Baricitinib for patients hospitalised with COVID-19 (adults and children aged 2 years and over)

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. It does not have a marketing authorisation for the treatment of COVID-19, so its use in these patients would be off-label (Please refer to the NHS Ayrshire & Arran Code of Practice for Medicines Governance Section 9 (b) "Off-label use of medicines" for further information).

The Scottish Medicines Consortium (SMC) collaborated with National Institute for Health and Care Excellence (NICE) on the Multiple Technology Appraisals (MTA) 878, but the use of baricitinib as an off-label treatment options for COVID-19 fell outside of the scope of the MTA and is for local determination. NICE's COVID-19 rapid guideline provides conditional recommendations on when baricitinib can be considered for the treatment of COVID-19.

1. Allowed Prescribers

Baricitinib for the treatment of COVID-19:

- must only be initiated by a Consultant.
- must be prescribed on the Hospital Electronic Prescribing & Medicine Administration (HEPMA) system.

2. Eligibility criteria

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

- Aged 2 years and over

AND

- 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

- need supplemental oxygen for the treatment of COVID-19;

AND

- are having or have completed a course of corticosteroids such as dexamethasone, unless they cannot have corticosteroids, (see ADTC 358: Corticosteroids in the treatment of suspected or confirmed COVID-19)

AND

- have no evidence of infection (other than SARS-CoV-2) that might be worsened by baricitinib

AND

- who cannot have tocilizumab.

NB: When there is clinical deterioration despite treatment with tocilizumab, it may be appropriate to add baricitinib.

[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.

3 Exclusions and cautions for use

3.1 Exclusions

Baricitinib should not be administered in the following circumstances:

- Known hypersensitivity to baricitinib or any of its excipients (refer to SmPC)
- 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.

[6] Please note that the drug criterion is taken directly from the RECOVERY trial, and the same criterion differs in the SmPC as this is for a short course in a high risk condition in an acute clinical context. 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.

3.2 Cautions

Please refer to the Summary of Product Characteristics (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.

3.3. Pregnancy, breastfeeding, use in women of childbearing potential and effect on fertility

In **all** cases of pregnancy and breastfeeding, senior Obstetric advice should be sought to ensure that theoretical risks to the fetus (or baby in the case of breastfeeding) do not outweigh proven benefits to the mother. In some cases of breastfeeding, it may be more appropriate to seek advice from a pediatrician.

Clinicians should refer to the baricitinib SmPC for further information on their use in pregnancy, breast feeding, women of childbearing potential and effects on fertility. In addition the current guidance from the Royal College of Obstetricians and Gynaecologists on Coronavirus (COVID-19), infection in pregnancy should be followed.

Baricitinib should **not** be used during pregnancy. The SmPC currently states "*baricitinib is contraindicated during pregnancy (see section 4.3 in the SmPC). 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 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 in SmPC). 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 therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman."*

4. Dosing schedules and supplies

- A Olumiant® (baricitinib) Patient Alert Card should be provided to patients when baricitinib is being administered or, if not appropriate at the time, prior to discharge from level 2 or level 3 care if this is within 1 week of the last dose being administered (patients should be advised to keep the card for one week after the end of treatment).

4.1 Dosing schedules

Baricitinib is available as 2mg or 4mg film coated tablets. Baricitinib should be taken with or without food, and may be taken at any time.

Recommended dose of baricitinib is 4mg orally once daily for 10 days (or until discharge if sooner) [7].

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

- Age 2 to <9 years[6] with eGFR ≥60 mL/min/1.73m^2
- Age ≥9 years[6] 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 (refer to section 6).

The dose should be reduced further to 2mg orally on alternate days in the following circumstances[6]:

- 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

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).

[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.*

Combination treatment

Baricitinib may be considered in people who meet the criteria in section 2 and who cannot have tocilizumab. When there is clinical deterioration despite treatment with tocilizumab, it may be appropriate to add baricitinib.

4.2 Supplies

Baricitinib tablets will be supplied from the pharmacy department.

A limited supply for use outwith pharmacy opening hours will also be available from:

- University Hospital Ayr - Emergency Drug cupboard
- University Hospital Crosshouse – Emergency Drug cupboard

5. Adverse effects

Refer to the baricitinib SmPC for further information on adverse effects.

6. Drug interactions

- No interactions are expected between baricitinib and the other available COVID-19 treatments e.g. corticosteroids (dexamethasone or hydrocortisone).
- Further information on interactions can be found within the baricitinib SmPC or via University of Liverpool COVID-19 Drug Interactions website.

7. Safety reporting

Any suspected adverse reactions (including congenital malformations and/or neurodevelopmental problems following treatment during pregnancy) from any of the treatments should be reported directly to the MHRA via the dedicated COVID-19 Yellow Card reporting site at: https://coronavirus-yellowcard.mhra.gov.uk/.

8. Communication

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 by including information on the immediate discharge letter and should also provide information to the patient to such effect.

9. Bibliography

1. CEM/CMO/2022/007: COVID-19 Therapeutic alert. Baricitinib for patients hospitalised due to COVID-19 (adults and children aged 2 years and over), issued 28 November 2022. Available from: CAS-ViewAlert (mhra.gov.uk) (accessed 07 April 2023.
2. Interim Clinical Commissioning Policy: Baricitinib for patients hospitalised due to COVID-19 (adults and children aged 2 years and over), issued 28 November 2022. Available from: CAS-ViewAlert (mhra.gov.uk) (accessed 07 April 2023).
3. CEM/CMO(2023)001. COVID Therapeutic Alert 2023 1 – Publication of NICE Multiple Technology Appraisal (MTA) – Treatment recommendation for COVID-19, Available from: COVID therapeutic alert 2023 1 – publication of NICE multiple technology appraisal (MTA) – treatment recommendations for COVID-19 (scot.nhs.uk) (accessed 07 April 2023).
4. NICE guideline [NG191]. COVID-19 rapid guideline: managing COVID-19. Published: 23 March 2021. Last updated: 29 March 2023. Available from: Overview | COVID-19 rapid guideline: managing COVID-19 | Guidance | NICE (accessed 07 April 2023).
5. RCOG, Royal College of Midwives, Royal College of Paediatrics and Child Health, Public Health England and Public Health Scotland. Coronavirus (COVID-19), infection in pregnancy, Version 16.0: updated Thursday 15 December 2022. Available from: Coronavirus (COVID-19), infection in pregnancy | RCOG (accessed 07 April 2023)
6. Olumiant® (baricitinib) 2 mg film-coated tablets Summary of Product Characteristics, last updated on eMC 23 March 2023. Available from https://www.medicines.org.uk/emc/product/2434/smpc (accessed 07 April 2023).