

Paxlovid (Nirmatrelvir and Ritonavir) for Eligible Non-Hospitalised patients (18 years and over) with COVID-19: Prescribing support document

What is it?

Paxlovid is the brand name for the combination of nirmatrelvir and ritonavir used to treat early COVID-19.

Nirmatrelvir is a peptidomimetic inhibitor of coronavirus 3C-like protease which prevents multiplication of SARS-CoV-2. Ritonavir inhibits CYP3A-mediated metabolism of nirmatrelvir, increasing the plasma concentration.

Paxlovid is licensed for the treatment of COVID-19 in adults who do not require supplemental oxygen and who are at increased risk for progression to severe COVID-19.

Results from the EPIC HR trial indicate that the dual oral antiviral nirmatrelvir/ritonavir resulted in a relative risk reduction of hospitalisation or death by 89% (within 3 days of symptom onset) and 88% (within 5 days of symptom onset) compared to placebo in non-hospitalised, high-risk adults with COVID-19.

NICE Guidance

[Overview | Casirivimab plus imdevimab, nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19 | Guidance | NICE](#)

In line with [NICE TA878](#) (updated 13 March 2024), Paxlovid is recommended as an option for treating COVID-19 in adults (18 years and over), only if they:

- do not need supplemental oxygen for COVID-19 and,
- they have any of the following:
 - an increased risk for progression to severe COVID-19, as defined in the [NICE TA](#).
 - people aged 85 years and over.
 - people with end-stage heart failure who have a long-term ventricular assistance device.
 - people on the organ transplant waiting list.
 - people aged 70 years and over, or who have a BMI of 35 kg/m² or more, diabetes or heart failure, and are resident in a care home, or are already hospitalised.

Licensed indication and prescribing good practice

Which health professionals will prescribe?

Paxlovid will be prescribed in the community by primary care prescribing clinicians who have completed the [eLearning package](#).

The patients will be identified by General Practice and Hospital specialists and will have access to NHS COVID-19 lateral flow device tests (LFD tests) via community pharmacies.

Preparations and Dosage

Summary of Product characteristics (SPC) [Paxlovid 150 mg/100 mg film-coated tablets](#).

Adult: 300 mg (two pink tablets) Nirmatrelvir and 100 mg (one white tablet) Ritonavir twice daily for 5 days, to be initiated as soon as possible after SARS-CoV-2 positive result and within 5 days of symptom onset, for each dose, nirmatrelvir (pink tablets) and ritonavir (white tablet) to be taken together.

The tablets are co-packaged in 5 daily-dose strips to aid compliance.

Renal impairment: eGFR ≥ 30 to < 60 ml/min. Dose of Paxlovid should be reduced to 150mg (one pink tablet) Nirmatrelvir and 100mg (one white tablet) Ritonavir. The remaining tablet of nirmatrelvir should be returned to the community pharmacy for disposal. Further information is available via [Renal Guidance](#).

Paxlovid is contraindicated in patients with severe renal impairment (eGFR < 30 mL/min).

Hepatic Impairment: No dosage adjustment of Paxlovid is needed for patients with either mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. Further information is available via [Hepatic Guidance](#).

Information to support patients with swallowing difficulties can be found at [Swallowing Guidance](#).

Contraindications and Cautions

Contraindications:

- Clinically significant hypersensitivity to either of the active ingredients or any of the excipients listed in the SPC.
- Severe hepatic impairment.
- Severe renal impairment.
- Co-administration with drugs that are highly dependent on CYP3A for clearance, and for which elevated concentrations are associated with serious and /or life-threatening reactions. See [drug interactions](#) for further information.

- Co-administration with drugs that are potent CYP3A inducers where significant reduction in plasma concentrations of nirmatrelvir and ritonavir may be associated with a loss of antiviral effect and possible resistance. See [drug interactions](#) for further information.

Cautions:

- [Interactions](#) with drugs metabolised by CYP3A may increase plasma concentrations of drugs metabolised by CYP3A.
- [Interactions](#) with drugs that inhibit or induce CYP3A may increase or decrease concentrations of Paxlovid, respectively.
 - These interactions may lead to:
 - Clinically significant adverse reactions, potentially leading to severe, life-threatening or fatal events from greater exposures of concomitant medicinal products.
 - Clinically significant adverse reactions from greater exposures of Paxlovid.
 - Loss of therapeutic effect of Paxlovid and possible development of viral resistance.
- Co-administration with calcineurin inhibitors and TOR inhibitors.
- Hypersensitivity reactions.
- Hepatotoxicity.
- HIV resistance.
- Contains lactose, patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- Should only be used in pregnancy if the potential benefits outweigh the potential risks for the mother and foetus.
- Patients using combined hormonal contraceptives should be advised to use an effective alternative contraceptive method or an additional barrier method of contraception during treatment and until after one complete menstrual cycle after stopping Paxlovid.
- Breastfeeding should be discontinued during treatment with Paxlovid and for 7 days after the last dose.

Drug Interactions

CYP3A inducers and inhibitors

There are clinically significant interactions with Paxlovid due to the metabolism of nirmatrelvir by CYP3A.

There is a drug interaction checker available at [Liverpool COVID-19 Interactions \(covid19-druginteractions.org\)](https://liverpool-covid-19-interactions.org/) where COVID-19 treatments and co-medications can be entered to search for interactions. A summary and description of the interaction, along with alternative treatments are provided. The interactions are ranked as below.

● Do Not Coadminister
 ■ Potential Interaction
 ▲ Potential Weak Interaction
 ◆ No Interaction Expected

Prior to prescribing Paxlovid all medications currently taken by any patient should be checked via the interaction checker or alternative resources (SPC, clinical system

interaction checker). This must include all regular and “as required” medicines, and any medicines purchased over-the-counter and currently in use.

Coadministration of Paxlovid with calcineurin inhibitors and mTOR inhibitors

Consultation of a multidisciplinary group (e.g., involving physicians, specialists in immunosuppressive therapy, and/or specialists in clinical pharmacology) is required to handle the complexity of this coadministration by closely and regularly monitoring immunosuppressant serum concentrations and adjusting the dose of the immunosuppressant in accordance with the latest guidelines. **In these individuals' consideration of sotrovimab as an alternative to Paxlovid, where the patient is eligible, could be considered.**

Adverse Effects

Common or very common adverse effects include diarrhoea, altered taste and vomiting.

Hypersensitivity reactions have been reported.

For full details on cautions, contraindications, drug interactions and adverse effects, please consult the latest edition of the [British National Formulary \(BNF\)](#) or [Summary of Product Characteristics \(SmPC\)](#).

References

1. National Institute for Health and Care Excellence [Casirivimab plus imdevimab, nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19](#) published 22 June 2023. (Accessed 30 Jan 2024).
2. National Institute for Health and Care Excellence Nirmatrelvir plus ritonavir for treated COVID-19 (partial review of TA878) draft guidance until publication Feb 2024.
3. Pfizer Ltd Summary of Product Characteristics Paxlovid 150mg/100mg film coated tablets 31 December 2021 Available at www.medicines.org.uk (Accessed 30 Jan 2024).
4. Hammond J, Leister-Tebbe H, Gardner A, et al. Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19. N Engl J Med. 2022;10.1056.

Document Ratification Details

Ratification Process	Details
Authored by:	Cambridgeshire and Peterborough Integrated Care Board
Ratified by:	Cambridgeshire and Peterborough Joint Prescribing Group
Date Ratified	April 2024
Review Date	April 2027
Version Number	1