Screening tool for Paxlovid® (nirmatrelvir and ritonavir) - DRAFT

Today's date: [dd/mm/yy]

Consultation is for patient: [Insert name]

DOB: [dd/mm/yyyy] NHS Number: [XXXXXXXXXX]

Name of representative if consultation is not with the patient: [Insert name]

If representative, state relation: [Parent/Guardian/Carer/Other _____]

Patient/Representative (delete as appropriate) contact number: _____

Referral from: [111, GP practice]

Patient's GP: [GP, Practice and Address]

Symptoms and Medical History

Criteria for Paxlovid®		
1	Patient DOES NOT have severe COVID-19 and is not experiencing at least one of the following as defined by NICE NG 191[1]: • Severe shortness of breath at rest or difficulty in breathing • Reduced oxygen saturation level measured by pulse oximetry (an oxygen level of 92% or below) - *caution patient's baseline oxygen level if e.g. COPD* • Coughing up blood • Blue lips or face • Feeling cold and clammy with pale or mottled skin • Collapse or fainting • New confusion • Becoming difficult to rouse • Reduced urine output	Yes – go to 2 No – refer patient to A&E if severe COVID-19
2	Patient is symptomatic with mild to moderate COVID-19 and showing no signs of clinical recovery COVID-19 symptoms and what to do - NHS (www.nhs.uk)[2] Current symptoms: Oxygen saturation (if available):	Yes – go to 3 No – if the patient is asymptomatic, this is not within the service scope and licence for Paxlovid® for COVID-19 treatment. Advise accordingly and refer back to GP as appropriate.

Criteria for Paxlovid®		
3	Patient has at least one of the following criteria: a) Patient has an increased risk for progression to severe COVID-19 as defined by Box 1 or Box 2[3]: Supporting information on risk factors for progression to severe COVID-19 | NICE TA 878[3] b) Or who are[3]: • aged 85 years and over or • have end-stage heart failure and have a long-term ventricular assistance device (a mechanical device that helps the heart pump blood) or • are on the organ transplant waiting list or • are a resident in a care home or already in hospital **AND** are: - aged 70 years and over or - who have a body mass index (BMI) of 35 kg/m^2 or more or - diabetes or - heart failure	Detail condition and details below Yes, in a) or b) – go to 4 No – not within service scope for COVID-19 treatment. Advise accordingly and refer back to GP as appropriate.
4	Patient has a positive COVID-19 Test (this can include verbal confirmation)	Yes – go to 5 No – refer back to GP and direct patient/patient rep to local pharmacy service for free LFD: Find a pharmacy that offers free COVID-19 rapid lateral flow tests - NHS (www.nhs.uk)
5	Patient is age 18 years or over	Yes – go to 6 No – see referral pathway, page 5
6	Symptoms started [dd/mm/yy] within the last 5 days	Yes – go to 7 No – presenting more than 5 days not within service scope for COVID-19 treatment. Discuss with CMDU GP lead and see 7 if appropriate.
7	The patient has **NOT** been treated with Paxlovid® within the last 3 months	Yes – go to Paxlovid® review tool, page 3 No – re-infection of COVID-19 in the first 30-90 days is uncommon. Prolonged viraemia and rebound infection can occur in this time period and does not routinely warrant re-treatment. Where re-infection is considered within this period (30-90 days), please refer to patient's parent team e.g. oncologist, rheumatologist etc. for analysis of SARS CoV-2 antibodies or other further investigations. See referral pathway, page 5.

Medical History	Current Medicines

Paxlovid® review tool

Consider standard dose Paxlovid® if the patient meets all the criteria below and screening tool.

Standard dose: 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet) all taken together orally twice daily for 5 days. Paxlovid® should be given as soon as possible after positive results of direct SARS-CoV-2 viral testing and within 5 days of onset of symptoms[4].

The patient is NOT pregnant (see additional guidance* on page 4 if patient is of child-bearing potential and referral pathway on page 5 if the patient is pregnant as Paxlovid® is contraindicated in pregnancy)
The patient does NOT have renal impairment (go to page 4 for further guidance if impairment or go to page 5 if dialysis)
The patient does NOT have liver impairment (go to page 4 for further guidance if impairment)

Drug interactions/drug contraindications have been checked.
 	
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. Initiation of medicinal products 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[4].
 	
