Ezmekly

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 /	This was an application for a group of	12/03/2026		SmPC	SmPC new text Section 5.2 In vitro, mirdametinib,

[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).

EMA/VR/0000313332	variations. 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 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 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 C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.13 Submission of additional clinical and non-clinical studies, including BE-studies. - Accepted C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.13 Submission of additional clinical and non-clinical studies, including BE-studies. - Accepted A grouped application consisting of: C.I.4: Update of section 5.2 of the SmPC in order to introduce the results from the in vitro				M15, and M22 are not inhibitors of CYP1A2, CYP2B6, CYP2C19, CYP2D6, or CYP3A4. Mirdametinib and M22 do not inhibit CYP2C8 or CYP2C9. M15 is an inhibitor of CYP2C8 and CYP2C9 in vitro, however there is a low potential for inhibition at clinically relevant concentrations. In vitro, M15 was not an inhibitor of the isoforms UGT1A3, UGT1A4, UGT1A6, UGT2B15, or UGT2B17. M15 is an inhibitor of UGT1A1, UGT1A9, UGT2B7 in vitro, however there is a low potential for inhibition at clinically relevant concentrations. In vitro, M22 does not inhibit P-gp, OATP1B3, OCT1, OCT2, OAT1, OAT3, MATE1 or MATE2K transporters. Based on in vitro studies, M22 inhibits BCRP, OATP1B1, and OATP2B1, however the clinical relevance of these effects cannot be established due to uncertainties regarding M22 maximal plasma concentrations and its protein binding. For more information, please refer to the Summary of Product Characteristics.

	study KC245128 investigating the reversible inhibitory potential of mirdametinib and PD-0315209 on CYP2C8, CYP2C9, CYP2C19, CYP1A2, CYP2D6, and CYP3A4. C.I.4: Update of section 5.2 of the SmPC in order to introduce the results from the in vitro study KC255037 investigating the potential inhibitory effect of PD-0315209 on UGT enzymes. C.I.4: Update of section 5.2 of the SmPC in order to introduce the results from the in vitro studies KC245140 and KC248110 investigating the CYP enzyme and transporter inhibitory potential of M22. C.I.13: Submission of the final report from the in vitro study KC255048 conducted to determine the mirdametinib Ki and Kinact for CYP2C19. C.I.13: Submission of the final report from from the in vitro investigation SPWT-20250515B (IVBU) of the pharmacological activity of M30.				
PSUR / EMA/PSUR/0000311173		12/03/2026			Maintenance