Advisory note: Paxlovid® COVID-19 antiviral treatment for non-hospitalised patients

April 2022

Advisory note: Paxlovid® COVID-19 antiviral treatment for non-hospitalised patients

April 2022

Introduction

The NHS is offering antibody and antiviral treatments to people with coronavirus (COVID-19) who are at highest risk of becoming seriously ill.

This advisory note provides links to information about the prescribing and adminsitration of Paxlovid® since it is being provided under a temporary authorisation, is subject to numerous drug-drug interactions and is a recommended first line treatment.

The treatments available are:

Priority	Drug	Class	Route	Patient age range
1st line	nirmatrelvir and ritonavir (Paxlovid®)	antiviral	oral	18 years+
1st line	sotrovimab (Xevudy)	nMAb*	intravenous	12 years+
2nd line	remdesivir (Veklury)	antiviral	intravenous	12 years+
3rd line	molnupiravir (Lagevrio)	antiviral	oral	18 years+

***nMAb = neutralising monoclonal antibody**

Paxlovid® received temporary authorisation under regulation 174 of the Human Medicines Regulations 2012 (as amended) on 31st December 2021, for supply to treat mild to moderate COVID-19 infection. It is only used in patients who are at increased risk for progression to severe COVID-19, including hospitalisation or death.

There are slightly different procedures for the supply of Paxlovid® depending on which of the four home nations patients reside in.

Indemnity

The PDA recognises that members may have concerns regarding indemnity cover and the potential for patient harm associated with the use of Paxlovid®, a new medicine with temporary authorisation being used to treat a rapidly changing viral infection which can cause hospitalisation, long term illness and death, with treatment risks exacerbated by a wide range of drug-drug interactions.

Liabilities linked to the inherent properties of the medications involved are not indemnified by the PDA as they are usually covered by the product liability insurance of the manufacturer for licensed products. In the case where no such license is yet available, the effects of this medicine should be covered by the Clinical Negligence Scheme for Coronavirus (CNSC) which was introduced at the time of the Coronavirus Act 2020.

There is also protection available from the Clinical Negligence Scheme for Trusts in England and the risk pool in Wales, or Clinical Negligence Scheme for General Practice in England depending on the sector worked in. Equivalent arrangements are in place in Scotland under the Clinical Negligence and Other Risk Indemnity Scheme (CNORIS) and in Northern Ireland under the NHS HSC scheme. In all four nations staff providing NHS services related to the coronavirus outbreak will have indemnity under the Act, where they are not already covered by an existing indemnity arrangement[1].

Brief information and signposting to the extensive information sources available are included in this advisory, and pharmacists with roles in assessment or prescribing need to ensure that they have followed national and local guidance and utilised all appropriate information sources available to make their professional decision on whether prescribing Paxlovid® is safe. Should a claim arise linked to a failure in this professional activity (as opposed to any detrimental effects of the Molecules in Paxlovid®), members will be covered by PDA indemnity

Patient groups and testing

Information on the groups of patients who may be eligible for Paxlovid® and the other treatments can be found by following these links with information being broadly similar across the nations:

- England: https://www.nhs.uk/conditions/coronavirus-covid-19/self-care-and-treatments-for-coronavirus/treatments-for-coronavirus/
- Wales: https://gov.wales/covid-19-treatments
- Scotland: https://www.nhsinform.scot/illnesses-and-conditions/infections-and-poisoning/coronavirus-covid-19/coronavirus-covid-19-treatments
- Northern Ireland: https://www.nidirect.gov.uk/articles/treatments-coronavirus-covid-19

Paxlovid® Eligibility criteria

Adults who have all 3 of the following are eligible to be assessed for treatment with Paxlovid®:

- Symptoms of coronavirus that started in the last 5 days with no signs of clinical recovery
- Are a member of one of the patient groups considered at high risk from coronavirus with a clinical condition prioritised for treatment (see information at the links above)
- Coronavirus is confirmed by either a positive PCR test or lateral flow device (LFD) test (some nations require PCR confirmation of positive LFT).

