EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Pregabalin Pfizer

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
IG/1690/G	This was an application for a group of variations. B.III.1.a.3 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition)	11/01/2024		Annex II and PL	

[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

	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				
PSUSA/2511/ 202301	Periodic Safety Update EU Single assessment - pregabalin	12/10/2023	07/12/2023	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2511/202301.
N/0054	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/09/2023	07/12/2023	PL	
IG/1622	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	31/07/2023	n/a		
N/0050	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	14/03/2023	07/12/2023	PL	
N/0049	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/07/2022	26/09/2022	PL	
WS/2293	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.z - 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 - Other variation	21/07/2022	26/09/2022	SmPC and PL	To update sections 4.4 and 4.8 of the SmPC and sections 2, 3 and 4 of the PL, to implement the wording related to the cases of abuse and dependence in patients without a history of substance disorder.

WS/2261	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of SmPC sections 4.4 and 4.8 with a warning regarding severe cutaneous adverse reactions (SJS and TEN). C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	10/06/2022	26/09/2022	SmPC and PL	
WS/2168	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.z - 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 - Other variation	22/04/2022	26/09/2022	SmPC and PL	
N/0046	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/03/2022	26/09/2022	PL	
N/0045	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/12/2021	26/09/2022	PL	
PSUSA/2511/ 202101	Periodic Safety Update EU Single assessment - pregabalin	16/09/2021	15/11/2021	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2511/202101.

WS/1919	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Submission of an updated RMP (version 13.2) to include results from recently completed PASS studies, namely: 1) study A0081359: a population-based cohort study of pregabalin to characterize pregnancy outcomes; 2) study A0081106: a 12-month open-label study to evaluate the safety and tolerability of pregabalin as adjunctive therapy in paediatric subjects 1 month to 16 years of age with partial onset seizures and paediatric and adult subjects 5 to 65 years of age with primary generalized tonic-clonic seizures; 3) study A0081042: a double-blind, placebo-controlled, parallel-group, multicentre study of the efficacy and safety of pregabalin as adjunctive therapy in children 1 month through <4 years of age with partial onset seizures; 4) study A0081105: a randomized, double-blind, placebo-controlled, parallel group, multicentre trial of pregabalin as adjunctive therapy in paediatric and adult subjects with primary generalized tonic-clonic seizures. In addition, information on A0081096: a prospective randomized 12-week controlled study of visual field change in subjects with partial seizures receiving pregabalin or placebo has been updated as well as A0081365: a phase 4, randomised, double-blind, double-dummy, placebo- and active-controlled, single-dose, six-way crossover study to evaluate the potential for abuse with pregabalin. However, further issues noted with the	28/10/2021	26/09/2022	SmPC and PL	The results from the pregnancy outcomes study provided additional information concerning the risks of pregabalin treatment during pregnancy; supporting that pregabalin should not be used during pregnancy unless clearly necessary and women of childbearing potential have to use effective contraception based on the new data on major congenital malformations. In addition, the data support that pregabalin may cross the human placenta. For more information, please refer to the Summary of Product Characteristics.

	RMP should be updated at the next regulatory opportunity. In the light of the results from the pregnancy outcomes study, section 4.6 of the SmPC is being updated concerning the risks of pregabalin treatment during pregnancy, indicating that women of childbearing potential have to use effective contraception, pregabalin may cross the human placenta and the description of major congenital malformations (MCM). In addition, section 4.4 is updated to highlight that pregabalin should not be used during pregnancy unless clearly necessary and women of childbearing potential have to use effective contraception based on the new data on MCM. 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				
N/0044	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/10/2021	26/09/2022	PL	
N/0042	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/08/2021	15/11/2021	PL	
WS/2015	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	25/03/2021	15/11/2021	SmPC and PL	

