Department of Health & Social Care

NHS

COVID-19 Therapeutic Alert

This alert replaces the previous alert CEM/CMO/2021/006 issued on 17th February 2021

CEM/CMO/2021/016 12 September 2021

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

Summary

A single UK Interim Clinical Commissioning Policy has now been published, recommending that equal consideration is given to two potential interleukin-6 (IL-6) inhibitor treatment options - tocilizumab or sarilumab - for adult patients (aged 18 years and older) hospitalised due to COVID-19 in accordance with the agreed criteria. The combined policy replaces previous separately published policies for sarilumab and tocilizumab respectively.

The policy takes into account evidence from the RECOVERY and REMAP-CAP trials, a rapid evidence review undertaken by the National Institute for Health and Care Excellence (NICE), updated guidelines (July 2021) from the World Health Organization (WHO) and currently available supplies of both medicines as a treatment for COVID-19 and other existing (routine) indications.

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. **Organisations are recommended to consider prescribing either tocilizumab or 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. 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.

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. For those organisations who have formally confirmed they wish to participate, supply will be managed, where required, by providing an indicative maximum order 'cap' by hospital / trust. 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.

5. 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.

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 Policy 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/good-practice-in-prescribing-and-managing-medicines-and-devices/prescribing-unlicensed-medicines

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 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.