Southern Health and Social Care Trust

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Reference Guide for the Management of Adults and Young People (age 12-17) in Community Setting who have an increased risk for progression to severe COVID-19 and require access to Antivirals or nMABs

Title:	Reference Guide for the Management of Adults and Young People (age 12-17) in Community Setting who have an increased risk for progression to severe COVID-19 and require access to Antivirals or nMABs
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Background

COVID-19 is a respiratory illness caused by the novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)

This reference guide for management of adult and young people (age 12-17) in community setting who have increased risk for progression to severe COVID-19 does not replace specialist guidance. The evidence base on treatment of COVID-19 is rapidly developing. You are advised to stay up-to-date with the latest developments.

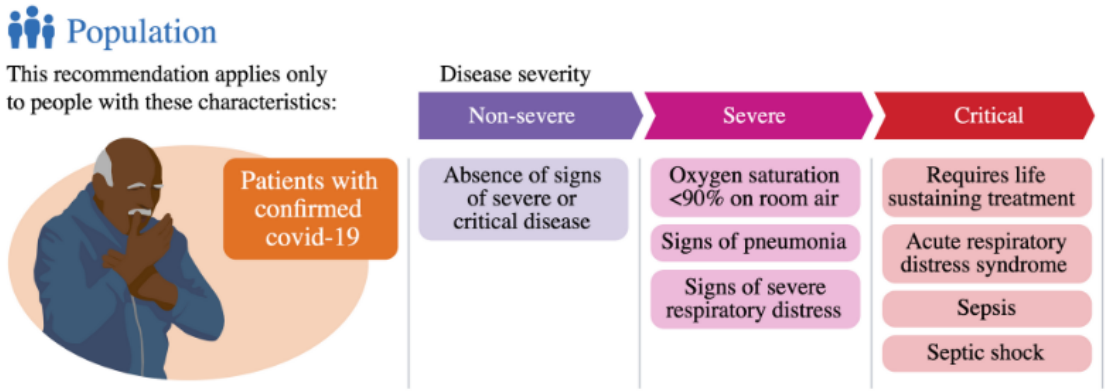
Disease Progression

- Incubation period 1-14 days
- Majority develop symptoms within 5-6 days
- Progression to pneumonia in 5-7 days
- Highest risk of respiratory failure at around 7-10 days from symptom onset

Signs and Symptoms

- Fever (may be absent).
- Fatigue, myalgia, anorexia, anosmia, ageusia.
- Lower respiratory symptoms – SOB, cough (new and continuous).
- Silent hypoxia" – respiratory compromise (Sats < 94%) without SOB especially elderly.
- Other non-specific symptoms include sore throat, headache, nasal congestion, diarrhoea, nausea, vomiting.

WHO definitions of disease severity for COVID-19



Infographic co-produced by the BMJ and MAGIC; designer Will Stahl-Timmins (see BMJ Rapid Recommendations).

Caution: The GDG noted that the oxygen saturation threshold of 90% to define severe COVID-19 was arbitrary, and should be interpreted cautiously when defining disease severity. For example, clinicians must use their judgment to determine whether a low oxygen saturation is a sign of severity or is normal for a given patient with chronic lung disease. Similarly, clinicians may interpret a saturation of 90–94% on room air as abnormal in the patient with normal lungs, and as an early sign of severe disease in patients with a downward clinical trajectory. Generally, in cases where there is doubt, the GDG suggested erring on the side of considering disease as severe.

Eligibility criteria

Non-hospitalised patients are eligible for treatment if the following ***initial*** criteria are met:

- SARS-CoV-2 infection is confirmed by either
    - Lateral flow test (registered via gov.uk) OR
    - Polymerase chain reaction (PCR) testing

AND

- Symptomatic with COVID-19 and showing no signs of clinical recovery

AND

- The patient is a member of a 'highest' risk group (see below)

Risk factors for progression to severe COVID-19 in adults

List available at: 5 Supporting information on risk factors for progression to severe COVID-19 | Casirivimab plus imdevimab, nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19 | Guidance | NICE

Risk factors for progression to severe COVID-19 in adults defined by the independent advisory group commissioned by the Department of Health and Social Care (June 2023)

