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Rapid Policy Statement

Interim Clinical Commissioning Policy: Sarilumab for critically ill patients with COVID-19 pneumonia (adults)

22 February 2021

Commissioning position

The commissioning position is: sarilumab 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.

Evidence summary

A rapid evidence review published by the National Institute for Health and Care Excellence (NICE) on 20 January 2021 suggested that any mortality or recovery benefit from sarilumab is seen only in the most severely ill patients given sarilumab soon after organ support is started, when any developing organ dysfunction may be more reversible.

https://www.nice.org.uk/advice/es34/chapter/Product-overview

Implementation

Eligibility criteria

Patients must meet all of the eligibility criteria and none of the exclusion criteria. Hospitalised patients are eligible to be considered for sarilumab if[1]:

- 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
- Treated with respiratory support (high-flow nasal oxygen, continuous positive airway pressure (CPAP) or non-invasive ventilation, or invasive mechanical ventilation);[2, 3] and

[1] Sarilumab should only be considered in patients who have not already received tocilizumab (or other IL-6 inhibitor).
[2] 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).
[3] The decision to treat with sarilumab should be made by two consultants, of whom one should be experienced in respiratory support (as defined above).

- Less than 24 hours[4] have elapsed since commencement of respiratory support (high-flow nasal oxygen, continuous positive airway pressure (CPAP) or non-invasive ventilation, or invasive mechanical ventilation).

Exclusion criteria

Sarilumab should not be administered in the following circumstances:

- Known hypersensitivity to sarilumab
- Co-existing infection[5] that might be worsened by sarilumab
- A baseline alanine aminotransferase (ALT) or aspartate aminotransferase (AST) more than 5 times the upper limit of normal (caution is recommended if hepatic enzymes are more than 1.5 times the upper limit of normal)
- A baseline platelet count of less than 150 x 10^9/L
- A pre-existing condition or treatment resulting in ongoing immunosuppression

Please refer to the Summary of Product Characteristics (SmPC) for sarilumab for contraindications and cautions for use.

Caution is necessary when prescribing sarilumab to patients with neutropaenia. Please note that C-reactive protein (CRP) levels may be depressed for some time after treatment with sarilumab.

Pregnancy and women of childbearing potential

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 sarilumab should be consulted if further information is required.

For women who are breast-feeding, the SmPC states "*It is unknown whether sarilumab is excreted in human milk or absorbed systemically after ingestion. The excretion of sarilumab in milk has not been studied in animals. Because IgG1 are excreted in human milk, a decision should be made whether to discontinue breast-feeding or to discontinue sarilumab therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman."*

Dose

The recommended dose of sarilumab is 400mg to be delivered as a once-only intravenous infusion. **Please note that the use of sarilumab intravenously in COVID-19 is off label.**

[4] This can be extended up to a maximum of 48 hours for relevant clinical reasons, such as transfer of patients. However, the principle is to treat patients as early as possible in their critical illness.
[5] Any active, severe infection other than COVID-19; caution is advised when considering the use of sarilumab in patients with a history of recurring or chronic infections or with underlying conditions which may predispose patients to infections.

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[6].

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).

Co-administration

Corticosteroids

Administration of systemic dexamethasone or hydrocortisone (corticosteroid CAS alert) is recommended in the management of patients with severe or critical COVID-19. Corticosteroids are not suggested in non-severe COVID-19 disease. Updated WHO guidance on the use of systemic corticosteroids in the management of COVID-19 can be found here. Sarilumab should not be regarded as an alternative to corticosteroids.

There is no interaction of sarilumab with either dexamethasone or hydrocortisone expected. For further information please visit the University of Liverpool COVID-19 Drug Interactions website (https://www.covid19-druginteractions.org/checker).

Remdesivir

The Clinical Commissioning Policy for the use of remdesivir in hospitalised patients with COVID-19 who require supplemental oxygen can be found here. There is no interaction of sarilumab with remdesivir expected. For further information please visit the University of Liverpool COVID-19 Drug Interactions website (https://www.covid19-druginteractions.org/checker).

Safety reporting

This medicine does not yet have a licence (marketing authorisation) for use in COVID-19 and therefore 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 sarilumab can lower the ability of the immune system to fight infections which could increase the risk of getting infection or make any infection the patient contracts worse. It also causes prolonged depression of CRP levels, making it 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 also 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 sarilumab and provide information to the patient to such effect.

Marketing authorisation

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.**

[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

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 sarilumab 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