Chief Medical Officer Directorate
Pharmacy and Medicines Division

Scottish Government
Riaghaltas na h-Alba
gov.scot

T: 0131-244-2528
E: irene.fazakerley@gov.scot

URGENT MESSAGE TO:

1. Directors of Pharmacy
2. Medical Directors NHS Boards

29 November 2022

Dear Healthcare Professional,

COVID THERAPEUTIC ALERT 2022 18 - INTERLEUKIN-6 INHIBITORS (TOCILIZUMAB OR SARILUMAB) FOR ADULT PATIENTS HOSPITALISED DUE TO COVID-19

Please see the attached CMO letter,Interim Clinical Commissioning Policy and guidelines regarding the use of Interleukin-6 inhibitors (tocilizumab or sarilumab) for adult patients hospitalised due to COVID-19. The published policy, providing access to interleukin-6 (IL-6) inhibitors has been updated following consideration of the recommendations of the updated World Health Organization (WHO) clinical guideline. An IL-6 inhibitor 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. The WHO makes a strong recommendation for IL-6 inhibitors in all patients with severe/critical COVID-19, and also states that they may be co-administered with baricitinib and corticosteroids. Where supply is available sarilumab (Kevzara), an off-label treatment for this indication, should continue to be considered where tocilizumab is not available or cannot be used, for dissemination to relevant healthcare professionals for onward transmission as detailed below:-

Could all Directors of Pharmacy please forward this alert to:-

- Hospital Pharmacists
- Procurement Pharmacists

Please could Medical Directors arrange to forward this alert on to:-

- Accident & Emergency Departments
- Paediatric Critical Care
- Nurses
- Infectious Disease Consultants
- Directors of Public Health
- Relevant Clinics
- Chief Executives of NHS Board

Thank you for your co-operation.

Yours sincerely

IRENE FAZAKERLEY
Medicines Policy Team

St Andrew's House, Regent Road, Edinburgh EH1 3DG
www.gov.scot

Department of Health & Social Care

NHS

COVID-19 Therapeutic Alert

This alert replaces the previous alert CEM/CMO/2022/004 issued on 31 January 2022

CEM/CMO/2022/018 29 November 2022

Interleukin-6 inhibitors (tocilizumab or sarilumab) for adult patients hospitalised due to COVID-19

Summary

The published policy, providing access to interleukin-6 (IL-6) inhibitors (tocilizumab (RoActemra) or sarilumab (Kevzara)) to adult patients hospitalised due to COVID-19, has been updated following consideration of the recommendations of the updated World Health Organization (WHO) clinical guideline. An IL-6 inhibitor 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. The WHO makes a strong recommendation for IL-6 inhibitors in all patients with severe/critical COVID-19, and also states that they may be co-administered with baricitinib and corticosteroids.

Where supply is available sarilumab (Kevzara), an off-label treatment for this indication, should continue to be considered where tocilizumab is not available or cannot be used.

The linked clinical guide summarising the main COVID treatment options available to patients admitted to hospital due to COVID, has been updated accordingly to support clinical decision making.

The policy is supported by evidence from the RECOVERY and REMAP-CAP trials, the COVID-19 Rapid Guideline developed by the National Institute for Health and Care Excellence (NICE), and guidelines from the World Health Organization (WHO).

Action

NHS acute trusts / health boards are asked to take the following immediate steps to support treatment of adult patients hospitalised due to COVID-19:

1. **Consider prescribing tocilizumab (or, by exception, sarilumab) to adult patients hospitalised with COVID-19 in line with the criteria set out in the published policy**. In the absence of a confirmed virological diagnosis, tocilizumab or sarilumab should only be used when a multidisciplinary team has a high level of confidence that the clinical and radiological features suggest that COVID-19 is the most likely diagnosis.

2. Maintain access to intravenous tocilizumab for existing (non-COVID-19) indications including treatment of cytokine storm (CRS) following CAR-T cell therapy, rheumatoid arthritis (where appropriate), and paediatric indications.

