European Union Safety Risk Management Plan

Pregabalin

(25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg and 300 mg, Hard capsules)

Risk Management Plan (RMP) version to be assessed as part of this application	
Active substances (INN or common name)	Pregabalin
Document status	Final
RMP version number	4.0
Data lock point for this RMP	21 Feb 2025
Date of final sign off	10 Apr 2025
Rationale for submitting an updated RMP	The RMP has been updated to align with the safety concerns of the reference RMP Lyrica v14.1 by removing the important identified risk of "Abuse and drug dependence" followed by targeted follow up questionnaire (TFUQ) Abuse. The RMP has been updated with Marketing Authorization Holder (MAH) name to Sandoz following the completion of its spin-off from Novartis and to align to the Sandoz template.

Summary of significant changes in this RMP Version:

RMP part/module	**High level description of major changes**
Part I Product overview	Marketing Authorisation Holder (MAH) name has been updated from Novartis to Sandoz. Removed Centralized procedure (EMEA/H/C/4070) details, as this was withdrawn.
Part II Safety specification Module I to Module VI	None.
Part II - Module VII Identified and potential risks	Updated as per good pharmacovigilance practices (GVP) module V revision 2 RMP format.
Part II - Module SVIII Summary of the safety concerns	Removed important identified risk 'Abuse and drug dependence' to align with the reference product RMP.
Part III	Removed information regarding TFUQ named 'abuse' for the important identified risk of "Abuse and drug dependence".

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RMP part/module	High level description of major changes
Pharmacovigilance plan (including post-authorisation safety studies)	
Part IV Plans for post-authorisation efficacy studies	None.
Part V Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)	Updated as per good pharmacovigilance practices (GVP) module V revision 2 RMP format.
Part VI Summary of the risk management plan	Removed the important identified risk 'Abuse and drug dependence' to align with the reference product RMP. This section has been updated aligning with the Part 1 product overview.
Part VII Annexes	Annex 4 - Removed the information regarding TFUQ named abuse for the risk for important identified risk of "Abuse and drug dependence Annex 7: • Updated with the latest updated summary of product characteristics (SmPC) dates. • Removed Centralized procedure (EMEA/H/C/4070) details which as this was withdrawn. Annex 8: Updated table 'Summary of changes to the risk management plan over time'.
Others	The RMP has been updated aligning to the Sandoz template.

Other RMP versions under evaluation	
RMP Version number	Not applicable.
Submitted on	Not applicable.
Procedure number	Not applicable.

Details of the currently approved RMP	
Version number	1.0
Approved with procedure	DE/H/4164+ 4167/001-008
Date of approval (opinion date)	04 Dec 2014

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Details of the currently approved RMP	
Version number	1.0
Approved with procedure	DE/H/7029-7030/001-008
Date of approval (opinion date)	02 Dec 2022

Details of the currently approved RMP	
Version number	3.0
Approved with procedure	SE/H/1711, EMEA/H/C/4010-4070
Date of approval (opinion date)	05 Jan 2023, 16 Nov 2022

Qualified Person for Pharmacovigilance (QPPV) Details	
QPPV name:	Dr. Mohammad Ali Kotal
QPPV oversight declaration:	The content of this RMP has been reviewed and approved by the marketing authorization holder´s QPPV/deputy.
QPPV/deputy signature:	I am approving this document as Deputy QPPV on behalf of the EU QPPV.

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LIST OF ABBREVIATIONS

ATC	Anatomical Therapeutic Chemical (Classification System)
CHMP	Committee for Medicinal Products for Human Use
CHF	Congestive heart failure
CP	Centralized Procedure
DE	Germany
EEA	European Economic Area
EMEA (EMA)	European Medicines Agency
EPAR	European Public Assessment Report
EU	European Union
GAD	Generalized Anxiety Disorder
GVP	Good Pharmacovigilance Practices
HCPs	Healthcare Professionals
INN	International Non-Proprietary Name
MAH	Marketing Authorization Holder
mg	Milligram
PL	Package Leaflet
PRAC	Pharmacovigilance Risk Assessment Committee
QPPV	Qualified Person for Pharmacovigilance
RMP	Risk Management Plan
SE	Sweden
SmPC	Summary of Product Characteristics
TFuQ	Target Follow Up Questionnaire

