Duloxetine Lilly

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
PSUSA/1187/ 202308	Periodic Safety Update EU Single assessment - duloxetine	25/04/2024	20/06/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1187/202308.
IG/1625	B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect	17/08/2023	n/a		

[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).

	the product information				
WS/2220/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.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	10/03/2022	n/a		
N/0024	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/12/2021	20/06/2024	PL	
PSUSA/1187/202008	Periodic Safety Update EU Single assessment - duloxetine	11/03/2021	n/a		PRAC Recommendation - maintenance
IG/1355/G	This was an application for a group of variations. B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability -	24/02/2021	n/a		

	Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material) B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material) B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material) B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material) B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material) B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material)				

WS/1879	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. This worksharing variation is being submitted to present and discuss the results of Study F1J-MC-B034 Pregnancy Registry to meet the commitment made during the previous procedure No. EMEA/H/C/WS1527/G which received positive CHMP opinion on 25 July 2019. As a consequence of the submission of the F1J-MC-B034 Study Report, the Risk Management Plan (RMP) for duloxetine has been updated. The RMP for all Lilly duloxetine products are combined. The changes introduced are not specific to one product and are therefore the same for all products. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	03/09/2020	n/a		
WS/1755	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. As agreed in the procedure WS-1527G in order to address the foetal outcomes, submission of the final report from study FIJ-MC-B059 'Observational Study to Assess Fetal Outcomes Following Maternal	11/06/2020	17/06/2021	SmPC and PL	As agreed in the procedure WS-1527G in order to address the foetal outcomes, submission of the final report from study FIJ-MC-B059 'Observational Study to Assess Fetal Outcomes Following Maternal Exposure to Duloxetine' and the revised final report from study Study F1J-MC-B057 'Observational Studies to Assess Maternal and Fetal Outcomes Following Exposure to Duloxetine'.

	Exposure to Duloxetine' and the revised final report from study Study F1J-MC-B057 'Observational Studies to Assess Maternal and Fetal Outcomes Following Exposure to Duloxetine'. Section 4.6 of the SmPc and section 2 of the PL were updated to reflect the available knowledge with regard to the usBe of duloxetine during pregnancy. The MAH took also the opportunity to include the declaration of sodium in the Product Information following the guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. During the assessment and following a transfer of MAH, Xeristar was removed from the WS procedure. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				Section 4.6 of the SmPc and section 2 of the PL were updated to reflect the available knowledge with regard to the usBe of duloxetine during pregnancy. The MAH took also the opportunity to include the declaration of sodium in the Product Information following the guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. During the assessment and following a transfer of MAH, Xeristar was removed from the WS procedure.
IG/1134	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	14/08/2019	n/a		
R/0015	Renewal of the marketing authorisation.	29/05/2019	31/07/2019	SmPC, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Duloxetine Lilly in the approved indication remains favourable and therefore recommended the renewal of the

					marketing authorisation with unlimited validity.
IG/1126	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	25/07/2019	12/06/2020	SmPC and PL	
WS/1527/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. C.I.11.z (Type IB) - to stop enrolment of Study F1J-MC-B034 (study B034), another study included in the current EU-RMP as an additional pharmacovigilance activities to address missing information regarding duloxetine exposure due to pregnancy. C.I.4 (Type II) - Update of sections 4.4, 4.6 and 4.8 of the SmPC in order to add a warning on the risk of postpartum haemorrhage based on final results from study Study F1J-MC-B057 listed as a category 3 in the RMP; this is an observational study to assess maternal and foetal outcomes following exposure to duloxetine. The Package Leaflet is updated accordingly. The RMP version 13 has also been submitted. In addition, the Worksharing applicant (WSA) took the opportunity to correct the term "sucrase-isomaltase" in section 4.4 of the SmPC in line with the Annex to the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (EMA/CHMP/302620/2017 corr. 1*) and to bring the PI in line with the latest QRD	25/07/2019	12/06/2020	SmPC, Labelling and PL	Observational data have provided evidence of an increased risk (less than 2 -fold) of postpartum haemorrhage following duloxetine exposure within the month prior to birth. This risk is now reflected in the SmPC sections 4.4, 4.6 and 4.8.

	template version 10. The Xeristar 30 mg SmPC & Xeristar 60 mg SmPC and the Yentreve 20 mg SmPC & Yentreve 40 mg SmPC have been combined in a single SmPC, respectively, following the Policy on combined SmPCs (EMA/333423/2015). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation				
WS/1598	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH	14/06/2019	12/06/2020	SmPC	
WS/1619	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	06/06/2019	n/a		

IG/1055	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	18/01/2019	31/07/2019	SmPC and PL	
IG/0996	A.7 - Administrative change - Deletion of manufacturing sites	23/10/2018	n/a		
PSUSA/1187/ 201708	Periodic Safety Update EU Single assessment - duloxetine	12/04/2018	n/a		PRAC Recommendation - maintenance
WS/1264	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Submission of the final report from study F1J-MC-B056 listed as a category 3 study in the RMP. This is a non-interventional non-imposed study aimed to investigate the association between duloxetine exposure and suicide-related behaviours and ideation in women with stress urinary inconsistence (SUI). The RMP version 12.4 has also been updated to reflect the study results. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	08/02/2018	n/a		The association between suicide attempts and receipt of duloxetine treatment in women with stress urinary inconsistence (SUI) compared to women with SUI without duloxetine treatment has been assessed in study F1J-MC-B056. Study B056 has several limitations but in the light of the results the association between the risk of suicidality and duloxetine treatment cannot be completely ruled out. Currently, the risk of suicidality is an important identified risk for duloxetine-containing products and adequate warnings concerning this risk are already included in the SmPC. No further changes to the product information are warranted. The RMP is updated to reflect the study results and limitations and update the pharmacovigilance plan regarding this study.
WS/1331	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.h - Change in the specification parameters and/or limits of the finished product - Update of the	01/02/2018	n/a		

	dossier to comply with the provisions of an updated general monograph of the Ph. Eur. for the finished product				
WS/1109	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	26/01/2017	20/12/2017	SmPC, Annex II, Labelling and PL	
IG/0759/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or	11/01/2017	n/a		

	deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer				
WS/1015	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. To update the RMP to add a new Observational Study to Assess Maternal and Fetal Outcomes Following Exposure to Duloxetine (F1J-MC-B057), and to update the plans for the existing pregnancy registry (F1JMC-B034) in section III.4.3 of the RMP. 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	13/10/2016	n/a		
IG/0664	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	25/02/2016	n/a		
IG/0662	A.1 - Administrative change - Change in the name and/or address of the MAH	23/02/2016	04/07/2016	SmPC, Labelling and PL	
IB/0002	C.I.3.z - Change(s) in the SPC, Labelling or PL	21/07/2015	04/07/2016	SmPC and PL	

	intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Other variation				
WS/0758	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of section 4.8 of the SmPC in order to add microscopic colitis with frequency category 'rare' as a new ADR identified from post marketing experience. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant took the opportunity to make minor editorial changes in the SmPC and PL and to update the local representative for Italy in the Package Leaflet for Xeristar. Moreover, the Worksharing applicant took the opportunity to correct the stated mass of sucrose in capsule in section 2 of the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	09/07/2015	04/07/2016	SmPC and PL	