Public Health Link
From the Chief Medical Officer for Wales

Distribution: As Appendix 1

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Title: **COVID-19 Therapeutic Alert - Baricitinib for Patients Hospitalised Due to COVID-19 (Adults and Children Aged 2 Years and Over)**

Dear colleagues,

Baricitinib (Olumiant) is a selective and reversible Janus kinase (JAK) 1 and 2 inhibitor, licensed as an anti-inflammatory treatment for rheumatoid arthritis and atopic dermatitis. JAK-inhibitors are thought to control high levels of cytokines and inflammation, seen in patients with severe SARS-CoV-2 infection.

Data from the RECOVERY trial demonstrates that baricitinib reduces the risk of death when given to hospitalised patients with severe COVID-19. Between February and December 2021, 4,008 patients randomly allocated to usual care alone were compared with 4,148 patients who were randomly allocated to usual care plus baricitinib. Treatment with baricitinib significantly reduced deaths: 513 (12%) of the patients in the baricitinib group died within 28 days compared with 546 (14%) patients in the usual care group, a relative reduction of 13% (age-adjusted rate ratio 0.87, 95% confidence interval [CI] 0.77 to 0.98; p= 0.026). The benefit of baricitinib was consistent regardless of which other COVID-19 treatments the patients were also receiving, including corticosteroids, tocilizumab, or remdesivir.

Patients hospitalised due to COVID-19 are eligible for treatment with baricitinib under the published UK clinical access policy (attached) if the following criteria are met:

- COVID-19 infection is confirmed by microbiological testing or where a multidisciplinary team has a high level of confidence that the clinical and/or radiological features suggest that COVID-19 is the most likely diagnosis;

AND

- Viral pneumonia syndrome[1] is present

[1] Viral pneumonia syndrome. In general, as per the RECOVERY trial protocol, viral pneumonia should be suspected when a patient presents with: typical symptoms (e.g. influenza-like illness with fever and muscle pain, or respiratory illness with

AND

- Receiving supplemental oxygen or respiratory support[2] for the treatment of COVID-19;

AND

- Receiving dexamethasone or an equivalent corticosteroid[3] (corticosteroid alert) unless contraindicated.

Baricitinib can be considered in children (age 2 to 17 years inclusive) with severe COVID- 19, guided by clinical judgement and multi-disciplinary team assessment. Although the RECOVERY trial included this age group, it should be noted that this cohort was too small to reach statistical significance, the summary of product characteristics (SmPC) is only for adults, and there are limited data on both clinical effectiveness and safety in children. Use in all ages is off-label.

Please refer to the full UK clinical access policy (attached) and linked summary clinical guide for further information, including cautions and exclusion criteria.

ACTION

Health boards and Trusts are asked to take the following immediate steps to support the treatment of patients in hospital with COVID-19 infection:

1. **Clinicians are asked to consider prescribing baricitinib to patients hospitalised due to COVID-19 in line with the published policy** (available here).

   In the absence of a confirmed virological diagnosis, the treatment 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.

   Baricitinib should not be used during pregnancy.

2. Any provider organisation treating patients admitted to hospital due to COVID with baricitinib, as an off-label treatment, will be required to assure itself that the appropriate internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the health board / hospital / trust drugs and therapeutics committee, or equivalent.

3. Clinicians are encouraged to proactively support recruitment into trials developing further evidence in the treatment of COVID-19. Patients admitted to hospital due to COVID may be considered for entry into the RECOVERY or REMAP-CAP trials.

4. **Noting the important role of surveillance, treating clinicians are asked to support testing and / or data requirements as recommended under country specific or UK wide surveillance programmes, where laboratory capacity and resourcing allows.** Sequencing is an important part of surveillance activities to monitor for the development

cough and shortness of breath); AND compatible chest X-ray findings (consolidation or ground-glass shadowing); AND alternative causes have been considered unlikely or excluded (e.g. heart failure, bacterial pneumonia).

[2] Defined as: high-flow nasal oxygen, continuous positive airway pressure (CPAP) or non-invasive ventilation, or invasive mechanical ventilation.

[3] Patients are expected to be on a corticosteroid as the current standard of care, except where there is a strong contraindication against its use.

of new variants and drug resistance. Genotype results do not form part of the eligibility criteria for treatment with baricitinib in this policy and treatment should not be delayed pending these results.

5. Discharge letters to primary care should explicitly record the treatment that has been given, together with the dose and date of administration.

6. Order supply of baricitinib through existing (business as usual) routes.

7. Split packs of baricitinib (supplied in packs of 28 tablets) to provide the daily dose and duration of treatment recommended for individual patients under this policy. As the 2mg and 4mg tablets are priced the same, where patients are prescribed the 4mg daily dose, hospitals are asked to use the 4mg tablet (rather than 2 x 2mg tablets) where stock allows.

8. Maintain access to baricitinib for existing (non-COVID) indications including treatment of rheumatoid arthritis and atopic dermatitis. Regular stock updates should be provided to trust / hospital and regional pharmacy procurement lead / chief pharmacists.

Product Details

Baricitinib (Olumiant) is supplied by Eli Lilly and Company. Baricitinib is licensed for use in the treatment of moderate to severe rheumatoid arthritis and moderate to severe atopic dermatitis. **The use of baricitinib as a treatment for COVID-19 is off-label.**

Baricitinib is administered orally. The recommended dose of baricitinib in the management of COVID is 4mg once daily for 10 days (or until discharge, if sooner).

The dose should be halved to 2mg once daily in the following circumstances:

- Age 2 to <9 years with eGFR ≥60 mL/min/1.73m2;
- Age ≥9 years with eGFR 30 to <60 mL/min/1.73m2;
- Co-administration of an Organic Anion Transporter 3 (OAT3) inhibitor with a strong inhibition potential, such as probenecid.

The dose should be reduced further to 2mg on alternate days in the following circumstances:

- Age 2 to <9 years with eGFR 30 to <60 mL/min/1.73m2;
- Age ≥9 years with eGFR 15 to <30 mL/min/1.73m2;

There are limited safety data on the use of baricitinib in people with severe acute or chronic renal impairment. Prescribers should use clinical judgement and exercise caution with regards to dosing in those with unstable renal function in the context of acute kidney injury.

Further information on dose and administration can be found in the full clinical policy (attached).

Co-Administration

There is no interaction expected for baricitinib with other routine treatments for COVID available under published UK clinical access policies - dexamethasone or hydrocortisone, remdesivir, or tocilizumab or sarilumab.
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

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 record that an antiviral or monoclonal antibody has been given, together with the dose and date of administration.

Healthcare professionals are asked to report any suspected adverse reactions via the United Kingdom Yellow Card Scheme www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Yours sincerely

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