

# Guideline for the treatment of hospitalised adult patients with COVID-19 on oxygen (Group 1)

|  |  |
| --- | --- |
| Version | 2.1 |
| Approved by | Clinical Advisory Group and Medicines Governance Committee |
| Date approved | 5th December 2022 |
| Name of author(s) | Prof Martin Llewelyn, Dr Bethany Davies  Dr Racheol Sierra,  Aoife Hendrick  David Hilbert, Jo Munns |
| Name of responsible committee | Medicines Governance Group  Clinical Advisory Group |
| Date issued | December 2022 |
| Review date | December 2023 or sooner if clinical information changes |
| Target audience | Health care professionals (nurses/doctors/pharmacists) |

**Scope**

This document provides guidance for healthcare professionals considering the following treatments (IL-6 Inhibitor (Tocilizumab and Sarilumab), Remdesivir and Baricitinib) for patients hospitalised due to COVID-19. It follows recommendations from the following alerts:

* CMO alert [CEM/CMO/2022/018](https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103222) dated 29th November 2022 (Tocilizumab and Sarilumab)
* CMO alert [CEM/CMO/2022/016](https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103220) dated 28th November 2022 (Remdesivir)
* CMO alert [CEM/CMO/2022/017](https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103221) dated 28th November 2022 (Baricitinib)

**Evidence summary**

On the 11th February 2021 the RECOVERY trial announced the findings of tocilizumab use in a broader hospitalised population, which indicated a relative reduction in mortality of 14% at 28 days in hospitalised COVID-19 patients with hypoxia and systemic inflammation. This benefit was additional to that seen with systemic corticosteroids. A rapid evidence review published by NICE on 15th January 2021 was based on the findings of REMAP-CAP trial in critically ill adult patients, the review was updated with the RECOVERY trial results and new guidance NICE Rapid Guideline on managing COVID-19 published in March 2021 and since updated, most recently on the 11th November 2022 version 27.6.

New evidence and guidance have since emerged supporting equivalence of the two IL-6 inhibitors. Further evidence from the REMAP-CAP trial has demonstrated equivalent effects of both IL-6 inhibitors on survival and requirement for organ support (84.9% posterior probability of equivalence).

The licence for tocilizumab, which was updated in December 2021 to include authorisation for use in the treatment of COVID-19 in adults who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation. This now places tocilizumab as the first-line IL-6 inhibitor for hospitalised patients with COVID-19. Patients may continue to be considered for treatment with sarilumab where tocilizumab is unavailable for this indication or cannot be used.

Results from the RECOVERY trial demonstrate that baricitinib significantly reduces the risk of death when given to hospitalised patients with severe COVID-19, 12% of the patients in the baricitinib group died within 28 days compared with 14% patients in the usual care group, a relative reduction of 13%. The benefit of baricitinib was consistent regardless of which other COVID-19 treatments the patients were also receiving, including corticosteroids, tocilizumab, or remdesivir.

Current evidence shows that remdesivir improves clinical outcomes in both hospitalised and non-hospitalised patients with COVID-19. Evidence from the ACTT-1 trial showed that remdesivir improved time to recovery in patients hospitalised with COVID-19 by 5 days compared to placebo (Beigel et al, 2020).This conflicts with the conclusion of the WHO Solidarity trial in which remdesivir appeared to have little or no effect on hospitalised Covid-19, as indicated by mortality, initiation of ventilation and duration of hospital stay (Pan et al, 2020).

The World Health Organization (WHO) updated its ’[Therapeutics and COVID-19: Living guideline](https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2022.5)’ on 16 September 2022 and the recommendations have been considered in the development of the commissioning policies, on which this guidance is based.

**Indication**

Tocilizumab, sarilumab, remdesivir or baricitinib should be considered as **adjuvant treatment to dexamethasone** (as standard care) in eligible **hospitalised** patients.

Patients must meet all of the eligibility criteria and none of the exclusion criteria below. The eligibility and exclusion criteria will vary for each of the drugs.

IL-6 inhibitors may be administered in combination with baricitinib (as well as corticosteroids, unless contraindicated), according to clinical judgement, in patients with severe or critical COVID-19.

