Department of Health & Social Care

NHS

COVID-19 Therapeutic Alert

CEM/CMO/2021/004 01 February 2021

Interleukin-6 inhibitors (tocilizumab or sarilumab) for critically ill patients with COVID-19 pneumonia (adults)

Summary

UK Interim Clinical Commissioning Policies have now been published, recommending that two Interleukin-6 (IL-6) inhibitors - tocilizumab and sarilumab - are made available as a treatment option for critically ill adult patients (aged 18 years and older) hospitalised with COVID-19 in accordance with the agreed criteria.

The REMAP-CAP trial has reported a finding of survival and time to recovery benefits for tocilizumab or sarilumab, over and above current standard of care (including corticosteroids), in the immune modulation therapy domain of the REMAP-CAP platform trial. Mortality was reported as 35.8% in the standard of care group, compared to 27.3% in the treatment group, an overall reduction in the relative risk of death of 24%. The treatment also reduced the time patients spent in the intensive care unit (ICU) by more than a week on average.

Rapid evidence reviews were subsequently published by the National Institute for Health and Care Excellence (NICE) for tocilizumab (15th January), and sarilumab (20th January), respectively. These reviews suggested that any mortality or recovery benefit from tocilizumab or sarilumab is seen only in the most severely ill patients who are given these agents soon after organ support is started, when any developing organ dysfunction may be more reversible.

Recruitment has now closed to the tocilizumab arm of the RECOVERY trial and the results are currently awaited. The policies will be further updated as required, once further data are available.

Please note that in addition to the tocilizumab supply arrangements put in place to support access under the previously published interim position statement, sarilumab supply will now also be available from early February.

Action

NHS acute trusts / health boards are asked to take the following immediate steps to support treatment of critically ill patients with COVID-19:

1. **Organisations are recommended to consider prescribing either tocilizumab or sarilumab to hospitalised patients with COVID-19 pneumonia being treated with non-invasive ventilation (including high-flow nasal oxygen therapy or continuous positive airway pressure ventilation) or invasive mechanical ventilation.** Any organisation treating patients with either IL-6 inhibitor, as off-label products, 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.

2. Ensure that the criteria described in the published Interim Clinical Commissioning Policies are used to identify patients with COVID-19 related pneumonia who may be suitable for treatment with tocilizumab or sarilumab. 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.

3. In England, trusts who have not yet done so should register (by site) to participate in COVID-19 specific tocilizumab and sarilumab supply arrangements, respectively, via Blueteq™. Blueteq should also then be used to confirm pre-authorisation for individual patients. Blueteq forms are now also available for post pubescent children under NHS England's Medicines for Children Policy. 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.

4. Order tocilizumab and sarilumab supply through existing (business as usual) routes. Arrangements have been made with Roche CHUGAI and Sanofi to secure initial supply to the UK to meet potential COVID-19 treatment requirements, alongside existing (licensed) clinical indications. For those organisations who have formally confirmed they wish to participate, the additional supply will be managed by providing an indicative maximum order 'cap' by hospital / trust (based on modelled intensive care activity). Retrospective reimbursement of medicines costs will continue to be managed as usual through the excluded drugs funding route in England. Further advice on this will follow for Northern Ireland, Scotland and Wales.

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

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

7. 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 for intravenous use 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.

The published Interim Clinical Commissioning Policies cover off-label use of tocilizumab or sarilumab in adults as an intravenous infusion.

Prescribing

Tocilizumab and sarilumab are not licensed for use in COVID-19. As such, clinicians prescribing either tocilizumab or 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/prescribing-and-managing-medicines-and-devices/prescribing-unlicensed-medicines#paragraph-71

Administration

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

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.

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).

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

Co-Administration

Corticosteroids

Administration of systemic dexamethasone or hydrocortisone 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. There is no interaction of tocilizumab or sarilumab with either dexamethasone or hydrocortisone expected.

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 either tocilizumab, or sarilumab, with remdesivir expected.

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

Monitoring, tracking and follow-up

IL-6 inhibitors are immunosuppresants 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.