DRUG TREATMENTS OF COVID-19 IN HOSPITALISED ADULT PATIENTS

UNCONTROLLED IF PRINTED.

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BACKGROUND

These guidelines outline the available therapies for symptomatic hospitalised adult patients with COVID-19 within NHS Lothian. This document is based on the guidelines NG191 published by the National Institute for Health a Care Excellence (NICE) [last updated 08 May 2024; last accessed 07 June 2024] which were adopted by the Scottish Medicines Consortium and describes the local implementation. It will be updated if this is superseded or if the evidence base for these therapies changes significantly.

However, NHS Lothian has made several local adaptations and in some parts deviates from national guidelines. Some key differences between the NHS Lothian and the national guidelines are:

- Nirmatrelvir/ritonavir (Paxlovid®), molnupiravir (Lagevrio®), or remdesivir (Veklury®) will **only be available for patients at increased risk for progression to severe COVID-19**, as defined in section 5 of NICE's technology appraisal guidance (TA878) on nirmatrelvir plus ritonavir, sotrovimab and tocilizumab [https://www.nice.org.uk/guidance/ta878/chapter/5-Supporting-information-on-risk-factors-for-progression-to-severe-COVID19 ; last accessed 12 June 2024]. A list of eligible condition can also be found in this document.
- However, NHS Lothian will not expand the availability of nirmatrelvir/ritonavir (Paxlovid®) to additional groups currently defined by NICE beyond the above list (TA878).
- Furthermore, NHS Lothian will **not** automatically include the following criteria listed in TA878 for the use of remdesivir (Veklury®), molnupiravir (Lagevrio®) or nirmatrelvir/ritonavir (Paxlovid®):
    - body mass index [BMI] greater than 30
    - diabetes mellitus
    - hypertension
    - Where the responsible consultant looking after any patient who falls into these categories wishes to pursue antiviral treatment a further discussion with the infectious diseases consultant on-call is required.
- A monoclonal antibody, sotrovimab, delivered intravenously is accepted for restricted use within the NHS in England, Scotland and Wales for the treatment of symptomatic adults, and adolescents (aged 12 years and over and weighing at least 40kg) with acute COVID-19 infection who do not require oxygen supplementation and who are at increased risk of progressing to severe COVID-19 infection. However, **sotrovimab is not currently routinely available in Lothian**.
- In NHS Lothian, for hospitalised adult inpatients not requiring oxygen with symptomatic COVID-19 nirmatrelvir/ritonavir (Paxlovid®) can be considered for eligible highest-risk patients as first-line therapy (see list of risk factors for progression to severe COVID-19 in adults). Molnupiravir (Lagevrio®) will be offered to eligible highest-risk patients who cannot receive nirmatrelvir/ritonavir (Paxlovid®). For highest-risk patients not on oxygen, remdesivir (Veklury®) will generally only be offered if neither nirmatrelvir/ritonavir nor molnupiravir can be given.
- For all antivirals, some indications from NICE TA878 require specific approval by an infectious diseases consultant (see above and remdesivir section for details).

These decisions have been made locally following review of the clinical evidence and cost-effectiveness predictions by Infectious Diseases Consultants, Medical Director (Acute), Director of Pharmacy, and has been supported by the Executive Leadership Team and Drugs and Therapeutics Committee.

This document covers the following therapeutics:

- Antivirals
    - Nirmatrelvir plus ritonavir (Paxlovid®)
    - Molnupiravir (Lagevrio®)
    - Remdesivir (Veklury®)
- Corticosteroids
- Interleukin-6 inhibitors
    - Tocilizumab
- JAK inhibitors
    - Baricitinib

TREATMENT OVERVIEW

This document is a guide of the available drug treatments for adult patients hospitalised with COVID-19. It does currently not cover supportive treatments, e.g. oxygen, thromboprophylaxis, pain relief, anxiolytics, etc.

Each section contains details regarding indications, contraindications, cautions, dosing & administration, and advice relating to the pregnant patient. But for full details, the individual summaries of product characteristics should be consulted. Below figure 1 gives a quick overview of the available therapeutic management based on disease severity. Please note that the graphic does not contain exact indications or contraindications and hence should not be used as a standalone guide, but rather as an overview of which treatments to consider in which scenario. For more details see the specific chapters for each drug.

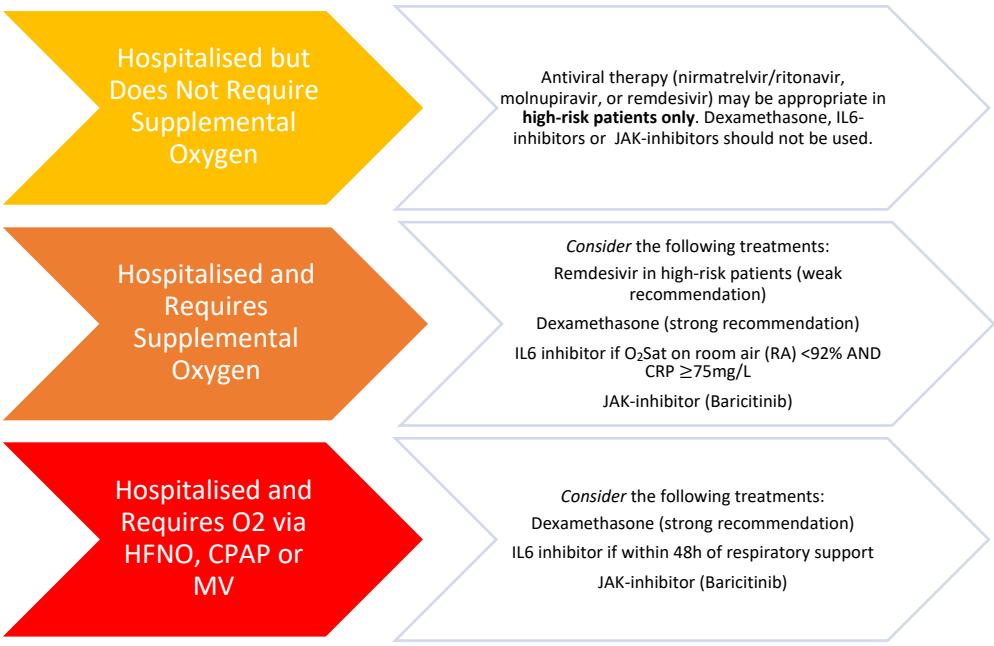

Figure 1: Overview of the therapeutic drug management of adult patients hospitalised with COVID-19 in NHS Lothian based on disease severity. For more details, please see the chapters for each drug.

