Orgovyx

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
PSUSA/10994 /202401	Periodic Safety Update EU Single assessment - relugolix	19/09/2024	18/11/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10994/202401.
IA/0025	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	04/11/2024	n/a		

[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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II/0024	Update of section 4.8 of the SmPC in order to amend the frequency of an existing adverse drug reactions (ADRs) 'Myocardial infarction' from 'rare' to 'uncommon' following PSUSA 00010994/202401 procedure and based on the current available clinical trial data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to add editorial changes. C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH	31/10/2024		SmPC and PL	SmPC new text Uncommon Myocardial infarction For more information, please refer to the Summary of Product Characteristics.
IB/0022	B.II.e.1.b.1 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Solid, semi-solid and non-sterile liquid pharmaceutical forms	06/09/2024	n/a		
II/0020	Update of sections 4.2 and 4.5 of the SmPC to add information on "Combination with other medicines for advanced hormone-sensitive prostate cancer" based on clinical studies and literature. In addition, the MAH took the opportunity to update section 5.1 of the SmPC with 2 minor corrections. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	27/06/2024	18/11/2024	SmPC	SmPC new text Potential for other medicinal products to affect the exposure to relugolix Clinical interaction studies with P-gp inhibitors (erythromycin and azithromycin) and combined P-gp and strong CYP3A4 inducers (rifampicin) have shown to affect the exposure of relugolix to a clinically relevant extent. Effect of co-administration on the exposure to relugolix and associated dosing recommendations are summarised in Table 1. This list also includes expected effect and

					recommendations with other potentially interacting medicinal products. For more information, please refer to the Summary of Product Characteristics.
PSUSA/10994 /202307	Periodic Safety Update EU Single assessment - relugolix	08/02/2024	n/a		PRAC Recommendation - maintenance
IA/0019	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	09/01/2024	n/a		
N/0018	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	20/12/2023	18/11/2024	PL	
PSUSA/10994 /202301	Periodic Safety Update EU Single assessment - relugolix	14/09/2023	20/11/2023	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10994/202301.
IB/0017	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	24/10/2023	n/a		
IB/0015/G	This was an application for a group of variations. 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 B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.2.a - Change to importer, batch release	25/08/2023	n/a		

	arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation 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				
II/0012	Update of section 4.5 of the SmPC based on final results from study MVT-601-9039; this is an In vitro Interaction Study of Relugolix with human OATP2B1 Uptake Transporter. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	01/06/2023	15/09/2023	SmPC	SmPC new text Transporter systems: Relugolix is not an inhibitor of OATP2B1
II/0009	Update of section 4.5 of the SmPC to include the result from study MVT-601-057. This is a Phase I, two-part, open-label, fixed (single)-sequence, two-treatment, two-period crossover study to assess the effects of relugolix on the pharmacokinetics of total dabigatran upon co-administration of relugolix and the P-gp substrate dabigatran etexilate in healthy adult men and women. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	25/05/2023	15/09/2023	SmPC	SmPC new text Upon co-administration of a single 150 mg dose of dabigatran etexilate, a P-gp substrate, with a single 120 mg dose of relugolix, the AUC0-inf and Cmax of total dabigatran was increased by 17% and 18%, respectively, which is not considered to be clinically meaningful. Therefore, clinically meaningful effects of a 120 mg dose relugolix on other P gp substrates are not expected. Considering that the 360 mg loading dose of relugolix has not been tested, dose separation of the loading dose of relugolix from administration of other P-gp substrates is

					advised.
II/0008	Update of section 4.5 of the SmPC to include the result from study MVT-601-055; this is an open-label, fixed (single)-sequence crossover phase 1 study to assess the sufficiency of dose separation to mitigate absorption-mediated increases in exposure to relugolix resulting from inhibition of intestinal P-gp by azithromycin in healthy adult men. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	25/05/2023	15/09/2023	SmPC	Upon co-administration of a 120 mg dose of relugolix and a single 500 mg dose of azithromycin the AUC and Cmax of relugolix were increased by 1.5- and 1.6-fold, respectively, although in the median concentration-time curves increases in relugolix exposure up to 5-fold were observed 1-3 hours after dosing. When the single dose of azithromycin was administered 6 hours after the 120 mg relugolix dose, the AUC and Cmax of relugolix were increased by 1.4- and 1.3-fold, respectively; the increase in relugolix exposure in the median concentration-time curves was maximally 1.6-fold in the window 1-3 hours after dosing. Due to limited number of subjects (n=18) and high PK variability, confidence intervals around these increases were wide (for AUC from 1.0- to 2.1-fold).
IAIN/0014	B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site	21/04/2023	n/a		
IB/0011	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	31/03/2023	15/09/2023	SmPC, Labelling and PL	Product information updated to add a new pack-size of 90 (3 packs of 30) film-coated tablets for Orgovyx 120 mg film-coated tablets (EU/1/22/1642/002)
PSUSA/10994 /202207	Periodic Safety Update EU Single assessment - relugolix	09/02/2023	n/a		PRAC Recommendation - maintenance
II/0007	Submission of the bioanalytical report for testosterone measurement in the clinical study MVT-601-3201.	02/02/2023	n/a		Not applicable

	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
IAIN/0010	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	13/01/2023	n/a		
IAIN/0005	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	25/08/2022	n/a		
IAIN/0003/G	This was an application for a group of variations. B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	17/08/2022	15/09/2023	Annex II and PL	
IA/0004	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	12/08/2022	n/a		
T/0002	Transfer of Marketing Authorisation	15/06/2022	08/07/2022	SmPC, Labelling and	

				PL	
IAIN/0001	C.I.11.a - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of wording agreed by the competent authority	07/06/2022	n/a		