NHS South Yorkshire Integrated Care Board

Paxlovid™ (nirmatrelvir plus ritonavir) and Molnupiravir for treatment of COVID-19

The details of side-effects, cautions, contraindications and interactions are not a complete list and the current BNF (https://bnf.nice.org.uk/) and the SPC (https://www.medicines.org.uk/emc/) remain authoritative.

The SY ICB Medicines Optimisation Team will alert primary care prescribers if any significant changes in review or monitoring arrangements of the products they prescribe are recommended.

Background Information	**General Eligibility Criteria** Patients should meet all of the eligibility criteria and none of the exclusion criteria. Non-hospitalised patients with onset of COVID-19 are eligible to be considered for the treatments above if: • SARS-CoV-2 infection is confirmed by either: o Polymerase chain reaction (PCR) testing OR o Lateral flow test (registered via gov.uk) AND • Symptomatic with COVID-19 and showing no signs of clinical recovery. • The patient is a member of a 'highest' risk group (as defined in Appendix 1) • Treatment is commenced within 7 days of symptom onset (off label) • Aged 16 and over (seek MDT support from Children's Trust for 16 - 18 year olds) **Molnupiravir Eligibility Criteria** If the initial criteria above are met, patients should only be considered for treatment with molnupiravir if: • Treatment with Paxlovid™ is contraindicated or not possible AND • Treatment is commenced within 7 days of symptom onset (off label) • Patients are over 18 The following are considered symptoms of COVID-19: feverish, chills, sore throat, cough, shortness of breath or difficulty breathing, nausea, vomiting, diarrhoea, headache, red or watery eyes, body aches, loss of taste or smell, fatigue, loss of appetite, confusion, dizziness, pressure or tight chest, chest pain, stomach ache, rash, sneezing, sputum or phlegm, runny nose
Therapeutic class	Antiviral Treatment

<table>
<tr><td>Indication</td><td>

1st line Paxlovid™ 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.
2nd line Molnupiravir for use in the treatment of mild to moderate COVID-19 in adults (aged 18 years and over) with a positive SARS-CoV-2 diagnostic test and who have at least one risk factor for developing severe illness.
3rd line – refer to Trusts

</td></tr>
<tr><td>Dosage and administration</td><td>
<h2>Paxlovid™ Dosing and administration</h2>
The recommended dose of Paxlovid™ (nirmatrelvir plus ritonavir) is

300mg (two 150mg tablets) nirmatrelvir with
100mg (one 100mg tablet) ritonavir taken together orally twice daily for 5 days only. Treatment must not be extended beyond 5 days.

Dose Reduction Stage 3 Chronic Kidney Disease (eGFR 30-59ml/min)
The recommended dose of Paxlovid™ (nirmatrelvir plus ritonavir) is

150mg (one 150mg tablet) nirmatrelvir with
100mg (one 100mg tablet) ritonavir taken together orally twice daily for 5 days only. Treatment must not be extended beyond 5 days.

<table>
<tr><td>Renal Function</td><td>Proposed Dose</td></tr>
<tr><td>eGFR < 30 ml/min</td><td>300mg nirmatrelvir + 100mg ritonavir once daily D1
Followed by
150mg nirmatrelvir + 100mg ritonavir once daily D2-5</td></tr>
<tr><td>Dialysis</td><td>Patients ≥ 40kg – to be given after dialysis
300mg nirmatrelvir + 100mg ritonavir once daily D1
Followed by
150mg nirmatrelvir + 100mg ritonavir once daily D2-5

Patients < 40kg – to be given after dialysis
150mg nirmatrelvir + 100mg ritonavir once daily D1, D3, D5 ie every 48h for THREE doses only,</td></tr>
</table>
<h2>Molnupiravir Dosing & Administration</h2>
The recommended dose of molnupiravir is 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days only. Treatment must not be extended beyond 5 days
</td></tr>
</table>

Cautions and Contraindications	• Requirement for hospitalisation for COVID-19 • Known hypersensitivity reaction to the active substances or to any of the excipients of medications as listed in their respective Summary of Product Characteristics (SmPC). • New or additional oxygen requirements. Paxlovid™ (nirmatrelvir plus ritonavir): • The patient does NOT have stage 4-5 chronic kidney disease (eGFR <30ml/min). • Paxlovid™ is not licensed for the treatment of patients with advanced decompensated liver cirrhosis or stage 4-5 chronic kidney disease who are not hospitalised. However, off-label, adjusted dosing can be used in stage4-5 chronic kidney disease patient group and also in dialysis patients after appropriate evaluation and discussion of risks/benefits with the patient • Children aged less than 16 years • Pregnancy or breastfeeding • The patient is taking any of the medications listed in Appendix 2. Please contact pharmacy teams if further advice on potential interactions are required • pre-existing liver diseases, liver enzyme abnormalities or hepatitis **Molnupiravir Additional Exclusion Criteria** The following additional exclusion criteria applies if considering treatment with molnupiravir: Children aged less than 18 years **Molnupiravir Cautions** Please refer to the SmPC for molnupiravir for special warnings and precautions for use.
Pregnancy and breast feeding	Pregnant and breastfeeding patients are excluded from receiving this treatment in the community and should be referred to Trusts
Adverse Drug Reactions	Possible gastro-intestinal side-effects of treatment with nirmatrelvir/ritonavir (e.g. nausea, vomiting). If such side-effects are experienced, anti-emetics should be considered that are not contra-indicated. If nirmatrelvir/ritonavir treatment cannot be tolerated, an alternative treatment can be considered within the options and criteria of this guidance The most common adverse reactions to molnupiravir (≥1% of subjects) reported during treatment and during 14 days after the last dose of molnupiravir were diarrhoea (3%), nausea (2%), dizziness (1%) and headache (1%) all of which were Grade 1 (mild) or Grade 2 (moderate).
Monitoring	• None • Paxlovid and molnupiravir are ▼ black triangle drugs; report ALL suspected adverse reaction to the MHRA via the Yellow Card scheme: www.mhra.gov.uk/yellowcard
Interactions	• Initiation of Paxlovid™, a CYP3A inhibitor, in patients receiving medicinal products metabolised by CYP3A or initiation of medicinal products metabolised by CYP3A in patients already receiving

	Paxlovid™, may increase plasma concentrations of medicinal products metabolised by CYP3A	
Additional information	• Link to algorithm • Liverpool COVID-19 Interactions • Treatments for COVID-19 - NHS • 5 Supporting information on risk factors for progression to severe COVID-19 |	
Patient information	• It is the responsibility of the initiating clinician to share and discuss the patient information with the patient	
Ordering information	• Stock available is through community pharmacy. These products are unlikely to be in stock and patients should be informed that they should check with the pharmacy as to when to collect	

References

- NHS Greater Glasgow and Clyde Covid 19 Clinical Guideline

https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf

Interim Clinical Commissioning Policy: Antivirals or neutralising monoclonal antibodies for non-hospitalised patients with COVID-19 (Version 6)

Development Process

This guidance has been produced by Alex Molyneux. This guideline has been subject to consultation and endorsement by Primary Care Sheffield, SY ICB Medicines Optimisation Team and was ratified by IMOC on <insert date>.