Figure 2 provides an illustrative flow diagram of the treatments in various scenarios. It is important to refer to the exact indications and contraindications in the respective summaries of product characteristics and the text below for each drug.

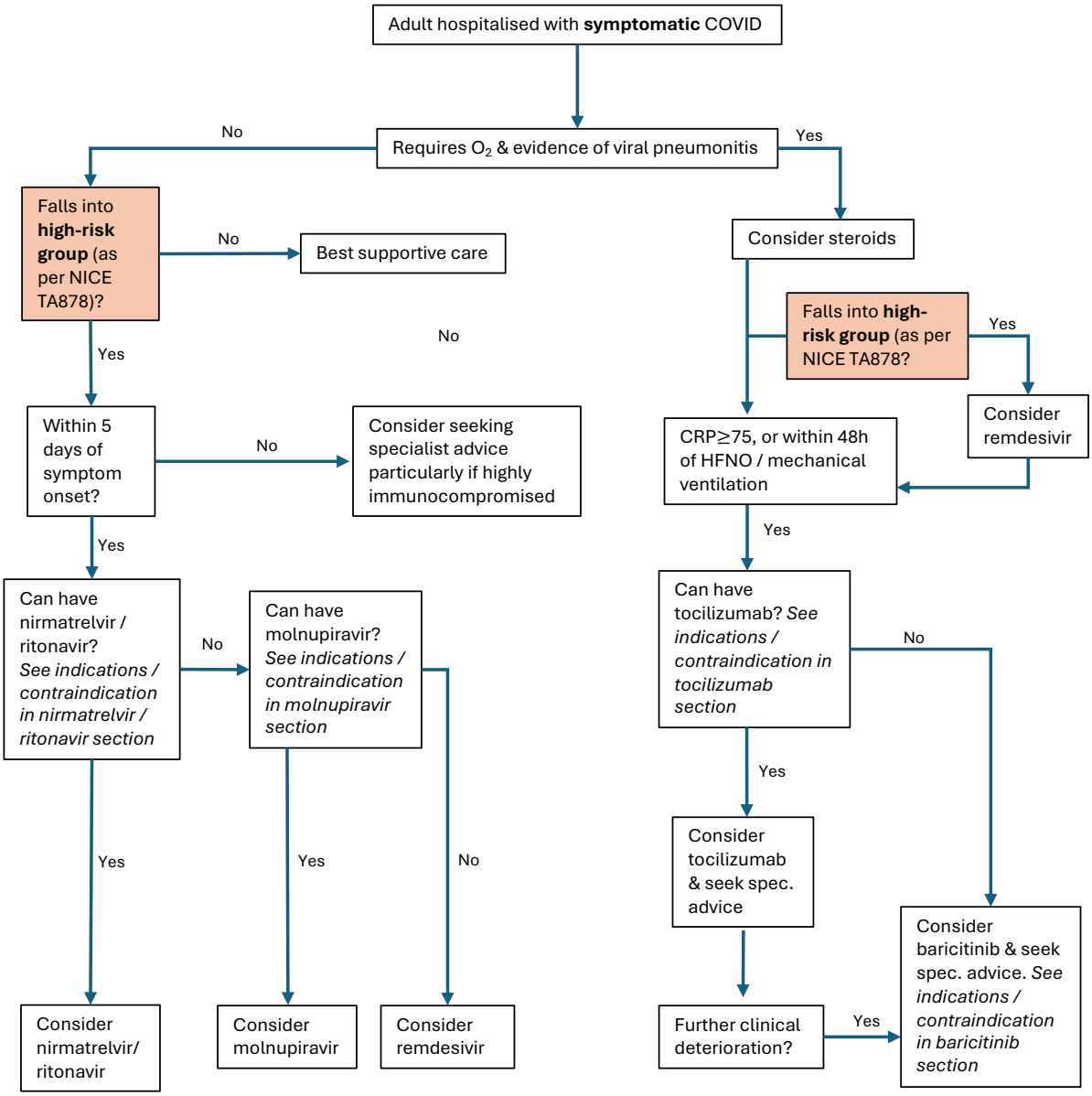

Figure 2: Simplified illustrative decision flow diagram for COVID-19 therapeutics for adult patients hospitalised with symptomatic COVID-19 in NHS Lothian. For full list of indications please see individual drug sections. While generic drug names are referred to in the diagram, some are better known under their brand name: nirmatrelvir/ritonavir (Paxlovid®), molnupiravir (Lagevrio®), remdesivir (Veklury®), tocilizumab (RoActemra® or Tyenne®), baricitinib (Olumiant®). Please note that this decision flow chart applies to NHS Lothian and may not be applicable in other health boards. For severely unwell patients and those who fall outside defined criteria consider seeking specialist infectious diseases advice.

RISK FACTORS FOR PROGRESSION TO SEVERE COVID-19 IN ADULTS

Since the start of the pandemic the landscape of COVID-19 diseases has changed. The SARS-CoV2 virus continues to evolve and mutate. And much of the UK population has now been vaccinated. Therefore, admissions to hospital with severe disease are now far less common than in early 2020.

Several therapeutics against COVID-19 (remdesivir, molnupiravir and nirmatrelvir/ritonavir) have shown highest efficacy when used in patients at highest risk for progression to severe COVID-19 and should now largely only be used in this group of individuals.

Risk factors for progression to severe COVID-19 in adults were defined by the independent advisory group commissioned by the Department of Health and Social Care (June 2023). They can be found below and in Technology Appraisal Guidance (TA878) [https://www.nice.org.uk/guidance/ta878/chapter/5-Supporting-information-on-risk-factors-for-progression-to-severe-COVID19; last accessed 12 June 2024].