3. Maintain access to subcutaneous sarilumab for existing rheumatoid arthritis patients.

4. Any organisation treating patients with sarilumab, as an off-label product, will be required to assure itself that the necessary internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the health board / trust drugs and therapeutics committee, or equivalent.

5. Ensure that discharge letters to primary care, and other handovers between care settings, explicitly record the treatment that has been given, together with the dose and date of administration. The following **SNOMED codes should be used** to support evaluation and to inform subsequent treatment decisions:

   Administration of Tocilizumab

   Procedure code: 47943005 |Administration of anti-infective agent (procedure)|

   Presentation:

   - Tocilizumab 80mg/4ml solution for infusion vials – 16102111000001109
   - Tocilizumab 200mg/10ml solution for infusion vials – 16101911000001101
   - Tocilizumab 400mg/20ml solution for infusion vials – 16102011000001108

   Administration of Sarilumab

   Procedure code: 47943005 |Administration of anti-infective agent (procedure)|

   Presentation:

   - Sotrovimab 500mg/8ml solution for infusion vials - 40227411000001101

6. In England, trusts who have not yet done so should register (by site) to participate in COVID-19 specific supply arrangements, respectively, via Blueteq™. Blueteq should also then be used to confirm pre-authorisation for individual patients. HSC Trusts in Northern Ireland should liaise with the Regional Pharmaceutical Procurement Service to register interest. In Scotland, Health Board Directors of Pharmacy should notify NHS National Procurement if they wish to participate. Health Boards in Wales should notify the All Wales Specialist Procurement Pharmacist of their intention to participate.

7. Order tocilizumab and sarilumab supply through existing (business as usual) routes. Retrospective reimbursement of medicines costs will continue to be managed as usual through the excluded drugs funding route in England. Further advice on this is available for Northern Ireland, Scotland and Wales.

8. Provide regular updates on the stock position to trust / hospital and regional pharmacy procurement lead / chief pharmacists.

Product Details

Tocilizumab (RoActemra) is supplied to the UK by Roche CHUGAI. It is a humanised monoclonal antibody against the interleukin-6 (IL-6) receptor.

Tocilizumab has a marketing authorisation in Great Britain (under the Medicines and Healthcare products Regulatory Authority), and in Northern Ireland (under the European Medicines Agency) for use in the treatment of coronavirus disease 2019 (COVID-19) in adults who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation. Tocilizumab for intravenous use also has a marketing authorisation for adults in the treatment of moderate to severe rheumatoid arthritis. Tocilizumab for intravenous use has marketing authorisations for children 2 years and over in the treatment of active systemic juvenile idiopathic arthritis, juvenile idiopathic polyarthritis and CAR-T induced cytokine release syndrome (CRS).

Sarilumab (Kevzara) is supplied to the UK by Sanofi (Aventis Pharma Ltd). It is a human monoclonal antibody that specifically binds to interleukin-6 receptors and blocks the activity of pro-inflammatory cytokines.

Sarilumab for subcutaneous use has a marketing authorisation for adults with moderate to severe rheumatoid arthritis. **Use of sarilumab under this policy as a treatment for COVID-19 is off-label.**

Prescribing Sarilumab As An Off-Label Product

Sarilumab is not licensed for use in COVID-19. As such, clinicians prescribing sarilumab for this indication should follow trust / hospital governance procedures in relation to the prescribing of off-label medicines.

Further guidance on the prescribing of off-label medicines can be found below:

- https://www.gov.uk/drug-safety-update/off-label-or-unlicensed-use-of-medicines-prescribers-responsibilities
- https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/prescribing-unlicensed-medicines
- https://www.rpharms.com/Portals/0/RPS%20document%20library/Open%20access/Professional%20standards/Prescribing%20competency%20framework/prescribing-competency-framework.pdf

Administration

Tocilizumab should be administered as an intravenous infusion at a dose of 8mg per kg, up to a maximum dose of 800mg. 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[1].

