Arava

Procedural steps taken and scientific information after the authorisation*

*Due to the Agency`s update of its procedure management systems, an additional document, reflecting the historical lifecycle may be available in the 'Assessment history' section. For the complete product lifecycle procedures, you may need to also refer to **EPAR - Procedural steps taken and scientific information after authorisation (archive)**.

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
Variation type II / EMA/VR/0000309158		10/04/2026		SmPC and PL	Haemophagocytic lymphohistiocytosis (HLH), including macrophage activation syndrome (MAS), has been reported in patients treated with

[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).

	Outcome: C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.4 Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data - Accepted Update of section 4.4 of the SmPC in order to add a new warning on leflunomide and hemophagocytic lymphohistiocytosis (HLH) and DRESS/HLH overlap syndrome in patients with rheumatoid arthritis and psoriatic arthritis (PsA) based on postmarketing data. The Package Leaflet is updated accordingly.				leflunomide. Although rare, Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) associated with leflunomide may be complicated by HLH or MAS. Cases of HLH/MAS have also been reported independently of DRESS. HLH/MAS is a serious and potentially life-threatening hyperinflammatory condition. Clinical features may include persistent fever, rash, neurological symptoms, hepatosplenomegaly, lymphadenopathy, cytopenias, markedly elevated serum ferritin, hypertriglyceridaemia, and abnormalities of liver function and coagulation. Patients should be informed about the signs and symptoms associated with HLH/MAS and advised to seek medical attention immediately if such symptoms occur during leflunomide treatment. If patients develop any of these conditions, stop leflunomide treatment and perform an accelerated drug elimination procedure (see section 4.4). Early recognition and prompt management are important to improve outcomes. For more information, please refer to the Summary of Product Characteristics.
Variation type IA_IN / EMA/VR/0000333754	Outcome: Q.III.1.a) European Pharmacopoeial certificate of suitability to the relevant Ph. Eur. Monograph(*) - Q.III.1.a.1 New certificate of suitability (CEP) (including replacement or addition) - Refused	13/03/2026			
Variation type II / EMA/VR/0000264105		12/03/2026		Annex II	For more information, please refer to the Summary of Product Characteristics.

	Outcome: C.I.11 Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the risk management plan - C.I.11.b Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment by the competent authority is required* - Accepted Submission of an updated RMP version 6.1 in order to address query raised by PRAC EMEA/H/C/PSUSA/00001837/202309 on the effectiveness and usefulness of the additional risk minimization measures (aRMMs) specifically related to the safety concerns hepatic reactions, blood cytopenia, and infections. In addition, the key elements of the physician leaflet and patient information sheet of the Annex II.D of the product information are updated.				
Variation type IB / EMA/VR/0000320658	Outcome: B.II.d.2 Change in test procedure for the finished product - B.II.d.2.d Other changes to a test procedure (including replacement or addition) - Accepted	23/02/2026			

Variation type II / EMA/VR/0000279486	Outcome: C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.z Change(s) in the Summary of product Characteristics, Labelling or Package Leaflet intended to implement the outcome of a PRAC signal recommendation: implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH - Accepted To update sections 4.4 and 4.8 of the SmPC and section 4 of the PL to implement the signal recommendations on pulmonary nodule (EPITT no 20155) adopted at the 13 March 2025 PRAC meeting. In addition, the MAH took the opportunity to update the EU local representatives.	04/09/2025		SmPC and PL	Interstitial lung disease, as well as rare cases of pulmonary hypertension and pulmonary nodules have been reported during treatment with leflunomide (see section 4.8). The risk interstitial lung disease and pulmonary hypertension can be increased in patients with a history of interstitial lung disease. Interstitial lung disease is a potentially fatal disorder, which may occur acutely during therapy. Pulmonary symptoms, such as cough and dyspnoea, may be a reason for discontinuation of the therapy and for further investigation, as appropriate. For more information, please refer to the Summary of Product Characteristics.