



Ryego

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
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	18/01/2024		SmPC, Labelling and PL	

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).



PSUSA/10942 /202305	Periodic Safety Update EU Single assessment - relugolix / estradiol / norethisterone acetate	11/01/2024	n/a		PRAC Recommendation - maintenance
IB/0023	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate	05/01/2024	n/a		
II/0020/G	<p>This was an application for a group of variations.</p> <p>B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes</p> <p>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)</p> <p>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)</p> <p>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)</p> <p>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</p>	07/12/2023	n/a		

	<p>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)</p> <p>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</p>				
II/0019/G	<p>This was an application for a group of variations.</p> <p>B.I.a.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant update to the relevant AS section in the dossier</p> <p>B.III.1.a.3 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition)</p> <p>B.III.1.a.3 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition)</p>	07/12/2023	n/a		
II/0013/G	<p>This was an application for a group of variations.</p> <p>Extension of indication to include symptomatic treatment of endometriosis for RYEQO in adult women of reproductive age with a history of previous medical or surgical treatment for their endometriosis, based on final results from studies MVT-601-3101</p>	14/09/2023	30/10/2023	SmPC and PL	Please refer to Scientific Discussion 'Ryeqo-H-C-005267-II-0013-G

and MVT-601-3102 and final results up to 104 weeks from study MVT-601-3103. Studies 3101 and 3102 are pivotal, phase III, randomised, double-blind, placebo-controlled, safety and efficacy studies to evaluate relugolix with E2 and NETA as a combination therapy for pain associated with endometriosis. Study 3103 is an open-label extension study including patients who completed one of the two pivotal studies and met the eligibility criteria, regardless of their treatment assignment in the pivotal studies. In the extension part all patients received relugolix combination therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC were updated. The Package Leaflet is updated in accordance.

Update of section 4.5 of the SmPC to update information regarding Drug-Drug Interaction based on final results of DDI studies MVT-601-54, MVT-601-55 and MVT-601-57. Study MVT-601-54 is a 2-part interventional open-label study to assess the potential effects of erythromycin on the PK of the 3 components of Ryeqo. Study MVT-601-55 is an interventional open label fixed single sequence cross-over study to assess whether a 6-hour dose separation is sufficient to mitigate absorption mediated increased exposure to relugolix and study MVT-601-057 is a 2-part study to assess the potential effect of relugolix on the PK of total dabigatran.

The updated RMP version (2.1) has also been submitted. As part of the application, the MAH also requests an extension of the market protection by

	<p>one additional year.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p> <p>C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one</p>				
IB/0017/G	<p>This was an application for a group of variations.</p> <p>C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation</p> <p>C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation</p>	18/08/2023	n/a		
PSUSA/10942 /202211	<p>Periodic Safety Update EU Single assessment - relugolix / estradiol / norethisterone acetate</p>	06/07/2023	n/a		PRAC Recommendation - maintenance
IB/0016/G	<p>This was an application for a group of variations.</p> <p>B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer</p> <p>B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer</p>	24/05/2023	n/a		
IA/0018	<p>B.II.d.2.a - Change in test procedure for the finished</p>	23/05/2023	n/a		

	product - Minor changes to an approved test procedure				
PSUSA/10942 /202205	Periodic Safety Update EU Single assessment - relugolix / estradiol / norethisterone acetate	26/01/2023	31/03/2023	SmPC and PL	<p>Scientific conclusions and grounds for variation to the terms of the marketing authorisations</p> <p>In view of available data on urticaria and angioedema from clinical trials and spontaneous reports including cases with close temporal relationship, a positive de-challenge and/or re-challenge, and in view of a plausible mechanism of action, the PRAC considers a causal relationship between the combination relugolix/estradiol/norethisterone acetate and urticaria and angioedema is at least a reasonable possibility. The PRAC concluded that the product information of medicinal products containing the combination relugolix/estradiol/norethisterone acetate should be amended accordingly.</p>
II/0012	B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	23/02/2023	n/a		
II/0009	<p>Update of sections 5.3 and 6.6 of the SmPC based on final results from MVT-601-9030_Relugolix_ZEOGRT_Study (Rec); this is a fish, full life cycle test performed in the context of the Environmental Risk Assessment of relugolix. The Package Leaflet is updated accordingly.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>	30/06/2022	31/03/2023	SmPC and PL	Please refer to Scientific Discussion 'Ryeqo-H-C-5267-II-09'.

IB/0010	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	20/06/2022	22/07/2022	SmPC	
PSUSA/10942 /202111	Periodic Safety Update EU Single assessment - relugolix / estradiol / norethisterone acetate	10/06/2022	n/a		PRAC Recommendation - maintenance
IB/0008	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	11/05/2022	n/a		
II/0006	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	05/05/2022	n/a		
IB/0005	B.I.b.z - Change in control of the AS - Other variation	22/12/2021	n/a		
IA/0004/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites	11/10/2021	22/07/2022	Annex II and PL	
IB/0002/G	This was an application for a group of variations. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	02/09/2021	n/a		

	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation				
IB/0001	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	27/08/2021	22/07/2022	SmPC, Labelling and PL	
IA/0003/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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	05/08/2021	n/a		