Department of Health & Social Care

NHS

COVID-19 Therapeutic Alert

This alert replaces the previous alert CEM/CMO/2021/016 issued on 12 September 2021

CEM/CMO/2022/004 31 January 2022

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

Summary

The published policy has been updated to reflect that tocilizumab (RoActemra) is now licensed as a treatment for adult patients hospitalised due to COVID-19 who are receiving systemic corticosteroids and require supplementary oxygen or mechanical ventilation. Please note that additional exclusion criteria now apply. Where supply is available sarilumab (Kevzara), an off-label treatment for this indication, should continue to be considered where tocilizumab is not available or cannot be used.

The policy is supported by evidence from the RECOVERY and REMAP-CAP trials, the COVID-19 Rapid Guideline developed by the National Institute for Health and Care Excellence (NICE), and guidelines from the World Health Organization (WHO).

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 tocilizumab (or, by exception, 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. 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.

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

4. Any organisation treating patients with sarilumab, 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 drugs and therapeutics committee, or equivalent.

5. In England, trusts who have not yet done so should register (by site) to participate in COVID-19 specific 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.

6. Order tocilizumab and sarilumab supply through existing (business as usual) routes. 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.

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 has a marketing authorisation in Great Britain (under the Medicines and Healthcare products Regulatory Authority), and in Northern Ireland (under the European Medicines Agency) for use in the treatment of coronavirus disease 2019 (COVID-19) in adults who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation. Tocilizumab for intravenous use also 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. **Use of sarilumab under this policy as a treatment for COVID-19 is off-label.**

Prescribing Sarilumab As An Off-Label Product

Sarilumab is not licensed for use in COVID-19. As such, clinicians prescribing 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
- https://www.rpharms.com/Portals/0/RPS%20document%20library/Open%20access/Professional%20standards/Prescribing%20competency%20framework/prescribing-competency-framework.pdf

Administration

Tocilizumab should be administered as an intravenous infusion at a dose of 8mg per kg, up to a maximum dose of 800mg. Tocilizumab should be diluted in a 100mL bag of 0.9% sodium chloride, after removing an equivalent volume of saline (total volume 100mL) and given over 1 hour[1].

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).

Co-Administration

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

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

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

[1] 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.

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.