**Eligibility criteria for all of the treatments discussed in this guideline:**

* SARS-CoV-2 infection confirmed by PCR/LFT **OR** in the absence of a confirmed virological diagnosis **only** when a multidisciplinary team have a high level of confidence that the clinical and radiological features suggest that COVID-19 is the most likely diagnosis
* Receiving (or have completed a course of) dexamethasone or equivalent corticosteroid to treat COVID-19 unless contraindicated
* Receiving supplemental oxygen or respiratory support for the treatment of COVID-19, if this does not apply please see [COVID-19 Guidance for Group 2 Patients](https://viewer.microguide.global/BSUH/COVIDBSUH#content,033d17b1-66d9-45eb-a2c0-185dec8ef706)
* Please see additional criteria for each drug

**IL-6 Inhibitors (tocilizumab and sarilumab) additional eligibility criteria**

* Patient must be either:
  + Not requiring respiratory support:
    - CRP ≥ 75mg/L (Note: CRP levels may be depressed for up to 3 months after treatment with tocilizumab or sarilumab)
    - **AND** sustained O2 saturation of < 92% on room air or an on-going requirement for supplemental oxygen
  + Critical illness requiring respiratory support – is within 48 hours of starting respiratory support (high flow nasal oxygen, continuous positive airway pressure (CPAP), non-invasive ventilation or invasive mechanical ventilation), regardless of CRP

**Baricitinib additional eligibility criteria**

* Viral pneumonia syndrome is present
  + Typical symptoms (influenza-like illness with fever and muscle pain, or respiratory illness with cough and shortness of breath)
  + AND compatible chest X-ray findings (consolidation or ground-glass shadowing)
  + AND alternative causes have been considered unlikely or excluded (heart failure, bacterial pneumonia)
  + 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

**Remdesivir additional eligibility criteria**

* With pneumonia requiring low-flow supplemental oxygen (facemask or nasal cannula at a flow rate usually up to 15L/min). ***This criterion does not apply to those with significant immunosuppression[[1]](#footnote-1)***
* No more than 10 days since the onset of symptoms ***This criterion does not apply to those with significant immunosuppression1***
* Not eligible for treatment with IL-6 inhibitor or Baricitinib
* Patients re-admitted for symptoms of COVID-19 (and meeting the eligibility criteria, with the exception of the requirement on the timing from symptom onset) are permitted a second course of up to 5 days upon readmission.

**See individual drugs for exclusion criteria:**

**IL-6 Inhibitors (tocilizumab and sarilumab)**

* Previous use of an IL-6 inhibitor for COVID-19 during this admission
* Known hypersensitivity to tocilizumab or sarilumab
* Baseline platelet count < 50 x 109/L for tocilizumab and < 150 x 109 /L for sarilumab
* ALT or AST > 10 times upper limit of normal for tocilizumab or > 5 times upper limit of normal for sarilumab OR active hepatic disease
* Neutrophil count < 1 x 109/L for tocilizumab and < 2 x 109 /L for sarilumab

**Use with caution**

* Clinically significant active bacterial infection (N.B. not including possible bacterial superinfection of COVID-19 being treated with antibiotics) that might be worsened by IL-6 inhibitor therapy
* Active fungal infection, tuberculosis or herpes zoster
* Active diverticulitis, bowel perforation or at increased risk of bowel perforation
* If the patient has a pre-existing condition or treatment resulting in on-going immunosuppression, please see appendix 1 for list of conditions and treatments.

**Baricitinib**

* Known hypersensitivity to baricitinib
* eGFR/CrCl < 15 mL/min (see dose and administration section as reduced dose needed if eGFR/CrCl < 60 mL/min)
* Receiving dialysis or haemofiltration
* Neutrophil count < 0.5 x 109/L
* Active tuberculosis
* Treatment with baricitinib can lower the ability of the immune system to fight infections. Consider risk/benefit in patients with on-going immunosuppression
* Unable to take oral medication
* Pregnancy or breastfeeding

