From the Chief Medical Officer
Prof Sir Michael McBride

Department of Health
An Roinn Sláinte
Männystrie O Poustie
www.health-ni.gov.uk

HSS(MD) 57/2022

FOR ACTION
Chief Executives, Public Health Agency/HSC Trusts/ NIAS/ Deputy Secretary SPPG

PLEASE SEE ATTACHED FULL CIRCULATION LIST

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Our Ref: HSS(MD) 57/2022
Date: 1 December 2022

Dear Colleague

COVID-19 THERAPEUTIC ALERT: INTERLEUKIN-6 INHIBITORS (TOCILIZUMAB OR SARILUMAB) FOR ADULT PATIENTS HOSPITALISED DUE TO COVID-19

This letter supersedes HSS (MD) 05/2022

The published policy, providing access to interleukin-6 (IL-6) inhibitors (tocilizumab (RoActemra) or sarilumab (Kevzara)) to adult patients hospitalised due to COVID-19, has been updated following consideration of the recommendations of the updated World Health Organization (WHO) clinical guideline. An IL-6 inhibitor may be administered in combination with baricitinib (as well as corticosteroids, unless contraindicated), according to clinical judgement, in patients with severe or critical COVID-19. The WHO makes a strong recommendation for IL-6 inhibitors in all patients with severe/critical COVID-19, and also states that they may be co-administered with baricitinib and corticosteroids.

The linked clinical guide, summarising the main COVID treatment options available to patients admitted to hospital due to COVID, has been updated accordingly to support clinical decision making.

Action required

HSC Trusts are asked to take the following immediate steps to support treatment of adult patients hospitalised due to COVID-19:

1. **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 HSC Trust drugs and therapeutics committee, or equivalent.

5. Ensure that discharge letters to primary care, and other handovers between care settings, explicitly record the treatment that has been given, together with the dose and date of administration.

6. HSC Trusts should liaise with the Regional Pharmaceutical Procurement Service to register interest in COVID-19 specific supply arrangements. Trusts should 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 Trust.

7. Provide regular updates on the stock position to HSC Trust Heads of Pharmacy and Medicines Management, pharmacy procurement leads and the Regional Pharmaceutical Procurement Service.

The **Strategic Planning and Performance Group** is asked to:

8. Work with HSC Trusts and the Regional Pharmaceutical Procurement Service to develop proportionate interim arrangements to monitor uptake of treatment, pending consideration for routine commissioning in line with extant Managed Entry arrangements.

Summary

The published policy, providing access to interleukin-6 (IL-6) inhibitors (tocilizumab (RoActemra) or sarilumab (Kevzara)) to adult patients hospitalised due to COVID-19, has been updated following consideration of the recommendations of the updated World Health Organization (WHO) clinical guideline. An IL-6 inhibitor may be administered in combination with baricitinib (as well as corticosteroids, unless contraindicated), according to clinical judgement, in patients with severe or critical COVID-19. The WHO makes a strong recommendation for IL-6 inhibitors in all patients with severe/critical COVID-19, and also states that they may be co-administered with baricitinib and corticosteroids.

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 linked clinical guide summarising the main COVID treatment options available to patients admitted to hospital due to COVID, has been updated accordingly to support clinical decision making.

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).

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 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.

[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.

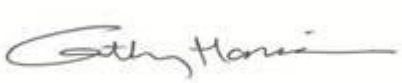
Monitoring, tracking and follow-up

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.

Further enquiries should in the first instance be directed to your hospital pharmacy team.

Yours sincerely



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