	To update Section 5.1 of the SmPC following completion of a paediatric study (A0081105) in line with the outcome of the Article 46 (EMEA/H/C/003880/P46/006.1 and EMEA/H/C/003880/P46/006) and Post-authorisation Measure (PAM) procedure (EMEA/H/C/000546/P46/053.1 and EMEA/H/C/003880/P46/006.1). In addition the MAH brought that annexes in line with QRD version 10.1 and a reference to the reporting of side effects that had been duplicated was removed. C.I.3.a - 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 - Implementation of wording agreed by the competent authority				
PSUSA/2511/202001	Periodic Safety Update EU Single assessment - pregabalin	17/09/2020	18/11/2020	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2511/202001.
N/0039	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/10/2020	15/11/2021	Labelling	
WS/1798	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update Section 4.8 and Section 5.1 SmPC to reflect data from study A0081106 "A 12-Month Open-Label	03/09/2020	18/11/2020	SmPC, Labelling and PL	Section 4.8 and Section 5.1 of the SmPC were updated to reflect safety results from study A0081106 "A 12-Month Open-Label Study to Evaluate the Safety and Tolerability of Pregabalin as Adjunctive Therapy in Pediatric Subjects 1 Month to 16 Years of Age With Partial Onset Seizures and Pediatric and Adult Subjects 5 to 65 Years of Age With

	Study to Evaluate the Safety and Tolerability of Pregabalin as Adjunctive Therapy in Pediatric Subjects 1 Month to 16 Years of Age With Partial Onset Seizures and Pediatric and Adult Subjects 5 to 65 Years of Age With Primary Generalized Tonic-Clonic Seizures". C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				Primary Generalized Tonic-Clonic Seizures". For more information, please refer to the Summary of Product Characteristics.
T/0035	Transfer of Marketing Authorisation	03/04/2020	02/06/2020	SmPC, Labelling and PL	
IG/1245/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 - 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	29/05/2020	n/a		

	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)				
N/0034	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	25/03/2020	02/06/2020	PL	
WS/1605	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Addition of a warning in section 4.4. regarding an increased risk for opioid related death in patients who took concomitant opioids. A statement on the observation of a trend for a greater risk at higher doses was also included. Section 4.5 has been updated to reflect the findings of the case-control study regarding concomitant use of pregabalin and opioids. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/11/2019	09/03/2020	SmPC and PL	Based on published literature and a cumulative review of cases in the MAH's safety database, there is a strong signal for an increased risk of opioid-related death in patients concomitantly receiving opioids and pregabalin compared to treatment with opioids alone. Consequently, a new warning regarding an increased risk for opioid related death in patients who took concomitant opioids has been added in SmPC section 4.4. Moreover, Section 4.5 has been updated to reflect the findings of the case-control study regarding concomitant use of pregabalin and opioids.
N/0032	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/11/2019	09/03/2020	PL	
PSUSA/2511/ 201901	Periodic Safety Update EU Single assessment - pregabalin	05/09/2019	n/a		PRAC Recommendation - maintenance

IG/1123	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	30/08/2019	n/a		
N/0030	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/05/2019	09/03/2020	PL	
IG/1103	B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes	17/05/2019	09/03/2020	SmPC, Labelling and PL	
WS/1495	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	28/02/2019	09/03/2020	SmPC	
R/0025	Renewal of the marketing authorisation.	18/10/2018	12/12/2018		Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Pregabalin Pfizer in the approved indication remains unchanged and therefore recommended the renewal of the marketing authorisation with unlimited validity.
WS/1364	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	29/11/2018	n/a		

	Introduction of an updated RMP version 12.3 in order to include the changes proposed by EMEA/H/C/PSUSA/00002511/201701, updating the safety concerns and risk minimisation measures. The pharmacovigilance plan has also been updated. The protocol for non-interventional non-imposed PASS (A0081359) titled "A population-based cohort study of Pregabalin to characterize pregnancy outcomes" has been approved. 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/2511/ 201801	Periodic Safety Update EU Single assessment - pregabalin	06/09/2018	n/a		PRAC Recommendation - maintenance
T/0024	Transfer of Marketing Authorisation	11/07/2018	30/07/2018	SmPC, Labelling and PL	
IG/0938/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	13/07/2018	n/a		

