RC GP LEARNING

# Top tips on new treatments for COVID-19

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

For most of the pandemic, the primary care management of those with COVID-19 was supportive – if the patients weren't unwell enough to be admitted then we managed them in the same way as patients with other viral respiratory tract infections. This changed in early 2022 with the arrival of new community treatments which can be divided into two groups – antivirals and neutralising monoclonal antibodies (nMABs).

NICE[1] has approved two drugs for use in the community. The first is nirmatrelvir plus ritonavir (an antiviral, given orally) and it is approved for adults who do not need supplemental oxygen for COVID-19 and have an increased risk for progression to severe COVID-19. The second option is sotrovimab (an nMAB, given intravenously), which is approved for adults and children who are at least 12 and weigh at least 40kg, for whom nirmatrelvir plus ritonavir is contraindicated or unsuitable. They also have to have no need for supplemental oxygen and be in the group with an increased risk for progression to severe COVID-19.

## 2) Only the highest risk patients are eligible for these treatments

Patients who are a member of the 'highest risk group' should have all received a letter from NHSEI telling them about these new treatments. They were also initially sent a PCR test kit to keep at home so that they can test promptly if they have symptoms of COVID-19. Advice has now changed and they are advised to take a lateral flow test as soon as possible if they have any symptoms that could be COVID-19[2]. If positive, this should be uploaded online.

The group of patients defined as being in the 'highest risk group' is given in the table below – it is not identical to the group who were asked to shield during the pandemic, nor is it the same as the group who are usually invited for flu vaccinations.

The following patient cohorts were determined by an independent advisory group commissioned by the Department of Health and Social Care (DHSC)[1].

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| **Down's syndrome and other genetic disorders** | • All individuals with Down's syndrome or other chromosomal disorders known to affect immune competence. |
| **Solid cancer** | • Metastatic or locally advanced inoperable cancer.<br>• Lung cancer (at any stage).<br>• People receiving any chemotherapy (including antibody-drug conjugates), PI3K inhibitors or radiotherapy within 12 months. |

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| | • People who have had cancer resected within 3 months and who received no adjuvant chemotherapy or radiotherapy.<br>• People who have had cancer resected within 3 to 12 months and receiving no adjuvant chemotherapy or radiotherapy are expected to be at less risk (and thus less priority) but still at increased risk compared with the non-cancer populations. |
| **Haematological diseases and recipients of haematological stem cell transplant (HSCT)** | • Allogeneic HSCT recipients in the last 12 months or active graft versus host disease (GVHD) regardless of time from transplant (including HSCT for non-malignant diseases).<br>• Autologous HSCT recipients in the last 12 months (including HSCT for non-malignant diseases).<br>• Individuals with haematological malignancies who have received CAR-T cell therapy in the last 24 months, or until the lymphocyte count is within the normal range.<br>• Individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months, or radiotherapy in the last 12 months.<br>• All people who do not fit the criteria above, and are diagnosed with:<br>  • myeloma (excluding monoclonal gammopathy of undetermined significance [MGUS])<br>  • AL amyloidosis<br>  • chronic B-cell lymphoproliferative disorders (chronic lymphocytic leukaemia, follicular lymphoma)<br>  • myelodysplastic syndrome (MDS)<br>  • chronic myelomonocytic leukaemia (CMML)<br>  • myelofibrosis<br>  • any mature T-cell malignancy.<br>• All people with sickle cell disease.<br>• People with thalassaemia or rare inherited anaemia with any of the following:<br>  • severe cardiac iron overload (T2 * less than 10 ms)<br>  • severe to moderate iron overload (T2 * greater than or equal to 10 ms) plus an additional comorbidity of concern (for example, diabetes, chronic liver disease or severe hepatic iron load on MRI).<br>• Individuals with non-malignant haematological disorders (for example, aplastic anaemia or paroxysmal nocturnal haemoglobinuria) receiving B-cell depleting systemic treatment (for example, anti-CD20, anti-thymocyte globulin [ATG] and alemtuzumab) within the last 12 months. |
| **Renal disease** | • Renal transplant recipients (including those with failed transplants within the past 12 months), particularly those who have: |