**Remdesivir**

* Known hypersensitivity reaction to the active substances or to any of the excipients
* eGFR/CrCl < 30mL/min excluding patients on haemodialysis
* ALT > 5 times upper limit of normal
* Remdesivir should not be initiated in patients who are unlikely to survive (determined by clinical judgement). The 4C mortality score can help support clinical judgement. The calculator can be accessed [here](https://isaric4c.net/risk/) [advise using in Firefox or Google Chrome browser] (see Appendix 2 treatment pathway)
* Remdesivir should not be initiated in patients who are highly likely to recover without treatment with remdesivir (low 4C Mortality Score (0 to 3))

**Infection Screening for IL-6 Inhibitor (tocilizumab and sarilumab)**

* Serology should be sent for Hepatitis B/C, HIV, VZV, EBV, and CMV for all patients started on tocilizumab/sarilumab unless positive status already known but this should not delay initiating treatment. Meta-analyses have demonstrated little or no risk of reactivation of latent TB in patients undergoing tocilizumab/sarilumab therapy

**Approval & Governance**

A decision to prescribe these drugs should be made by a multi-disciplinary team consisting of:

1. The consultant who has responsibility for the patient’s care
2. Infection specialist
   * RSCH/PRH: ext. 65207 during working hours (or out of hours on-call consultant via switchboard)
   * Worthing: ext. 85398 during working hours (or out of hours on-call microbiologist via switchboard)
   * SRH: ext. 33547 during working hours (or out of hours on-call microbiologist via switchboard)
3. Pharmacy
   * RSCH/PRH: infection/critical care specialist pharmacist via their bleep during working hours (or out of hours and weekends on-call pharmacist via switchboard)
   * Worthing/SRH: ward pharmacist via their bleep (or on-call pharmacist at weekends after 2pm via switchboard)

For patients hospitalised with acute COVID-19 and on general wards these drugs will be available to be administered between 8.00am and 8.00pm. Last supply orders for these should be received in pharmacy by 6.00pm in order to deliver to wards and allow nursing staff to administer.

For patients in critical care, these drugs are available at all times.

Completion of a Blueteq form is mandatory for approval and supply.

RSCH/PRH

The Blueteq form must be completed by the specialist pharmacist for all requests. The pharmacist supplying the medication should inform the infection specialist pharmacist via email or on bleep 8033.

Worthing/SRH

The Blueteq form must be completed by the prescribing clinician and processed by the ward pharmacist. This is available on the [intranet](http://nww.westernsussexhospitals.nhs.uk/departments/pharmacy/covid-19-treatment/). Blueteq forms must be emailed to [uhsussex.COVIDdrugforms@nhs.net](mailto:uhsussex.COVIDdrugforms@nhs.net) and [uhsussex.research@nhs.net](mailto:uhsussex.research@nhs.net) by the ward pharmacist to be reviewed by the antimicrobial pharmacists.

**Continuing care**

All handovers of clinical care (including between hospitals if patients are transferred, between levels of care and clinical teams within hospitals) must explicitly mention that IL-6 Inhibitor, Baricitinib or Remdesivir has been given and the date of administration.

The GP should be informed on the discharge summary that an IL-6 Inhibitor, Baricitinib or Remdesivir has been prescribed specifying the date of administration.

A patient information leaflet for IL-6 Inhibitor should be provided prior to hospital discharge and this is available [here](https://www.sps.nhs.uk/wp-content/uploads/2021/03/COVID-19-Patient-Discharge-Information-Leaflet-Tocilizumab-Sarilumab.pdf).

**Dose & Administration**

**IL-6 Inhibitors**

Tocilizumab should be considered the first line IL-6 Inhibitor as it is now a licensed medication for this indication. Sarilumab does not yet have a licence (marketing authorisation) for use in COVID-19 but may be used in place of tocilizumab if stock of tocilizumab cannot be obtained or there is a national shortage of tocilizumab.