A single dose is to be administered. A second dose should not be considered, given the uncertainty over evidence of additional benefit as well as the need to maximise available supply.

[1] The following infusion rate is recommended: 10ml/hour for first 15 minutes then 130ml/hour for the remaining 45 minutes followed by a 20ml normal saline flush.

Sarilumab should be administered as a single dose of 400mg (using 2 x 200mg pre-filled syringes) as an intravenous infusion.

The Medusa monograph is available here (registration / log-on required).

Co-Administration

For further information please visit the University of Liverpool COVID-19 Drug Interactions website (https://www.covid19-druginteractions.org/checker).

Neither tocilizumab nor sarilumab should be infused concomitantly in the same IV line with other medications.

Monitoring, tracking and follow-up

IL-6 inhibitors are immunosuppressants which can suppress C-Reactive Protein (CRP) response for up to 3 months after administration. Monitoring of longer-term progress is recommended via recruitment of patients receiving these agents to the ISARIC-CCP study.

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) should explicitly mention that an IL-6 inhibitor has been given and the date of administration.

Distribution

NHS Trusts (NHS boards in Scotland and Wales)
Regional Medical Directors
Regional Chief Pharmacists
Lead/Senior Pharmacists and Regional Procurement Pharmacy Leads
Trust/Hospital Medical Directors to circulate to medical and nursing staff managing COVID-19 patients

Enquiries

England
Enquiries from NHS trusts in England should in the first instance be directed to your trust pharmacy team who will escalate issues to the Regional Chief Pharmacist and national teams if required. Further information can be requested from the dedicated email address: england.spoc-c19therapeutics@nhs.net.

Northern Ireland
Enquiries from hospitals in Northern Ireland should in the first instance be directed to your hospital pharmacy team who will escalate issues to the Regional Pharmaceutical Procurement Service or Pharmaceutical Directorate at the Department of Health if required Further information can be obtained by contacting RPHPS.Admin@northerntrust.hscni.net

Scotland
Enquiries from hospitals in Scotland should in the first instance be directed to your hospital pharmacy team who will escalate issues to either NHS National Procurement or

the Scottish Government's Medicines Policy Team if required. Contact should be made using the following emails: nss.nhssmedicineshortages@nhs.scot or medicines.policy@gov.scot

Wales

Enquiries from hospitals in Wales should in the first instance be directed to the health board's Chief Pharmacist who will escalate issues to the Pharmacy and Prescribing Team at Welsh Government if required. Enquiries to the Welsh Government should be directed to: COVID-19.Pharmacy.Prescribing@gov.wales.

Rapid Policy Statement

Interim Clinical Commissioning Policy: IL-6 inhibitors (tocilizumab or sarilumab) for hospitalised patients with COVID-19 (adults)

Publication date: 28 November 2022
Effective from: 28 November 2022

Commissioning position

Tocilizumab is recommended to be available as a treatment option through routine commissioning for adult patients (aged 18 years and older) hospitalised with COVID- 19 in accordance with the criteria set out in this document. Patients may alternatively be considered for treatment with sarilumab where tocilizumab is unavailable for this indication or cannot be used.

Evidence and policy summary

This updated UK Clinical Commissioning Policy for IL-6 inhibitors reflects the change in 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.

Evidence from the REMAP-CAP trial demonstrates a clinical benefit with the use of tocilizumab or sarilumab in patients with COVID-19 requiring organ support. In February 2021, the RECOVERY trial announced the findings of tocilizumab use in a broader hospitalised population, which indicated that tocilizumab significantly improved survival and other clinical outcomes in patients with hypoxaemia and systemic inflammation (severe COVID-19).

New evidence and guidance have since emerged to indicate the possibility of equivalence between the two IL-6 inhibitors, which is summarised below:

- 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).

- A prospective meta-analysis of clinical trials of IL-6 inhibitors in patients hospitalized for COVID-19 showed that they were associated with lower 28-day all-cause mortality.

