HSE Clinical Guidance on Paxlovid™ (nirmatrelvir/ritonavir) for use in the Treatment of COVID-19

This document is intended for use by healthcare professionals only.

This guidance is specific to the management of patients with COVID-19 disease.

While the guidance is intended to strengthen clinical management of these patients it does not replace clinical judgement or specialist consultation.

Issued January 2025 by the Office of the Chief Clinical Officer

KEY RECOMMENDATION

1. **Paxlovid™ (nirmatrelvir/ritonavir) is not recommended for routine use in treatment of COVID-19**
2. **Treatment may be considered for selected seriously immunocompromised COVID-19 patients for the licensed indication.**
3. **Particular care is required in balancing potential risk with evidence based expectation of benefit in relation to patients in the "use with caution" category (see below).**
4. **The following is intended to guide use of Paxlovid™ (nirmatrelvir/ritonavir) in those selected seriously immunocompromised COVID-19 patients in whom Paxlovid™ (nirmatrelvir/ritonavir) is prescribed for the licensed indication.**
5. **Paxlovid™ (nirmatrelvir/ritonavir) should not be used outside of the licensed indication.**

LICENSED INDICATION FOR USE: [1]

Refer to Summary of Product Characteristics (SmPC) of Paxlovid™ (nirmatrelvir/ritonavir) for full prescribing information https://www.ema.europa.eu/en/documents/product-information/paxlovid-epar-product-information_en.pdf[1]

TREATMENT	INDICATION	ICD10	PROTOCOL CODE
Paxlovid™ (nirmatrelvir/ritonavir)	For the treatment of COVID-19 in adults patients (over 18) who: • Are less than or equal to 5 days of symptom onset • COVID-19 confirmed **within the last 5 days** • do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19	U07.1	COVID001

TREATMENT: [1]

Drug	Treatment
Paxlovid™ (nirmatrelvir/ritonavir)	300mg nirmatrelvir (two 150mg tablets) with 100mg ritonavir (one 100mg tablet) all taken **together** orally every 12 hours for 5 days.

A dose reduction is recommended in patients with moderate renal impairment

eGFR (mL/min)	Dose of nirmatrelvir	Dose of Ritonavir	Frequency	Duration
Greater than or equal to 60	300 mg	100 mg	12 hourly	5 days
30-60	150 mg	100 mg	12 hourly	5 days
Less than 30	Not recommended in Summary of Product Characteristics *			

*There is limited evidence available for the use of low dose Paxlovid™ (nirmatrelvir/ritonavir) regimens in patients with eGFR less than 30mL/min or those on dialysis (i.e. advanced Chronic Kidney Disease) who are at high risk of progressing to severe COVID-19. This should be discussed with local infectious diseases and renal teams prior to prescribing[2,3,4,5].

ELIGIBILE PATIENTS:

Selected seriously immunocompromised patients who meet all criteria outlined in the indication section.

EXCLUSION CRITERIA:

Patients who do not meet the eligibility criteria above

CONTRAINDICATIONS: [1]

- Severe renal impairment, (eGFR less than 30mL/min), including patients with End Stage Renal Disease under haemodialysis*
- Severe liver disease- Child Pugh Class C
- Co-administration of medicinal products that are highly dependent on CYP3A for clearance and for which elevated concentrations are associated with serious and/or life threatening reactions.
- Co-administration of medicinal products that are potent CYP3A inducers where significantly reduced Paxlovid™ (nirmatrelvir/ritonavir) plasma concentrations may be associated with potential for loss of virologic response and possible resistance.
- Hypersensitivity to the active substance or to any other ingredients
- Any contraindications to Paxlovid™ (nirmatrelvir/ritonavir) as listed in the Summary of Product Characteristics.

USE WITH CAUTION: [1]

- In patients with moderate renal impairment (eGFR less than or equal to 60mL/min), the dose of Paxlovid™ (nirmatrelvir/ritonavir) should be reduced to 150mg/100mg every 12 hours for 5 days.