Paxlovid key points:

- Paxlovid® is for use in non-hospitalised symptomatic adult patients with COVID-19 who have at least one prespecified risk factor for progressing to severe COVID.
- In the study Paxlovid® significantly reduced the proportion of participants with

[1] Coronavirus-outbreak-indemnity-FAQs.pdf (resolution.nhs.uk)

COVID-19 related hospitalisation or death by 89.1%, compared with placebo. (Trial participants had not receieved any coronavirus vaccine or had a SARS-CoV-2 infection, meaning that those in the placebo arm were completely unprotected and virus naïve)

- Treatment should be started within 3-5 days of symptom onset.
- Treatment may be contra-indicated in patients with renal or liver disease. **Whilst the SPC suggests prescribing a lower dose for patients with CKD3, the national commissioning policy does not recommend the use of Paxlovid® in patients with CKD3 outside of a hospital setting.**
- There are a large number of drug-drug interactions, some being a complete contraindication, whilst others require careful clinical consideration. It is therefore essential to take an accurate drug history and utilise relevant information before prescribing Paxlovid®. An NHS Education for Scotland Powerpoint presentation with information on risk-assessing interactions can be found in the information section.
- The UK home nations have variations in the assessment, prescribing and supply process.
- **Patients not in the highest risk groups who are over 50 or aged 18-49 with a health condition putting them at high risk who develop Covid-19 symptoms may be able to access Covid-19 treatments by enrolling on the Panoramic study: https://www.panoramictrial.org/**

Practicalities

Symptoms: Whilst the NHS England website page still only lists the 'main' symptoms of Covid, the CMO letters contain the following COVID-19 symptoms: 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.

England: Patients in highest risk groups should have been informed by letter or by their specialist and provided with lateral flow or PCR tests so that they can test themselves if they develop symptoms. Positive PCR tests will be picked up centrally, positive lateral flow tests should be reported via the UK Government website: Report a Covid-19 Lateral Flow Test result or by calling NHS 119.

If symptomatic, but with a negative lateral flow, patients should perform a PCR test and send it for analysis to ensure they receive treatment if positive. Assesment and prescribing should usually take place via Covid Medicine Delivery Units which are located across England. A link to a directory of CMDUs can be found here: Covid Medicines Delivery Unit directory

Wales: Patients in highest risk groups should have been informed by letter or by their specialist and provided with lateral flow or PCR tests so that they can test themselves if they

develop symptoms. Positive lateral flow tests should be reported via the UK Government website: Report a Covid-19 Lateral Flow Test result or by calling NHS 119.

Patients eligible for assessment will be contacted within 48 hours of a positive PCR or lateral flow test by specially trained pharmacists who will ask about their medicines and decide which treatment is the most appropriate. The medicine will then be delivered to their homes within 24 hours[2].

Scotland: Each Health Board has established a single point of contact telephone number for eligible high-risk individuals to contact for an assessment of their suitability for treatment. Everyone on the high risk list should have been informed of their status by letter from the CMO.

Aseessment of patients and prescribing will be provided by advanced nurse practitioners and prescribing pharmacists via the central assessment and prescribing facility in each Health Board. Supply of oral anti-virals will mainly be via dispensing and delivery from community pharmacies which have been commissioned to dispense and supply them (not all pharmacies are part of the scheme). In HB areas which have not commissioned community pharmacy, supply may be via hospital day clinics. A table listing the dedicated HB telephone numbers can be found here: https://www.nhsinform.scot/illnesses-and-conditions/infections-and-poisoning/coronavirus-covid-19/coronavirus-covid-19-treatments

Northern Ireland: HSC trusts are commissioned to provide Outpatient Covid Services (OCS) under the national guideline. SARS-CoV-2 infection is confirmed via PCR or lateral flow test (registered via gov.uk or NHS 119).

HSC trusts have been asked to consider prescribing and administering an antiviral or monoclonal antibody treatment in line with the published national policy and associated clinical guide to non-hospitalised patients. Trusts will contact eligible patients with positive test results to discuss treatment. If patients believe they are eligible but have not been contacted by a trust within 24 hours, they should contact their GP who will then contact the HSC Trust on their behalf.

Pregnancy

PF-07321332(nirmatrelvir) plus ritonavir (Paxlovid®), and molnupiravir, are not recommended during pregnancy. All individuals of childbearing potential who are prescribed molnupiravir should be advised to use effective contraception for the duration of treatment and for 4 days after the last dose of molnupiravir.

The use of 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 and until after one complete menstrual cycle after stopping Paxlovid®.[3]

All healthcare professionals are asked to ensure that any patients who receive a COVID antiviral while pregnant are reported to the UK COVID-19 antivirals in pregnancy registry on 0344 892 0909. For more information, go to http://www.uktis.org/.

