

EU Risk Management Plan for Pregabalin Zentiva (pregabalin)

No 70/25

RMP version to be assessed as part of this application:

RMP Version number:	V 3.1	
Data lock point for this RMP:	11 August 2025	
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Rationale for submitting an updated RMP:	Harmonisation of the list of safety concerns and pharmacovigilance plan with the reference product Lyrica. Specific follow up questionnaire for abuse was removed.	
Summary of significant changes in this RMP:	Part II: Module SVII Identified and Potential Risks	This section was harmonized with the RMP V14.2 for reference product Lyrica. Removal of Abuse and drug dependence from <i>Important identified risks</i> and Pregnancy and lactating women from <i>Missing information</i> was realized.
	Part II: Module SVIII Summary of the Safety Concerns	Harmonised with the reference product.
	Part III: Pharmacovigilance Plan	The targeted questionnaire for events of abuse was removed to be in line with the reference product.
	Part VI: Summary of the RMP	Updated to be in line with the changes made.
	Part VII: Annexes	Annex 4: Updated to be in line with the reference product and above mentioned changes. Specific adverse reaction follow-up questionnaire for Abuse was removed. Annex 7: List of reference material was updated. Annex 8: Updated based on the above mentioned changes.
Other RMP versions under evaluation:	RMP version number:	Not applicable
	Submitted on:	Not applicable
	Procedure number:	Not applicable
Details of the currently approved RMP:	RMP version number:	V 3.0
	Approved with procedure:	EMA/H/C/003900
	Date of approval (opinion date):	26 March 2020
QPPV name:	Miloslava NYKODEMOVÁ, MD	
QPPV (or delegate) signature:	The content of this RMP has been reviewed and approved by the marketing authorisation holder's QPPV. The electronic signature is available on file.	

Table of contents

List of Abbreviations	3
Part I: Product(s) Overview	4
Part II: Safety Specification.....	6
Part II: Module SI - Epidemiology of the indication(s) and target population(s).....	6
Part II: Module SII - Non-clinical part of the safety specification	6
Part II: Module SIII - Clinical trial exposure	6
Part II: Module SIV - Populations not studied in clinical trials.....	6
Part II: Module SV - Post-authorisation experience	6
Part II: Module SVI - Additional EU requirements for the safety specification	6
Part II: Module SVII - Identified and potential risks	6
Part II: Module SVIII - Summary of the safety concerns.....	7
Part III: Pharmacovigilance Plan (including post-authorisation safety studies).....	8
III.1 Routine pharmacovigilance activities	8
III.2 Additional pharmacovigilance activities	8
III.3 Summary Table of Additional Pharmacovigilance Activities.....	8
Part IV: Plans for Post-authorisation Efficacy Studies.....	9
Part V: Risk Minimisation Measures (including evaluation of the effectiveness of risk minimisation activities)	10
Part VI: Summary of the Risk Management Plan.....	11
I. The medicine and what it is used for	11
II. Risks associated with the medicine and activities to minimise or further characterise the risks	11
II.A List of important risks and missing information.....	12
II.B Summary of important risks.....	12
II.C Post-authorisation development plan.....	12
Part VII: Annexes.....	13
Annex 1 – EudraVigilance Interface	14
Annex 2 – Tabulated summary of planned, ongoing, and completed pharmacovigilance study programme	15
Annex 3 - Protocols for proposed, on-going and completed studies in the pharmacovigilance plan	16
Annex 4 - Specific adverse drug reaction follow-up forms.....	17
Annex 5 - Protocols for proposed and on-going studies in RMP part IV.....	18
Annex 6 - Details of proposed additional risk minimisation activities (if applicable)	19
Annex 7 - Other supporting data (including referenced material)	20
Annex 8 – Summary of changes to the risk management plan over time	21