**Tocilizumab**

* The recommended dose of tocilizumab is 8mg/kg IV as a single dose (maximum 800mg)
* The vials come in 80mg, 200mg and 400mg sizes; round doses to nearest vial size to reduce wastage

|  |  |
| --- | --- |
| Actual body weight (kg) | Recommended dose of tocilizumab |
| < 41kg | 320mg |
| 41 - 45kg | 360mg |
| 46 - 55kg | 400mg |
| 56 - 65kg | 480mg |
| 66 - 80kg | 600mg |
| 81 - 90kg | 680mg |
| ≥ 91kg | 800mg |

* Administer[[2]](#footnote-2) in 100mL 0.9% sodium chloride, after removing an equivalent volume of saline (total volume 100mL).
* Administer over 60 minutes via an infusion pump.
* Tocilizumab should not be infused concomitantly in the same IV line with other medications

**Sarilumab**

* The recommended dose of sarilumab is always 400mg IV as a single dose
* There are no dose adjustments with respect to extremes of body weight
* 2 x 200mg pre-filled syringes should be added to 100mL sodium chloride 0.9% and the infusion bag inverted at least 10 times to ensure mixing[[3]](#footnote-3)
* Administer using a low protein-binding 0.2micron filter
  + At RSCH/PRH: these are available from pharmacy and should be dispensed with Sarilumab syringes. **Note for pharmacy**: the filters are profiled on WellSky as ‘Paclitaxel Pump Admin Set or Infliximab Filter 0.2 microns’
  + At Worthing/SRH these are available on the wards at Worthing/SRH from medicines management
* Initial infusion rate should be 10mL/hour for first 15 minutes then 130mL/hour for the remaining 45 minutes (total infusion time = 1 hour)
* Sarilumab should not be infused concomitantly in the same IV line with other medications

**IL-6 inhibitors should not be prepared or administered by pregnant members of staff or those of childbearing potential who are actively trying to conceive.** A disposable apron, gloves, FFP3 mask and eye protection should be worn when preparing and administering.

In order to improve the traceability of biological medicines, the batch number should be recorded.

**Baricitinib**

* eGFR/CrCl > 60 mL/min - 4mg once daily orally for 10 days (or until discharge if sooner)
* eGFR/CrCl 30 to 60 mL/min - 2mg once daily orally for 10 days (or until discharge if sooner)
* eGFR/CrCl 15 to 30 mL/min - 2mg on alternate days orally for 10 days (or until discharge if sooner)
* Baricitinib may be taken at any time of the day, it is recommended that it continues to be taken at the same time each day

**Remdesivir**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Loading Dose** | **Maintenance Dose** | **Number of days Treatment** | **Other** |
| **Group 1** | 200mg on day 1 | 100mg OD on days 2 – 5 | 5 days | May be extended to a maximum of 10 days in significantly immunocompromised1 patients following discussion with the MDT |

**Reassessment and Review Remdesivir**

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 remdesivir
* The patient continues to deteriorate despite 48 hours of sustained mechanical ventilation

**Prescribing & Administration Remdesivir**

Two formulations are available for use. **Information on preparation and administration** can be found on the **Injectable Medicines Guide** accessed via the Pharmacy homepage on the Trust intranet.

|  |  |  |  |
| --- | --- | --- | --- |
| **Formulation** | **Infusion fluid** | **Infusion time** | **Storage** |
| Concentrate for  Solution for Infusion  100mg in 20mL vial | 250mL sodium  chloride 0.9% | 30 – 120 minutes | Fridge (2 – 8◦c) |
| Powder for  Concentrate for  Solution for Infusion  100mg vial | 100 - 250mL sodium  chloride 0.9% | 30 – 120 minutes | Room temperature  (<30◦c) |

All unused vials should be returned without delay to Pharmacy.

**Co-administration**

IL-6 inhibitors may be administered in combination with baricitinib (as well as corticosteroids, unless contraindicated), according to clinical judgement, in patients with severe or critical COVID-19.

Use of baricitinib in the treatment of COVID-19 should also 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.

**Drug Interactions**

Further information of potential drug interactions may be found via [the University of Liverpool COVID-19 drug interactions](https://www.covid19-druginteractions.org/) website.

**Pregnancy & Breastfeeding**

**IL-6 Inhibitor (tocilizumab and sarilumab)**

Tocilizumab

Animal studies have shown an increased risk of spontaneous abortion / embryo-foetal death with high doses of tocilizumab. The risk in humans is unknown.

Sarilumab

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. There are no or limited amount of data from the use of sarilumab in pregnant women.

