TEPMETKO

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
II/0011	Update of section 4.2 of the SmPC in order to add alternative methods of administration dispersed in water, as oral drinking suspension or via feeding tubes based on the available physicochemical and clinical pharmacology data. The Section 3 of the Package Leaflet is updated accordingly.	18/04/2024		SmPC and PL	SmPC new text Section 4.2 of the SmPC is updated as follow in order to include alternative methods of administration : If the patient is unable to swallow, the tablets can be dispersed in 30 mL of non-carbonated water. No other liquids should be used or added. The tablets should be

[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).

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				dropped in a glass with water without crushing, stir until the tablets dispersed into small pieces which may take a few minutes (the tablet will not completely dissolve). The dispersion should be swallowed within 1 hour. Rinse the glass with additional 30 mL to ensure that no residues remain in the glass and drink immediately. If an administration via a naso gastric tube (with at least 8 French gauge) is required, the tablets should be dispersed in 30 mL of non-carbonated water as described above. The 30 mL of liquid should be administered within 1 hour as per naso gastric tube manufacturer's instructions. Immediately rinse twice with 30 mL each to ensure that no residues remain in the glass or syringe and the full dose is administered. For more information, please refer to the Summary of Product Characteristics.
PSUSA/10979 /202309	Periodic Safety Update EU Single assessment - tepotinib	11/04/2024	n/a		PRAC Recommendation - maintenance
II/0012	B.I.e.2 - Introduction of a post approval change management protocol related to the AS	15/02/2024	n/a		
IA/0014	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	03/01/2024	n/a		
PSUSA/10979 /202303	Periodic Safety Update EU Single assessment - tepotinib	26/10/2023	n/a		PRAC Recommendation - maintenance

II/0009	Update of sections 4.8 and 5.1 of the SmPC in order to update safety and efficacy information based on updated results from study VISION (MS200095-0022); this is a Phase II, multicenter, open-label, single-arm study to evaluate the efficacy and safety/tolerability of the recommended dose of tepotinib in participants with advanced NSCLC of all histology types who tested positive for METex14 skipping alterations by next-generation sequencing in tissue (RNA-based) or plasma (circulating tumor DNA based). The RMP version 2.0 is agreed. In addition, the MAH took the opportunity to implement editorial changes to the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	31/08/2023		SmPC	SmPC new text Sections 4.8 and 5.1 of the SmPC have been revised in order to reflect the updated efficacy and safety results from the pivotal trial 'Vision', a single-arm, open-label, multicentre study in adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) harbouring METex14 skipping alterations. The updated efficacy and safety results remain consistent with those of the primary analysis for this study. For more information, please refer to the Summary of Product Characteristics.
IA/0010	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	17/07/2023	n/a		
II/0005	Update of sections 4.4, 4.5 and 5.2 of the SmPC in order to remove the warnings on interactions with 'CYP and P-gp inducers' and 'dual strong CYP3A and P-gp inhibitors, and P-gp inhibitors' and to update pharmacokinetic information based on final results from the drug-drug interaction (DDI) studies MS200095-0051 and MS200095-0053. Study MS200095-0051 is a phase 1, open-label, single-sequence, cross-over study to evaluate the effect of	15/06/2023		SmPC, Annex II and PL	SmPC new text Based on the final results of drug-drug interactions studies, sections 4.4, 4.5 and 5.2 of the SmPC have been updated in order to delete the warning that concomitant use of TEPMETKO with strong CYP and P gp inducers or dual strong CYP3A and P gp inhibitors should be avoided. These interactions are no longer considered clinically relevant and no dose adjustment is needed.

	multiple doses of carbamazepine on single-dose tepotinib pharmacokinetics in healthy participants, while study MS200095-0053 is a phase 1, open-label, single-sequence, cross-over study to evaluate the effect of multiple doses of itraconazole on single-dose tepotinib pharmacokinetics in healthy participants. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor changes to the PI and to remove a sentence from the annex II section about PSURs, as the first PSUR was submitted in due time in June 2022. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				For more information, please refer to the Summary of Product Characteristics.
IA/0007	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	14/06/2023	n/a		
PSUSA/10979 /202209	Periodic Safety Update EU Single assessment - tepotinib	14/04/2023	n/a		PRAC Recommendation - maintenance
IB/0004	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	07/11/2022	n/a		
PSUSA/10979 /202203	Periodic Safety Update EU Single assessment - tepotinib	27/10/2022	n/a		PRAC Recommendation - maintenance
IB/0003/G	This was an application for a group of variations.	06/10/2022	n/a		

	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				
IA/0002/G	This was an application for a group of variations. B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol 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	30/08/2022	n/a		

	manufacturer of a novel excipient B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				