This list may be subject to change, and it remains the responsibility of the prescribing clinician to access the latest guidance and list on the website of the National Institute for Health and Care Excellence (NICE).

Marked in red are conditions where further discussion with the infectious diseases consultant on-call is required before antivirals (nirmatrelvir/ritonavir, molnupiravir, or remdesivir) can be used in NHS Lothian.

RISK FACTORS FOR PROGRESSION TO SEVERE COVID-19 IN ADULTS (AGED 18 AND OVER) 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 that would in isolation make them eligible for monoclonals or oral antivirals
- Non-transplant renal patients who have received a comparable level of immunosuppression
- 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
- 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, ofatumumab, 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 10 mg or more per day of prednisolone) for at least the 28 days prior to positive PCR or relevant COVID test
- 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 or relevant COVID test); and/or (b) other high risk comorbidities (for example, body mass index [BMI] greater than 30, diabetes mellitus, hypertension[1], 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
- 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

[1] For the indications highlighted in red approval by the infectious diseases consultant on-call is required.

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 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:
    - 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

ANTIVIRALS

NIRMATRELVIR AND RITONAVIR (PAXLOVID®)

Nirmatrelvir plus ritonavir (Paxlovid®) is recommended as an option for treating COVID-19 in adults, only if they:

- are within 5 days of symptoms onset ***and***
- do not need supplemental oxygen for COVID-19 ***and***
- are at an **increased risk for progression to severe COVID-19**, as defined in section 5 of NICE's technology appraisal guidance (TA878) on nirmatrelvir plus ritonavir, sotrovimab and tocilizumab. The list of eligible conditions can also be found in this document

DOSING

The recommended dosage is 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.

POSOLOGY, CONTRAINDICATIONS AND CAUTIONS

RENAL IMPAIRMENT

In patients with moderate renal impairment (CKD stage 3), the dose of nirmatrelvir/ritonavir should be reduced to nirmatrelvir/ritonavir 150 mg/100 mg (1 tablet of each) twice daily for 5 days:

- Moderate renal impairment (eGFR 30 to 59 mL/min): Half dose: nirmatrelvir 150mg (ONE tablet instead of TWO with full dose ritonavir)
- Severe renal impairment (eGFR <30mL/min): Not recommended

For full prescribing information including contraindications and cautions please see SmPC and BNF. Please note that Paxlovid® can interact with many other medications. It is therefore vital that a drug-drug interaction check is undertaken prior to prescribing Paxlovid®. A useful interaction checker can be found at: https://covid19-druginteractions.org/checker

MOLNUPIRAVIR (LAGEVRIO®)

Consider a 5-day course of molnupiravir for adults with COVID-19 who:

- do not need supplemental oxygen for COVID-19 ***and***

- are within 5 days of symptom onset ***and***
- are thought to be at high risk of progression to severe COVID-19 (See list included in this document and NICE TA878) ***and***
- where nirmatrelvir/ritonavir (Paxlovid®) is contraindicated or unsuitable.

When assessing the person, take into account their likely response to any vaccinations already given, any comorbidities or risk factors, and whether their condition is deteriorating.

Do not offer molnupiravir to children and young people aged under 18, or pregnant women.

DOSING

The recommended dose of molnupiravir is 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days.

For contraindications, cautions and interactions please consult the SmPC and BNF.

REMDESIVIR (VEKLURY®)

INDICATIONS

Remdesivir is recommended as an option for treating COVID-19 in hospitals in:

- adults, **only if they have a high risk of serious illness** (risk factors as defined in section 5 of NICE's technology appraisal guidance on nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19). A list of eligible condition is included in this document.

Please note that NHS Lothian will not automatically include the following criteria mentioned in TA878 for the use of remdesivir:

- body mass index [BMI] greater than 30
- diabetes mellitus
- hypertension

Where the responsible consultant looking after any patient who falls into these categories wishes to pursue antiviral treatment a further discussion with the infectious diseases consultant on-call is required.

Please note these guidelines only apply to adults aged 18 and over. For babies, children and young people please refer to NICE guidance and take advice from paediatrics.

Remdesivir is likely to work best early in the disease process and should therefore not generally be started beyond 10 days after the onset of symptoms.

INITIATION OF TREATMENT

- Remdesivir is an expensive treatment, and the principle of cost-effective prescribing should be followed.
- The decision to initiate treatment with remdesivir should be made by the admitting care consultant. The decision to treat with remdesivir is not an emergency and should be made judiciously after assessment and in a timely manner.
- Remdesivir should not be initiated in patients who present to hospital and are unlikely to survive (determined by clinical judgement).
- Remdesivir should **generally not be initiated** in patients who present to hospital **more than 10 days after symptom onset.** Where use is considered beyond 10 days of symptoms onset (e.g. in heavily immunocompromised patients) this should be discussed with the infectious diseases consultant on-call.
- Where the only eligibility criteria from TA878 are either BMI>30, diabetes mellitus, or hypertension approval from the infectious diseases consultant on-call is required.

DURATION

The treatment course for high-risk patients not on oxygen is **3 days**.

For patients on oxygen for COVID-19 pneumonitis the course is **5 days**. Any extension of these durations needs approval by the infectious diseases consultant on-call.

Significantly immunocompromised patients may be eligible for an extended course of remdesivir (up to 10 days), but only if agreed and approved by the ID consultant on-call.

REASSESSMENT AND REVIEW

The use of remdesivir should be reassessed daily. Consider stopping remdesivir if:

- The patient clinically improves and no longer requires supplemental oxygen 72 hours after commencement of treatment; or
- The patient continues to deteriorate despite 48 hours of sustained mechanical ventilation.

DOSING AND ADMINISTRATION

DOSE & DURATION

- The recommended dosage is a single loading dose of remdesivir 200mg intravenously on day 1, followed by a once daily maintenance dose of remdesivir 100 mg for the remainder of the treatment course. For duration of treatment see above.

ADMINISTRATION

- Given via IV infusion over 30 – 120 minutes
- Flush with at least 30mL 0.9% sodium chloride after infusion complete

PRECAUTIONS FOR USE

For full list please SmPC and BNF for remdesivir.