List of Abbreviations

ATC	Anatomical Therapeutic Chemical classification
CHF	Congestive Heart Failure
EMA	European Medicines Agency
EU	European Union
EEA	European Economic Area
eCTD	Electronic Common Technical Document
GAD	Generalised Anxiety Disorder
INN	International Nonproprietary Name
MAA	Marketing Authorisation Applicant
MAH	Marketing Authorisation Holder
PL	Package Leaflet
RMP	Risk Management Plan
QPPV	Qualified Person for Pharmacovigilance
SmPC	Summary of Product Characteristics

Part I: Product(s) Overview

Table Part I.1 – Product Overview

Active substance(s) (INN or common name)	Pregabalin
Pharmacotherapeutic group(s) (ATC Code)	Analgesics, other analgesics and antipyretics (N02BF02)
Marketing Authorisation Holder/Applicant	ZENTIVA, K.S.
Medicinal products to which this RMP refers	8
Invented name(s) in the European Economic Area (EEA)	Pregabalin Zentiva 25 mg hard capsules Pregabalin Zentiva 50 mg hard capsules Pregabalin Zentiva 75 mg hard capsules Pregabalin Zentiva 100 mg hard capsules Pregabalin Zentiva 150 mg hard capsules Pregabalin Zentiva 200 mg hard capsules Pregabalin Zentiva 225 mg hard capsules Pregabalin Zentiva 300 mg hard capsules
Marketing authorisation procedure	Centralised EMA/H/C/003900
Brief description of the product	<u>Chemical class:</u> The active substance, pregabalin, is a gamma-aminobutyric acid analogue ((S)-3-(aminomethyl)-5-methylhexanoic acid). <u>Summary of mode of action:</u> Pregabalin binds to an auxiliary subunit ($\alpha_2\text{-}\delta$ protein) of voltage-gated calcium channels in the central nervous system. <u>Important information about its composition:</u> None.
Hyperlink to the Product Information	Please refer to section 1.3.1 in eCTD.
Indication(s) in the EEA	<u>Current:</u> <u>Neuropathic pain</u> Pregabalin Zentiva is indicated for the treatment of peripheral and central neuropathic pain in adults. <u>Epilepsy</u> Pregabalin Zentiva is indicated as adjunctive therapy in adults with partial seizures with or without secondary generalisation. <u>Generalised anxiety disorder</u> Pregabalin Zentiva is indicated for the treatment of generalised anxiety disorder (GAD) in adults. <u>Proposed:</u> Not applicable
Dosage in the EEA	<u>Current:</u>

	<p>The dose range is 150 to 600 mg per day given in either two or three divided doses.</p> <p><i>Neuropathic pain</i> 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.</p> <p><i>Epilepsy</i> 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.</p> <p><i>Generalised anxiety disorder</i> 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.</p> <p><i>Discontinuation of pregabalin</i> 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.</p> <p><u>Method of administration</u> Pregabalin Zentiva may be taken with or without food. Pregabalin Zentiva is for oral use only.</p> <p><i>For details please refer to section 1.3.1 in eCTD</i></p> <p><u>Proposed:</u> Not applicable</p>
<p>Pharmaceutical form(s) and strengths</p>	<p><u>Current:</u> Capsule, hard 25, 50, 75, 100, 150, 200, 225, 300 mg</p> <p><u>Proposed:</u> Not applicable</p>
<p>Is/will the product be subject to additional monitoring in the EU?</p>	<p>No</p>

Part II: Safety Specification

Part II: Module SI - Epidemiology of the indication(s) and target population(s)

Not applicable for generic products as per Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 2) effective since 31 March 2017.

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

Not applicable for generic products as per Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 2) effective since 31 March 2017.

Part II: Module SIII - Clinical trial exposure

Not applicable for generic products as per Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 2) effective since 31 March 2017.

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

Not applicable for generic products as per Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 2) effective since 31 March 2017.

Part II: Module SV - Post-authorisation experience

Not applicable for generic products as per Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 2) effective since 31 March 2017.

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

Potential for misuse for illegal purposes

Not applicable for generic products as per Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 2) effective since 31 March 2017.

