EU RISK MANAGEMENT PLAN for

[redacted]

(Tapentadol 25 mg, 50 mg, 100 mg, 150 mg, 200 mg, 250 mg Prolonged release capsule, hard)

RMP version to be assessed as part of this application:

RMP Version number: 0.1

Data lock point for this RMP: 30.11.2020

Date of final sign off: 17.12.2020

QPPV deputy name: [redacted]

Email: [redacted]

QPPV deputy signature:

[redacted]

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Abbreviations

CMDh	Co-ordination Group for Mutual Recognition and Decentralised procedures - Human
DCP	Decentralised procedure
EEA	European Economic Area
EU QPPV	European Pharmacovigilance Qualified person
GVP	Good Pharmacovigilance Practices
MAH	Marketing authorization holder
NA (N/A)	Not applicable
PAES	Post-authorisation efficacy study
PI	Principal investigator
PV	Pharmacovigilance
QPPV	Pharmacovigilance Qualified person
RMP	Risk Management Plan
SmPC (SPC)	Summary of Products Characteristics

ADDITIONAL CLARIFICATION:

The report follows the general format and content described in the Guideline on Good Pharmacovigilance Practices (GVP) Module V – Risk management systems Rev. 2 (31 March 2017) and the Guidance on the format of the risk management plan (RMP) in the EU – in integrated format Rev.2.0.1 (31 October 2018).

According to GVP Module V Rev. 2, for RMPs involving initial marketing authorization applications according to Article 10(1) of Directive 2001/83/EC (generic), Modules II.SI-SVI may be omitted. Module II. SVII may be omitted if the originator product has an RMP and/or its safety profile is published on CMDh website. Part IV is applicable only when a PAES was imposed for the originator product. In addition, in Part V a statement of alignment of safety information in PI is sufficient, unless the medicinal product has additional risk minimisation activities.

PART I- PRODUCT OVERVIEW

This Risk Management Plan is intended to support a hybrid product license for [redacted]25 mg, 50 mg, 100 mg, 150 mg, 200 mg, 250 mg Prolonged release capsule, hard, namely a national procedure for Tapentadol.

The reference product for this hybrid application is Palexia, approved by MAH Grünenthal Ltd.

Table Part I.1 – Product Overview

Active substance(s) (INN or common name):	Tapentadol phosphate
Pharmaco-therapeutic group **(ATC Code):**	Other opioids (N02AX06)
Marketing Authorisation Applicant	Neuraxpharm UK Limited
Medicinal products to which this RMP refers	6
Invented name(s)	[redacted]25, 50, 100, 150, 200, 250 mg prolonged-release capsules, hard
Marketing authorisation procedure	National procedure for UK PL 49718/0080 PL 49718/0081 PL 49718/0082 PL 49718/0083 PL 49718/0084 PL 49718/0085
Brief description of the product	**Chemical class** Tapentadol is an alkylbenzene.
	Summary of mode of action Tapentadol is a strong analgesic with μ-agonistic opioid and additional noradrenaline reuptake inhibition properties. Tapentadol exerts its

	analgesic effects directly without a pharmacologically active metabolite.
	Important information about its composition: NA
Hyperlink to the Product Information	Please refer to CTD Module 1.3.1.
Indication(s)	**Proposed:** Tapentadol is indicated for the management of severe chronic pain in adults, which can be adequately managed only with opioid analgesics.
Dosage	**Proposed:** The dosing regimen should be individualised according to the severity of pain being treated, the previous treatment experience and the ability to monitor the patient. Tapentadol should be taken twice daily, approximately every 12 hours. Total daily doses of tapentadol greater than 500 mg have not yet been studied and are therefore not recommended.
Pharmaceutical form(s) and strengths	**Proposed:** 25 mg, 50 mg, 100 mg, 150 mg, 200 mg, 250 mg prolonged-release capsules, hard
Is/will the product be subject to additional monitoring in the EU?	No

Part II: Safety Specification

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

Not applicable since this module is not required for hybrid type of application, based on risk proportionality principle, if no new data are generated to address the differences with the originator product.

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

Not applicable since this Module is not required for hybrid type of application.

Part II: Module SIII - Clinical trial exposure

Not applicable since this module is not required for hybrid type of application, based on risk proportionality principle, if no new data are generated to address the differences with the originator product.

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

Not applicable since this Module is not required for hybrid type of application.

Part II: Module SV - Post-Authorisation Experience

Not applicable since this Module is not required for hybrid type of application.

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

Not applicable since this Module is not required for hybrid type of application.

Part II: Module SVII - Identified and potential risks

Not applicable since this module is not required for hybrid type of application, based on risk proportionality principle, if no new data are generated to address the differences with the originator product.

Part II: Module SVIII - Summary of safety concerns

Summary of safety concerns	
Important identified risks	• Drug abuse and drug dependence
Important potential risks	• None
Missing information	• None

PART III- Pharmacovigilance Plan (including post-authorisation safety studies)

III.1 Routine pharmacovigilance activities

No routine pharmacovigilance activities beyond adverse reactions reporting and signal detection are in place for the products included in this RMP.

III.2 Additional pharmacovigilance activities

No additional pharmacovigilance activities are required to assess effectiveness of risk minimisation measures.

III.3 Summary Table of additional Pharmacovigilance activities

Not applicable

PART IV- Plans for post-authorisation efficacy studies

No post-authorisation efficacy studies are planned therefore the remainder of this section is not applicable.

PART V- Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)

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

PART VI- Summary of the risk management plan

Summary of risk management plan for [redacted].

This is a summary of the risk management plan (RMP) for [redacted]. The RMP details important risks of [redacted], how these risks can be minimized, and how more information will be obtained about [redacted] ´s risks and uncertainties (missing information).

[redacted]´s summary of product characteristics (SmPC) and their package leaflet give essential information to healthcare professionals and patients on how these products should be used.

I. The medicine and what it is used for

[redacted] is indicated for the management of severe chronic pain in adults, which can be adequately managed only with opioid analgesics (see SmPC for the full indication)

It contains tapentadol as the active substance, and it is given by oral administration.

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

Important risks of [redacted], together with measures to minimise such risks and the proposed studies for learning more about [redacted] 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, including PSUR assessment, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of [redacted] is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of [redacted] are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 [redacted]. 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).

Summary of safety concerns	
Important identified risks	• Drug abuse and drug dependence
Important potential risks	• None
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.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 [redacted].

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

There are no studies required for [redacted].

PART VII- ANNEXES

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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, on-going 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 on-going studies in RMP part IV

Not applicable.

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

Not applicable.

Annex 7 – Other supporting data (including referenced material)

Not applicable.

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

Not applicable