HEPATIC IMPAIRMENT

Manufacturer advises caution — treatment should not be started if ALT is ≥5 times the upper limit of normal. If ALT increases during treatment, remdesivir may need to be withheld, consult product literature for further information.

RENAL IMPAIRMENT

Manufacturer advises avoid if eGFR less than 30 mL/minute/1.73 m^2 (except in patients with end-stage renal disease on haemodialysis).

PREGNANCY AND BREASTFEEDING

Remdesivir should be avoided in pregnancy unless the clinician believes the benefits of treatment outweigh the risks to the individual. The care and treatment of pregnant women with COVID-19 should be discussed with a senior obstetrician.

MONITORING

Renal and liver function should be monitored carefully during treatment with remdesivir as clinically appropriate.

Remdesivir may prolong the QT interval, and a patient risk-assessment should be undertaken prior to initiation of treatment. A baseline ECG should be performed, with monitoring of QTc interval from days 1 to 3 in patients at increased risk, eg who are prescribed additional QT prolonging medication. Seek advice from cardiology as necessary.

DOCUMENTATION

- The consultant / team in charge of the patient should:
  - Check the patient meets the remdesivir eligibility criteria as detailed above.
  - Document remdesivir prescription in the patient's TRAK notes using the short code **\remd** .
  - Discuss with infectious diseases consultant on-call if using out with above listed criteria and indications or using when elevated BMI, diabetes or hypertension are the sole eligibility criteria.

- Nursing staff should order the remdesivir on a pharmacy order form from pharmacy; include the patient's name and CHI number on the order.
- When ordering supply, the full course of remdesivir should be requested and transferred with the patient.
- With the exception of critical care areas, remdesivir will only be supplied by pharmacy 9am to 4pm (Mon to Fri) and during pharmacy opening-hours at weekends, which vary across the acute hospitals. Out of hours requests from non-critical care areas will not be processed until the following morning unless an urgent supply is requested by the ID consultant on call.

STOPPING CRITERIA

Remdesivir should be discontinued in patients who develop any of the following:

- ALT ≥ 5 times the upper limit of normal during treatment with remdesivir (remdesivir may be restarted when ALT is < 5 times the upper limit of normal)
- ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or international normalised ratio (INR)
- eGFR <30 mL/min(except in patients with end-stage renal disease on haemodialysis).

CORTICOSTEROIDS

INDICATIONS

Corticosteroids are indicated for the treatment of adult patients hospitalised with COVID-19 who:

- have a diagnosis of COVID-19 based on confirmatory PCR or strong suspicion on the basis of chest imaging and clinical history **AND**
- need supplemental oxygen (due to COVID-19) to meet their prescribed oxygen saturation levels **OR**
- need non-invasive ventilation or invasive mechanical ventilation **OR**
- have a level of hypoxia that needs supplemental oxygen but who are unable to have or tolerate it.

Do not routinely use corticosteroids to treat COVID-19 in people who do not need supplemental oxygen, unless there is another medical indication to do so.

DOSING AND ADMINISTRATION

For **dexamethasone** the recommended adult dose schedule is:

Route of administration	Formulation	Dose
Oral	2mg tablet	6mg once daily for 7-10 days[2]
Oral or NG	2mg soluble tablet	6mg once daily for 7-10 days
	2mg/5ml oral solution	6mg (15ml) once daily for 7-10 days
IV	3.3mg (**base**) / ml intravenous 1ml ampoules	5.94 mg **base** (1.8ml) once daily for 7-10 days

Oral administration should be used first line where possible. IV administration should be limited to patients with no alternative route of administration. Treatment should stop if discharged from hospital within the 10 days.

For **hydrocortisone** the recommended adult dose schedule is:

- 50mg hydrocortisone administered intravenously three times per day for 7-10 days
- A longer low dose duration can be considered for patients with septic shock

[2]Course generally 10 days but this can be shortened if the patient has made a full recovery prior to that, or if the risk of side effects by that point significantly outweighs benefit.

Please note that the majority of evidence in the published meta-analysis emanates from the assessment of dexamethasone in the RECOVERY trial.

PREGNANCY AND BREASTFEEDING

For information on use in pregnant or breastfeeding women, please refer to the Summary of Product Characteristics (SPC) for dexamethasone(https://www.medicines.org.uk/emc/product/5411/smpc#gref) and hydrocortisone (https://www.medicines.org.uk/emc/product/9377/smpc#gref).The care and treatment of pregnant women with COVID-19 should be discussed with a senior obstetrician.

Dexamethasone crosses the placenta and repeated courses of maternal dexamethasone have been linked with developmental delay in children. Guidance by the Royal College of Obstetricians and Gynaecologists suggests 40mg oral prednisolone (instead of dexamethasone). Where the oral route is not available intravenous hydrocortisone 80 mg twice daily can be used. Where the mother has had two doses IM dexamethasone for foetal lung maturation start prednisolone after completion of dexamethasone if still appropriate.

ADVERSE EFFECTS AND ADDITIONAL PRESCRIBING CONSIDERATIONS

Adverse effects include gastrointestinal discomfort, dyspepsia, peptic ulceration, sleep disturbances, nausea and anxiety. Please refer to the BNF for further details.

Gastrointestinal: Advise patients to take oral dexamethasone with or after food. When prescribing dexamethasone, consider the patient's risk factors for gastrointestinal ulceration. A proton pump inhibitor should be strongly considered for high-risk patients for the duration of the course but should be discontinued once dexamethasone has stopped.

***Diabetes*:** High Blood Glucose levels with COVID-19 infection have been shown to result in worse patient outcomes. All patients who have diabetes or who are persistently hyperglycaemic should be discussed with the diabetes team.

- **Glucose monitoring frequency** (Target glucose 6.0 -10.0 mmol/L; up to 12.0 mmol/L is acceptable)
    - **People not known to have diabetes**
        - Check the glucose 4 times daily (before meals and at bedtime). If after 48 hours all glucose results are <10.0 mmol/L reduce frequency to once daily at 17.00-18.00 hrs. Continue until dexamethasone is stopped.
        - If any fasting glucose is above 10.0 mmol/L continue 4 times daily monitoring and discuss with the diabetes team.
    - **People with diabetes**
        - Throughout the admission, check fasting glucose at least 6 hourly, or more frequently if the glucose is outside the 6.0 -10.0 mmol/L range. Inform the diabetes team of admission.

