Department of Health & Social Care

NHS

COVID-19 Therapeutic Alert

CEM/CMO/2021/001 8 January 2021

Interleukin-6 inhibitors (tocilizumab or sarilumab) for patients admitted to ICU with COVID-19 pneumonia (adults)

Summary

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 placebo group, compared to 27% in the treatment group, an overall reduction in the 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. The published UK wide Interim Position Statement has therefore been revised to support access to either tocilizumab or sarilumab (when available), administered intravenously, for eligible COVID-19 positive patients in the intensive care setting.

As supply of sarilumab is more limited at the current time, provision is likely to need to initially focus predominantly on tocilizumab. Initial stocks of additional tocilizumab supply for the UK have been secured.

Work is now underway to develop a UK clinical commissioning policy for tocilizumab and sarilumab, which will be based on a NICE review of the available research evidence. The policy will replace the Interim Position Statement.

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. RECOVERY trial sites should continue to enrol patients into the study to help determine whether tocilizumab has a role in the future routine treatment of the wider cohort of admitted COVID-19 positive patients.

2. **Organisations are encouraged to consider prescribing either tocilizumab or sarilumab in the treatment of patients admitted to intensive care with COVID-19 pneumonia.** Any organisation treating patients with either intervention, 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 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. 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 revised Interim Position Statement are used to identify patients with COVID-19 related pneumonia who may be potentially 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.

5. Continue to order tocilizumab supply through existing (business as usual) routes. Arrangements have been made with Roche CHUGAI 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.

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.

7. Maintain access to subcutaneous sarilumab for existing rheumatoid arthritis patients. Updates will be provided on additional sarilumab supply, via pharmacy lead networks and their equivalents in Northern Ireland, Scotland and Wales, as soon as further information is available.

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 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).

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 Position Statement covers off-label use of both tocilizumab and 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.
The following dose bandings are suggested:

Weight	Dose
<41kg	8mg/kg, rounded to 20mg
≥ 41kg and ≤ 45kg	360mg
≥ 46kg and ≤ 55kg	400mg
≥ 56kg and ≤ 65kg	480mg
≥ 66kg and ≤ 80kg	600mg
≥ 81kg and ≤ 90kg	680mg
≥91kg	800mg

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

Sarilumab should be administered as a single dose of 400mg as an intravenous infusion.

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).

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.