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| | • received B-cell depleting therapy within the past 12 months (including alemtuzumab, rituximab [anti-CD20], ATG)<br>• an additional substantial risk factor that would in isolation make them eligible for monoclonals or oral antivirals.<br>• Non-transplant renal patients who have received a comparable level of immunosuppression.<br>• People with chronic kidney disease (CKD) stage 4 or 5 (an estimated glomerular filtration rate [eGFR] less than 30 ml per min per 1.73 m2) without immunosuppression. |
| **Liver diseases** | • People with cirrhosis Child-Pugh (CP) class A, B and C, whether receiving immune suppressive therapy or not. Those with decompensated liver disease (CP B and C) are at greatest risk.<br>• People with a liver transplant.<br>• People with liver disease on immune suppressive therapy (including people with and without cirrhosis). |
| **Solid organ transplant recipients** | Solid organ transplant recipients not in any of the above categories.<br><br>**Immune-mediated inflammatory disorders (diseases in which autoimmune or autoinflammation-based pathways are implicated in disease, for example, inflammatory arthritis, connective tissue diseases, inflammatory skin diseases, inflammatory gastrointestinal disease).**<br><br>• People who have received a B-cell depleting therapy (anti-CD20 drug, for example, rituximab, ocrelizumab, ofatumumab, obinutuzumab) in the last 12 months.<br>• People who have been treated with cyclophosphamide (IV or oral) in the 6 months prior to positive PCR or relevant COVID test.<br>• People who are on corticosteroids (equivalent to 10 mg or more per day of prednisolone) for at least the 28 days prior to positive PCR or relevant COVID test.<br>• People who are on biologics or small molecule JAK inhibitors.<br>• People who are on current treatment with mycophenolate mofetil, oral tacrolimus, azathioprine, mercaptopurine, or similar agents (for major organ involvement such as kidney, gastro-intestinal tract, liver, lung, brain), methotrexate (for interstitial lung disease or asthma only) and/or ciclosporin. No minimum dose threshold is suggested.<br>• People who are on current treatment (or within the last 6 months) with S1P modulators (fingolimod, ponesimod or siponimod), or alemtuzumab or cladribine within the last 12 months. |

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| | • People who exhibit at least one of: (a) uncontrolled or clinically active disease (that is, required recent increase in dose or initiation of new immunosuppressive drug or IM steroid injection or course of oral steroids within the 3 months prior to positive PCR or relevant COVID test); and/or (b) other high risk comorbidities (for example, body mass index [BMI] greater than 30, diabetes mellitus, hypertension, major organ involvement such as significant kidney, liver, nervous system or lung inflammation or significantly impaired renal, liver, nervous system and/or lung function). |
| **Respiratory** | • Asthma in people on oral corticosteroids (defined above). Any asthma patient taking immunosuppressants for their asthma including but not exclusively methotrexate, ciclosporin. Frequent exacerbations requiring 4 or more courses of prednisolone per year, usually 40 mg per day for 5 days or more.<br>• COPD on long term home non-invasive ventilation (NIV). Patients on long term oxygen therapy. People with moderate or severe disease (FEV1 less than or equal to 50% predicted) who have required 4 or more courses of prednisolone 30 mg for 5 days or greater in last 12 months.<br>• Interstitial lung disease (ILD) – all patients with idiopathic pulmonary fibrosis.<br>• Sub-types of ILD, for example, connective tissue disease related, sarcoidosis, hypersensitivity pneumonitis, NSIP (non-specific interstitial pneumonia) who have received a B-cell depleting therapy in last 12 months, or IV or oral cyclophosphamide in the 6 months prior to testing positive for COVID-19. Any ILD patient on current treatment with corticosteroids, mycophenolate mofetil, azathioprine, tacrolimus, cyclosporin or methotrexate. No minimum dose criteria.<br>• Any people with any type of ILD who may not be on treatment due to intolerance but has severe disease with an FVC predicted less than 60%.<br>• NIV and tracheostomy ventilated – all patients requiring this type of support regardless of the underlying disorder (which might include COPD, obesity hypoventilation syndrome, scoliosis, bronchiectasis, neurodisability and genetic muscular diseases [refer to neurology section]).<br>• Lung cancer patients, refer to 'Solid cancer' section above.<br>• Lung transplant patients (refer to solid organ transplant section).<br>• Pulmonary hypertension (PH): groups 1 and 4 from PH classification. |

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| **Immune deficiencies** | • Common variable immunodeficiency (CVID).<br>• Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig).<br>• Hyper-IgM syndromes.<br>• Good's syndrome (thymoma plus B-cell deficiency).<br>• Severe combined immunodeficiency (SCID).<br>• Autoimmune polyglandular syndromes or autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome).<br>• Primary immunodeficiency associated with impaired type 1 interferon signalling.<br>• X-linked agammaglobulinaemia (and other primary agammaglobulinaemias).<br>• Any person with secondary immunodeficiency receiving, or eligible for, immunoglobulin replacement therapy. |
| **HIV/AIDS** | • People with high levels of immune suppression, have uncontrolled or untreated HIV (high viral load) or present acutely with an AIDS defining diagnosis.<br>• People on treatment for HIV with CD4 less than 350 cells per mm3 and stable on HIV treatment or CD4 greater than 350 cells per mm3 and additional risk factors (for example, age, diabetes, obesity, cardiovascular, liver or renal disease, homeless, alcoholic dependency). |
| **Neurological disorders** | • Conditions associated with neuromuscular respiratory failure requiring chronic ventilatory support:<br>  • motor neurone disease<br>  • Duchenne muscular dystrophy.<br>• Conditions that require use of specific immunotherapies:<br>  • multiple sclerosis (MS)<br>  • myasthenia gravis (MG)<br>  • other immune-mediated disorders.<br>• Dementia, neurodegenerative and neuroimmune disorders when associated with severe frailty (for example, levels 7 or 8 on Clinical Frailty Scale, as part of a personalised care plan):<br>  • Alzheimer's disease, vascular disease, Lewy body disease, or frontotemporal atrophy<br>  • Parkinson's disease<br>  • Huntington's disease<br>  • progressive supranuclear palsy and multiple system atrophy<br>  • motor neurone disease<br>  • multiple sclerosis and other immune-mediated neurological disorders. |
| **Children and young people (CYP) at substantial risk** | Complex life-limiting neurodisability with recurrent respiratory infections or compromise. |

