Xadago

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
N/0045	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/10/2023		PL	
PSUSA/10356 /202302	Periodic Safety Update EU Single assessment - safinamide	28/09/2023	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).

IB/0044	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	18/08/2023	n/a		
IA/0042/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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)	20/02/2023	n/a		
IB/0040/G	This was an application for a group of variations. 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 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 B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an	03/08/2022	n/a		

	ASMF 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 B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure 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 B.I.z - Quality change - Active substance - Other variation				
IB/0041/G	This was an application for a group of variations. 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.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 B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The	29/07/2022	n/a		

	proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer				
N/0039	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/10/2021		PL	
IB/0038	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	29/06/2021	n/a		
IA/0037	B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold	27/05/2021	n/a		
II/0034	B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a manufacturer of the AS supported by an ASMF	11/02/2021	n/a		
PSUSA/10356 /202002	Periodic Safety Update EU Single assessment - safinamide	01/10/2020	n/a		PRAC Recommendation - maintenance
II/0035	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	01/10/2020	n/a		
R/0032	Renewal of the marketing authorisation.	25/07/2019	19/09/2019	SmPC and PL	
PSUSA/10356	Periodic Safety Update EU Single assessment -	05/09/2019	n/a		PRAC Recommendation - maintenance

/201902	safinamide				
II/0031	Submission of an updated RMP version 6.1 in order to implement RMP rev 2 template and introduce changes to pre-clinical, clinical and post-marketing exposure information and update the due date of DUS Z7219N02 from July 2019 to 28 February 2020. 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	05/09/2019	n/a		
PSUSA/10356 /201808	Periodic Safety Update EU Single assessment - safinamide	14/03/2019	n/a		PRAC Recommendation - maintenance
N/0030	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/03/2019	18/07/2019	PL	
IB/0028/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure 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	14/12/2018	n/a		

II/0027	Update of sections 4.4 and 4.5 of the SmPC in order to implement information regarding interaction of safinamide and rosuvastatin, following results from study CRO-PK-17-318. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Ireland in the Package Leaflet and to include editorial changes in the English, German and Spanish product information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	18/10/2018	18/07/2019	SmPC and PL	Safinamide may transiently inhibit BCRP in vitro. In drug-drug-interaction studies in human, a weak interaction was observed with rosuvastatin (AUC increase between 1.25 and 2.00 fold) but no significant interaction was found with diclofenac. It is recommended to monitor patients when safinamide is taken with medicinal products that are BCRP substrates (e.g., rosuvastatin, pitavastatin, pravastatin, ciprofloxacin, methotrexate, topotecan, diclofenac or glyburide) and to refer to their SmPCs to determine if a dose adjustment is needed.
PSUSA/10356 /201802	Periodic Safety Update EU Single assessment - safinamide	06/09/2018	n/a		PRAC Recommendation - maintenance
IB/0026/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site 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	27/07/2018	18/07/2019	Annex II and PL	

	packaging, for non-sterile medicinal products B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process				
II/0020	B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a manufacturer of the AS supported by an ASMF	22/03/2018	n/a		
PSUSA/10356 /201708	Periodic Safety Update EU Single assessment - safinamide	08/03/2018	n/a		PRAC Recommendation - maintenance
IA/0024	B.II.d.1.i - Change in the specification parameters and/or limits of the finished product - Ph. Eur. 2.9.40 uniformity of dosage units is introduced to replace the currently registered method, either Ph. Eur. 2.9.5 or Ph. Eur. 2.9.6	06/03/2018	n/a		
IA/0023/G	This was an application for a group of variations. 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 B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	25/01/2018	n/a		

IB/0022	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)	20/12/2017	19/04/2018	SmPC	
PSUSA/10356 /201702	Periodic Safety Update EU Single assessment - safinamide	28/09/2017	n/a		PRAC Recommendation - maintenance
II/0019	B.I.b.1.g - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Widening of the approved specs for starting mat./intermediates, which may have a significant effect on the quality of the AS and/or the FP	21/09/2017	n/a		
N/0018	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/06/2017	19/04/2018	PL	
PSUSA/10356 /201608	Periodic Safety Update EU Single assessment - safinamide	09/03/2017	n/a		PRAC Recommendation - maintenance
II/0014	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	23/02/2017	n/a		
IB/0016/G	This was an application for a group of variations. A.6 - Administrative change - Change in ATC Code/ATC Vet Code B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test	01/02/2017	19/04/2018	SmPC, Annex II, Labelling and PL	

	procedure 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)				
PSUSA/10356 /201602	Periodic Safety Update EU Single assessment - safinamide	02/09/2016	n/a		PRAC Recommendation - maintenance
II/0005	Update of Section 4.5 of the SmPC for Xadago based on the results of the final report of the in vitro studies "In vitro Interaction Studies of Safinamide and NW-1153 with Selected human BCRP Efflux (ABC) Transporter, and with human OATP1B1, OATP1B3, OATP1A2, OAPT2B1, OCT1, OCT2, OAT1, OAT3, MATE1 and MATE2-K Uptake Transporters". C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	26/05/2016	11/01/2017	SmPC	In an in vitro Study, the non-specific binding of safinamide and whether safinamide is a substrate for BCRP, OATP1B1 and OATP1B3 were investigated. Based on the results of this and previous studies, it can be concluded that safinamide did not show any non-specific binding and safinamide is not a substrate for BCRP, OATP1B1 and OATP1B3 at clinically relevant concentrations. Safinamide is, however, an inhibitor of OCT1 at clinically relevant portal vein concentrations and may lead to interactions with concomitantly taken drugs that are also substrates of OCT1. Therefore, Information that Safinamide may lead to interactions when taken concomitantly with drugs such as metformin, acyclovir, ganciclovir was added to Section 4.5 of the SmPC.
IB/0012/G	This was an application for a group of variations. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	21/04/2016	n/a		
IB/0011	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale	17/03/2016	11/01/2017	SmPC and PL	

	(supported by real time data)				
PSUSA/10356 /201508	Periodic Safety Update EU Single assessment - safinamide	17/03/2016	n/a		PRAC Recommendation - maintenance
II/0008	Update of sections 4.5 and 5.2 of the SmPC to introduce information on safinamide effects on BCRP based on the results of a drug-drug interaction study (category 3 study in the RMP). The RMP is updated accordingly. In addition, the MAH took the opportunity to update the list of Local Representatives for Ireland and UK in the PL. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	28/01/2016	11/01/2017	SmPC and PL	Safinamide may transiently inhibit BCRP in vitro. However, in a drug-drug-interaction study with diclofenac in humans no significant interactions were observed. Therefore, no precautions are necessary when safinamide is taken with medicinal products that are BCRP substrates (e.g., pitavastatin, pravastatin, ciprofloxacin, methotrexate, topotecan, diclofenac or glyburide).
IAIN/0010/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	14/12/2015	n/a		
N/0007	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/10/2015	11/01/2017	PL	
IB/0006	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	02/09/2015	n/a		

IB/0003/G	This was an application for a group of variations. B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF 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 B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.e - Change in test procedure for AS or	20/08/2015	n/a		

	starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate				
IB/0002	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	24/07/2015	n/a		
IA/0001/G	This was an application for a group of variations. B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	13/05/2015	n/a		