Rapid Policy Statement

Interim Clinical Commissioning Policy: Baricitinib for patients hospitalised due to COVID-19 (adults and children aged 2 years and over)

Publication date: 28 November 2022
Effective from: 28 November 2022

Commissioning position

Baricitinib is recommended to be available as a treatment option through routine commissioning for adults and children (aged 2 years and over) hospitalised with COVID-19 in accordance with the criteria set out in this document. Baricitinib may be used as an alternative to interleukin-6 (IL-6) inhibitors, or in combination with corticosteroids and IL-6 inhibitors, according to clinical judgement. Use of baricitinib in the treatment of COVID-19 is off-label.

Evidence and policy summary

Baricitinib is an anti-inflammatory treatment licensed for use in moderate to severe rheumatoid arthritis, moderate to severe atopic dermatitis and severe alopecia areata 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).

Results from the RECOVERY trial demonstrate 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 (RECOVERY Collaborative Group, 2022).

The World Health Organization (WHO) updated its 'Therapeutics and COVID-19: Living guideline' on 16 September 2022 and the recommendations have been considered in the development of this policy. 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).

Implementation

Eligibility criteria

Patients must meet all the eligibility criteria and none of the exclusion criteria. Patients hospitalised due to COVID-19 are eligible[1] to be considered for **baricitinib** if the following criteria are met:

- COVID-19 infection is confirmed by microbiological testing or where a multi-disciplinary 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[2] is present;

  AND

- Aged 2 years and over;[3]

  AND

- Receiving supplemental oxygen or respiratory support[4] for the treatment of COVID-19;

  AND

- Receiving dexamethasone or an equivalent corticosteroid[5] (corticosteroid CAS alert) unless contraindicated.

Exclusion criteria and cautions

Baricitinib should not be administered in the following circumstances:

- Known hypersensitivity to baricitinib;
- eGFR <15 mL/min/1.73m^2 [If the individual being treated is <9 years, this exclusion criteria should be eGFR <30 mL/min/1.73m^2];[6]
- Receiving dialysis or haemofiltration;[6]
- Absolute neutrophil count (ANC) less than 0.5 x 10^9 cells/L;[6]
- Active tuberculosis;
- Pregnancy or breastfeeding.

Please refer to the Summary of Product Characteristics (SmPC) for baricitinib (in Northern Ireland, refer to the EMA SmPC for baricitinib) for special warnings and precautions for use, although some may not be relevant for use in the acute setting, as the licensed indications address long-term use for chronic conditions.

Pregnancy and women of childbearing potential

Baricitinib should not be used during pregnancy.

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[1] The decision to initiate treatment with baricitinib should be made by the receiving consultant, with support from multi-disciplinary colleagues in cases of uncertainty.

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

[3] 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.

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

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

[6] Please note that the drug criterion used here in this policy is taken directly from the RECOVERY trial, and the same criterion differs in the SmPC. The key reason for the difference is that the SmPC is written for long-term use in a low-risk condition, whereas this policy is for a short course in a high-risk condition in an acute clinical context (where the balance of benefits and risks is different). Please see the SmPC for further information. Clinical judgement should be exercised as appropriate. Additionally, although the SmPC lists an absolute lymphocyte count (ALC) of <0.5 x 10^9 cells/L as an exclusionary criterion for licensed indications, this was not used in the RECOVERY trial.

The SmPC for baricitinib currently states that: *"The JAK/STAT pathway has been shown to be involved in cell adhesion and cell polarity which can affect early embryonic development. There are no adequate data from the use of baricitinib in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). Baricitinib was teratogenic in rats and rabbits. Animal studies indicate that baricitinib may have an adverse effect on bone development in utero at higher dosages.*

Olumiant [baricitinib] *is contraindicated during pregnancy (see section 4.3). Women of childbearing potential have to use effective contraception during and for at least 1 week after treatment. If a patient becomes pregnant while taking Olumiant* [baricitinib] *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 Olumiant [baricitinib] *should not be used during breast-feeding. A decision must be made whether to discontinue breast-feeding or to discontinue Olumiant* [baricitinib] *therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman."*

Dose and administration

The recommended dose of baricitinib is 4mg once daily for 10 days (or until discharge if sooner)[7]. The dose should be halved to 2mg once daily in the following circumstances:

- Age 2 to <9 years with eGFR ≥60 mL/min/1.73m^2;[6]
- Age ≥9 years with eGFR 30 to <60 mL/min/1.73m^2;[6]
- 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/1.73m^2;[6]
- Age ≥9 years with eGFR 15 to <30 mL/min/1.73m^2.[6]

Baricitinib should be taken with or without food and may be taken at any time.

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).

Combination treatment

Baricitinib may be administered in combination with IL-6 inhibitors, tocilizumab or sarilumab (as well as corticosteroids, unless contraindicated), according to clinical judgement in patients with severe or critical COVID-19.

If an IL-6 inhibitor is not deemed suitable, or eligibility criteria (for an IL-6 inhibitor) are unmet, baricitinib treatment may still be considered.

[7] 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.

Co-administration

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).

Please refer to other published UK clinical commissioning policies setting out available COVID-19 treatments here.

Safety reporting

It is vital that any serious suspected adverse reactions are 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, ideally using SNOMED codes, 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.

Marketing authorisation

Baricitinib has marketing authorisation for:

- Oral use in adults with moderate to severe active rheumatoid arthritis.
- Oral use in adults with moderate to severe atopic dermatitis.

The use of baricitinib in COVID-19 is off label.

Governance

Off-label use of medication

Any provider organisation treating patients admitted due to COVID-19 with baricitinib, as an off-label product, will be required to assure itself that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the health board/hospital/trust's drugs and therapeutics committee, or equivalent.

Data collection requirement

Provider organisations in England should register all patients using prior approval software (alternative arrangements in Scotland, Wales and Northern Ireland will be communicated) and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined.

Recruitment into COVID-19 Therapeutic Clinical Trials

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

Effective from

This policy will be in effect from the date of publication.

Policy review date

This is an interim rapid clinical policy statement, which means that the full process of policy production has been abridged: public consultation has not been undertaken. This policy may need amendment and updating if, for instance, new trial data emerges, supply of the drug changes, or a new evidence review is required. A NICE Technology Appraisal or Scottish Medicines Consortium

(SMC) Health Technology Assessment or All Wales Medicines Strategy Group (AWMSG) appraisal of baricitinib for COVID-19 would supersede this policy when completed.

Equality statement

Promoting equality and addressing health inequalities are at the heart of the four nations' values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010 or equivalent equality legislation) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Definitions

COVID-19	Refers to the disease caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus

References

RECOVERY Collaborative Group. (2022). Baricitinib in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial and updated meta-analysis. Lancet (London, England), 400(10349), pp. 359-368. https://doi.org/10.1016/S0140-6736(22)01109-6

Walz L, Cohen AJ, Rebaza AP, Vanchieri J, Slade MD, Dela Cruz CS, Sharma L. (2020). Janus Kinase-Inhibitor and Type I Interferon Ability to Produce Favorable Clinical Outcomes in COVID-19 Patients: A Systematic Review and Meta-Analysis. *medRxiv : the preprint server for health sciences*, 2020.08.10.20172189. https://doi.org/10.1101/2020.08.10.20172189