IL-6 inhibitors should not be used during pregnancy unless clinical benefit outweighs risk. Please follow [RCOG Guidance](https://www.rcog.org.uk/guidance/coronavirus-covid-19-pregnancy-and-women-s-health/) for use of Tocilizumab or Sarilumab during pregnancy . Persons of childbearing potential should use effective contraception for 3 months following administration of an IL-6 inhibitor.

For women who are breast-feeding, the SmPCs for both tocilizumab and sarilumab state: “It is unknown whether tocilizumab/sarilumab is excreted in human breast milk. The excretion of tocilizumab/sarilumab in milk has not been studied in animals. A decision on whether to discontinue breast-feeding or to discontinue IL-6 inhibitor therapy should be made taking into account the benefit of breast-feeding to the child and the benefit of therapy to the woman.”

**Baricitinib**

Baricitinib is not recommended during pregnancy. Persons of childbearing potential should use effective contraception during and for at least 1 week after treatment.

Breastfeeding is not recommended with Baricitinib.

**Remdesivir**

There are limited data from the use of remdesivir in pregnant women. Remdesivir should be avoided in pregnancy unless clinicians believe the benefits of treatment outweigh the risks to the individual (please see [SmPC](https://www.medicines.org.uk/emc/product/11597) for further information). Please follow [RCOG Guidance](https://www.rcog.org.uk/guidance/coronavirus-covid-19-pregnancy-and-women-s-health/) for use of Remdesivir during pregnancy. Women of child-bearing potential have to use effective contraception during treatment.

It is unknown whether remdesivir is excreted in human milk or the effects on the breast-fed infant, or the effects on milk production. In animal studies, the nucleoside analog metabolite GS-441524 has been detected in the blood of nursing rat pups of mothers given remdesivir. Therefore, excretion of remdesivir and/or metabolites into the milk of lactating animals can be assumed. Because of the potential for viral transmission to SARS-CoV-2-negative infants and adverse reactions from the drug in breast-feeding infants, a decision must be made whether to discontinue breast-feeding or to discontinue/abstain from remdesivir therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

**Monitoring**

**IL-6 Inhibitor (tocilizumab and sarilumab) and Baricitinib**

Treatment with tocilizumab/sarilumab and baricitinib can lower the ability of the immune system to fight infection. This means potentially:

* Increased risk of acquiring infection
* Attenuated clinical and laboratory signs of infection for a prolonged period e.g. CRP response for up to 3 months
* Worse outcome of any infection the patient contracts

It is important therefore that clinicians are alert to any intercurrent infection in patients who have received tocilizumab/sarilumab or baricitinib.

Clinicians should ensure:

* Microbiological samples (e.g. cultures) are sent if there is any concern about infection
* Prompt antibiotic treatment is given if infection is suspected and reviewed with senior infection input as soon as possible
* GP is aware the patient has received an IL-6 inhibitor or baricitinib
* Patient is informed of risk.

Tocilizumab monitoring during infusion[[4]](#footnote-4)

Hypersensitivity reactions including anaphylaxis, flushing, fever, chills, rash, pruritus, urticaria, headache, hypertension can occur.  
Monitor: Pulse, blood pressure, temperature & respiration rate for any signs of hypersensitivity reaction. Monitor baseline observations after 15 minutes, then every 30 minutes and post infusion.

Sarilumab monitoring during infusion[[5]](#footnote-5)

Infusion-related reactions: may include chills, nausea, headache, wheezing, itching, flushing, pyrexia, dizziness. If a mild to severe infusion related reaction (grade 1-3) occurs stop treatment and treat symptoms. Reduce infusion rate by at least 50% when re-starting infusion.  
Monitor: for infusion-related reactions during and after infusion (if they occur, likely to be within first 24 hours).

**Remdesivir**

Renal and hepatic function should be monitored **daily throughout treatment.**

* Discontinue remdesivir if ALT ≥ 5 times upper limit of normal or ALT elevation with signs or symptoms of liver inflammation or increasing bilirubin, alkaline phosphatase or INR
* Discontinue remdesivir if CrCl <30mL/min or renal replacement therapy required

Hypersensitivity reactions including infusion-related and anaphylactic reactions have been observed during and following administration of remdesivir. **The patient should be monitored closely during infusion and for one hour after the infusion** Signs and symptoms may include hypotension, hypertension, tachycardia, bradycardia, hypoxia, fever, dyspnoea, wheezing, angioedema, rash, nausea, vomiting, diaphoresis, and shivering.

