

Top tips on new treatments for COVID-19

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1) There are new treatments available for community management of COVID-19

So far in the pandemic, the primary care management of those with COVID-19 has been supportive – if the patients weren't unwell enough to be admitted then we have managed in the same way as other viral respiratory tract infections. This is beginning to change with the arrival of two new community treatments.

Molnupiravir is an antiviral drug which is given orally as a five-day course, which has to be started within five days of symptom onset. It is a pro-drug and the active metabolite causes copying errors in the mRNA genome of the virus, which inhibits viral replication.

Sotrovimab is a combination synthetic monoclonal antibody, a class of drug which bind to the spike protein of the virus, stopping it entering the host cell. It is delivered intravenously as a single infusion¹.

2) Very-high risk patients should have received information about this already.

Patients who have PCR confirmed COVID-19 with onset of symptoms in the last five days and are a member of the 'highest risk group' should have all received a letter from NHSEI telling them about these new treatments². They have also been sent a PCR test kit to keep at home so that they can test promptly if they have symptoms of COVID-19 and were told to contact 119 if they had not received their test kit by January 10th.

The group of patients defined as being in the 'highest risk group' is given in the table below.

The following patient cohorts were determined by an independent advisory group commissioned by the Department of Health and Social Care (DHSC)⁷.

Cohort	Description
Down's syndrome	All patients with Down's syndrome
Patients with a solid cancer	<ul style="list-style-type: none"> Active metastatic cancer and active solid cancers (at any stage) All patients receiving chemotherapy within the last 3 months Patients receiving group B or C chemotherapy 3-12 months prior (see Appendix 2) Patients receiving radiotherapy within the last 6 months
Patients with a haematological diseases and stem cell transplant recipients	<ul style="list-style-type: none"> Allogeneic haematopoietic stem cell transplant (HSCT) recipients in the last 12 months or active graft vs host disease (GVHD) regardless of time from transplant (including HSCT for non-malignant diseases) Autologous HSCT recipients in the last 12 months (including HSCT for non-malignant diseases) Individuals with haematological malignancies who have

	<ul style="list-style-type: none"> ○ received chimaeric antigen receptor (CAR)-T cell therapy in the last 24 months, or ○ radiotherapy in the last 6 months ● Individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months except patients with chronic phase chronic myeloid leukaemia (CML) in molecular response or first or second line tyrosine kinase inhibitors (TKI). ● All patients with myeloma (excluding MGUS) or chronic B-cell lymphoproliferative disorders (e.g., chronic lymphocytic leukaemia, follicular lymphoma) or myelodysplastic syndrome (MDS) who do not fit the criteria above. ● All patients with sickle cell disease. ● Individuals with non-malignant haematological disorder (e.g., aplastic anaemia or paroxysmal nocturnal haemoglobinuria) receiving B-cell depleting systemic treatment (e.g., anti-CD20, anti-thymocyte globulin [ATG] and alemtuzumab) within the last 12 months.
Patients with renal disease	<ul style="list-style-type: none"> ● Renal transplant recipients (including those with failed transplants within the past 12 months), particularly those who: <ul style="list-style-type: none"> ○ Received B cell depleting therapy within the past 12 months (including alemtuzumab, rituximab [anti-CD20], anti-thymocyte globulin) ○ Have an additional substantial risk factor which would in isolation make them eligible for nMABs or oral antivirals ○ Not been vaccinated prior to transplantation ● Non-transplant patients who have received a comparable level of immunosuppression ● Patients with chronic kidney stage (CKD) 4 or 5 (an eGFR less than 30 ml/min/1.73m²) without immunosuppression
Patients with liver disease	<ul style="list-style-type: none"> ● Patients with cirrhosis Child's-Pugh class B and C (decompensated liver disease). ● Patients with a liver transplant ● Liver patients on immune suppressive therapy (including patients with and without liver cirrhosis) ● Patients with cirrhosis Child's-Pugh class A who are not on immune suppressive therapy (compensated liver disease)
Patients with immune-mediated inflammatory disorders (IMID)	<ul style="list-style-type: none"> ● IMID treated with rituximab or other B cell depleting therapy in the last 12 months ● IMID with active/unstable disease on corticosteroids, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate. ● IMID with stable disease on either corticosteroids, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate. IMID patients with active/unstable disease including those on biological monotherapy and on combination biologicals with thiopurine or methotrexate
Primary immune deficiencies	<ul style="list-style-type: none"> ● Common variable immunodeficiency (CVID) ● Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig) ● Hyper-IgM syndromes ● Good's syndrome (thymoma plus B-cell deficiency) ● Severe Combined Immunodeficiency (SCID) ● Autoimmune polyglandular syndromes/autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)

	<ul style="list-style-type: none"> • Primary immunodeficiency associated with impaired type I interferon signalling • X-linked agammaglobulinaemia (and other primary agammaglobulinaemias)
HIV/AIDS	<ul style="list-style-type: none"> • Patients with high levels of immune suppression, have uncontrolled/untreated HIV (high viral load) or present acutely with an AIDS defining diagnosis • On treatment for HIV with CD4 <350 cells/mm³ and stable on HIV treatment or CD4>350 cells/mm³ and additional risk factors (e.g., age, diabetes, obesity, cardiovascular, liver or renal disease, homeless, those with alcohol-dependence)
Solid organ transplant recipients	All recipients of solid organ transplants not otherwise specified above
Rare neurological conditions	<ul style="list-style-type: none"> • Multiple sclerosis • Motor neurone disease • Myasthenia gravis • Huntington's disease

⁷ For paediatric/adolescent patients (aged 12-17 years inclusive), paediatric multi-disciplinary team (MDT) assessment should be used to determine clinical capacity to benefit from the treatment

Table 1: Patient cohorts considered at highest risk from COVID-19 and to be prioritised for treatment with nMABs. NHS England and NHS Improvement coronavirus. Interim Clinical Commissioning Policy: Neutralising monoclonal antibodies or antivirals for non-hospitalised patients with COVID-19. Published on: 24 December 2021.

