Scemblix

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/0017	Submission of a comprehensive final analysis of the data from study CABL001X2101, listed as a category 3 study in the RMP. This is a phase I, multicenter, open-label study of oral asciminib in patients with chronic myelogenous leukemia or Philadelphia Chromosome-positive acute lymphoblastic leukemia. The RMP version 2.1 has also been submitted.	13/03/2025	n/a		The purpose of this procedure is to assess and discuss the results from the final analysis of Study CABL001X2101 (also referred as Study X2101) of asciminib in patients with Ph+ CML- CP previously treated with two or more TKIs. The final analysis of Study X2101 addresses mainly safety concerns related to long-term safety, acute pancreatitis (including isolated pancreatitis enzyme elevations), myelosuppression, QTc prolongation, and hepatotoxicity as

[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).

	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				listed in the RMP and includes data from an additional approximately 18 months of treatment relative to the Primary Analysis. In summary, the benefit-risk balance after longer exposure from the now available final analysis for Study X2101 remain positive.
IAIN/0018	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	04/12/2024		Annex II and PL	
PSUSA/11008 /202404	Periodic Safety Update EU Single assessment - asciminib	28/11/2024	n/a		PRAC Recommendation - maintenance
PSUSA/11008 /202310	Periodic Safety Update EU Single assessment - asciminib	30/05/2024	19/07/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/11008/202310.
II/0013/G	This was an application for a group of variations. Grouped application comprising three type II variations as follows: • C.I.4 - Update of sections 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information with P-gp Substrates based on the final results from studies 2301078, CABL001A2301 and CABL001X2101, listed as a category 3 study in the RMP. • C.I.4 - Update of section 4.8 of the SmPC in order to update the Summary of the safety profile and safety information based on final results from	13/06/2024		SmPC and PL	For more information, please refer to the Summary of Product Characteristics.

	study CABL001A2301 and CABL001X2101 • C.I.4 - Update of section 5.1 of the SmPC in order to update safety information based on final results from study CABL001A2301. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IAIN/0015	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	13/03/2024	n/a		
IA/0014	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	07/03/2024	n/a		
II/0009	Update of section 5.3 of the SmPC in order to update preclinical safety data based on final results from study R1570226: this is a 2-year rat carcinogenicity study. In addition, the MAH took the opportunity to implement editorial changes to the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to	29/02/2024	19/07/2024	SmPC	SmPC new text: In a 2-year rat carcinogenicity study, non-neoplastic proliferative changes consisting of ovarian Sertoli cell hyperplasia were observed in female animals at doses equal to or above 30 mg/kg/day. Benign Sertoli cell tumours in the ovaries were observed in female rats at the highest dose of 66 mg/kg/day. AUC exposures to asciminib

	new quality, preclinical, clinical or pharmacovigilance data				in female rats at 66 mg/kg/day were generally 8-fold higher than those achieved in patients at the dose of 40 mg twice daily. The clinical relevance of these findings is currently unknown. For more information, please refer to the Summary of Product Characteristics.
II/0008	Update of sections 4.5 and 5.2 of the SmPC in order to add interaction information between asciminib and OATP1B and BCRP substrates. The Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/12/2023	19/07/2024	SmPC and PL	SmPC new text: Medicinal products that may have their plasma concentrations altered by asciminib (…) OATP1B, BCRP substrates or substrates of both transporters Based on PBPK modelling, caution should be exercised during concomitant administration of asciminib with substrates of OATP1B, BCRP or both transporters, including, but not limited to sulfasalazine, methotrexate, pravastatin, atorvastatin, pitavastatin, rosuvastatin and simvastatin. No clinical drug interaction study was performed. In vitro evaluation of drug interaction potential Asciminib is metabolised by several pathways, including the CYP3A4, UGT2B7 and UGT2B17 enzymes, and biliary secreted by the transporter BCRP. Medicinal products inhibiting or inducing the CYP3A4, UGT and/or BCRP pathways may alter asciminib exposure. (…)

					Asciminib inhibits BCRP, P gp and OATP1B with Ki values of 24, 22 and 2 micromolar, respectively Based on PBPK models, asciminib may increase the exposure of medicinal products which are substrates of these transporters. For more information, please refer to the Summary of Product Characteristics.
IAIN/0011/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	07/12/2023	n/a		
PSUSA/11008 /202304	Periodic Safety Update EU Single assessment - asciminib	30/11/2023	n/a		PRAC Recommendation - maintenance
II/0004/G	This was an application for a group of variations. Grouped application comprising two type II variations as follows: - Submission of the final reports from studies DMPK-R2200470 (REC). This is an in vitro evaluation of inducibility of OATP1V1, MDR1 and CYP3A4 by asciminib using human hepatocytes. - Submission of the final report from study DMPK-	31/08/2023	n/a		

	R2270399 (REC). This is a physiologically based PK modelling and simulations to characterize the effect of cyclodextrins on the exposure of asciminib. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
IA/0010	A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)	17/08/2023	n/a		
PSUSA/11008 /202210	Periodic Safety Update EU Single assessment - asciminib	25/05/2023	24/07/2023	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/11008/202210.
IB/0005	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	05/07/2023	n/a		
IB/0003	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)	02/03/2023	24/07/2023	SmPC	
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	14/12/2022	24/07/2023	SmPC, Labelling and PL	The Product Information was updated to add a new pack-size of 180 tablets (multipack) in blister for Scemblix 40 mg film-coated tablet (EU/1/22/1670/005).
