Department of Health & Social Care

NHS

COVID-19 Therapeutic Alert

CEM/CMO/2020/038 25 November 2020

Publication of an interim position statement: Tocilizumab for patients admitted to ICU with COVID-19 pneumonia (adults)

Summary

Following early positive signals of benefit from the immune modulation therapy domain of the REMAP-CAP platform trial, a UK wide position statement has been agreed to support off-label prescribing and access to tocilizumab, administered intravenously, for eligible COVID positive patients in the intensive care setting.

The interim position statement will be reviewed as further evidence becomes available, including from the REMAP-CAP trial.

Action

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

1. REMAP-CAP trial centres should continue to enrol patients into the study. The trial Data and Safety Monitoring Board (DSMB) has determined that it is ethically imperative to withdraw the standard-of-care control arm of the immunomodulatory domain. However, the domain will continue, with all patients receiving an immune modulator to determine relative effectiveness.

2. **Confirm whether or not the organisation wishes to prescribe tocilizumab in the treatment of patients admitted to intensive care with COVID-19 outside of a trial.** Any provider organisation treating patients with this intervention, 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's drugs and therapeutics committee (or equivalent).

3. In England, trusts should register to participate in COVID-19 specific tocilizumab supply arrangements 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

4. Ensure that the criteria described in the interim position statement are used to identify patients with COVID-related pneumonia who may be potentially suitable for treatment with tocilizumab. In the absence of a confirmed virological diagnosis, tocilizumab

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.

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

6. 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. With the exception of CRS, patients can alternatively be switched to the subcutaneous formulation of tocilizumab. To assess suitability for available subcutaneous formulations for rheumatoid arthritis (RA) and paediatric arthritis patients, please consult the relevant Summary of Product Characteristics.

7. Provide regular updates on the stock position to trust / hospital and regional procurement pharmacy 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 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-induced cytokine release syndrome (CRS).

The published interim position statement covers off-label use of tocilizumab in adults as an intravenous infusion.

Prescribing

Tocilizumab is not licensed for use in COVID-19. As such clinicians prescribing tocilizumab for this indication should follow trust / hospital governance procedures in relation to the prescribing of unlicensed/off label medicines. Further information on the prescribing of unlicensed/off label medicines can be found here:

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 second infusion may be given after 12-24 hours if after the initial dose there has not been sufficient clinical improvement.

Tocilizumab should not 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 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 tocilizumab with remdesivir expected.

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

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