EU Risk Management Plan for Niapelf (paliperidone)

RMP version to be assessed as part of this application:

RMP version number: 0.3

Data lock point for this RMP: 31 October 2023

Date of final sign-off: 04 December 2023

Rationale for submitting an updated RMP: Not applicable

Summary of significant changes in this RMP: Not applicable

Other RMP versions under evaluation: Not applicable

Details of the currently approved RMP: Not applicable

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List of Abbreviations

ATC	Anatomical Therapeutic Chemical classification
CMDh	Coordination Group for Mutual Recognition and Decentralised Procedures - human
EEA	European Economic Area
EU	European Union
GVP	Good Pharmacovigilance Practices
INN	International Non-proprietary Names
QPPV	Qualified Person for Pharmacovigilance
RMP	Risk Management Plan
SmPC	Summary of Product 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 European Union (EU) – in integrated format Rev.2.0.1 (31 October 2018).

According to GVP Module V Rev. 2, for RMPs involving initial marketing authorisation 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 Coordination Group for Mutual Recognition and Decentralised Procedures - human (CMDh) website. Part IV is applicable only when a post-authorisation efficacy study was imposed for the originator product. In addition, in Part V a statement of alignment of safety information in the product information is sufficient, unless the medicinal product has additional risk minimisation activities.

Part I: Product(s) Overview

Table Part I.1 – Product(s) Overview

Active substance(s) (INN or common name)	Paliperidone.
Pharmacotherapeutic group(s) (ATC Code)	Pharmacotherapeutic group: Psycholeptics, other antipsychotics. ATC code: N05AX13.
Marketing Authorisation Applicant	Neuraxpharm Pharmaceuticals, S.L.
Medicinal products to which this RMP refers	6
Invented name(s) in the European Economic Area (EEA)	Niapelf
Marketing authorisation procedure	Centralised Procedure (EMEA/H/C/006185).
Brief description of the product	Chemical class Paliperidone contains a racemic mixture of (+)- and (-)-paliperidone. Paliperidone is a selective blocking agent of monoamine effects, whose pharmacological properties are different from that of traditional neuroleptics.
	Summary of mode of action Paliperidone binds strongly to serotonergic 5-HT2- and dopaminergic D2-receptors. Paliperidone also blocks alpha 1-adrenergic receptors and slightly less, H1-histaminergic and alpha 2-adrenergic receptors. The pharmacological activity of the (+)- and (-)-paliperidone enantiomers are qualitatively and quantitatively similar. Paliperidone is not bound to cholinergic receptors. Even though paliperidone is a strong D2-antagonist, which is believed to relieve the positive symptoms of schizophrenia, it causes less catalepsy and decreases motor functions less than traditional neuroleptics. Dominating central serotonin antagonism may reduce the tendency of paliperidone to cause extrapyramidal side effects.
	Important information about its composition: Not applicable.
Hyperlink to the Product Information	Please refer to the product information text in module 1.3.1.
Indication(s) in the EEA	Current: Maintenance treatment of schizophrenia in adult patients stabilised with paliperidone or risperidone. In selected adult patients with schizophrenia and previous responsiveness to oral paliperidone or risperidone, Niapelf may be used without prior stabilisation with oral treatment if psychotic

	symptoms are mild to moderate and a long-acting injectable treatment is needed.
	Proposed: Not applicable.
Dosage in the EEA	Current: Recommended initiation of paliperidone is with a dose of 150 mg on treatment day 1 and 100 mg one week later (day 8), both administered in the deltoid muscle in order to attain therapeutic concentrations rapidly. The third dose should be administered one month after the second initiation dose. The recommended monthly maintenance dose is 75 mg; some patients may benefit from lower or higher doses within the recommended range of 25 to 150 mg based on individual patient tolerability and/or efficacy. Patients who are overweight or obese may require doses in the upper range. Following the second initiation dose, monthly maintenance doses can be administered in either the deltoid or gluteal muscle. Adjustment of the maintenance dose may be made monthly. When making dose adjustments, the prolonged release characteristics of Niapelf should be considered, as the full effect of maintenance doses may not be evident for several months.
	Proposed: Not applicable.
Pharmaceutical form(s) and strengths	Current: Prolonged release suspension for injection containing 25 mg, 50 mg, 75 mg, 100 mg or 150 mg of paliperidone.
	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 indication(s) and target population(s)

Not applicable since this module is not required for generic type of application.

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

Not applicable since this module is not required for generic type of application.

Part II: Module SIII - Clinical trial exposure

Not applicable since this module is not required for generic type of application.

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

Not applicable since this module is not required for generic type of application.

Part II: Module SV - Post-authorisation experience

Not applicable since this module is not required for generic type of application.

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

Not applicable since this module is not required for generic type of application.

Part II: Module SVII - Identified and potential risks

Not applicable since this module is not required for generic type of application.

Part II: Module SVIII - Summary of the safety concerns

The following summary of safety concerns has been obtained from the list of safety concerns published on CMDh website for Paliperidon-ratiopharm 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 100 mg + 150 mg Depot-Injektionssuspension (ratiopharm GmbH) (version 2.0, dated 25 September 2020):

Table SVIII.1: Summary of safety concerns

Summary of safety concerns	
Important identified risks	• None
Important potential risks	• None
Missing information	• Exposure during pregnancy

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 will be conducted for the products included in this RMP.

III.2 Additional pharmacovigilance activities

No additional pharmacovigilance activities will be conducted.

III.3 Summary Table of additional Pharmacovigilance activities

Not applicable.

Part IV: Plans for post-authorisation efficacy studies

No planned or on-going imposed post-authorisation efficacy studies have been conducted.

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

Risk Minimisation Plan

The safety information in the proposed 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

Summary of risk management plan for Niapelf (paliperidone)

This is a summary of the Risk Management Plan (RMP) for Niapelf. The RMP details important risks of Niapelf, how these risks can be minimised, and how more information will be obtained about Niapelf's risks and uncertainties (missing information).

Niapelf's Summary of Product Characteristics (SmPC) and their package leaflet give essential information to healthcare professionals and patients on how Niapelf should be used.

This summary of the RMP for Niapelf 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 Niapelf's RMP.

I. The medicine and what it is used for

Niapelf is authorised for maintenance treatment of schizophrenia in adult patients stabilised with paliperidone or risperidone. In selected adult patients with schizophrenia and previous responsiveness to oral paliperidone or risperidone, the medicine may be used without prior stabilisation with oral treatment if psychotic symptoms are mild to moderate and a long-acting injectable treatment is needed (see SmPC for the full indication). It contains paliperidone as the active substance and it is administered by intramuscular injection as a prolonged-release suspension in prefilled syringes containing 25 mg, 50 mg, 75 mg, 100 mg, or 150 mg of paliperidone.

Further information about the evaluation of Niapelf's benefits can be found in Niapelf'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/niapelf.

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

Important risks of Niapelf, together with measures to minimise such risks and the proposed studies for learning more about Niapelf'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***.

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

II.A List of important risks and missing information

Important risks of Niapelf 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 Niapelf. 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	• None
Important potential risks	• None
Missing information	• Exposure during pregnancy

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 Niapelf.

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

There are no studies required for Niapelf.