Prescribers must have available accurate information on the patient's medicines to check for drug interactions. Some examples are listed below:
• OTC medicines (including herbal remedies)
• Illicit or recreational drugs
• Prescription medicines, from primary and secondary/tertiary care. Consider asking about:
  ○ Received medicines prescribed or administered by secondary/tertiary care (including medicines delivered to the home, injections or infusions administered in out-patients or clinics, depot injections)
  ○ Received medicines if attended a walk-in clinic, A&E, acute medical unit or day case admission
  ○ Discharge from hospital and if they were prescribed/given medicines
 	
Supporting resources:
• Home - electronic medicines compendium (emc) [Paxlovid][4] + [patient's medication]
• Liverpool COVID-19 Interactions (covid19-druginteractions.org)[5]
• Medicines Advice Service – Medicines Advice contact details – SPS - Specialist Pharmacy Service[6]
• CMDU GP Lead
• Specialist advice

The patient is NOT breast-feeding* (see additional guidance* in page 4)
The patient can swallow tablets* (see additional guidance* in page 4 if swallowing difficulties)
The patient does NOT have a history of clinically significant hypersensitivity to the active substances (nirmatrelvir/ritonavir) or to any of the excipients listed in: See contraindications - Home - electronic medicines compendium (emc) [Paxlovid][4]

***Additional guidance**

Circumstance	Guidance
Breast-feeding	Caution: Breast-feeding should be discontinued during treatment with Paxlovid® and for 7 days after the last dose of Paxlovid[4].
Difficulty in swallowing or enteral feeding tubes	Paxlovid® can be crushed or split and mixed with food or liquid, including dairy containing products (off-label)[6]
Child-bearing potential	Patients using combined hormonal contraceptives should be advised to use an effective alternative contraceptive method or an additional barrier method of contraception (applicable during treatment and until after one complete menstrual cycle after stopping Paxlovid®).[4]

Conditions requiring dose adjustment and contraindications for Paxlovid®
Refer to SPC for further details: Home - electronic medicines compendium (emc) [Paxlovid][4]

Renal Impairment (and check drug interaction sources)[4]	
Mild (eGFR ≥ 60 mL/min)	No dose adjustment is needed.
Moderate (eGFR ≥ 30 to < 60 mL/min)	The dose of Paxlovid® should be reduced to nirmatrelvir/ritonavir 150 mg/100 mg (1 tablet of each) twice daily for 5 days. The remaining tablets of nirmatrelvir should be disposed of by taking this to the local community pharmacy.
Severe (eGFR < 30 mL/min)	Do not prescribe, contraindicated – go to referral pathway, page 5.
Liver impairment (and check drug interaction sources)[4]	
Mild (Child-Pugh Class A)	No dose adjustment is needed
Moderate (Child-Pugh Class B)	No dose adjustment is needed
Severe (Child-Pugh Class C)	Do not prescribe, contraindicated – go to referral pathway, page 5

Other patient factors to consider:

- Is the patient's current medication a complete and accurate list?
- Caution - medication history taking by proxy
- Patients on clinical trials
- Dossette box requirements
- If the patient is considered **not suitable for Paxlovid®, go to page 5**

North West London referral pathway to specialist/hospital for eligible patients who are not suitable for Paxlovid®

Risk cohorts
a) Patient has an increased risk for progression to severe COVID-19 as defined by Box 1 or Box 2 as per NICE TA878[3]:
Supporting information on risk factors for progression to severe COVID-19 | NICE TA 878[3]

b) Patients who are **not in risk cohort a) and are[3]:**

- aged 85 years and over or
- have end-stage heart failure and have a long-term ventricular assistance device (a mechanical device that helps the heart pump blood) or
- are on the organ transplant waiting list or
- are a resident in a care home or already in hospital **AND** are:
  - aged 70 years and over or
  - who have a body mass index (BMI) of 35 kg/m^2 or more or
  - diabetes or
  - heart failure

Nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19 NICE TA 878[3]

Note: do not refer to Same Day Emergency Care (SDEC) if the patient is classified in risk cohort b) – alternative treatments if Paxlovid® is deemed unsuitable are currently not recommended by NICE[3]

