SUMMARY OF RISK MANAGEMENT PLAN FOR PAXLOVID (NIRMATRELVIR/ RITONAVIR)- VERSION 3.0

This is a summary of the risk management plan (RMP) for Paxlovid. The RMP details important risks of Paxlovid, how these risks can be minimized, 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.

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 authorized 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.

II. Risks associated with medicine and activities to minimize or further characterize the risks.

Important risks of Paxlovid, together with measures to minimize such risks and the proposed studies for learning more about Paxlovid’s risks, are outlined below.

Measures to minimize 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 public (e.g. with or without prescription) can help to minimizes its risks.

Together, these measures constitute routine risk minimization measures.

In addition to these measures, information about adverse events is collected continuously and regularly analysed, including PSUR assessment, so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

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II.A List of important risks and missing information

Important risks of Paxlovid hydrochloride are risks that need special risk management activities to further investigate or minimize 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 hydrochloride. 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	• 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

Missing information: Use of Paxlovid with the addition of sildenafil in children	
Risk minimization measures	**Routine risk minimisation measures** SmPC Section 4.2 Posology and method of administration Section 4.4 Special warnings and precautions for use 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.

Missing information: Use in children with renal function impairment	
Risk minimization 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-authorization development plan

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

There are no studies, which are conditions of the marketing authorization or specific obligation of Paxlovid.

II.C.2 Other studies in post-authorization 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.