Baricitinib for Patients Hospitalised Due to COVID-19 (Adults and Children aged 2 years and older) Guidelines for NHS GGC

Background and Evidence

Baricitinib is an anti-inflammatory treatment licensed for use in moderate to severe rheumatoid arthritis and moderate to severe atopic dermatitis, and has been studied in patients who are hospitalised due to COVID-19. It is a selective and reversible Janus kinase (JAK) 1 and 2 inhibitor. JAK-inhibitors are thought to control high levels of cytokines and inflammation, seen in patients with severe SARS-CoV-2 infection (Walz et al 2020).

The RECOVERY trial demonstrated 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.

The World Health Organization (WHO) updated its 'Therapeutics and COVID-19: Living guideline' on 16 September 2022 and the WHO makes a strong recommendation for use of baricitinib in patients with severe COVID-19 illness, and in patients with critical COVID-19 illness. (WHO, September 2022).

Eligibility criteria

Patients hospitalised due to COVID-19 are eligible for treatment with baricitinib if they fulfil the following eligibility criteria:

•SARS-CoV-2 infection is confirmed by microbiological testing or where a multidisciplinary team (MDT) 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 is present*

AND

•Aged 2 years and over**

AND

•Requiring supplemental oxygen or respiratory support for the treatment of COVID-19. Respiratory support is defined as: high-flow nasal oxygen, continuous positive airway pressure (CPAP) or non-invasive ventilation, or invasive mechanical ventilation.

AND

•Receiving dexamethasone or an equivalent corticosteroid unless contraindicated.

*****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 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)

** 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 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

Exclusion criteria and cautions

Patients who meet any of the following exclusion criteria are NOT eligible for treatment in any of the above groups with remdesivir:

- Children aged less than 2 years
- Known hypersensitivity reaction to the active substances or to any of the excipients of baricitinib as listed in the Summary of Product Characteristics for Great Britain and Northern Ireland.
- eGFR <15 mL/min/1.73m^2 (If the individual being treated is <9 years, this exclusion criteria is eGFR <30 mL/min/1.73m^2)
- Receiving dialysis or haemofiltration;
- Absolute neutrophil count (ANC) less than 0.5 x 10^9 cells/L;
- Active tuberculosis;
- Pregnancy or breastfeeding.

The decision to initiate baricitinib must be made by a Consultant and be within the defined criteria. If a patient does not meet the eligibility criteria and remdesivir therapy is still felt to be a therapeutic consideration, the Consultant in charge of the patient's care must discuss the case with at least one other Consultant who has expertise in the management of COVID, for example the on call Infectious Diseases or Respiratory Consultant. It may be that a broader MDT discussion is required in complex cases. The summary and outcome of this discussion, along with the names of the clinicians involved in the discussion, must be clearly documented in a clinical note on Portal.

Baricitinib Supply, Dosing, Duration and Administration

Supply

Supplies can be obtained from departments of pharmacy during opening hours via an indent for a named patient supply. Please do not call an on-call pharmacist out for supply.

Dose

The recommended dosage for patients hospitalised due to symptoms of COVID-19 is as below:

The use of baricitinib as a treatment for COVID-19 is off-label. Baricitinib is administered orally. Baricitinib can be taken with or without food, and may be taken at any time.

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 for 10 days** (or until discharge, if sooner) in the following circumstances:

- Age 2 to <9 years with eGFR ≥60 mL/min/1.73m^2
- Age ≥9 years with eGFR 30 to <60 mL/min/1.73m^2
- 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 for 10 days** (or until discharge, if sooner) in the following circumstances:

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

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.

Individuals who are being considered for treatment under this policy, who are already taking baricitinib for a licenced indication at the dose of 4mg per day, should not receive additional baricitinib doses. However, if such individuals are already taking baricitinib at a dose of 2mg per day, the dose may be increased for the recommended treatment interval as described in this policy provided all eligibility criteria are met and provided the increased dose is deemed clinically appropriate (which includes the patient not being within the dose reduction categories described).

Pregnancy & Breast Feeding

Baricitinib should not be used during pregnancy. Women of child-bearing potential have to use effective contraception during treatment and for at least 1 week after treatment. If a patient becomes pregnant while taking baricitinib the SmPC must be reviewed and the parents should be informed of the potential risk to the foetus.

For women who are breast-feeding, the SmPC for baricitinib states: “It is unknown whether baricitinib/metabolites are excreted in human milk. Available pharmacodynamic/toxicological data in animals have shown excretion of baricitinib in milk (see section 5.3). A risk to newborns/infants cannot be excluded and baricitinib should not be used during breast-feeding. A decision must be made whether to discontinue breast-feeding or to discontinue baricitinib therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.”

Co-administration

Use of baricitinib in the treatment of COVID-19 should be considered as ‘additive’ to the use of an IL-6 inhibitor (tocilizumab or sarilumab), rather than an alternative. A patient may be given an IL-6 inhibitor after treatment with baricitinib has been commenced (or vice versa), according to clinical judgement. Baricitinib should not routinely be co-administered with an IL-6 inhibitor (where co-administration means given simultaneously). However, in the situation of illness requiring critical care support or where a patient has deteriorated despite treatment, clinical judgement may deem co administration appropriate.

There is no interaction expected between baricitinib with the other commissioned COVID-19 treatments. For further information please visit the University of Liverpool COVID-19 Drug Interactions website (https://www.covid19-druginteractions.org/checker).

Safety reporting

Any suspected adverse drug reactions (ADRs) for patients receiving remdesivir should be reported directly to the MHRA via the new dedicated COVID-19 Yellow Card reporting site at: https://coronavirus-yellowcard.mhra.gov.uk

Treatment with baricitinib can lower the ability of the immune system to fight infections. This could increase the risk of getting a new infection or make any infection the patient contracts worse. 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) must explicitly mention that baricitinib has been given, and the date of administration. Clinicians must ensure the GP is aware the patient has received baricitinib and should provide information to the patient to such effect.

References

RECOVERY Collaborative Group, Horby PW, Emberson JR, Mafham M Campbell M, Peto L, Pessoa-Amorim G, Spata E, Staplin N, Lowe C, Chadwick DR, Brightling C, Stewart R, Collini P, Ashish A, Green CA, Prudon B, Felton T, Kerry A, Baillie JK, Buch M, Day JN, Faust SN, Jaki T, Jeffery K, Juszczak E, Knight M, Lim WS, Montgomery A, Mumford A, Rowan K, Thwaites G, Haynes R, Landray MJ. 2022. Baricitinib in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial and updated meta-analysis. Preprint available at: https://www.medrxiv.org/content/10.1101/2022.03.02.22271623v1. Accessed on 3/3/2022

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WHO: Therapeutics and COVID-19: Living guideline, 16 September 2022 https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2022.5

COVID-19
CLINICAL GUIDELINE

Note: This guideline has been fast-tracked for approval for use within NHSGGC

Covid-19 Baricitinib for Patients Hospitalised Due to COVID-19 (Adults and Children aged 2 years and older)

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

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