Distribution: As Appendix 1

From: Chief Pharmaceutical Officer, Andrew Evans

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Reference: CEM/CPhA/2021/27

Category: Immediate – Action within 24 hours

Title: Covid-19 Therapeutic Alert: Interleukin-6 inhibitors (tocilizumab or sarilumab) for adult patients hospitalised due to COVID-19

For Action by:

Chief Pharmacists - Action as below.
Medical Directors – Action as below.

Why has it been sent: For your information, action and to pass on to colleagues.

Issue

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 (issued in Wales under CEM/CMO/2021/10 on 19th February 2021)

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:

Health Boards/ Trusts 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. Health Boards/ Trusts in Wales should notify the All Wales Specialist Procurement Pharmacist of their intention to participate in COVID-19 specific tocilizumab and sarilumab supply arrangements if they have not already done so.

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 / Health Board. 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.

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

6. Provide updates on the stock position to the All Wales Specialist Procurement Pharmacist procurement lead as requested. Health Boards should continue to identify usage of tocilizumab and sarilumab for the treatment of COVID as per exisiting arrangements.

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.

Appendix 1

To: Chief Executives of Health Boards and NHS Trusts

Medical Directors of Health Boards

Nurse Directors Health Boards

Directors of Public Health

Hospital Principals and Chief Pharmacists to action as per alert

NHS Direct

AWTTC

To: **NHS Wales Shared Services Partnership for information.**