Part I: Product Overview

Table 2 Part I.1 – Product Overview

Active substance (INN or common name)	Pregabalin
Pharmacotherapeutic group (ATC Code)	Anti-epileptics, other anti-epileptics Anatomical therapeutic chemical classification System (ATC) code: N03AX16
Marketing Authorization Holder	Sandoz
Medicinal products to which this RMP refers	08
Invented name in the European Economic Area (EEA)	[Nationally completed name] 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg and 300 mg, Hard capsules
Marketing authorization procedure	Decentralized Procedure (DCP), Centralized Procedure (CP) and Mutual Recognition Procedure (MRP)
Brief description of the product	Chemical class: Anti-epileptics, other anti-epileptics.
	Summary of mode of action: Pregabalin binds to an auxiliary subunit (alpha (α) 2-delta (δ) protein) of voltage-gated calcium channels in the central nervous system (CNS).
	Important information about its composition: For DE/H/4164/001-008, DE/H/4167/001-008 Pregabalin contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.
Hyperlink to the Product Information	Current Summary of Product Characteristics
Indication(s) in the EEA	Current: Posology Neuropathic pain Pregabalin is indicated for the treatment of peripheral and central neuropathic pain in adults. Epilepsy Pregabalin is indicated as adjunctive therapy in adults with partial seizures with or without secondary generalization. Generalized Anxiety Disorder (GAD) Pregabalin is indicated for the treatment of GAD in adults.

	Proposed: Not Applicable
Dosage in the EEA	Current: Posology Neuropathic pain Pregabalin treatment can be started at a dose of 150 mg per day given as two or three divided doses. Based on individual patient response and tolerability, the dose may be increased to 300 mg per day after an interval of 3 to 7 days, and if needed, to a maximum dose of 600 mg per day after an additional 7-day interval. The dose range is 150 to 600 mg per day given in either two or three divided doses. Epilepsy Pregabalin treatment can be started with a dose of 150 mg per day given as two or three divided doses. Based on individual patient response and tolerability, the dose may be increased to 300 mg per day after 1 week. The maximum dose of 600 mg per day may be achieved after an additional week. Generalized Anxiety Disorder (GAD) The dose range is 150 to 600 mg per day given as two or three divided doses. The need for treatment should be reassessed regularly. Pregabalin treatment can be started with a dose of 150 mg per day. Based on individual patient response and tolerability, the dose may be increased to 300 mg per day after 1 week. Following an additional week, the dose may be increased to 450 mg per day. The maximum dose of 600 mg per day may be achieved after an additional week. Discontinuation of pregabalin In accordance with current clinical practice, if pregabalin has to be discontinued, it is recommended this should be done gradually over a minimum of 1 week independent of the indication. For detailed information on dosage in special population (Renal impairment, hepatic impairment, pediatric population and elderly), please refer to current SmPCs. Method of administration Pregabalin may be taken with or without food. Pregabalin is for oral use only.
	Proposed: Not applicable
Pharmaceutical form(s) and strengths	Current: Hard capsule; 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg and 300 mg
	Proposed: Not applicable
Is/will the product be subject to additional monitoring in the EU?	No

Part II: Safety specification

Part II: Module SI - Epidemiology of the indications and target populations

Not applicable.

Part II: Module SII - Non-clinical part of the safety specification

Not applicable.

Part II: Module SIII - Clinical trial exposure

Not applicable.

Part II: Module SIV - Populations not studied in clinical trials

Not applicable.

Part II: Module SV - Post-authorization experience

Not applicable.

Part II: Module SVI - Additional EU requirements for the safety specification

Potential for misuse for illegal purposes

Not applicable.

Part II: Module SVII - Identified and potential risks

The summary of safety concerns has been aligned to the latest list of safety concerns of Lyrica, Pregabalin Pfizer (pregabalin) RMP v.14.1 dated 22-Feb-2024 (MAH: Upjohn EESV) published on the European Medicines Agency (EMA) webpage (02 Jul 2024). (RMP 2024)

No new data in comparison to the information of the reference medicinal product is available.

SVII.1 Identification of safety concerns in the initial RMP submission

Not applicable.

SVII.2 New safety concerns and reclassification with a submission of an updated RMP

The following important identified risk has been removed to align with the reference RMP Lyrica:

Important Identified Risk:

- Abuse and drug dependence

SVII.3 Details of important identified risks, important potential risk, and missing information

Not applicable.