3) Providing treatment to this group of patients should not involve the GP...

The intention is that this group of patients is now centrally known. If a patient in this group returns a positive PCR test which has been registered against their NHS number, they will be contacted centrally within 24 hours and offered an appointment at their local COVID-19 medicine delivery unit (CMDU) where they will receive the appropriate treatment.

4) ... but some will always slip through the net

COVID-19 and the shielding programme revealed some of the limitations of coding and it is likely that there will be patients in the highest risk group who aren't contacted directly and will seek advice via their GP, having read about these treatments in the media. The letter being sent to the highest risk patients² also says that if they haven't been contacted within 24 hours of a positive PCR result they should call their GP surgery or 111, so we are likely to get calls about these treatments. This may happen if the test was not accurately registered against the patient's NHS number.

5) Referring to a CMDU should be easy

If you have a patient who you think needs to be seen at a CMDU then you can refer directly, via e-RS. Your local CMDU should be found within the infectious diseases menu and a list of all the CMDUs has also been published³. At the moment neither molnupiravir or sotrovimab can be prescribed by a GP or by any doctor outside of a CMDU; community pharmacies will not carry stocks of molnupiravir⁵.

6) Lower risk patients can access these drugs via the PANORAMIC trial

The Platform Adaptive trial of NOvel antiVIRals for eArly treatMent of Covid-19 In the Community trial⁴ is also open to those with PCR proven COVID-19 whose symptoms have started in the last five days, but unlike CMDU provision those who want to join the trial can have a wider range of medical co-morbidities. The range of co-morbidities accepted for the trial, listed below, is closer to the flu vaccination group than the shielding group and those aged 50 or over can join the trial even in the absence of a pre-existing condition.

<ul style="list-style-type: none"> • Chronic Respiratory disease (including chronic obstructive pulmonary disease (COPD), cystic fibrosis and asthma requiring at least daily use of preventative and/or reliever medication) • Chronic heart or vascular disease • Chronic kidney disease • Chronic liver disease • Chronic neurological disease (including dementia, stroke, epilepsy) 	<ul style="list-style-type: none"> • Severe and profound learning disability • Down's syndrome • Diabetes mellitus (Type I or Type II) • Immunosuppression: primary (e.g., Inherited immune disorders resulting from genetic mutations, usually present at birth and diagnosed in childhood) or Secondary due to disease or treatment (e.g., sickle cell, HIV, cancer, chemotherapy) 	<ul style="list-style-type: none"> • Solid organ, bone marrow and stem cell transplant recipients • Morbid obesity (BMI >35) • Severe mental illness • Care home resident • Judged by recruiting clinician or research nurse (registered medical practitioner or trained study nurse) to be clinically vulnerable
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Table 2: Who can join the PANORAMIC Study. The Platform Adaptive trial of NOvel antiVIRals for eArly treatMent of Covid-19 In the Community trial. University of Oxford. Reproduced with permission.

7) The trial involves a treatment group and a control group

Those who join the PANORAMIC trial will be assigned to usual NHS care, or usual NHS care plus molnupiravir – there is no group which will be given a placebo antiviral. Women who are pregnant or breastfeeding are excluded from the trial.

8) GPs have been encouraged to help recruit to the PANORAMIC trial...

NHSEI have written to GPs⁵ to ask for our help in recruiting to the PANORAMIC trial by reviewing the daily lists of positive tests and signposting those who fit the criteria to the PANORAMIC website or referring to a local GP recruitment hub if one is available.

9) ...but those who are eligible for CMDU treatment should not join the trial

Participants in the PANORAMIC trial have only a 50% chance of being in the treatment arm. Those who are in the highest risk group and are eligible for CMDU treatment should therefore go down that route rather than joining the trial.

10) The PANORAMIC trial may help with our understanding of long COVID and any future treatments

Those who take part in the PANORAMIC trial will have to answer questions online for 28 days (a phone call will be offered for those who do not have internet access) and will be contacted at three and six months to be asked about longer-term COVID-19 symptoms. It has been designed as a multi-platform trial so if any future treatments become available, they will be added to the same trial.

References

- 1) <https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2021/12/C1530-Interim-clinical-commissioning-policy-neutralising-monoclonal-antibodies-or-antivirals-for-non-hospitali.pdf>
- 2) <https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2021/12/C1480-patient-notification-letter-important-information-about-new-treatments-for-coronavirus.pdf>
- 3) <https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2021/12/cmdu-directory-v1.8.pdf>
- 4) <https://www.panoramictrial.org/participant-information>
- 5) <https://www.england.nhs.uk/coronavirus/publication/deployment-of-covid-19-treatments-for-highest-risk-non-hospitalised-patients/>