Special attention for patients with moderate renal impairment

The daily blister contains two separated parts each containing two tablets of nirmatrelvir and one tablet of ritonavir corresponding to the daily administration at the standard dose. Therefore, patients with moderate renal impairment should be provided with only one tablet of nirmatrelvir with the tablet of ritonavir to be taken every 12 hours.

- Caution is advised in patients with pre-existing liver diseases, liver enzyme abnormalities or hepatitis, due to a risk of hepatotoxicity.
- Ritonavir is a CYP3A inhibitor (and PgP inhibitor). Nirmatrelvir is a substrate of CYP3A. Interactions with other medicinal products could lead to **clinically significant reactions, including potentially life-threatening or fatal reactions, loss of therapeutic effect of** Paxlovid™ (nirmatrelvir /ritonavir) **and possible development of viral resistance.**
- Carefully review concomitant medicines before and during treatment. Monitor the patient for adverse reactions associated with any concomitant medicine. Paxlovid™ (nirmatrelvir/ritonavir) should not be started immediately after discontinuation of certain contraindicated medicines, see Summary of Product Characteristics for further information.
- The COVID-19 Drug Interactions tool developed by the University of Liverpool (https://www.covid19-druginteractions.org/) should be used to check for potential drug interactions. A mobile app of the Liverpool Covid-19 tool is also available. Further information on medicines contraindicated for concomitant use with Paxlovid™ (nirmatrelvir/ritonavir) and for potential significant interactions with other medicinal products are also available from the Summary of Product Characteristics[1].
- Ritonavir may reduce the efficacy of combined hormonal contraceptives. Patients using combined hormonal contraceptives should be advised to use an effective alternative contraceptive method or an additional barrier method of contraception during treatment with Paxlovid™ (nirmatrelvir ritonavir), and until one menstrual cycle after stopping treatment.

OTHER INFORMATION:

Completion of the full 5-day treatment course is recommended even if the patient develops severe or critical COVID-19 after starting treatment[1].

Method of Administration:

Oral

DRUG INTERACTIONS:

Refer to Summary of Product Characteristics

ATC CODE:

Antivirals for systemic use, protease inhibitors, J05AE30

REFERENCES:

1. Summary of Product Characteristics Paxlovid 150mg + 100mg film-coated tablets. Available from: https://www.ema.europa.eu/en/documents/product-information/paxlovid-epar-product-information_en.pdf Accessed online: 13.01.2025
2. Hiremath S, McGuinty M, Argyropoulos C, Brimble KS, Brown PA, Chagla Z, Cooper R, Hoar S, Juurlink D, Treleaven D, Walsh M, Yeung A, Blake P. Prescribing Nirmatrelvir/Ritonavir for COVID-19 in Advanced CKD. Clin J Am Soc Nephrol. 2022 Aug;17(8):1247-1250. doi: 10.2215/CJN.05270522. Epub 2022 Jun 9. PMID: 35680135; PMCID: PMC9435977.
3. Hiremath S, Blake PG, Yeung A, McGuinty M, Thomas D, Ip J, Brown PA, Pandes M, Burke A, Sohail QZ, To K, Blackwell L, Oliver M, Jain AK, Chagla Z, Cooper R. Early Experience with Modified Dose Nirmatrelvir/Ritonavir in Dialysis Patients with Coronavirus Disease 2019. Clin J Am Soc Nephrol. 2023 Apr 1;18(4):485-490. doi: 10.2215/CJN.0000000000000107. Epub 2023 Mar 1. PMID: 36723285; PMCID: PMC10103226.
4. Renal Drug Database. Available from: https://renaldrugdatabase.com/monographs/paxlovid-nirmatrelvirritonavir. Accessed online: 13.01.2025
5. Guidance for the use of nirmatrelvir/ritonavir in patients with advanced chronic kidney disease and patients on dialysis. www.covid19-druginteractions.org/prescribing_resources/paxlovid-renal-dosing. Accessed online: 13.01.2025