The World Health Organization (WHO) updated its 'Therapeutics and COVID-19: Living guideline' on 16 September 2022 and the recommendations have been considered in the development of this policy. The guideline did not recommend the use of one IL- 6 inhibitor over the other. (WHO, September 2022).

The NICE Rapid Guideline on managing COVID-19 recommends the use of sarilumab for adults in hospital with COVID-19 if tocilizumab cannot be used or is unavailable. These guidelines were developed based on the consensus of a separate expert group and an independent evidence summary which states there is significant uncertainty around the efficacy and safety of sarilumab compared to standard care in treating patients with COVID-19.

Implementation

Eligibility criteria

Patients must meet all the eligibility criteria and none of the exclusion criteria. Hospitalised patients are eligible[1] to be considered for **tocilizumab** 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[2] (corticosteroid CAS alert) unless contraindicated;

  AND

  Either

  - Hypoxaemia with evidence of inflammation but not yet critically ill requiring respiratory support[3] 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;

[1] 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

[2] Patients are expected to be on a corticosteroid as the current standard of care, except where there is a strong contraindication against its use. Patients may be commenced on both a corticosteroid and tocilizumab simultaneously if deemed clinically appropriate.

[3] In the context of the COVID-19 pandemic, treatment of patients critically unwell with COVID-19 can be in the following (critical care equivalent) settings: designated intensive care unit (ICU); surge ICU; or other hospital settings delivering an equivalent level of respiratory care (such as respiratory ward, infectious disease ward).

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[4] 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.

Sarilumab should be considered as an alternative option if tocilizumab is unavailable for this indication or cannot be used, and the above criteria are met.

Exclusion criteria and cautions

Tocilizumab should not be administered in the following circumstances:

- Known hypersensitivity to tocilizumab
- Liver enzymes [alanine aminotransferase (ALT) or aspartate aminotransferase (AST)] ten times or greater the upper limit of normal
- Absolute neutrophil count of less than 1 x 10^9/L
- Platelet count of less than 50 x 10^3/µL

Sarilumab should not be administered in the following circumstances:

- Known hypersensitivity to sarilumab
- Liver enzymes [alanine aminotransferase (ALT) or aspartate aminotransferase (AST)] more than 5 times the upper limit of normal
- A baseline platelet count of less than 150 x 10^9/L
- Absolute neutrophil count of less than 2 x 10^9/L

Please refer to the Summary of Product Characteristics (SmPC) for tocilizumab and sarilumab (in Northern Ireland, refer to the EMA SmPCs for tocilizumab and sarilumab) 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.

Caution should be exercised when considering treatment with IL-6 inhibitors in the following circumstances:

- Co-existing infection[5] 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 thrombocytopenia. Please note that C-reactive protein (CRP) levels may be depressed for some time after treatment with tocilizumab. Consequently, in this setting, caution should be exercised in the interpretation of CRP as a marker of infection.

---

[4] Treatment should be started as early as possible

[5] Any active, severe infection other than COVID-19; caution is advised when considering the use of tocilizumab or sarilumab in patients with a history of recurring or chronic infections or with underlying conditions which may predispose patients to infections.

Pregnancy and women of childbearing potential

Tocilizumab and sarilumab should not be used during pregnancy unless clinically necessary.

The SmPC for tocilizumab currently states that: "*Women of childbearing potential must use effective contraception during and up to 3 months after treatment. There are no adequate data from the use of tocilizumab in pregnant women. A study in animals has shown an increased risk of spontaneous abortion/embryo-foetal death at a high dose. The potential risk for humans is unknown. RoActemra should not be used during pregnancy unless clearly necessary."*

The SmPC for sarilumab currently states that: *"Women of childbearing potential should use effective contraception during and up to 3 months after treatment. There are no or limited amount of data from the use of sarilumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. Kevzara should not be used during pregnancy unless the clinical condition of the woman requires treatment with sarilumab."*

The SmPC for tocilizumab and sarilumab should be consulted if further information is required.

