CAMZYOS

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/G	This was an application for a group of variations. C.I.4: Update of section 4.2 of the SmPC to change the echocardiography monitoring frequency once a patient is on a stable dose of mavacamten. The proposed update is supported by the clinical data from interim Clinical study report of MAVA-LTE (CV027-003) study: "A Long-term Safety Extension	12/12/2024		SmPC and PL	Modification to section 4.2 were introduced to reduce the frequency of echo monitoring, once a patient is on a stable dose of mavacamten after week 12 in those patients with a LVEF > 55% and Valsalva LVOT gradient < 30 mmHg. Safety data comparing cardiac adverse event rates up to week 156 versus those up to week 204, where 6 month monitoring was applied after 156 weeks, suggest no increased incidence rate of such events. In particular, no

[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).

	Study of Mavacamten in Adults with Hypertrophic Cardiomyopathy who have completed the MAVERICK-HCM (MYK-461-006) or EXPLORER-HCM (MYK-461-005) trials", modelling & simulation results and safety data from post-approval safety database. Update of section 4.5 of the SmPC to clarify that the effect of strong CYP3A4 inhibitors on the PK of mavacamten was not investigated in a clinical drug drug interaction study to align it with similar wording for other CYP enzyme interactions based on the PBPK modelling. In addition, editorial changes were included in section 4.8 of the SmPC. The Package Leaflet is updated accordingly. The RMP version 4.1 has also been submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				additional LVEF < 50% events were observed during this additional period, although limited number of patients were treated beyond 180 days, to some degree limiting drawing strong conclusion. These data have been somewhat supported by modelling data, also suggesting no important increase in such events. For more information, please refer to the Summary of Product Characteristics.
IA/0013/G	This was an application for a group of variations. B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling	11/12/2024	n/a		

	down to 10-fold B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer				
PSUSA/74/202404	Periodic Safety Update EU Single assessment - mavacamten	28/11/2024	n/a		PRAC Recommendation - maintenance
IAIN/0012/G	This was an application for a group of variations. B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer B.I.a.2.a - Changes in the manufacturing process of	17/10/2024	n/a		

	the AS - Minor change in the manufacturing process of the AS				
II/0006	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	11/07/2024		SmPC and PL	Based on final results from study CV027043 (single-centre, open-label, randomized, parallel-group study to evaluate the effects of co-administration of activated charcoal with sorbitol on the single-dose PK of mavacamten in healthy subjects) in healthy subjects fasted overnight, administration of activated charcoal 2 hours after ingestion of a 15 mg dose of mavacamten reduced absorption as expressed by AUC0 72 by 20%. Administration of activated charcoal 6 hours after the mavacamten dose had no effect on the absorption.
II/0009	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	27/06/2024	05/08/2024	SmPC, Labelling and PL	
II/0008	C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required	13/06/2024	n/a		
PSUSA/74/2022310	Periodic Safety Update EU Single assessment - mavacamten	16/05/2024	n/a		PRAC Recommendation - maintenance
IA/0005	B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size	05/10/2023	n/a		

IA/0004	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	04/09/2023	n/a		
IA/0003	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	04/09/2023	n/a		
IA/0002	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	04/09/2023	n/a		
IB/0001/G	This was an application for a group of variations. B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes	04/08/2023	05/08/2024	SmPC, Labelling and PL	
