RXULTI

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/0015	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	30/01/2025	07/03/2025	SmPC and PL	
PSUSA/10698 /202407	Periodic Safety Update EU Single assessment - brexpiprazole	13/02/2025	n/a		PRAC Recommendation - maintenance

[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).

R/0014	Renewal of the marketing authorisation.	30/03/2023	26/05/2023	SmPC, Annex II and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of RXULTI in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity. RXULTI (brexpiprazole) is removed from the additional monitoring list as a new active substance following five years of authorisation. Therefore, the statement that this medicinal product is subject to additional monitoring and that this will allow quick identification of new safety information, preceded by an inverted equilateral black triangle, is removed from the summary of product characteristics and the package leaflet. A few minor changes were also made to the PI to bring it in line with the current Agency/QRD template, SmPC guideline and other relevant guideline(s).
PSUSA/10698 /202107	Periodic Safety Update EU Single assessment - brexpiprazole	10/02/2022	n/a		PRAC Recommendation - maintenance
IB/0013/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.	17/11/2021	31/10/2022	SmPC, Labelling and PL	To introduce additional pack sizes (EU/1/18/1294/008-011) in the Product Information and in "EPAR – all Authorised presentations". To update the wording related to lactose in section 2 of the Summary of Product Characteristics (SmPC) and to update local representatives in the Package Leaflet. To update Section 6.5 of the Danish SmPC.

	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				
PSUSA/10698 /202101	Periodic Safety Update EU Single assessment - brexpiprazole	02/09/2021	n/a		PRAC Recommendation - maintenance
PSUSA/10698 /202007	Periodic Safety Update EU Single assessment - brexpiprazole	11/02/2021	n/a		PRAC Recommendation - maintenance
IA/0010	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	20/11/2020	n/a		
PSUSA/10698 /202001	Periodic Safety Update EU Single assessment - brexpiprazole	03/09/2020	n/a		PRAC Recommendation - maintenance
IB/0008/G	This was an application for a group of variations. 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 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	19/08/2020	n/a		

	control/testing takes place 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.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation				
IB/0007	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	22/07/2020	05/11/2020	SmPC and PL	
PSUSA/10698 /201907	Periodic Safety Update EU Single assessment - brexpiprazole	16/01/2020	n/a		PRAC Recommendation - maintenance
II/0003	Based on the Company Core Data Sheet of brexpiprazole, update of section 4.4 of the SmPC to add information regarding Impulse-control disorders and section 4.8 to add the adverse reactions 'Gambling disorder', 'Impulsive behaviour', 'Binge eating', 'Compulsive shopping' and 'Compulsive sexual behaviour' with a frequency 'unknown'. The Package Leaflet (PL) is updated accordingly. In addition, the MAH took the opportunity to clarify the wording regarding the posology in 'Patients taking strong CYP3A4 inducers' in SmPC section 4.2 as requested by EMA, and to perform additional editorials and minor changes throughout the Product Information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/11/2019	05/11/2020	SmPC, Annex II and PL	Considering all available data, the CHMP agrees that the cases reported are suggestive of the possibility to develop impulse control disorders (ICDs) especially if brexpiprazole is co-administered with other medications, used off label, or in patients with co-morbidities. Brexpiprazole mechanism of action and its similarities with aripiprazole, despite not being alone sufficient to establish a causal relationship between ICDs and brexpiprazole use, are also suggestive of the possibility to develop gambling and other impulse control disorders. Accordingly, section 4.4 of the SmPC is updated to add information regarding Impulse-control disorders and section 4.8 to add the adverse reactions 'Gambling disorder', 'Impulsive behaviour', 'Binge eating', 'Compulsive shopping' and 'Compulsive sexual behaviour' with a frequency 'unknown'. The Package Leaflet (PL) is updated accordingly.

IB/0005	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	31/10/2019	n/a		
PSUSA/10698 /201901	Periodic Safety Update EU Single assessment - brexpiprazole	05/09/2019	n/a		PRAC Recommendation - maintenance
T/0001	Transfer of Marketing Authorisation	02/10/2018	12/12/2018	SmPC, Labelling and PL	