Bylvay

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/0022/G	This was an application for a group of variations. A grouped application including two type II variations: - Update of sections 4.2, 4.4, 4.8, and 5.1 of the SmPC based on the clinical study report for the completed 72 weeks of Study A4250-008; an open-label, phase III study to evaluate the long-term	13/03/2025	02/05/2025	SmPC and PL	Please refer to Scientific Discussion Bylvay-H-C-004691-II-0022/G.

[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).

	efficacy and safety of odevixibat in children with PFIC (category 3 study in the RMP; MEA 002). The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and the Package Leaflet. An updated RMP version 6.3 was included in this submission. - Submission of the clinical study report for Study A4250-J001; a Phase I PK study in healthy Japanese adult male patients. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
PSUSA/10949 /202407	Periodic Safety Update EU Single assessment - odevixibat	13/02/2025	n/a		PRAC Recommendation - maintenance
S/0023	3rd annual re-assessment	30/01/2025	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Bylvay should be maintained.
PSUSA/10949 /202401	Periodic Safety Update EU Single assessment - odevixibat	19/09/2024	22/11/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10949/202401.
II/0018	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	27/06/2024	24/07/2024	SmPC and PL	SMPC section 4.2 Posology and Method of Administration is updated to include instructions for administration of Bylvay

	data				pellets in age-appropriate liquids in addition to the pre-existing instructions for administration in soft foods. The package leaflet is updated accordingly.
T/0017	Transfer of Marketing Authorisation	31/01/2024	16/02/2024	SmPC, Labelling and PL	
PSUSA/10949 /202307	Periodic Safety Update EU Single assessment - odevixibat	08/02/2024	n/a		PRAC Recommendation - maintenance
S/0016	2nd annual re-assessment	25/01/2024	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Bylvay should be maintained.
PSUSA/10949 /202301	Periodic Safety Update EU Single assessment - odevixibat	31/08/2023	n/a		PRAC Recommendation - maintenance
II/0013	Update of sections 4.4, 4.5 and 4.6 of the SmPC in order to update an existing warning, add drug-drug interaction (DDI) information with oral contraceptives and update information for women of childbearing potential, based on study A4250-022 listed as a category 3 study in the RMP; this is an open-label, phase 1 DDI study to evaluate the interaction of odevixibat with oral lipophilic contraceptives in healthy volunteers. The Package Leaflet and the RMP vs 4.1 is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	12/05/2023	16/02/2024	SmPC and PL	Interaction study A4250-022 with a lipophilic combination oral contraceptive containing ethinyl estradiol (EE) (0.03 mg) and levonorgestrel (LVN) (0.15 mg) conducted in adult healthy females, concomitant use of odevixibat had no impact on the AUC of LVN and decreased the AUC of EE by 17%, which is not considered clinically relevant. Interaction studies with other lipophilic medicinal products have not been performed, therefore, an effect on the absorption of other fat-soluble medicinal products cannot be excluded.

	data				
IB/0012	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	13/03/2023	n/a		
PSUSA/10949 /202207	Periodic Safety Update EU Single assessment - odevixibat	09/02/2023	n/a		PRAC Recommendation - maintenance
S/0008	1st annual re-assessment	15/12/2022	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Bylvay should be maintained.
IB/0009/G	This was an application for a group of variations. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	20/09/2022	n/a		
PSUSA/10949 /202201	Periodic Safety Update EU Single assessment - odevixibat	01/09/2022	n/a		PRAC Recommendation - maintenance
IB/0005	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	09/06/2022	n/a		
IB/0006	B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other	30/05/2022	31/05/2023	SmPC	

	variation				
IA/0004	B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place	02/03/2022	n/a		
II/0001	B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	11/11/2021	n/a		
IB/0002	B.I.b.1.h - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition or replacement (excl. Biol. or immunol. substance) of a specification parameter as a result of a safety or quality issue	05/10/2021	n/a		