	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/1137	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of sections 4.8 and 5.1 of the SmPC in order to reflect final results from paediatric study A0081041: "A Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study of the Efficacy and Safety of Pregabalin as Adjunctive Therapy in Children 4-16 Years of Age with Partial Onset Seizures". C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	16/11/2017	07/03/2018	SmPC	In the 12 week placebo controlled study, paediatric patients were assigned to pregabalin 2.5 mg/kg/day (maximum, 150 mg/day), pregabalin 10 mg/kg/day (maximum, 600 mg/day), or placebo. The percentage of subjects with at least a 50% reduction in partial onset seizures as compared to baseline was 40.6% of subjects treated with pregabalin 10 mg/kg/day (p=0.0068 versus placebo), 29.1% of subjects treated with pregabalin 2.5 mg/kg/day (p=0.2600 versus placebo) and 22.6% of those receiving placebo. The most common adverse events observed in the 12 week study with pregabalin treatment were somnolence, pyrexia, upper respiratory tract infection, increased appetite, weight increased, and nasopharyngitis.

	data				
WS/1213	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	14/09/2017	n/a		
PSUSA/2511/201701	Periodic Safety Update EU Single assessment - pregabalin	01/09/2017	n/a		PRAC Recommendation - maintenance
WS/1200	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	06/07/2017	07/03/2018	SmPC, Labelling and PL	
WS/1121	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	16/03/2017	07/03/2018	SmPC, Labelling and PL	
PSUSA/2511/201601	Periodic Safety Update EU Single assessment - pregabalin	15/09/2016	11/11/2016	SmPC, Annex II, Labelling and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2511/201601.

N/0014	Update of the package leaflet with revised contact details of the local representative for Germany. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/06/2016	11/11/2016	PL	
IG/0683	B.III.2.a.1 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - AS	13/05/2016	n/a		
IA/0011/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.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	04/04/2016	n/a		

	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)				
N/0010	Update of the Annex IIIA for the bottle label for Pregabalin Pfizer 75 mg hard capsules (pack of 200) presentation (EU/1/14/916/018) to align with the currently approved text for the brand product, Lyrica. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/02/2016	11/11/2016	Labelling	
IA/0008	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	16/10/2015	n/a		
IB/0009	B.I.c.1.z - Change in immediate packaging of the AS - Other variation	14/10/2015	n/a		
PSUSA/2511/ 201501	Periodic Safety Update EU Single assessment - pregabalin	10/09/2015	n/a		PRAC Recommendation - maintenance
IAIN/0007	C.I.11.a - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of wording agreed by the competent authority	31/07/2015	n/a		
N/0005	Minor change in labelling or package leaflet not	24/06/2015	11/11/2016	PL	

	connected with the SPC (Art. 61.3 Notification)				
WS/0690	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update paediatric information as requested after assessment of studies A0081074 & A0081075 submitted as post authorisation measure P46 045. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/03/2015	08/07/2015	SmPC	Paediatric information has been added to the SmPC after final assessment of data from two clinical studies assessed during a P46 procedure.
WS/0628	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of sections 4.6 (Fertility, pregnancy, and lactation) and 5.2 (Pharmacokinetic properties) of the SmPC to reflect new data available for lactation, based on the results of a recently completed study, A0081181: A multiple dose pharmacokinetic open label study of pregabalin (LYRICA) in healthy lactating women. Package leaflet is updated accordingly. Furthermore editorial changes have been introduced throughout the PI. In addition, the MAH took the opportunity to align the product information with the latest QRD template version	18/12/2014	08/07/2015	SmPC, Annex II, Labelling and PL	This variation updated sections 4.6 (Fertility, pregnancy, and lactation) and 5.2 (Pharmacokinetic properties) of the SmPC to reflect new data available for lactation, based on the results of a recently completed study, A0081181: A multiple dose pharmacokinetic open label study of pregabalin (LYRICA) in healthy lactating women.

	9.0. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
N/0003	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/09/2014	08/07/2015	PL	
IB/0001	C.I.3.z - 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 - Other variation	24/07/2014	08/07/2015	SmPC and PL	