Slower infusion rates, with a maximum infusion time of up to 120 minutes, may prevent these signs and symptoms but if clinically significant hypersensitivity occurs immediately discontinue remdesivir and manage the reaction appropriately.

**Safety reporting**

Tocilizumab has recently been approved for use for ‘the treatment of COVID-19 in adults who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation’.

Sarilumab does not yet have a licence (marketing authorisation) for use in COVID-19 and therefore tocilizumab as the licensed preparation should be used first line for the above indication where national stock levels allow. Sarilumab may otherwise be used in place of tocilizumab if stock cannot be obtained.

Baricitinib has a marketing authorisation for use in adults with moderate to severe active rheumatoid arthritis and adults with moderate to severe atopic dermatitis. The use of baricitinib in COVID-19 is off label.

Remdesivir delivered intravenously has conditional marketing authorisation in the UK for treatment of COVID-19 in adults and adolescents (aged 12 years and over and weighing at least 40kg) with pneumonia requiring supplemental oxygen (low- or high-flow oxygen or other non-invasive ventilation at start of treatment), for a treatment duration of 5-10 days.

Marketing authorisation variation for Great Britain is currently being considered by the Medicines and Healthcare products Regulatory Authority (MHRA) under the ‘reliance route’.

It is vital that any serious suspected adverse reactions from any of the drugs in this guideline drug are reported directly to the MHRA via the new dedicated COVID-19 Yellow Card reporting site at: <https://coronavirus-yellowcard.mhra.gov.uk/>

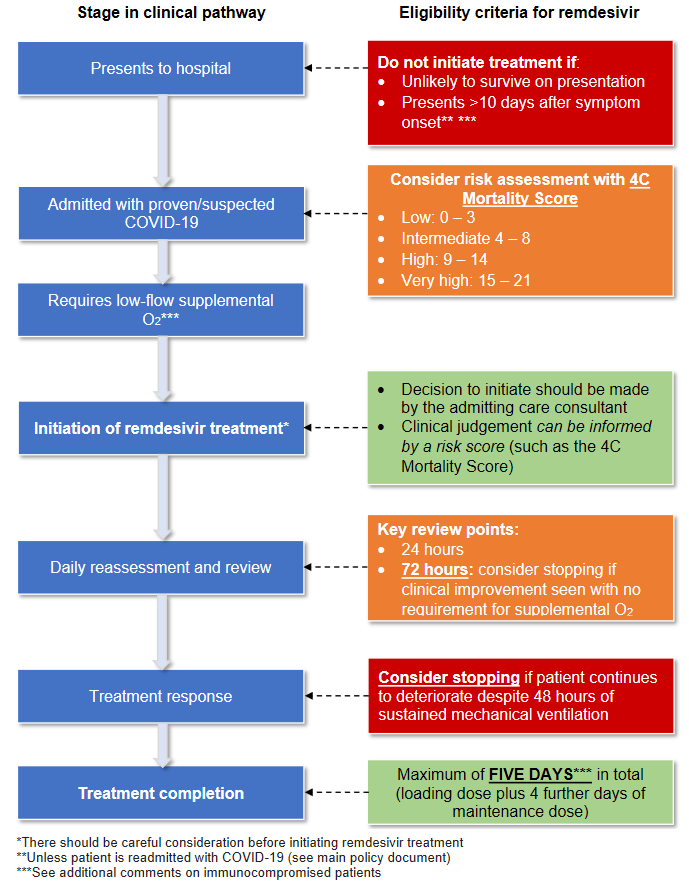
**Appendix 1**

List of conditions and treatments resulting in on-going immunosuppression (Reference JCVI List immunosuppressed individuals NHS Official Letter Reference [C1399](https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2021/09/C1399-Updated-JCVI-guidance-for-vaccinating-immunosuppressed-individuals-with-third-primary-dose.pdf) 2nd September 2021)