- National guidance is available at:*https://www.diabetes.org.uk/professionals/resources/coronavirus-clinical-guidance#inpatient-guidance*

Frailty /Elderly: Use with caution in the elderly; in addition to common side-effects consider increased risk of delirium, agitation, falls and fluid retention. If patients are already on maintenance steroids (acute/maintenance) discuss with local endocrinology team. Duration of dexamethasone may require review if side-effects in the elderly are significant.

Sleep disorders: Dexamethasone should be given in the morning to minimise sleep disruption.

All adverse drug reactions for patients receiving dexamethasone for COVID-19 must be reported to the using MHRA using COVID-19 Yellow Card reporting site: https://coronavirus-yellowcard.mhra.gov.uk/

INTERACTIONS

Please refer to the BNF or Summary of product characteristics for a list of potential drug interactions.

For drug interactions please also see the COVID-19 drug interaction checker: https://www.covid19-druginteractions.org/

INTERLEUKIN-6 INHIBITORS

TOCILIZUMAB / SARILUMAB

Tocilizumab is now licensed for use in the treatment of COVID-19 in adults who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation [16]. This now places **tocilizumab as the first-line IL-6 inhibitor for hospitalised patients with COVID-19**. This document therefore only includes administration guidance for tocilizumab.

Patients may continue to be considered for treatment with sarilumab where tocilizumab is unavailable for this indication or cannot be used. A separate protocol for the administration of sarilumab is available on request via infectious diseases.

Clinicians should consider prescribing intravenous IL-6 inhibitors (tocilizumab or sarilumab) following the criteria defined below.

ELIGIBILITY CRITERIA

Patients must meet all of the eligibility criteria and none of the exclusion criteria. Hospitalised patients are eligible to be considered for an IL-6 inhibitor (tocilizumab or sarilumab) if:

- COVID-19 infection is confirmed by microbiological testing or where a multidisciplinary team has a high level of confidence that the clinical and/or radiological features suggest that COVID-19 is the most likely diagnosis;

  AND

- They have not already been treated during this episode with tocilizumab or sarilumab

  AND

- They are receiving (or have completed a course of) dexamethasone or an equivalent corticosteroid unless contraindicated.

  AND

  Either

  - Hypoxaemia with evidence of inflammation but not yet critically ill requiring respiratory support defined as:
    - C-reactive protein level of at least 75mg/L; AND
    - an oxygen saturation of <92% on room air OR requirement for supplemental oxygen;

  Or

- In the early stages of critical illness requiring respiratory support (if an IL-6-inhibitor has not been already administered for COVID-19) defined as:
    - Within 48 hours of commencement of respiratory support (high-flow nasal oxygen, continuous positive airway pressure (CPAP) or non-invasive ventilation, or invasive mechanical ventilation), regardless of C-reactive protein level.

EXCLUSION CRITERIA

- Tocilizumab should not be administered in the following circumstances:
    - Known hypersensitivity to tocilizumab
    - Liver enzymes [alanine aminotransferase (ALT) or aspartate aminotransferase (AST)] more than ten times the upper limit of normal
    - Absolute neutrophil count of less than 1 x 10^9/L
    - Platelet count of less than 50 x 10^9/L

Please refer to the Summary of Product Characteristics (SmPC) for tocilizumab (https://www.medicines.org.uk/emc/product/15244/smpc) for special warnings and precautions for use, although some may not be relevant for use in the acute setting, as the licensed indications address long-term use.

CAUTIONS

- Co-existing infection that might be worsened by IL-6 inhibitor therapy
- A pre-existing condition or treatment resulting in ongoing immunosuppression.

Caution is also necessary when prescribing IL-6 inhibitors to patients with neutropenia or thrombocytopaenia. Please note that C-reactive protein (CRP) levels may be depressed for some time after treatment with IL-6 inhibitors.

RISK OF INFECTIONS

Serious and sometimes fatal infections have been reported in patients receiving immunosuppressive agents including IL-6 inhibitors. While being on antibiotics per se is not a contraindication, IL-6 inhibitor treatment generally must not be initiated in patients with active, severe bacterial (including active tuberculosis), fungal, viral, or other infection (besides COVID19). Healthcare professionals should exercise caution when considering the use of IL-6 inhibitors in patients with a history of recurring or chronic infections.

Of note is that the limited trial evidence of using IL-6 inhibitors in COVID-19 has not demonstrated significant safety concerns, which may be in part due the fact that only one or two doses were given as opposed to repeated doses over weeks or months.

The SmPC states that patients should be screened for latent tuberculosis (LTBI). However, data on a large number of tocilizumab exposed patients from clinical trials indicate a very low or absent risk of TB reactivation

[Cantini, F., et al. Risk of Tuberculosis Reactivation in Patients with Rheumatoid Arthritis, Ankylosing Spondylitis, and Psoriatic Arthritis Receiving Non-Anti-TNF-Targeted Biologics. Mediators Inflamm. 2017; 2017: 8909834.]. It is likely not feasible to screen for LTBI prior to commencing tocilizumab for severe COVID-19.

Viral reactivation (e.g. hepatitis B virus) has been reported with biologic therapies for rheumatoid arthritis. In clinical studies with tocilizumab, patients who screened positive for hepatitis were excluded. However, screening for viral hepatitis was not required for RECOVERY or REMAP-CAP. Given the acuity of the presentation of patients with COVID-19 screening would not be feasible in a timely manner prior to consideration of tocilizumab. Instead, clinicians should be aware of the theoretical risk, and blood borne virus serology could be undertaken with routine bloods in due course. Patients with active hepatitis B or C infection should be discussed with the infectious diseases team.

MONITORING

No specific monitoring is required post infusion. Raised ALT/AST and neutropenia can occur, particularly with longer treatment courses.

Both tocilizumab and sarilumab cause **prolonged depression of CRP levels, making CRP a less reliable marker of active infection**. All handovers of clinical care (including between hospitals if patients are transferred, between levels of care and clinical teams within hospitals, and between hospitals and primary care) must explicitly mention that an IL-6 inhibitor has been given and the date of administration. Clinicians **must ensure the GP is aware the patient has received tocilizumab or sarilumab** and provide information to the patient to such effect.

