Summary of the risk management plan (version 1.2) for Paxlovid (nirmatrelvir/ritonavir)

Introduction

This document is a summary of the risk management plan (RMP) for Paxlovid (nirmatrelvir/ritonavir). The RMP was created by the drug manufacturer and is submitted to medicine regulators as part of the approval and safety monitoring processes.

The RMP details important risks of Paxlovid, how these risks can be minimised, and how more information will be obtained about Paxlovid's risks and uncertainties (missing information). Important new changes or changes to the current ones will be included in updates of the RMP by the drug manufacturer.

The Paxlovid data sheet and Consumer Medicine Information (CMI) give essential information for healthcare professionals and patients on how to use this medicine.

See also the European Public Assessment Report (EPAR), including the risk management plan, available on the European Medicines Agency website.

RMP Definitions

Important risks

Important risks need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely used.

Important risks are classified as identified or potential.

- Identified risks are concerns for which there is sufficient proof of a link with the use of the medicine.
- 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

Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (eg, on the long-term use of the medicine).

Activities to minimise or further characterise identified risks

Measures to minimise the identified risks for medicinal products may include:

- specific information for healthcare professionals and patients, such as warnings, precautions and advice on correct use, in the data sheet, consumer medicine information and package leaflet
- 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 (eg, 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 events is collected continuously by the company and regularly analysed, so that immediate action can be taken by the company as necessary. These measures constitute *routine pharmacovigilance activities*.

Other non-routine measures to further characterise the risks include safety and efficacy studies. The studies may be in particular risk groups or for particular safety concerns. They may also be a condition of the medicine's approval. These measures constitute *additional pharmacovigilance activities*.

Paxlovid (nirmatrelvir/ritonavir) RMP

The medicine and what it is used for

Paxlovid is an oral antiviral medicine used for the treatment of coronavirus disease 2019 (COVID-19) in adults 18 years of age and older, who do not require supplemental oxygen due to COVID-19 and are at increased risk of progression to hospitalisation or death.

Paxlovid contains two active substances: nirmatrelvir in combination with ritonavir.

Important risks, missing information and additional pharmacovigilance activities

The tables below summarise the risks for Paxlovid, as described in the RMP.

- Table 1 is a list of the important risks (identified and potential) and missing information.
- Tables 2 to 4 provide risk minimisation measures and a list of additional pharmacovigilance activities.
- Table 5 summarises the additional pharmacovigilance activities.

Table 1: List of important risks and missing information

Important identified risks	None
Important potential risks	None
Missing information	Safety in patients with hepatic impairment Safety in patients with renal impairment Safety during use in pregnancy and lactation

Table 2: Missing information: Safety in patients with hepatic impairment

Risk minimisation measures	Sections 4.2, 4.4 and 5.2 of the data sheet Pack size Medicine's legal status
Additional pharmacovigilance activities	Study C4671010 Post-authorisation safety study in moderate and severe hepatic impairment

Table 3: Missing information: Safety in patients with renal impairment

Risk minimisation measures	Sections 4.2, 4.4 and 5.2 of the data sheet Pack size Medicine's legal status
Additional pharmacovigilance activities	Post-authorisation safety study in moderate and severe renal impairment

Table 4: Missing information: Safety during use in pregnancy and lactation

Risk minimisation measures	Section 4.6 of the data sheet Pack size Medicine's legal status
Additional pharmacovigilance activities	Post-authorisation safety study in pregnant and breastfeeding women Pharmacokinetic and safety study in lactating adult women

Table 5: Summary of the additional pharmacovigilance activities

Study C4671010 To characterise the effect of hepatic impairment on the plasma pharmacokinetics of Paxlovid. Findings from this study will be used to develop dosing recommendations so that the dose and/or dosing interval may be adjusted appropriately in the presence of hepatic disease. The objective of this study is to evaluate the safety and tolerability of Paxlovid in participants with moderate hepatic impairment and in healthy participants with normal hepatic function.
Post-authorisation safety study in moderate and severe hepatic impairment To assess the safety of Paxlovid in patients with moderate and severe hepatic impairment.
Post-authorisation safety study in moderate and severe renal impairment To assess the safety of Paxlovid in patients with moderate and severe renal impairment.
Post-authorisation safety study in pregnant and breastfeeding women To assess use of Paxlovid during pregnancy and, if feasible, lactation. The objectives of the study are to evaluate the safety of Paxlovid in pregnant and lactating women, including pregnancy outcomes and other safety events of interest in exposed and unexposed women. As feasible, maternal, and infant outcomes will be assessed in lactating women.
Pharmacokinetic and safety study in lactating adult women To assess penetration of nirmatrelvir in human breast milk and to measure the concentration of nirmatrelvir in breast milk in healthy women.