XOSPATA

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
IAIN/0018	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	12/04/2024		Annex II and PL	
PSUSA/10832 /202309	Periodic Safety Update EU Single assessment - gilteritinib	11/04/2024	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).

II/0013	Update of sections 4.2, 4.4 and 5.2 in order to update the information on renal impairment based on final results from study 2215-CL-0114, listed as a category 3 study in the RMP. Study 2215-CL-0114 is a phase 1, single-dose, open-label study to investigate the effect of renal impairment on gilteritinib pharmacokinetics, safety and tolerability in 9 participants with severe renal impairment compared to 8 participants with normal renal function. The RMP version 5.0 has also been agreed during the procedure and submitted. In addition, the MAH took the opportunity to introduce editorial changes. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	12/10/2023		SmPC	The pharmacokinetics of gilteritinib were evaluated in five subjects with severe (CrCL 15 - <30 mL/min) renal impairment and in four subjects with end stage renal disease (CrCL <15 mL/min). A 1.4-fold increase in mean Cmax and 1.5 fold increase in mean AUCinf of gilteritinib was observed in subjects with severe renal impairment or end stage renal disease compared to subjects with normal renal function (n=8). No dose adjustment is necessary in patients with mild, moderate or severe renal impairment. Gilteritinib exposure may be increased in patients with severe renal impairment or end stage renal disease. Patients should be closely monitored for toxicities during administration of Xospata. For more information, please refer to the Summary of Product Characteristics.
IB/0014/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 B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process	14/08/2023	n/a		

	of the AS B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
IB/0015	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	14/07/2023	n/a		
II/0012	Submission of the final report from study 2215-PV-0001 - Evaluation of the effectiveness of the Xospata Routine Risk Minimization Measures (RMMs) and an additional Risk Minimisation Measure (aRMM): A Cross sectional study among Healthcare Professionals to assess awareness and knowledge, listed as a category 3 study in the RMP. The RMP version 3.1 has also been submitted. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	06/07/2023	n/a		
PSUSA/10832 /202209	Periodic Safety Update EU Single assessment - gilteritinib	14/04/2023	n/a		PRAC Recommendation - maintenance

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)	08/06/2022	n/a		
IA/0009/G	This was an application for a group of variations. 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 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	08/06/2022	n/a		
II/0007	Submission of the report of an integrated analysis to demonstrate the safety of long term treatment with gilteritinib when all patients enrolled in studies 2215-CL-0101, 2215-CL-0102 and 2215-CL-0301 have completed at least 3 years of treatment with gilteritinib or have withdrawn prior to completing at least 3 years of treatment. The studies refer to: 1) study 2215-CL-0101: a phase 1/2 open-label, dose escalation study investigating the safety, tolerability, pharmacokinetics, and pharmacodynamics of ASP2215 (gilteritinib) in patients with relapsed or refractory acute myeloid leukaemia (AML); 2) study	05/05/2022	n/a		

	2215-CL-0102: a phase 1 open-label, dose escalation study investigating the safety, tolerability, pharmacokinetics, and pharmacodynamics of ASP2215 in Japanese patients with relapsed or refractory AML; 3) study 2215-CL-0301: a phase 3 open-label, multicentre, randomized study of ASP2215 versus salvage chemotherapy in patients with relapsed or refractory AML with FMS-like tyrosine kinase 3 (FLT3) mutation. The RMP (version 2.0) is updated in order to address the missing information regarding the safety of Xospata (gilteritinib). C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required				
PSUSA/10832 /202109	Periodic Safety Update EU Single assessment - gilteritinib	07/04/2022	n/a		PRAC Recommendation - maintenance
PSUSA/10832 /202103	Periodic Safety Update EU Single assessment - gilteritinib	28/10/2021	n/a		PRAC Recommendation - maintenance
IA/0006	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	13/08/2021	09/12/2021	SmPC and PL	
PSUSA/10832 /202009	Periodic Safety Update EU Single assessment - gilteritinib	09/04/2021	n/a		PRAC Recommendation - maintenance

II/0003	Update of section 4.4, 4.5 and 5.2 of the SmPC in order to update information about Transporter drug-drug interactions based on final results from in vitro transporter studies identified as recommendations by CHMP (REC003) during the initial approval. In addition, the MAH took the opportunity to perform minor corrections and editorial changes in the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	03/12/2020	09/12/2021	SmPC, Labelling and PL	SmPC new text Sections 4.4 a warning is added for concominant administration of gilteritinib with medicinal products that are strong inhibitors of breast cancer resistant protein (BCRP) Section 4.5 Interactions:"Strong inhibitors of BCRPP can increase gilteritinib plasma concentrations" Effects of Xospata on other medicinal products: Effect of gliteritinib on medicinal products which are P-gp substrates is removed Section 5.2 Transporter drug drug interactions;section is modified to reflect new data: In vitro experiments demonstrated that gilteritinib is a substrate of P-gp and BCRP. Gilteritinib may potentially inhibit BCRP, and P gp, OATP1B1 in the small intestine, and OCT1 in the liver at clinically relevant concentrations (see section 4.5). For more information, please refer to the Summary of Product Characteristics.
II/0001	Submission of a pooled analysis report from studies 2215-CL-0101 (Phase 1/2), 2215-CL-0102 (Phase 1), 2215-CL-0301, 2215-CL-9100 (phase 3) listed as "Other forms of routine pharmacovigilance activities in section III.1 of the RMP". This is a pooled analysis to characterize gilteritinib-related differentiation syndrome, specifically incidence, observed signs and symptoms, duration, and response to intervention based on patient-level data from on-going trials in patients with acute myeloid leukemia.	26/11/2020	n/a		

	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
PSUSA/10832 /202003	Periodic Safety Update EU Single assessment - gilteritinib	29/10/2020	n/a		PRAC Recommendation - maintenance