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
- lung cancer (at any stage)
- people receiving any chemotherapy (including antibody-drug conjugates), PI3K inhibitors or radiotherapy within 12 months
- people who have had cancer resected within 3 months and who received no adjuvant chemotherapy or radiotherapy
- 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)
- autologous HSCT recipients in the last 12 months (including HSCT for non-malignant diseases)
- 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
- individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months, or radiotherapy in the last 12 months
- all people who do not fit the criteria above, and are diagnosed with:
    - myeloma (excluding monoclonal gammopathy of undetermined significance [MGUS])
    - AL amyloidosis
    - chronic B-cell lymphoproliferative disorders (chronic lymphocytic leukaemia, follicular lymphoma)

    - myelodysplastic syndrome (MDS)
    - chronic myelomonocytic leukaemia (CMML)
    - myelofibrosis
    - any mature T-cell malignancy
- all people with sickle cell disease
- people with thalassaemia or rare inherited anaemia with any of the following:
    - severe cardiac iron overload (T2 * less than 10 ms)
    - 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)
- 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:
    - received B-cell depleting therapy within the past 12 months (including alemtuzumab, rituximab [anti-CD20], ATG)
    - an additional substantial risk factor which would in isolation make them eligible for monoclonals or oral antivirals
- non-transplant renal patients who have received a comparable level of immunosuppression
- patients with chronic kidney disease (CKD) stage 4 or 5 (an estimated glomerular filtration rate [eGFR] less than 30 ml per min per 1.73 m^2) 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
- people with a liver transplant
- 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

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)

- people who have received a B-cell depleting therapy (anti-CD20 drug, for example, rituximab, ocrelizumab, ofatumab, obinutuzumab) in the last 12 months
- people who have been treated with cyclophosphamide (IV or oral) in the 6 months prior to positive PCR or relevant COVID test
- people who are on corticosteroids (equivalent to or greater than 10 mg per day of prednisolone) for at least the 28 days prior to positive PCR
- people who are on biologics or small molecule JAK inhibitors
- 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
- 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
- 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); 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
- 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
- interstitial lung disease (ILD) – all patients with idiopathic pulmonary fibrosis
- 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
- 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%
- 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]).
- lung cancer patients, refer to 'Solid cancer' section above
- lung transplant patients (refer to solid organ transplant section)
- pulmonary hypertension (PH): groups 1 and 4 from PH classification

Immune deficiencies

- 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 or autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)
- primary immunodeficiency associated with impaired type 1 interferon signalling
- X-linked agammaglobulinaemia (and other primary agammaglobulinaemias)
- 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
- people on treatment for HIV with CD4 less than 350 cells per mm^3 and stable on HIV treatment or CD4 greater than 350 cells per mm^3 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:
    - motor neurone disease
    - Duchenne muscular dystrophy
- Conditions that require use of specific immunotherapies:
    - multiple sclerosis (MS)
    - myasthenia gravis (MG)
    - other immune-mediated disorders
- 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):
    - Alzheimer's disease, vascular disease, Lewy body disease, or frontotemporal atrophy
    - Parkinson's disease
    - Huntington's disease
    - progressive supranuclear palsy and multiple system atrophy
    - motor neurone disease
    - multiple sclerosis and other immune-mediated neurological disorders

Risk factors for progression to severe COVID-19 in young people aged 12 to 17 years

Pathway for PCR positive symptomatic cases aged older than 12 and younger than 18 years, greater than 40 kg weight, and clinical concern: defined by the independent advisory group commissioned by the Department of Health and Social Care (March 2023)

Non-hospitalised individuals in the older than 12 and younger than 18 years age range considered at high risk from COVID-19 and to be prioritised for consideration of treatment with neutralising monoclonal antibodies when symptomatic and SARS-CoV-2 PCR positive. Concerned clinicians should refer for regional multidisciplinary team (MDT) case discussion through local established pathways, who will confirm eligibility and consider risk benefit and whether to proceed with offer of treatment.

Children and young people (CYP) at substantial risk

Complex life-limiting neurodisability with recurrent respiratory infections or compromise.

