EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Repso

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/0020	A.7 - Administrative change - Deletion of manufacturing sites	30/03/2016		Annex II and PL	
R/0018	Renewal of the marketing authorisation.	19/11/2015	18/01/2016	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, including all variations introduced since the marketing authorisation was granted, the CHMP considered that the benefit-risk balance of Repso in the approved indications remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited

[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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					validity.
IAIN/0019	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	18/08/2015	18/01/2016	SmPC and PL	
IA/0017/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 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 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 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 A.7 - Administrative change - Deletion of manufacturing sites	01/07/2015	n/a		
IB/0016/G	This was an application for a group of variations. To update sections 4.3 and 4.4 of the SmPC	14/04/2015	18/01/2016	SmPC, Annex II and PL	

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	contraindicating and including a warning on teriflunomide the active metabolite of leflunomide; To update section 4.5 of the SmPC for leflunomide related to the study reports HWA486/1032/001 (interaction cimetidine) and To update section 4.5 of the SmPC for leflunomide related to the study reports HWA486/2F0.1 (interaction with methotrexate); To update section 4.5 of the SmPC for lefluomide related to the following Study reports INT11697 To update section 4.5 of the SmPC for leflunomide related to the following Study reports-INT11720 To update section 4.5 of the SmPC for leflunomide related to the following Study reports-INT12503 To update section 4.5 of the SmPC for leflunomide related to the following Study reports-INT12500 To update section 4.5 of the SmPC for leflunomide related to the following Study reports INT10564 To update section 4.5 of the SmPC for leflunomide related to the following Study reports-INT6040 In addition and following CHMP request section 4.4 of the SmPC was updated to include a warning for patients to be evaluated for tuberculosis before starting treatment with leflunomide. The PL was revised to reflect the above warnings and interactions. Furthermore, the MAH took the opportunity of this procedure to reflect the interaction studies in the RMP and to include DRESS syndrome in the RMP as requested by PRAC.				

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	Furthermore the MAH took this opportunity to make minor editorial changes and to update the annexes to the latest QRD version. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation 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				

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	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 the MAH				
T/0014	Transfer of Marketing Authorisation from Teva Pharma B.V. (Utrecht) to Teva B.V. (Haarlem). Transfer of Marketing Authorisation	13/10/2014	07/11/2014	SmPC, Labelling and PL	

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IB/0013	To update sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information on DRESS (drug reaction with eosinophilia and systemic symptoms). The Package Leaflet is updated accordingly. In addition, the MAH took this opportunity to update to the latest QRD template version and to update the contact details for the local representatives in IS, CY, LV, LU, HU, MT. 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	11/07/2014	07/11/2014	SmPC, Annex II and PL	
PSUSA/1837/ 201309	Periodic Safety Update EU Single assessment - LEFLUNOMIDE	10/04/2014	n/a		PRAC Recommendation - maintenance
N/0012	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/01/2014	06/02/2014	PL	
IAIN/0010	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	28/06/2013	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	28/01/2013	06/02/2014	SmPC and PL	

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IA/0008/G	This was an application for a group of variations. B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold B.II.b.3.a - Change in the manufacturing process of the finished product - Minor change in the manufacturing process of an immediate release solid oral dosage form or oral solutions	29/11/2012	n/a		
IB/0007	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	11/06/2012	29/10/2012	SmPC, Annex II, Labelling and PL	Implementation of changes approved in the reference product – update of section 4.4 to add a warning for peripheral neuropathy and the frequency of this event has been changed to 'commom' in section 4.8 as requested by CHMP. The PIL has been updated accordingly. Further updates concern the implementation of the latest QRD template. In addition, the MAH updated the list of local representatives for Austria, Germany, Finland, Ireland, Malta and Norway.
IB/0006	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	19/04/2012	n/a		
IB/0005	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	05/12/2011	06/03/2012	SmPC and Labelling	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. The MAH also took the opportunity to update sections 8 and 9 of the SmPC and section 12 in the labelling with the EU numbers and the date of authorisation.

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IA/0004	A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release)	26/09/2011	n/a		
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	06/09/2011	n/a	SmPC	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.
IB/0002	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, Annex II 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 Annex IIB and the implementation of the latest QRD template.
IB/0001/G	This was an application for a group of variations. 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 B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.2.a - Change to batch release arrangements	08/06/2011	n/a		

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	and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place				

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