[2] https://gov.wales/thousands-benefit-antiviral-medicine-wales
[3] https://hscbusiness.hscni.net/pdf/ANTIVIRALS%20OR%20NEUTRALISING%20MONOCLONAL.....pdf

Conclusion

Paxlovid® is one of four therapies available for the treatment of highest risk patients with Covid-19 infection in the community. Patients will be assessed to see if they meet the criteria for inclusion and will need careful checking to see if Paxlovid® therapy is safe due to the significant number of drug interactions. Assessment and prescribing are provided via dedicated services with dispensing and supply arranged by the central supply service or via participating community pharmacies.

Pharmacists are playing an integral part in the supply chain, whether as Chief Pharmacists in hospital trusts dealing with order and supply of medications and medicines information, trained pharmacist assessors in the Welsh service or in both the prescribing anddispensing and delivery of antivirals in the Scottish service.

Every pharmacist can support this service by making themselve familiar with service set up in their area so that they can provide advice and signposting to healthcare colleagues and patients.

Pharmacists working in general practice may also be able to help with identifying newly diagnosed highest risk patients – whilst most of this group should already have been identified and contacted, no system is entirely foolproof.

Patients in England who have tested positive but have not been picked up by the digital cohorting sytem will need to proactively contact their GP or 111 for a referral to their local CMDU for assessment and treatment[4]. Practice pharmacists can support their GP by ensuring that all required information about the patient's drug history is available to forward to the CMDU with the referral. Community pharmacists contacted by patients in the highest risk cohort with positive PCR or lateral flow tests should advise them to stay at home and contact their GP for a referral to a CMDU, or to call NHS 111 out of hours if they have not been contacted within 24 hours of their positive test result.

We hope that the information and links in this document will enable members to play their part in making this service successful across the four UK nations and reducing the risk of negative outcomes for the most vulnerable patients.

Information sources

Chief Medical Officer Communications:

England:
https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103191

Scotland:https://static1.squarespace.com/static/601d44b7e8475c7d8be2ea36/t/61e062231d047c44be1452a0/1642095140184/Circular+PCA%28P%29%282022%29+03+-+Deployment+of+COVID-19+Antiviral+Treatment+in+non-hospitalised+patients+%28002%29.pdf

Wales: https://awttc.nhs.wales/files/covid-hub/covid-19-therapies/interim-clinical-commissioning-policy-nmabs-in-non-hospitalised-patients-24-feb-pdf/

[4] https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2021/12/C1574-Letter-to-general-practices-deployment-of-COVID-19-treatments-for-highest-risk-non-hospitalised-patients.pdf

Northern Ireland:
https://hscbusiness.hscni.net/pdf/ANTIVIRALS%20OR%20NEUTRALISING%20MONOCLONAL.....pdf

Drug information (Paxlovid®)

- Pfizer SPC. This contains two drug tables, one with absolute contraindications and one where caution is required. At least one drug appears in both tables.: Summary of Product Characteristics for Paxlovid® - GOV.UK (www.gov.uk)
- NHS Education for Scotland presentation about Paxlovid® prescribing with well set out rationale for consideration of the potential risks of relevant drug interactions: https://www.glasgowlmc.co.uk/download/Links/test/2022/25_feb/Prescribing-of-Paxlovid®-for-COVID-19.pdf

Policies

- UK Rapid Policy Statement: Interim Clinical Commissioning Policy: Antivirals or neutralising monoclonal antibodies for non-hospitalised patients with COVID-19 (Version 5):
- DHSC England, Clinical Guide This guide has information on treatment pathways, information on medical contraindications to treatment and information on drugs which are contraindicated: Therapies for symptomatic non-hospitalised patients with COVID-19
- Specialist Pharmacy Service (SPS) page with links to guidance on the use of oral COVID-19 treatments: https://www.sps.nhs.uk/home/guidance/covid-19-treatments/oral-antivirals/
- SPS page with information on use of neutralising monoclonal antibodies for Covid-19: https://www.sps.nhs.uk/home/guidance/covid-19-treatments/neutralising-monoclonal-antibodies/
- Liverpool Paxlovid® drug interaction checker – searchable online webpage (pdf table can be downloaded): https://covid19-druginteractions.org/checker
- SPS Using Paxlovid® in practice – provides advice on swallowing difficulties, pregnancy and breastfeeding. Also has further links, although some of these relate to secondary rather than primary care : https://www.sps.nhs.uk/articles/using-nirmatrelvir-and-ritonavir-Paxlovid®-in-practice/