PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

PAXLOVID (NIRMATRELVIR/RITONAVIR)

Marketing Authorization Number 68793

Film-coated Tablets, 150mg/100mg

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LIST OF ABBREVIATIONS

COVID-19	Coronavirus disease 2019
EMA	European Medicines Agency
EPAR	European Public Assessment Report
PASS	Post-Authorisation Safety Study
PK	Pharmacokinetic(s)
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan
SmPC	Summary of Product Characteristics (European Union)

OVERVIEW

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them. The RMP summary for Paxlovid is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g., by mentioning risks occurring in populations or indications not included in the Swiss marketing authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of Paxlovid in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorised by Swissmedic. Pfizer is fully responsible for the accuracy and correctness of the content of the published RMP summary of Paxlovid.

SUMMARY OF RISK MANAGEMENT PLAN FOR PAXLOVID (NIRMATRELVIR/RITONAVIR)

This is a summary of the risk management plan (RMP) for Paxlovid. 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).

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

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

I. The Medicine and What It Is Used For

Paxlovid is authorised for the treatment of coronavirus disease 2019 (COVID-19) in adults who do not require supplemental oxygen and who are at increased high risk for progressing to severe COVID-19 (see SmPC for full indication). It contains nirmatrelvir in combination with ritonavir as the active substances and it is given by oral route.

Further information about the evaluation of Paxlovid's benefits can be found in Paxlovid'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/paxlovid.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Paxlovid, together with measures to minimise such risks and the proposed studies for learning more about Paxlovid'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 (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 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 Paxlovid is not yet available, it is listed under 'missing information' below.

II.A. List of Important Risks and Missing Information

Important risks of Paxlovid 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 Paxlovid. 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 (eg, on the long-term use of the medicine).

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

II.B. Summary of Important Risks

Table 2. Missing information 1: Safety in patients with hepatic impairment

Risk minimisation measures	Routine risk minimisation measures SmPC Section 4.2 *Posology and method of administration*, Section 4.4 *Special warnings and precautions for use*, and Section 5.2 *Pharmacokinetic properties*. Pack size. Medicine's legal status. Additional risk minimisation measures None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: PASS in moderate and severe hepatic impairment; See PART II.C of this summary for an overview of the post-authorisation development plan.

Table 2. Missing information 1: Safety in patients with hepatic impairment

Table 3. Missing information 2: Safety in patients with renal impairment

Risk minimisation measures	Routine risk minimisation measures SmPC Section 4.2 *Posology and method of administration,* Section 4.4 *Special warnings and precautions for use* and Section 5.2 *Pharmacokinetic properties*. Pack size. Medicine's legal status. Additional risk minimisation measures* *Patient Cards* for normal dosage instructions and for dosage adjustment in patients with renal impairment. *Objectives:* The objective of the proposed additional measure is to provide an appropriate tool designed to enhance the awareness and knowledge of patients about the safety in patients with renal impairment and to ensure the optimal use of nirmatrelvir/ritonavir. *Rationale for the additional risk minimisation activities:* Additional awareness and knowledge of patients about the correct dosing and handling of nirmatrelvir/ritonavir. *Target audience and planned distribution path:* The target audience is patients via their prescribing physicians.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: PASS in moderate and severe renal impairment; See PART II.C of this summary for an overview of the post-authorisation development plan

*aRMM requested by Swissmedic. Applies to Switzerland only.

Table 4. Missing information 3: Safety during use in pregnancy and lactation

Risk minimisation measures	Routine risk minimisation measures SmPC Section 4.6 *Fertility, pregnancy and lactation*. Pack size. Medicine's legal status. Additional risk minimisation measures None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: PASS in pregnant and breastfeeding women and Study C4671039; See PART II.C of this summary for an overview of the post-authorisation development plan.

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 Paxlovid.

II.C.2. Other Studies in Post-Authorisation Development Plan

PASS in pregnant and breastfeeding women

Purpose of the study: To assess use of nirmatrelvir/ritonavir during pregnancy and, if feasible, lactation.

The objectives of the study are to evaluate the safety of nirmatrelvir/ritonavir 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.

Study C4671039

Purpose of the study: To assess penetration of nirmatrelvir in human breast milk and to measure the concentration of nirmatrelvir in breastmilk in healthy women.

PASS in moderate and severe renal impairment

Purpose of the study: To assess the safety of nirmatrelvir/ritonavir in patients with moderate and severe renal impairment.

PASS in moderate and severe hepatic impairment

Purpose of the study: To assess the safety of nirmatrelvir/ritonavir in patients with moderate and severe hepatic impairment.