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| **CYP at significant risk if 2 or more of these risk factors are present** | <u>Primary immunodeficiency:</u><br>▪ common variable immunodeficiency (CVID).<br>▪ primary antibody deficiency on immunoglobulin (or eligible for immunoglobulin replacement).<br>▪ hyper-IgM syndromes.<br>▪ Good's syndrome (thymoma plus B-cell deficiency)<br>▪ severe combined immunodeficiency (SCID).<br>▪ autoimmune polyglandular syndromes or autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome).<br>▪ primary immunodeficiency associated with impaired type 1 interferon signalling.<br>▪ X-linked agammaglobulinaemia (and other primary agammaglobulinaemias).<br><br><u>Secondary immunodeficiency:</u><br>▪ HIV CD4 count less than 200 cells per mm3.<br>▪ solid organ transplant.<br>▪ haematological stem cell transplant (HSCT) within 12 months, or with graft versus host disease (GVHD).<br>▪ CAR-T cell therapy in last 24 months.<br>▪ induction chemotherapy for acute lymphoblastic leukaemia (ALL), non-Hodgkin's lymphoma, chemotherapy for acute myeloid leukaemia (AML), relapsed and/or refractory leukaemia or lymphoma.<br><br>Immunosuppressive treatment:<br>▪ chemotherapy within the last 3 months.<br>▪ cyclophosphamide within the last 3 months.<br>▪ corticosteroids greater than 2 mg per kg per day for 28 days in last 4 weeks.<br>▪ B-cell depleting treatment in the last 12 months.<br><br>Other conditions:<br>▪ high body mass index (BMI; greater than 95th centile).<br>▪ severe respiratory disease (for example, cystic fibrosis or bronchiectasis with FEV1 less than 60%).<br>▪ tracheostomy or long-term ventilation.<br>▪ severe asthma (paediatric intensive care unit [PICU] admission in 12 months).<br>▪ neurodisability and/or neurodevelopmental disorders.<br>▪ severe cardiac disease.<br>▪ severe chronic kidney disease.<br>▪ severe liver disease.<br>▪ sickle cell disease or other severe haemoglobinopathy.<br>▪ trisomy 21.<br>▪ complex or chromosomal genetic or metabolic conditions associated with significant comorbidity.<br>▪ multiple congenital anomalies associated with significant comorbidity. |

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| | ▪ bronchopulmonary dysplasia – decisions should be made taking into account degree of prematurity at birth and chronological age. |

**Table 1**: Patient cohorts considered at highest risk from COVID-19 and to be prioritised for treatment with nMABs. Nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19. National Institute for Health and Care Excellence (NICE) Technology Appraisal (TA), 878, March 2023, last updated: 13 March 2024.

### 3) Commissioning of these treatments in England has changed.

When these treatments were first offered they were centrally commissioned - a high-risk patient in England who uploaded a positive COVID-19 test would be contacted directly by a COVID-19 medicine delivery unit (CMDU). Commissioning is now done locally[4] and patients need to make contact themselves. Depending on local arrangements, they may do this via the GP, via their hospital consultant, via 111 or by contacting the CMDU directly. As time passes, it may be that some areas choose to use a mechanism other than a CMDU to deliver care. It would be sensible to find out how care is offered in your area, before you need to signpost a patient to it. The provision of these medications is arranged differently in Scotland[5], Wales[6], and Northern Ireland[7].

In April 2024, the BMA issued guidance in this area, in response to suggestions from some ICBs that COVID-19 therapeutics should routinely be given by GPs. The BMAs position is that provision of therapeutics for COVID-19 should not be done by primary care, unless this is part of an appropriately commissioned service[9].

### 4) Some patients may not realise that they are at high risk.

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 are unaware of their risk, particularly if they have only recently acquired the condition which makes them high risk. If you speak to such a patient then you can let them know that they are at high risk and should have some COVID-19 tests at home, and how to access treatment in your area.

### 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. At the moment, none of these drugs can be prescribed by a GP or by any doctor outside of a CMDU and they are not stocked by community pharmacies. Some of them have significant drug interactions, so if referring from primary care it is important to provide a list of current medication.

### 6) The PANORAMIC trial[8] is now closed

The **P**latform **A**daptive trial of **NO**vel antivi**R**als for e**A**rly treat**M**ent of Covid-19 in the Community (PANORAMIC) was open to those with COVID-19 who did not fit the criteria for treatment from a CMDU but had a wider range of co-morbidities or were aged over 50. It

offered usual care or usual care plus a COVID-19 therapeutic. The group eligible for this trial were more similar to the group who are routinely offered flu vaccination, than to the shielding group. The trial is now closed to recruitment but will continue to collect data until September 2024. It is hoped that the date from PANORAMIC will inform our understanding about longer-term COVID-19 symptoms, as well as the use of antivirals, as participants will be contacted for six months after their enrolment in the trial.

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