CYP at significant risk if 2 or more of these risk factors are present

Primary immunodeficiency:

- common variable immunodeficiency (CVID)
- primary antibody deficiency on immunoglobulin (or eligible for immunoglobulin replacement)
- hyper-IgM syndromes
- Good's syndrome (thymoma plus B-cell deficiency)
- severe combined immunodeficiency (SCID)
- autoimmune polyglandular syndromes or autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)
- primary immunodeficiency associated with impaired type 1 interferon signalling
- X-linked agammaglobulinaemia (and other primary agammaglobulinaemias)

Secondary immunodeficiency:

- HIV CD4 count less than 200 cells per mm^3
- solid organ transplant
- haematological stem cell transplant (HSCT) within 12 months, or with graft versus host disease (GVHD)
- CAR-T cell therapy in last 24 months
- induction chemotherapy for acute lymphoblastic leukaemia (ALL), non-Hodgkin's lymphoma, chemotherapy for acute myeloid leukaemia (AML), relapsed and/or refractory leukaemia or lymphoma

Immunosuppressive treatment:

- chemotherapy within the last 3 months
- cyclophosphamide within the last 3 months
- corticosteroids greater than 2 mg per kg per day for 28 days in last 4 weeks
- B-cell depleting treatment in the last 12 months

Other conditions:

- high body mass index (BMI; greater than 95th centile)
- severe respiratory disease (for example, cystic fibrosis or bronchiectasis with FEV1 less than 60%)
- tracheostomy or long-term ventilation
- severe asthma (paediatric intensive care unit [PICU] admission in 12 months)
- neurodisability and/or neurodevelopmental disorders
- severe cardiac disease
- severe chronic kidney disease
- severe liver disease
- sickle cell disease or other severe haemoglobinopathy
- trisomy 21
- complex or chromosomal genetic or metabolic conditions associated with significant comorbidity
- multiple congenital anomalies associated with significant comorbidity
- bronchopulmonary dysplasia – decisions should be made taking into account degree of prematurity at birth and chronological age
- infants less than 1 year with congenital heart disease (CHD):
    - cyanotic CHD
    - haemodynamically significant acyanotic CHD and history of prematurity
    - those due for corrective surgery, to avoid complications or delay due to SARS-CoV-2 infection

Treatment options are:

First-line:	Nirmatrelvir plus ritonavir (Paxlovid®)	Antiviral
Second-line:	Sotrovimab	nMAB
Third-line:	Remdesivir	Antiviral
Fourth-Line	Molnupiravir	Antiviral

Please note:

Nirmatrelvir plus ritonavir (Paxlovid®), Sotrovimab and Molnupiravir are all licensed to be commenced within 5 days of symptom onset.

Remdesivir is licensed in patients who do not require supplemental oxygen and are at increased risk for progressing to severe COVID-19 within 7 days of symptom onset.

However off-label use of Nirmatrelvir plus ritonavir (Paxlovid®) and sotrovimab may be commenced of days 6 or 7 post symptom onset if deemed clinically appropriate by the prescriber. This is not referenced in COVID-19 rapid guideline: Managing COVID-19 published 23 March 2021 updated 22/06/2023 Accessed 19/07/2023 but is referenced in the Interim Clinical Commissioning Policy: Treatments for non-hospitalised patients with COVID-19. Publication date: 28th November 2022.

If prescribing Nirmatrelvir plus ritonavir (Paxlovid®) or sotrovimab on day 6-7 post symptom onset patients should be advised that this is “Off-label”.

Contact Details for Urgent Care Triaging Doctors

Urgent care co-ordinator	(028 375) 65207

Urgent Care Triaging Doctors

Dr Rosemary Sloan (Clinical Lead for Urgent Care)	Rosemary.Sloan@sourtherntrust.hscni.net
Dr Peter Wilson	Peter.Wilson@southerntrust.hscni.net
Dr Rachel Alister	rachel.alister@southerntrust.hscni.net
Dr David Burke	david.burke@southerntrust.hscni.net
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Dr Janine Redmond	Janine.Redmond@southerntrust.hscni.net
Dr Chike Aniekwena	Chike.Aniekwena@southerntrust.hscni.net
These Doctors are employed by the SHSCT and are therefore able to prescribe on SHSCT forms.	

Pharmacy information

Clinical queries

It is the responsibility of the prescribing clinician to review the patient's medications, both prescribed and non-prescribed and screen for interactions.

The University of Liverpool COVID-19 Drug Interaction website includes useful prescribing resources and an interaction checker, which is available at:

Liverpool COVID-19 Interactions (covid19-druginteractions.org)

Additional queries may be directed to Pharmacy Medicines Information

Email	MEDICINESINFO.CAH@southerntrust.hscni.net
Availability	Monday to Friday 8.30am to 4.30pm (excluding bank holidays)
Telephone	028 376 **63880 OPTION 3** **OR** 028375 63890 **OR** 02837563883

Calls should not be made to the ON-CALL pharmacy service or evening Extended Hours Service regarding outpatient antivirals or nMABs.