COMMON UNDESIRABLE EFFECTS

Please see SmPC for full list.

TOCILIZUMAB - DOSING & ADMINISTRATION

Biologics should be prescribed by brand name as per NHSL Medicines policy. The recommended dose of tocilizumab is 8mg/kg to be administered as an intravenous infusion. The total dose per infusion should not exceed 800mg. **A single dose is to be administered (no repeat dosing)** given the uncertainty over evidence of additional benefit of repeat dosing.

Tocilizumab should be diluted in a 100mL bag of 0.9% sodium chloride, after removing an equivalent volume of saline (total volume 100mL) and given over 1 hour. Please refer to the NHS Injectable Medicines Guide MEDUSA).

Estimated or measured weight	Dose	Vials
<41kg	8mg/kg, rounded to nearest 20mg	As required / available
≥41 and ≤45kg	360mg	As available
≥46 and ≤55kg	400mg	As available
≥56 and ≤65kg	480mg	As available
≥66kg and ≤80kg	600mg	As available
≥81 and ≤90kg	680mg	As available
≥91kg	800mg	As available

Tocilizumab should not be infused concomitantly in the same IV line with other medications.

DOCUMENTATION OF APPROVED USE

The use of IL-6 inhibitor therapy (tocilizumab or sarilumab) for the indication of COVID-19 pneumonitis in NHSL requires documentation on Trak using a specific shortcode. **It is important that the shortcode (see below) is used** as pharmacy will monitor use through a BOXI report which requires this particular shortcode.

The consultant in charge of the patient should:

- Check the patient meets the IL-6 inhibitor therapy approval criteria as detailed above.
- Where possible gain the agreement of the patient to use this medicine.
- Contact the clinical pharmacist responsible for their clinical area to advise which IL-6 inhibitor is currently in stock for use (this may change depending on supplies).
- The consultant in charge of the patient is responsible for:
    - Documenting the use of IL-6 inhibitor therapy in the patient's TRAK notes using the following short code: **\IL6COV**
    - Reporting any adverse drug reactions on the COVID-19 yellow card reporting site. https://coronavirus-yellowcard.mhra.gov.uk/
- **Important!** With the exception of critical care areas, IL-6 inhibitors will only be supplied by pharmacy 9am to 4pm (Mon to Fri) and during pharmacy opening-hours at weekends, which vary across the acute hospitals. Out of hours requests from non-critical care areas will not be processed until the following morning unless an urgent supply is requested by the ID consultant on call.
- Pharmacy staff will check Trak documentation by accessing the completed shortcode entry on TRAK (this will also inform stock holding).
- Locally stock will be held at all acute sites in NHS Lothian; RIE, WGH and SJH.

SAFETY REPORTING

Any suspected adverse drug reactions (ADRs) for patients receiving tocilizumab or sarilumab should be reported directly to the MHRA via the new dedicated COVID-19 Yellow Card reporting site at: https://coronavirus-yellowcard.mhra.gov.uk/

PREGNANCY AND WOMEN OF CHILDBEARING POTENTIAL

The REMAP-CAP trial excluded pregnant women, whereas the RECOVERY trial has included pregnant women. Please check the relevant SmPC for either tocilizumab or sarilumab. The SmPC for sarilumab and tocilizumab currently states: "*Women of childbearing potential must use effective contraception during and up to 3 months after treatment*." In relation to use in pregnancy, the SmPC for tocilizumab states there is no adequate data for the use in pregnant women. In relation to use in pregnancy, the SmPC for sarilumab states there is limited data for the use in pregnant women. A study in animals has shown an increased risk of spontaneous abortion/embryo-foetal death at a high dose with tocilizumab. Tocilizumab or sarilumab should not be used during pregnancy unless clearly clinically necessary. The Royal College of Obstetrics & Gynaecology state that tocilizumab should be considered if the woman fulfils above eligibility criteria.

For women who are breast-feeding, the SmPC states "*It is unknown whether tocilizumab is excreted in human breast milk. The excretion of tocilizumab in milk has not been studied in animals. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with RoActemra should be made taking into account the benefit of breast-feeding to the child and the benefit of RoActemra therapy to the woman.*"

The use of IL-6 inhibitor therapy in pregnant patients should ideally be discussed with the obstetric and/or infectious diseases team.

INTERACTIONS

There is no interaction of tocilizumab/sarilumab with either dexamethasone or hydrocortisone expected. There is no interaction of tocilizumab/sarilumab with remdesivir expected.

For drug interactions please also see the COVID-19 drug interaction checker: https://www.covid19-druginteractions.org/

JAK-INHIBITOR (BARICITINIB)

BARICITINIB

Baricitinib (Olumiant®) is a selective and reversible Janus kinase (JAK) 1 and 2 inhibitor, licensed as an anti-inflammatory treatment for rheumatoid arthritis and atopic dermatitis. JAK-inhibitors are thought to control high levels of cytokines and inflammation, seen in patients with severe SARS-CoV-2 infection. Results from the RECOVERY trial demonstrate that baricitinib reduces the risk of death when given to hospitalised patients with severe COVID-19.

Baricitinib can be considered in children (age 2 to 17 years inclusive) with severe COVID-19. However, this guidance only covers the use in adult patients. Any use in children should be discussed with paediatrics.

CO-ADMINISTRATION

Use of baricitinib in the treatment of COVID-19 should be considered as 'additive' to the use of an IL-6 inhibitor (tocilizumab or sarilumab), rather than an alternative. In other words, a patient may be given an IL-6 inhibitor after treatment with baricitinib has been commenced (or vice versa), according to clinical judgement.

Baricitinib may be administered in combination with IL-6 receptor blockers (as well as corticosteroids, unless contraindicated), according to clinical judgement, in patients with severe or critical COVID-19. If an IL-6 inhibitor is not deemed suitable, or eligibility criteria (for an IL-6 inhibitor) are unmet, baricitinib treatment may still be considered.