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."*

Dose

<u>Tocilizumab</u>

The recommended dose of tocilizumab is 8mg/kg to be administered as an intravenous infusion. The total dose should not exceed 800mg. 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[6].

A single dose is to be administered. A second dose should not be considered, given the uncertainty over evidence of additional benefit as well as the need to maximise available supply. Tocilizumab should not be infused concomitantly in the same IV line with other medications.

<u>Sarilumab</u>

The recommended dose of sarilumab is 400mg to be delivered as a once-only intravenous infusion. Sarilumab is available as a pre-filled syringe. For a 400mg dose two 200mg pre-filled syringes should be injected into a 100mL sodium chloride 0.9% infusion bag. The bag should be inverted at least 10 times to ensure thorough mixing and given over 1 hour[7].

---

[6] The following infusion rate is recommended: 10ml/hour for first 15 minutes then 130ml/hour for the remaining 45 minutes followed by a 20ml normal saline flush.

[7] The following infusion rate is recommended: 10ml/hour for first 15 minutes then 130ml/hour for the remaining 45 minutes followed by a 20ml normal saline flush

Sarilumab should not be infused concomitantly in the same IV line with other medications**.** Further information on the use of sarilumab intravenously is available at: https://medusa.wales.nhs.uk/ (registration may be required).

Combination treatment

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. The WHO makes a strong recommendation for IL-6 inhibitors in all patients with severe/critical COVID-19, and also states that they may be co-administered with baricitinib and corticosteroids. (WHO, September 2022).

Co-administration

There is no interaction expected between IL-6 inhibitors with other commissioned COVID-19 treatments. For further information please visit the University of Liverpool COVID-19 Drug Interactions website (https://www.covid19-druginteractions.org/checker).

Please refer to other published UK clinical commissioning policies setting out available COVID-19 treatments here.

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/.

In addition, treatment with IL-6 inhibitors 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. It also causes 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 an IL-6 inhibitor and provide information to the patient to such effect.

Marketing authorisation

Tocilizumab

Tocilizumab delivered intravenously is authorised for use in the treatment of coronavirus disease 2019 (COVID-19) in adults who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation. It is also licensed for use in moderate to severe active rheumatoid arthritis, some forms of juvenile idiopathic arthritis and for cytokine release syndrome as part of CAR-T therapy. NHS England also commissions off-label use of tocilizumab for Takayasu arteritis and Still's Disease.

Sarilumab

Sarilumab has marketing authorisation for subcutaneous use in adults with moderate to severe active rheumatoid arthritis. **The use of sarilumab intravenously in COVID-19 is off label.**

Governance

Off-label use of medication

Any provider organisation treating patients with these interventions will be required to assure itself that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the health board/hospital/trust's drugs and therapeutics committee, or equivalent.

Data collection requirement

Provider organisations in England should register all patients using prior approval software (alternative arrangements in Scotland, Wales and Northern Ireland will be communicated) and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined.

Clinical outcome reporting

Hospitals managing COVID-19 patients are strongly encouraged to submit data through the ISARIC 4C Clinical Characterisation Protocol (CCP) case report forms (CRFs), as coordinated by the COVID-19 Clinical Information Network (CO-CIN) (https://isaric4c.net/protocols/).

Effective from

This policy will be in effect from the date of publication.

Policy review date

This is an interim rapid clinical policy statement, which means that the full process of policy production has been abridged: public consultation has not been undertaken. This policy may need amendment and updating if, for instance, new trial data emerges, supply of the drug changes, or a new evidence review is required. A NICE Technology Appraisal or Scottish Medicines Consortium (SMC) Health Technology Assessment or All Wales Medicines Strategy Group (AWMSG) appraisal of tocilizumab for COVID-19 would supersede this policy when completed.

