DDPS Version 10), including a new Qualified person for Pharmacovigilance, which has not been assessed yet by EMA for another product of the same MAH.
IB/0001	B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation	08/03/2011	n/a	SmPC, Annex II and Labelling	