ELIGIBILITY CRITERIA

Patients must meet all the eligibility criteria and none of the exclusion criteria. Patients hospitalised due to COVID-19 are eligible to be considered for baricitinib if the following criteria are met:

- COVID-19 infection is confirmed by microbiological testing or where a multi-disciplinary team has a high level of confidence that the clinical and/or radiological features suggest that COVID-19 is the most likely diagnosis;

AND

- Viral pneumonia syndrome is present;

AND

- Aged 2 years and over;

AND

- Receiving supplemental oxygen or respiratory support[3] for the treatment of COVID-19;

AND

- Receiving dexamethasone or an equivalent corticosteroid unless contraindicated.

EXCLUSION CRITERIA AND CAUTIONS

Baricitinib should not be administered in the following circumstances:

- Known hypersensitivity to baricitinib;
- eGFR <15 ml/min/1.73m^2 (adult patients)
- Receiving dialysis or haemofiltration;
- Absolute neutrophil count (ANC) less than 0.5 x 10^9 cells/L;
- Active tuberculosis;
- Pregnancy or breastfeeding.

The summary of Product Characteristics (SmPC) for baricitinib also advises caution in severe hepatic impairment.

Please refer to Summary of Product Characteristics (SmPC) for baricitinib (https://www.medicines.org.uk/emc/product/2434/smpc#gref).

PREGNANCY / WOMEN OF CHILDBEARING POTENTIAL & BREASTFEEDING

Baricitinib should not be used during pregnancy.

For women who are breast-feeding, the SmPC for baricitinib states: "*It is unknown whether baricitinib/metabolites are excreted in human milk. Available pharmacodynamic/toxicological data in animals have shown excretion of baricitinib in milk. A risk to newborns/infants cannot be excluded and Olumiant [baricitinib] should not be used during breast-feeding. A decision must be made whether to discontinue breast-feeding or to discontinue Olumiant [baricitinib] therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman*."

DOSE AND ADMINISTRATION

The use of baricitinib in COVID-19 is off label.

The recommended dose of baricitinib is 4mg once daily for 10 days (or until discharge if sooner). The dose should be halved to 2mg once daily in the following circumstances:

- eGFR 30 to <60 mL/min/1.73m^2

[3] Defined as: high-flow nasal oxygen, continuous positive airway pressure (CPAP) or non-invasive ventilation, or invasive mechanical ventilation.

- Co-administration of an Organic Anion Transporter 3 (OAT3) inhibitor with a strong inhibition potential, such as probenecid.

The dose should be reduced further to 2mg on alternate days in the following circumstances:

- eGFR 15 to <30 mL/min/1.73m^2

Dosing of baricitinib has not been studied for an eGFR <30 mL/min/1.73m^2 and clinical judgement should be exercised prior to prescribing.

Baricitinib should be taken with or without food and may be taken at any time. Seek advice from pharmacist if patient requires NG or PEG tube administration.

Individuals who are being considered for treatment under this policy, who are already taking baricitinib for a licenced indication at the dose of 4mg per day, should not receive additional baricitinib doses. However, if such individuals are already taking baricitinib at a dose of 2mg per day, the dose may be increased for the recommended treatment interval as described in these guidelines provided all eligibility criteria are met and provided the increased dose is deemed clinically appropriate (which includes the patient not being within the dose reduction categories described).

DOCUMENTATION OF APPROVED USE

The use of baricitinib for the indication of COVID-19 pneumonitis in NHSL requires documentation on Trak using a specific shortcode. It is important that the shortcode (see below) is used as pharmacy will monitor use through a BOXI report which requires this particular shortcode. Weekly allocations to NHSL are provided based on usage.

- The consultant in charge of the patient should:
    - Check the patient meets the JAK-inhibitor therapy approval criteria as detailed above.
    - Where possible gain the agreement of the patient to use this medicine.
- The consultant in charge of the patient is responsible for:
    - Documenting the use of baricitinib in the patient's TRAK notes using the following short code: \baricov
    - Reporting any adverse drug reactions on the COVID-19 yellow card reporting site. https://coronavirus-yellowcard.mhra.gov.uk/
- **Important!** With the exception of critical care areas, baricitinib will only be supplied by pharmacy 9am to 4pm (Mon to Fri) and during pharmacy opening-hours at weekends, which vary across the acute hospitals. Out of hours requests from non-critical care areas will not be processed until the following morning unless an urgent supply is requested by the ID consultant on call.
- Pharmacy staff will check Trak documentation by accessing the completed shortcode entry on TRAK (this will also inform stock holding).

SAFETY REPORTING

It is vital that any serious suspected adverse reactions are reported directly to the MHRA via the new dedicated COVID-19 Yellow Card reporting site at: https://coronavirus- yellowcard.mhra.gov.uk/.

Treatment with baricitinib can lower the ability of the immune system to fight infections. This could increase the risk of getting a new infection or make any infection the patient contracts worse. All handovers of clinical care (including between hospitals if patients are transferred, between levels of care and clinical teams within hospitals, and between hospitals and primary care) must explicitly mention that baricitinib has been given and the date of administration. **Clinicians must ensure the GP is aware the patient has received baricitinib** and should provide information to the patient to such effect.

REFERENCES

1. NICE COVID-19 rapid guideline: managing COVID-19: https://www.nice.org.uk/guidance/ng191 [last accessed 11 June 2024]
2. NICE Technology appraisal guidance TA878. Nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19: https://www.nice.org.uk/guidance/ta878/chapter/5-Supporting-information-on-risk-factors-for-progression-to-severe-COVID19 [last accessed 11 June 2024]

ABBREVIATIONS

BNF	British National Formulary
COPD	Chronic obstructive airway disease
COVID-19	Coronavirus disease 2019
IL-6	Interleukin 6
IV	intravenous
mg	milligram
MHRA	Medicines & Healthcare products Regulatory Agency
ml	millilitre
mmol/l	millimole per litre
NG	nasogastric
NHSL	National Health Service Lothian
nMAB	Neutralising Monoclonal Antibody
O2	oxygen
PCR	polymerase chain reaction
POCT	Point-of –care-test
RA	Room air
RECOVERY (trial)	Randomised Evaluation of COVID-19 Therapy
REMAP-CAP	Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SmPC	Summary of Product Characteristics
WHO	World Health Organisation

APPENDIX 1

SHORTCODES

\REMD

This is the Trak short code to be used to document the use of remdesivir. It will generate the following canned text:

Remdesivir approval

Complete the sections in uppercase (without all fields completed – drug will not be supplied from pharmacy).