Equality statement

Promoting equality and addressing health inequalities are at the heart of the four nations' values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010 or equivalent equality legislation) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Definitions

COVID-19	Refers to the disease caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus
High-flow nasal cannula	An oxygen supply system capable of delivering up to 100% humidified and heated oxygen at a flow rate of up to 60L/minute
Continuous positive airway pressure	A type of positive airway pressure in which air flow is introduced into the airways to maintain a continuous pressure that constantly keeps the airways open
Non-invasive ventilation	The administration of breathing support for those unable to breathe on their own without using an invasive artificial airway
Invasive mechanical ventilation	A life support treatment which helps people breathe using an invasive artificial airway when they are not able to breathe enough on their own

References

1. Lescure FX, Honda H, Fowler RA, et al. Sarilumab in patients admitted to hospital with severe or critical COVID-19: a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Respir Med*. 2021;9(5):522-532. doi:10.1016/S2213-2600(21)00099-0
2. RECOVERY Collaborative Group. Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *Lancet*. 2021;397(10285):1637-1645. doi:10.1016/S0140-6736(21)00676-0
3. REMAP-CAP Investigators, Derde LPG, et al. Effectiveness of Tocilizumab, Sarilumab, and Anakinra for critically ill patients with COVID-19 The REMAP-CAP COVID-19 Immune Modulation Therapy Domain Randomized Clinical Trial. 2021. Preprint available at: https://www.medrxiv.org/content/10.1101/2021.06.18.21259133v2
4. REMAP-CAP Investigators, Gordon AC, Mouncey PR, et al. Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19. *N Engl J Med*. 2021;384(16):1491-1502. doi:10.1056/NEJMoa2100433
5. WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, Shankar-Hari M, Vale CL, et al. Association Between Administration of IL-6 Antagonists and Mortality Among Patients Hospitalized for COVID-19: A Meta-analysis. *JAMA*. 2021;326(6):499-518. doi:10.1001/jama.2021.11330

Clinical pathway: Therapies for patients hospitalised due to COVID-19

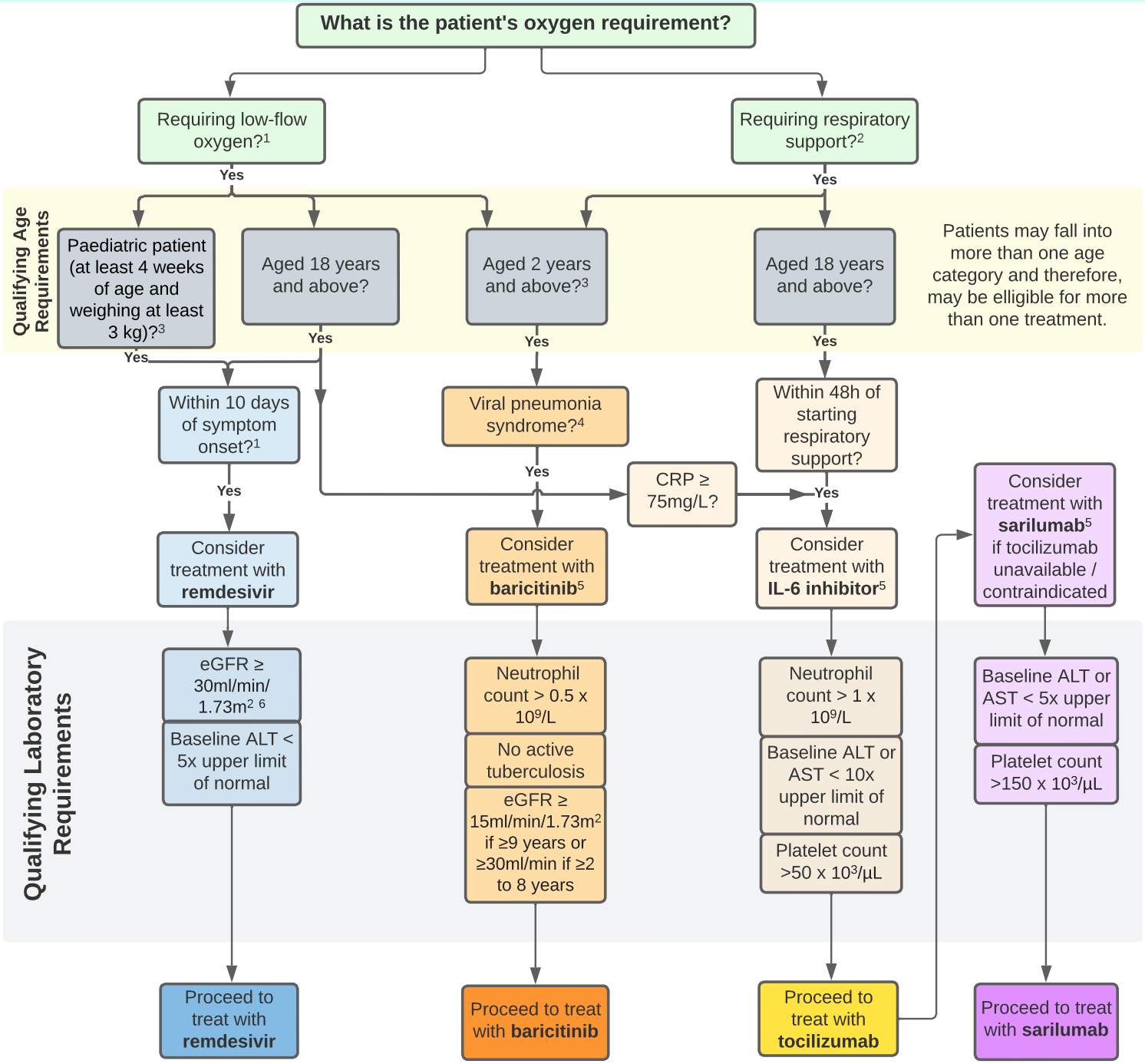
- This guide aims to support treatment decisions for commissioned COVID-19 therapies and outlines their position in the treatment pathway for patients hospitalised due to COVID-19. The relevant clinical commissioning policies should be consulted for further details
- Patients must be **hospitalised specifically for management of COVID-19** and must be **receiving supplemental oxygen or receiving respiratory support**
- Consult the relevant Summary of Product Characteristics for advice on contraception and use in pregnancy
- Please refer to the NICE COVID-19 Rapid Guideline (NG 191) for other treatments