Part II: Module SVIII - Summary of the safety concerns

Table 2 SVIII.1: Summary of safety concerns

Summary of safety concerns	
Important identified risks	Dizziness, somnolence, loss of consciousness, syncope, and potential for accidental injury
	Euphoria
	Discontinuation events
	Drug interactions [lorazepam, ethanol, and Central Nervous System depressants]
	Congestive heart failure (CHF)
	Vision-related events
Important potential risks	Suicidality
	Off-label use in pediatric patients
Missing information	None

Part III: Pharmacovigilance Plan (including post-authorization safety studies)

III.1 Routine pharmacovigilance activities

Routine pharmacovigilance activities beyond Adverse Drug Reactions (ADRs) reporting and signal detection:

Specific adverse reaction follow-up questionnaires:

None.

Other forms of routine pharmacovigilance activities:

None.

III.2 Additional pharmacovigilance activities

There are no planned, ongoing or completed additional pharmacovigilance activities.

III.3 Summary Table of additional Pharmacovigilance activities

There are no ongoing or planned categories 1-3 safety studies.

Part IV: Plans for post-authorization efficacy studies

No post-authorization efficacy studies are in place or planned.

Part V: Risk minimization measures (including evaluation of the effectiveness of risk minimization activities)

Risk Minimization Plan

The safety information in the proposed product information is aligned to the reference medicinal product.

V.1. Routine Risk Minimization Measures

Routine risk minimization measures are aligned to the reference medicinal product.

V.2. Additional Risk Minimization Measures

Routine risk minimization activities as described in Part V.1 are sufficient to manage the safety concerns of the medicinal product

V.3 Summary of risk minimization measures

Not applicable.

Part VI: Summary of the risk management plan

Summary of risk management plan for Pregabalin, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg and 300 mg hard capsules

This is a summary of the risk management plan (RMP) for pregabalin, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg and 300 mg, hard capsules (hereinafter referred as pregabalin). The RMP details important risks of pregabalin, how these risks can be minimized, and how more information will be obtained about pregabalin risks and uncertainties (missing information).

Pregabalin' summary of product characteristics (SmPCs) and its package leaflets (PLs) give essential information to healthcare professionals (HCPs) and patients on how pregabalin should be used.

This summary of the RMP for pregabalin should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR). Important new concerns or changes to the current ones will be included in updates of the pregabalin hard capsules' RMP.

I. The medicine and what it is used for

Pregabalin are authorized for:

Epilepsy

Pregabalin is indicated as adjunctive therapy in adults with partial seizures with or without secondary generalization.

Generalized Anxiety Disorder (GAD)

Pregabalin is indicated for the treatment of GAD in adults.

Neuropathic pain

Pregabalin is indicated for the treatment of peripheral and central neuropathic pain in adults.

It contains pregabalin as an active substance and is given orally as hard capsules (25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg and 300 mg).

Further information about the evaluation of pregabalin's benefits can be found in pregabalin's EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine's webpage: Pregabalin Sandoz |European Medicines Agency (EMA).

II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of pregabalin, together with measures to minimize such risks and the proposed studies for learning more about pregabalin's risks, are outlined below.

Measures to minimize the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the PLs and SmPCs addressed to patients and healthcare professionals (HCPs);
- Important advice on the medicine's packaging;
- The authorized pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimize its risks.

Together, these measures constitute routine risk minimization measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

II.A List of important risks and missing information

Important risks of pregabalin are risks that need special risk management activities to further investigate or minimize the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of pregabalin. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g., on the long-term use of the medicine).

List of important risks and missing information	
Important identified risks	Dizziness, somnolence, loss of consciousness, syncope, and potential for accidental injury
	Euphoria
	Discontinuation events
	Drug interactions [lorazepam, ethanol, and Central Nervous system depressants]
	Congestive heart failure (CHF)
	Vision-related events
Important potential risks	Suicidality
	Off-label use in pediatric patients
Missing information	None

II.B Summary of important risks

The safety information in the proposed product information is aligned to the reference medicinal product.

II. Post-authorization development plan

II.C.1 Studies which are conditions of the Marketing authorization

There are no studies which are conditions of the Marketing authorization or specific obligation of pregabalin.

II.C.2 Other studies in post-authorization development plan

There are no studies required for pregabalin.

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Annex 1 – EudraVigilance Interface

Not applicable.

Annex 2 – Tabulated Summary of Planned, Ongoing, and Completed Pharmacovigilance Study Programme

Not applicable.

Annex 3 - Protocols for Proposed, Ongoing and Completed Studies in the Pharmacovigilance Plan

Not applicable.

Annex 4 - Specific Adverse Drug Reaction Follow-Up Forms

Not applicable.

Annex 5 - Protocols for Proposed and Ongoing Studies in RMP part IV

Not applicable.

Annex 6 - Details of Proposed Additional Risk Minimization Activities

Not applicable.