ELIGIBLE CONDITION (RISK FACTOR FOR PROGRESSION TO SEVERE COVID-19 - SEE GUIDELINES):

PATIENT REQUIRING SUPPLEMENTAL OXYGEN?: YES / NO (delete as appropriate)

PLANNED DURATION OF TREATMENT: 3 DAYS / 5 DAYS / 10 DAYS (delete as appropriate)

Important: for indications, duration and dose please refer to hospital guidelines on the intranet.

NAME OF CONSULTANT IN CHARGE REQUESTING REMDESIVIR:

CURRENT PATIENT WARD:

Now prescribe remdesivir course on the drug chart / HEPMA.

\IL6COV

This is the Trak short code to be used to document the use of IL-6 inhibitors (tocilizumab/sarilumab). It will generate the following canned text:

Tocilizumab approval for COVID-19 / Sarilumab approval for COVID-19

Please read the COVID-19 treatment guidelines (available on the intranet) carefully.

Complete all the sections in uppercase.

IS THE PATIENT CURRENTLY BEING TREATED FOR COVID-19? Yes / No (delete as appropriate)

Patients must meet all the eligibility criteria and none of the exclusion criteria. Hospitalised patients are eligible to be considered for an IL-6 inhibitor (tocilizumab or sarilumab) if:

• COVID-19 infection is confirmed by microbiological testing or where a multidisciplinary team has a high level of confidence that the clinical and/or radiological features suggest that COVID-19 is the most likely diagnosis;

AND

• They have not already been treated during this episode with tocilizumab or sarilumab;

AND

• Receiving dexamethasone or an equivalent corticosteroid unless contraindicated;

AND

Either

o Hypoxaemia with evidence of inflammation but not yet critically ill requiring respiratory support defined as:

▪ C-reactive protein level of at least 75mg/L; AND

▪ an oxygen saturation of <92% on room air OR requirement for supplemental oxygen;

Or

o In the early stages of critical illness requiring respiratory support (if an IL-6-inhibitor

has not been already administered for COVID-19) defined as:

▪ Within 48 hours of commencement of respiratory support (high-flow nasal oxygen, continuous positive airway pressure (CPAP) or non-invasive ventilation, or invasive mechanical ventilation), regardless of C-reactive protein level.

DOES THE PATIENT FULFIL THE ABOVE INCLUSION CRITERIA? Yes / No (delete as appropriate)

DOES THE PATIENT FULFIL ANY EXCLUSION CRITERIA (SEE GUIDELINES)? Yes / No (delete as appropriate)

IS THE PATIENT PREGNANT OR BREASTFEEDING? Yes / No (delete as appropriate)

If pregnant or breastfeeding the patient should be discussed with obstetrics or infectious diseases.

Patient who do not fulfil above inclusion criteria or have exclusion criteria and where an IL-6 inhibitor is still being considered should be discussed with the infectious diseases consultant on-call.

The decision to initiate treatment with tocilizumab or sarilumab should be made by the receiving consultant and with the support from multi-disciplinary colleagues in cases of uncertainty.

PLEASE CONFIRM THE NAME OF THE RESPONSIBLE CONSULTANT WHO MADE THE DECISION TO TREAT WITH AN IL-6 INHIBITOR:

CURRENT PATIENT WARD:

IL-6 INHIBITOR USED (PHARMACY WILL ADVISE ON STOCK LEVELS DURING WORKING HOURS): tocilizumab (specify brand name: RoActemra or Tyenne) / sarilumab (delete as appropriate)

Single dose only (no additional doses recommended) - see intranet for dosing guidance.

FORM FILLED IN BY (NAME, DESIGNATION, CONTACT):

\PAXLOVID

PF-07321332 (nirmatrelvir) plus ritonavir for patients with COVID-19

Complete the sections in uppercase.

For indications and criteria please see latest guidance on the intranet.

I CONFIRM THAT I CHECKED THE INDICATIONS AND CONTRAINDICATIONS FOR PF-07321332 (NIRMATRELVIR) PLUS RITONAVIR: YES / NO

I CONFIRM THAT I HAVE CHECKED FOR DRUG-DRUG-INTERACTIONS WITH PATIENT'S REGULAR MEDICINES: YES / NO

eGFR IS GREATER THAN 59ML/MIN? YES / NO

If eGFR is greater than 59ml/min then use the following dose: PF-07321332 (nirmatrelvir) plus ritonavir is 300mg (two 150mg tablets) PF-07321332 with 100mg (one 100mg tablet) ritonavir taken together orally twice daily for 5 days.

For patients with moderate or severe renal impairment see guidance on the intranet or speak to specialist.

OUTCOME: PF-07321332 (NIRMATRELVIR) PLUS RITONAVIR PRESCRIBED: YES / NO

CURRENT PATIENT LOCATION: (please enter hospital and ward location; if outpatient write 'outpatient')

SIGNED BY:

\BARICOV

Baricitinib approval for COVID-19

Please read the COVID-19 treatment guidelines (available on the intranet) carefully.

Complete all the sections in uppercase.

IS THE PATIENT CURRENTLY BEING TREATED FOR COVID-19? Yes / No (delete as appropriate)

Patients must meet all the eligibility criteria and none of the exclusion criteria.

DOES THE PATIENT FULFIL THE INCLUSION CRITERIA (SEE GUIDELINES)? Yes / No (delete as appropriate)

DOES THE PATIENT FULFIL ANY EXCLUSION CRITERIA (SEE GUIDELINES)? Yes / No (delete as appropriate)

The decision to initiate treatment with baricitinib should be made by the receiving consultant and with the support from multi-disciplinary colleagues in cases of uncertainty.

CURRENT PATIENT WARD:

NAME OF CONSULTANT IN CHARGE REQUESTING BARICITINIB:

FORM FILLED IN BY (NAME, DESIGNATION, CONTACT):