Part II: Module SVII - Identified and potential risks

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 list of safety concerns has been harmonised with the reference product Lyrica (RMP V14.2, link: https://www.ema.europa.eu/en/documents/rmp/lyrica-epar-risk-management-plan_en.pdf).

Following safety concerns were removed:

Important identified risks

- Abuse and drug dependence

Missing information

- Pregnancy and lactating women

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

Not applicable

Part II: Module SVIII - Summary of the safety concerns

Table SVIII.1: Summary of safety concerns

Summary of safety concerns	
Important identified risks	<ul style="list-style-type: none"> • Dizziness, somnolence, loss of consciousness, Syncope and potential for accidental injury • Vision-related events • Discontinuation events • Congestive heart failure (CHF) • Drug interactions (lorazepam, ethanol and CNS depressants) • Euphoria
Important potential risks	<ul style="list-style-type: none"> • Suicidality • Off-label use in paediatric patients
Missing information	<ul style="list-style-type: none"> • None

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

III.1 Routine pharmacovigilance activities

Routine pharmacovigilance activities (such as adverse reactions reporting and signal detection) are considered sufficient for the product.

Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:

Specific adverse reaction follow-up questionnaires:

Not applicable

Other forms of routine pharmacovigilance activities:

Not applicable

III.2 Additional pharmacovigilance activities

Not applicable.

III.3 Summary Table of Additional Pharmacovigilance Activities

Not applicable.

Part IV: Plans for Post-authorisation Efficacy Studies

Not applicable.

Part V: Risk Minimisation Measures (including evaluation of the effectiveness of risk minimisation activities)**Risk Minimisation Plan**

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

V.1. Routine Risk Minimisation Measures

Not applicable

V.2. Additional Risk Minimisation Measures

Not applicable

V.3. Summary of Risk Minimisation Measures

Not applicable

Part VI: Summary of the Risk Management Plan

As the safety concerns and their management are identical for all products covered by this RMP, the information in Part VI is presented only once together for all products.

Summary of risk management plan for Pregabalin Zentiva 25/50/75/100/150/200/225/300 mg hard capsules (Pregabalin)

This is a summary of the risk management plan (RMP) for Pregabalin Zentiva. The RMP details important risks of Pregabalin Zentiva, how these risks can be minimised, and how more information will be obtained about Pregabalin Zentiva's risks and uncertainties (missing information).

Pregabalin Zentiva's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Pregabalin Zentiva should be used.

This summary of the RMP for Pregabalin Zentiva 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 Pregabalin Zentiva's RMP.

I. The medicine and what it is used for

Pregabalin Zentiva is authorised for the treatment of Neuropathic pain, Epilepsy and Generalised anxiety disorder (see SmPC for the full indication). It contains Pregabalin as the active substance and it is given by oral route of administration.

Further information about the evaluation of Pregabalin Zentiva's benefits can be found in Pregabalin Zentiva's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage <https://www.ema.europa.eu/en/medicines/human/EPAR/pregabalin-zentiva>.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

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

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

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised 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 minimise its risks.

Together, these measures constitute routine risk minimisation measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, 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 Zentiva are risks that need special risk management activities to further investigate or minimise 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 Zentiva. 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	<ul style="list-style-type: none"> • Dizziness, somnolence, loss of consciousness, Syncope and potential for accidental injury • Vision related events • Discontinuation events • Congestive heart failure (CHF) • Drug interactions (lorazepam, ethanol and CNS depressants) • Euphoria
Important potential risks	<ul style="list-style-type: none"> • Suicidality • Off-label use in paediatric patients
Missing information	<ul style="list-style-type: none"> • None

II.B Summary of important risks

The safety information in the approved Product Information is aligned to the reference medicinal product.

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Pregabalin Zentiva.

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

There are no studies required for Pregabalin Zentiva.

Annex 4 - Specific adverse drug reaction follow-up forms

Not applicable

Annex 6 - Details of proposed additional risk minimisation activities (if applicable)

Not applicable.