Annex 7 - Other Supporting Data (including referenced material)

References List

External references

[RMP, 2024] Human medicine European Public Assessment Report (EPAR): Lyrica Available from Search the website | European Medicines Agency (europa.eu). (Accessed on 05 Mar 2025).

(INN-pregabalin)

Internal references

[SmPC, 2024] Sandoz Summary of Product Characteristics - Pregabalin hard capsules (25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg and 300 mg), 06 Mar 2024 (DE/H/4164/001-008).

[SmPC, 2024] Sandoz Summary of Product Characteristics - Pregabalin hard capsules (25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg and 300 mg), 11 Mar 2024 (DE/H/4167/001-008).

[SmPC, 2025] Sandoz Summary of Product Characteristics - Pregabalin hard capsules (25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg and 300 mg), 18 Feb 2025 (EMEA/H/C/4010).

[SmPC, 2025] Sandoz Summary of Product Characteristics - Pregabalin hard capsules (25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg and 300 mg), 21 Jan 2025 (DE/H/7029- 7030/001-008).

[SmPC, 2024] Sandoz Summary of Product Characteristics - Pregabalin hard capsules (25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg and 300 mg), 21 Mar 2024 (SE/H/1711).

Annex 8 – Summary of changes to the risk management plan over time

Table 3 Annex 8 A list of all significant changes to the Risk Management Plan over time

Version	Approval date Procedure	Change
1.2	30 Apr 2015 EMEA/H/C/4010, EMEA/H/C/4070	The RMP was updated as per pharmacovigilance risk assessment committee (PRAC) rapporteur's RMP updated assessment report dated 20 Feb 2015 and following changes were made: • The routine risk minimization measures were amended (Part V.1): - *Safety concern: Weight gain* Reference to '5.3 section Preclinical safety data' was deleted. - *Safety concern: Hypersensitivity and allergic reactions* Reference to '4.3 section Contraindications' was included. Also, based on changes made in the risk minimization plan Part V and Part VI were aligned accordingly.
2.1	19 Jun 2020 EMEA/H/C/004070/R/0013 and EMEA/H/C/004010/R/0012 15 Jul 2021 SE/H/1711/01-08/IB/15	The RMP was updated to address Committee for Medicinal Products for Human Use (CHMP) and PRAC Rapporteurs Joint Assessment Report comment dated 20 Dec 2019 (EMA/CHMP/PRAC/539459/2019 and EMA/CHMP/PRAC/539382/2019); included TFuQ on "Abuse" for important identified risk of "Abuse and drug dependence" in Part III and appended in Annex. 4 of the RMP to be in line with the reference product (Lyrica).
3.0	16 Nov 2022 EMEA/H/C/4010 EMEA/H/C/4070 05 Jan 2023 SE/H/1711 Not applicable DE/H/7029-7030/001-008 DE/H/4164+ 4167/001-008	The RMP has been updated to remove the missing information "Pregnancy and lactating women" as per the latest EPAR RMP summary available for reference product (Lyrica) dated 21 Apr 2022 published on EMA webpage [EPAR, 2022]. The same has also been recommended in PRAC minutes of meeting on 07-10 June 2021 dated 10 Mar 2022 (EMA/PRAC/139868/2022). Following changes have been made: **Safety concerns Deleted** **safety concern:** *Missing information* Pregnancy and lactating women Additionally, deleted following wording "including PSURs assessment (if applicable)" from the "Part VI: II 'Risks associated with the medicine and activities to minimize or further characterize the risks of RMP" of the RMP since there is no PSUR requirement for Pregabalin as per European Union Reference Dates (EURD) list.

		Also, a consolidated RMP has been prepared combining all the applicable procedures (EMEA/H/C/4010,
4.0	Not applicable EMEA/H/C/4010 DE/H/7029-7030/001-008 DE/H/4164+4167/001-008 SE/H/1711	The RMP has been updated to align as per the latest RMP available for reference product (Lyrica) dated 22-Feb-2024 published on EMA webpage [RMP, Jul 2024]. The following changes have been made: The safety concern of *Important identified risk:* Abuse and drug dependence was deleted. Removed Centralized procedure (EMEA/H/C/4070) details from the whole RMP as this procedure was withdrawn. Removed the information regarding TFUQ named abuse for the risk for important identified risk of "Abuse and drug dependence". Annex 7 has been updated with the latest updated summary of product characteristics (SmPC) dates. Annex 8: Updated table 'Summary of changes to the risk management plan over time Others: The RMP has been updated aligning to the current Sandoz template and updated with Sandoz logo and QPPV details.