Weekend and bank holiday teams should only be contacted via the dispensary (028 37663880 option 1) in exceptional circumstances for clinical queries (e.g. when patient is day 7 of symptoms and treatment must be initiated same day).

Dispensing

Deliver original prescriptions (including fluid balance charts if required) to Pharmacy, CAH reception to be dispensed.

Outside of Pharmacy opening hours place prescriptions in the black post box. Envelopes should be marked as "Dispensary, COVID prescriptions" and not be marked for the attention of any one individual.

Paxlovid and Molnupiravir

Prescriptions for oral COVID-19 treatments (Paxlovid and molnupiravir) that are received before 3pm will be clinically screened and dispensed same day. After 3pm it will be next day.

For oral treatment Pharmacy will contact the patient/family to notify them when their prescription is ready for collection.

Sotrovimab and Remdesivir

Clinics for administration of sotrovimab and remdesivir should be pre-planned.

Only in exceptional circumstances will prescriptions be dispensed for same day administration.

Southern Area Hospice

Refer to full Southern Area Hospice (SAH) Pathway for full pathway

- COVID-19 positive patients in SAH to be referred to Urgent.Centre@southerntrust.hscni.net for triage.
- Triage form and Prescription to be written by Urgent Care Team.
- Original script to be delivered to Craigavon Area Hospital pharmacy.
- CAH or DHH Pharmacy will dispense the medication for the individual patient. If dispensed in CAH, transport will send this to DHH Pharmacy.
- Medication to be collected by SAH driver at DHH Pharmacy
- Note Sotrovimab is a fridge line and cold chain must be in place.
- Medications to be prescribed on Kardex in Southern Area Hospice by prescriber in Southern Area Hospice.

Accessing COVID-19 treatment elsewhere in UK and Ireland

If you're away from home and travelling elsewhere in the UK and need to access COVID-19 treatments, find out how to below.

England

In England, contact the nearest GP, or Out of Hours GP service via NHS 111 to allow you to access treatment within the recommended time.

Wales

In Wales, contact the nearest GP, or Out of Hours GP service via NHS 111 to allow you to access treatment within the recommended time.

Further information is available at:

- Antiviral services across Wales - Welsh Medicines Advice Service(external link opens in a new window / tab)

Scotland

If you are visiting Scotland and need access to COVID-19 treatments, you should contact the nearest Health Board to be assessed for your eligibility to access treatment.

The Health Board single point of contact details are available on the NHS Inform website(external link opens in a new window / tab).

If you need access to COVID-19 treatment out of hours, you should still use the Health Board single point of contact phone numbers on the NHS Inform website.

In some instances, you may reach an answering machine and be asked to leave a message. If so, you will receive a call back from the relevant Health Board.

Health Board contact numbers are not for use if you're seeking urgent medical advice or have a general health query.

Republic of Ireland

If you are travelling to the Republic of Ireland, you can access treatment by contacting the nearest GP, who can prescribe treatment for you in the same way to that available for their own patients.

References

WHO (2021). Living guidance for clinical management of COVID-19. Available at: WHO-2019-nCoV-clinical-2021.2-eng.pdf Accessed: 24/07/2023

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NI formulary. Managed Entry Decisions. Casirivimab/imdevimab (Ronapreve®), nirmatrelvir/ritonavir (Paxlovid®), sotrovimab (Xevudy®) and tocilizumab (RoActemra®). Last updated: 12/05/2023 Available at: Managed Entry Decisions | NI Formulary (hscni.net) Accessed: 24/07/2023

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NHS England: Rapid Policy Statement. Interim Clinical Commissioning Policy: Remdesivir and molnupiravir for non-hospitalised patients with COVID-19. Published: 11/05/2023 Available at: Microsoft Word - PRN00453_Rapid Policy Statement - Interim Clinical Commissioning Policy - remdesivir and molnupiravir for non-hospitalised patients with COVID-19_May 2023 (england.nhs.uk) Accessed: 24/07/2023

Updates

Date	Reason	Action
13/11/2023	Email address should be urgent.centre@southerntrust.hscni.net Not Urgent.care@southertrust.hscni.net	Email address amended by Anne McCord
13/11/2023	Email address updates for Dr Alister, Dr Murty, Dr Pope and Dr Aniekwena	Email addresses updated by Anne McCord