Lixiana

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
WS/2409	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	12/10/2023	29/11/2023	SmPC, Labelling and PL	Following the review of paediatric data it was concluded that edoxaban is not recommended for use in children and adolescents from birth to 18 years of age with confirmed VTE (PE and/or DVT) event as the efficacy has not been established. Available data in VTE patients are described in sections 4.8, 5.1 and 5.2. For more information, please refer to the Summary of Product Characteristics.
PSUSA/10387 /202210	Periodic Safety Update EU Single assessment - edoxaban	25/05/2023	26/07/2023	SmPC, Labelling and	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for

[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).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact Telephone +31 (0)88 781 6000

				PL	PSUSA/10387/202210.
WS/2510	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.c.1.z - Change in immediate packaging of the AS - Other variation	13/07/2023	n/a		
WS/2483	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	08/06/2023	n/a		
N/0048	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/05/2023	26/07/2023	Labelling	
WS/2444	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant update to the relevant AS section in the dossier	26/04/2023	n/a		
IG/1610	B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The	20/04/2023	n/a		

	proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer				
WS/2400	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	19/01/2023	n/a		
WS/2379/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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.z - Change in batch size (including batch size ranges) of AS or intermediate - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	10/11/2022	n/a		
IG/1569	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	01/11/2022	n/a		

PSUSA/10387 /202110	Periodic Safety Update EU Single assessment - edoxaban	10/06/2022	n/a		PRAC Recommendation - maintenance
WS/2190	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant update to the relevant AS section in the dossier	22/04/2022	n/a		Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Roteas in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IG/1484/G	This was an application for a group of variations. B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	23/03/2022	n/a		
WS/2078	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	24/02/2022	n/a		
IG/1454/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting	05/11/2021	n/a		

	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				
PSUSA/10387 /202010	Periodic Safety Update EU Single assessment - edoxaban	10/06/2021	n/a		PRAC Recommendation - maintenance
IG/1364	B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer	06/05/2021	n/a		
N/0032	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/03/2021	26/11/2021	PL	
WS/1895/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.e.1.b.1 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Solid, semi-solid and non-sterile liquid pharmaceutical forms B.II.e.1.b.1 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Solid, semi-solid and non-sterile liquid pharmaceutical forms	26/11/2020	26/11/2021	SmPC, Labelling and PL	

WS/1922	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/11/2020	26/11/2021	SmPC, Labelling and PL	
WS/1760	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	26/11/2020	n/a		
IAIN/0030	C.I.12 - Inclusion or deletion of black symbol and explanatory statements for medicinal products in the list of medicinal products that are subject to additional monitoring	29/10/2020	26/11/2021	SmPC and PL	
WS/1880	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer	10/09/2020	n/a		
WS/1756	This was an application for a variation following a	25/06/2020	26/11/2021	SmPC, Annex	

	worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data			II and PL	
PSUSA/10387 /201910	Periodic Safety Update EU Single assessment - edoxaban	14/05/2020	n/a		PRAC Recommendation - maintenance
R/0023	Renewal of the marketing authorisation.	12/12/2019	24/02/2020	SmPC, Annex II, Labelling and PL	
IAIN/0022	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	21/06/2019	25/07/2019	SmPC, Labelling and PL	
PSUSA/10387 /201810	Periodic Safety Update EU Single assessment - edoxaban	16/05/2019	n/a		PRAC Recommendation - maintenance
PSUSA/10387 /201804	Periodic Safety Update EU Single assessment - edoxaban	31/10/2018	n/a		PRAC Recommendation - maintenance
IG/0990/G	This was an application for a group of variations. B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting	30/10/2018	n/a		

	material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)				
IAIN/0018	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	03/08/2018	25/07/2019	SmPC and PL	
PSUSA/10387 /201710	Periodic Safety Update EU Single assessment - edoxaban	31/05/2018	26/07/2018	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10387/201710.
IB/0016	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	19/02/2018	28/05/2018	Labelling	
PSUSA/10387 /201704	Periodic Safety Update EU Single assessment - edoxaban	30/11/2017	n/a		PRAC Recommendation - maintenance
WS/1230	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	19/10/2017	n/a		
PSUSA/10387 /201610	Periodic Safety Update EU Single assessment - edoxaban	18/05/2017	13/07/2017	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10387/201610.
II/0012	Update of sections 4.2 and 5.1 of the SmPC in order to add information deriving from new clinical data for the use of edoxaban as anticoagulant therapy for patients with non-valvular atrial fibrillation undergoing	15/06/2017	28/05/2018	SmPC, Annex II, Labelling and PL	Lixiana can be initiated or continued in patients who may require cardioversion. For transoesophageal echocardiogram (TEE) guided cardioversion in patients not previously treated with anticoagulants, Lixiana treatment

	cardioversion (study ENSURE-AF). The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Portugal in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.0. In addition the MAH took the opportunity to introduce linguistic review in the Package Leaflet and to amend annex A as suggested during variation IA/05/G. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				should be started at least 2 hours before cardioversion to ensure adequate anticoagulation. Cardioversion should be performed no later than 12 hours after the dose of Lixiana on the day of the procedure. For all patients undergoing cardioversion, confirmation should be sought prior to cardioversion that the patient has taken Lixiana as prescribed. Decisions on initiation and duration of treatment should follow established guidelines for anticoagulant treatment in patients undergoing cardioversion.
PSUSA/10387 /201606	Periodic Safety Update EU Single assessment - edoxaban	12/01/2017	n/a		PRAC Recommendation - maintenance
IB/0009/G	This was an application for a group of variations. A.6 - Administrative change - Change in ATC Code/ATC Vet Code 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)	12/08/2016	14/10/2016	SmPC and PL	
PSUSA/10387 /201512	Periodic Safety Update EU Single assessment - edoxaban	07/07/2016	n/a		PRAC Recommendation - maintenance
N/0008	Update of the package leaflet with revised contact details of the local representative for Greece. In addition, the MAH took the opportunity to make minor linguistic amendments in the Bulgarian, Czech, Danish,	16/06/2016	14/10/2016	PL	

	Norwegian, Polish and Slovakian package leaflets. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)				
N/0007	Update of the package leaflet with revised contact details of the local representatives for Bulgaria, Croatia, Czech Republic, Denmark, Finland, Hungary, Iceland, Norway, Poland, Romania, Slovakia, Slovenia and Sweden. In addition the MAH took the opportunity to make a minor linguistic amendment in the Italian Patient Alert Card. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/03/2016	14/10/2016	PL	
IA/0005/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 B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	25/02/2016	n/a		

	B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)				
IB/0004	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	13/11/2015	n/a		
IB/0003/G	This was an application for a group of variations. B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new	13/11/2015	n/a		

	specification parameter to the specification with its corresponding test method B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method				
IB/0002	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)	08/10/2015	14/10/2016	SmPC and PL	
IB/0001	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	08/10/2015	n/a		