CORTICOSTEROIDS

Consider dexamethasone (or hydrocortisone or prednisolone if treatment with dexamethasone is unavailable/not possible) in patients who require supplemental oxygen to maintain prescribed oxygen saturation levels

TRIALS

All **hospitalised** patients can consider joining the RECOVERY trial or the pandemic aspects of the REMAP-CAP trial. To enter RECOVERY, they should have: a **viral pneumonia syndrome**; confirmed **SARS-CoV-2 infection**; and no **medical history** that might put the patient at risk from entering a trial. To enter REMAP-CAP, they should be in critical care with an **acute illness due to suspected pandemic illness**. Patients can be referred for entry into clinical trials at any stage in this clinical pathway and will continue to receive treatment under this pathway in addition to any trial medication prescribed.



Deterioration - Consider other therapeutic agent(s) from group above in accordance with respective clinical policies

[1] For treatment with remdesivir, the criteria relating to supplemental oxygen and the treatment window from symptom onset do not apply to significantly immunocompromised patients.
[2] Defined as: high-flow nasal oxygen, continuous positive airway pressure (CPAP) or non-invasive ventilation, or invasive mechanical ventilation.
[3] Clinicians should seek paediatric MDT advice for paediatric patients to determine clinical capacity to benefit from treatment.
[4] In general, viral pneumonia should be suspected when a patient presents with: a) typical symptoms (e.g. influenza-like illness with fever and muscle pain, or respiratory illness with cough and shortness of breath); AND b) compatible chest X-ray findings (consolidation or ground-glass shadowing); AND c) alternative causes have been considered unlikely or excluded (e.g. heart failure, bacterial pneumonia).
[5] 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.
[6] Patients with end-stage renal disease on haemodialysis are exempt from the specified eGFR threshold.

November 2022 Version 4. Not valid if printed.