1. Individuals with primary or acquired immunodeficiency states at the time of treatment due to conditions including:
   * acute and chronic leukaemias, and clinically aggressive lymphomas (including Hodgkin’s lymphoma) who were under treatment or within 12 months of achieving cure
   * individuals under follow up for chronic lymphoproliferative disorders including haematological malignancies such as indolent lymphoma, chronic lymphoid leukaemia, myeloma, Waldenstrom’s macroglobulinemia and other plasma cell dyscrasias (note: this list is not exhaustive)
   * immunosuppression due to HIV/AIDS with a current CD4 count of <200 cells/μl for adults or children
   * primary or acquired cellular and combined immune deficiencies – those with lymphopaenia (<1,000 lymphocytes/μl) or with a functional lymphocyte disorder
   * those who had received an allogeneic (cells from a donor) or an autologous (using their own cells) stem cell transplant in the previous 24 months
   * those who had received a stem cell transplant more than 24 months ago but had ongoing immunosuppression or graft versus host disease (GVHD)
   * persistent agammaglobulinaemia (IgG < 3g/L) due to primary immunodeficiency (for example, common variable immunodeficiency) or secondary to disease/therapy
2. Individuals on immunosuppressive or immunomodulating therapy at the time of treatment including:
   * those who were receiving or had received immunosuppressive therapy for a solid organ transplant in the previous 6 months
   * those who were receiving or had received in the previous 3 months targeted therapy for autoimmune disease, such as JAK inhibitors or biologic immune modulators including B-cell targeted therapies (including rituximab but in this case the recipient would be considered immunosuppressed for a 6-month period), T-cell co-stimulation modulators, monoclonal tumour necrosis factor inhibitors (TNFi), soluble TNF receptors, interleukin (IL)-6 receptor inhibitors, IL-17 inhibitors, IL 12/23 inhibitors, IL 23 inhibitors (note: this list is not exhaustive)
   * those who were receiving or had received in the previous 6 months immunosuppressive chemotherapy or radiotherapy for any indication
3. Individuals with chronic immune-mediated inflammatory disease who were receiving or had received immunosuppressive therapy prior to treatment including: (excluding Dexamethasone for COVID-19)
   * high-dose corticosteroids (equivalent to ≥ 20mg prednisolone per day) for more than 10 days in the previous month
   * long-term moderate dose corticosteroids (equivalent to ≥10mg prednisolone per day for more than 4 weeks) in the previous 3 months
   * non-biological oral immune modulating drugs, such as methotrexate >20mg per week (oral and subcutaneous), azathioprine >3.0mg/kg/day, 6-mercaptopurine >1.5mg/kg/day, mycophenolate >1g/day in the previous 3 months
   * certain combination therapies at individual doses lower than above, including those on ≥7.5mg prednisolone per day in combination with other immunosuppressants (other than hydroxychloroquine or sulfasalazine) and those receiving methotrexate (any dose) with leflunomide in the previous 3 months
4. Individuals who had received high-dose steroids (equivalent to >40mg prednisolone per day for more than a week) for any reason in the month before treatment. (excluding Dexamethasone for COVID-19)
   * Individuals who had received brief immunosuppression (≤40mg prednisolone per day) for an acute episode (for example, asthma / COPD / COVID-19) and individuals on replacement corticosteroids for adrenal insufficiency are not considered severely immunosuppressed sufficient to prevent treatment with an IL-6 Inhibitor.

**Appendix 2**

Clinical pathway and criteria for the use of **remdesivir** in patients hospitalised with COVID-19



1. Significant immunosuppression is defined as a significant impairment of humoral immune response (antibody production) and/or cellular immune competence. See appendix 1 below for list of conditions qualifying for considering for immunosuppression. [↑](#footnote-ref-1)
2. Injectable Medicines Guide ‘Medusa’ Tocilizumab accessed 2/12/22 [↑](#footnote-ref-2)
3. Injectable Medicines Guide ‘Medusa’ Sarilumab accessed 2/12/22 [↑](#footnote-ref-3)
4. Injectable Medicines Guide ‘Medusa’ Tocilizumab accessed 2/12/22 [↑](#footnote-ref-4)
5. Injectable Medicines Guide ‘Medusa’ Sarilumab accessed 2/12/22 [↑](#footnote-ref-5)