Scenario	Risk cohort	Refer to:
Severe symptoms of COVID-19	All	A&E
Pregnant (Paxlovid® is contraindicated in pregnancy)	All	Patient's obstetrician/midwife
Re-infection and prolonged viraemia with COVID-19 within 3 months of previous treatment with Paxlovid®	All	Patient's parent team e.g. oncologist, rheumatologist etc. for analysis of SARS CoV-2 antibodies or other further investigations
Age less than 18 years	a)	ICHT paediatric infectious diseases team
Renal Dialysis	a)	ICHT dialysis unit/renal team
Severe renal impairment	a)	SDEC
Severe liver impairment	a)	SDEC
Unavoidable contraindicated drug interactions as determined by supporting resources	a)	CMDU Clinical GP Lead SDEC
	b)	Do not refer to SDEC
Transplant (and transplant medicines)	a)	Patient's specialist
Severe neurological impairment	All	Discuss with patient's GP and/or specialist if a person lacks capacity if unable to make or communicate a decision/consent CMDU GP Lead

Further advice and guidance for the patient

Patient information for Paxlovid - GOV.UK (www.gov.uk)[7]
Patient Information Leaflet for Paxlovid - GOV.UK (www.gov.uk)[8]

How to take Paxlovid®

- Paxlovid® consists of 2 medicines: 2 tablets of PF-07321332 (nirmatrelvir) and 1 tablet of ritonavir.
- The blister foil for each day of treatment is divided in two different coloured sections to indicate which tablets need to be taken at each time of day – one side for the morning (AM) dose and the other side for the evening (PM) dose.
- Patient will need to take all 3 tablets behind the yellow foil in the morning and all 3 tablets behind the blue foil in the evening, for a total of 5 days.
- Paxlovid® can be taken with or without food. The tablets should be swallowed whole and not chewed, broken or crushed.

Missed doses

- A missed dose should be taken as soon as possible and within 8 hours of the scheduled time, and the normal dosing schedule should be resumed.
- If more than 8 hours has elapsed, the missed dose should not be taken and the treatment should resume according to the normal dosing schedule.

If patient feels better

- Patient should be counselled to complete a 5-day course of Paxlovid®, even if symptoms improve and/or patient feels better, to reduce the chances of a treatment-resistant version of the virus developing.

Possible side-effects

- Like all medicines, Paxlovid® can cause side effects, although not everybody gets them.
- Not many people have taken Paxlovid®. Serious and unexpected side effects may happen. Paxlovid is still being studied, so it is possible that all of the risks are not known at this time.

- Common: (*may affect up to 1 in 10 people)*
    - Diarrhoea
    - Vomiting
    - Altered sense of taste

Reporting of side effects

- Side effects can be reported directly via the Coronavirus Yellow Card Reporting site.

How to store Paxlovid®

- Store below 25 °C.
- Do not refrigerate or freeze.

References

1. NICE guideline [NG 191]. Covid-19 rapid guideline: managing COVID-19. May 2024. Available at: https://www.nice.org.uk/guidance/ng191. Accessed on: 17.06.2024.
2. NHS. COVID-19 symptoms and what to do. March 2023. Available at: https://www.nhs.uk/conditions/covid-19/covid-19-symptoms-and-what-to-do/ . Accessed on: 17.06.2024.
3. NICE Technology Appraisal [TA 878]. Nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19. Available at: https://www.nice.org.uk/guidance/ta878 . Accessed on: 17.06.2024.
4. Pfizer. Paxlovid 150 mg/100 mg film-coated tablets summary of product characteristics: Electronic Medicines Compendium. January 2024. Available at: https://www.medicines.org.uk/emc/product/13145. Accessed on 17.06.2024
5. University of Liverpool COVID-19 Drug Interaction checker. 2024. Available at: https://www.covid19-druginteractions.org/checker . Accessed at: 17.06.2024.
6. Specialist Pharmacy Service. Using nirmatrelvir and ritonavir (Paxlovid) in practice. Available at: https://www.sps.nhs.uk/articles/using-nirmatrelvir-and-ritonavir-paxlovid-in-practice/ . Accessed 17.06.2024.
7. UK Health Secretary Agency. Guidance: Patient information for Paxlovid. May2022. Available at: https://www.gov.uk/government/publications/covid-19-antiviral-treatment-paxlovid/patient-information-for-paxlovid . Accessed 17.06.2024.
8. Medicines & Healthcare products Regulatory Agency (MHRA). Decision: Patient Information Leaflet for Paxlovid. October 2022. Available at: https://www.gov.uk/government/publications/regulatory-approval-of-paxlovid/patient-information-leaflet-for-paxlovid#:~:text=Always%20take%20this%20medicine%20exactly,a%20lower%20dose%20of%20Paxlovid. Accessed 17.06.2024.