**Introduction**

The National COVID-19 Clinical Evidence Taskforce gives a conditional recommendation for use of baricitinib (Olumiant®) for the treatment of patients with COVID-19.

Baricitinib is not an alternative or substitute for vaccination. **Vaccination is the preferred and primary option for the prevention of COVID-19.**

This guideline requires endorsement by your local Drug and Therapeutics Committee (DTC) prior to implementation. Additional resources to support the safe and appropriate use of baricitinib are available [here](#).

**Drug class and mechanism of action**

Baricitinib belongs to a class of medicines called Janus Kinase (JAK) inhibitors. It works by inhibiting Janus kinases 1 and 2, suppressing the immune response.

**Indication**

Baricitinib is registered for use in Australia for the treatment of moderate-severe rheumatoid arthritis and moderate-severe atopic dermatitis, but not for the treatment of COVID-19. Therefore use for COVID-19 is considered ‘off-label’.

The National COVID-19 Clinical Evidence Taskforce gives a conditional recommendation for use of baricitinib for adults hospitalised with COVID-19 who require supplemental oxygen and/or mechanical ventilation or ECMO.

**Contraindications and precautions**

- Contraindicated in patients with known hypersensitivity to baricitinib or any of the excipients of this medicine (croscarmellose sodium, magnesium stearate, mannitol, microcrystalline cellulose, iron oxide red, lecithin, macrocol 3350, polyvinyl alcohol, purified talc, titanium dioxide).
- Safety and efficacy of baricitinib in children and adolescents aged 18 years and younger has not yet been established, therefore use in these patients is not recommended.
- Baricitinib must not be used in combination with biological disease modifying antirheumatic drugs (bDMARDs).
- Baricitinib may increase the risk of venous thromboembolism (VTE). Use with caution in patients with risk factors for deep vein thrombosis or pulmonary embolism (DVT/PE). Patients with multiple risk factors should be closely monitored and consideration should be given to appropriate VTE prophylaxis.
- Baricitinib may cause leucopenia, lymphopenia, neutropenia and anaemia. Cytopenias are generally reversible with treatment interruption. **Do not commence** if haemoglobin < 80 g/L, absolute lymphocyte count < 0.2 x 10^9/L or absolute neutrophil count < 0.5 x 10^9/L.
- Patients receiving baricitinib are at increased risk for serious infections, which may result in hospitalization and/or fatality. Do not initiate baricitinib in patients with active, serious infections (other than COVID-19), including localized infections.
  - Screen for viral hepatitis and latent tuberculosis (TB) (if positive, begin TB treatment for latent infection before starting baricitinib).
  - There is an increased risk of infection when baricitinib is used with other immunosuppressive agents (see Drug interactions section below).
  - Patients should be monitored for signs and symptoms of infection during and after treatment with baricitinib.
- Gastrointestinal (GI) perforations have been reported. Use with caution in patients at risk of GI perforation. Evaluate new onset abdominal symptoms.
- Live vaccines should not be given concomitantly.
Use of baricitinib tablets for COVID-19

- See Dose and route of administration section for dosing in renal impairment.
- See Pregnancy, breastfeeding and contraception section for recommendations in pregnancy, breastfeeding and contraception.

Pregnancy, breastfeeding and contraception

Pregnancy

Baricitinib has been classified pregnancy category D by the Therapeutics Goods Administration – it is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breastfeeding

Breastfeeding is not recommended during treatment with baricitinib – it is unknown whether baricitinib is present in human milk.

Contraception

Women of childbearing potential should take appropriate precautions to avoid becoming pregnant during treatment with baricitinib and for at least 1 week after the finishing treatment.

Drug interactions

Potential drug interactions have not been investigated in patients with COVID-19. Resources such as the Liverpool COVID-19 drug interactions tool and Micromedex drug interactions tool may be useful to check for specific drug-drug interactions. Generally:

- Baricitinib is contraindicated with other cytokine modulators (e.g. TNF-alpha antagonists, rituximab, tocilizumab). Such combinations increase the risk of infection.
- Baricitinib exposure is increased when baricitinib is used with strong organic anion transporter (OAT) 3 inhibitors e.g. probenecid and gemfibrozil. See Dose and route of administration section for dosing recommendation.
- Baricitinib may enhance the risk of agranulocytosis with clozapine. Monitor therapy.
- Live vaccines should be avoided just prior to and during treatment with baricitinib. Recommended interval between receipt of live vaccines and initiation of immunosuppressive agents such as baricitinib should follow current vaccination clinical guidelines – see Australian Immunisation Handbook or contact the NSW Immunisation Specialist Service (NSWISS) Advice Line (1800 679 477).

Presentation and storage

Baricitinib is available as 2 mg and 4 mg film-coated tablets. Store below 30°C in original package.

Dose and route of administration

For adult patients with normal renal function, the recommended dosing is:

**Baricitinib** 4 mg taken orally once daily for up to 14 days or until hospital discharge, whichever comes first. Baricitinib can be taken without regard to food. The tablets should be swallowed whole and not chewed, broken, or crushed.

Dose adjustments are required for:
- Renal impairment:
  - eGFR = 30 - 60 mL/min/1.73m² – reduce dose to 2 mg orally once daily

© 2022 – Clinical Excellence Commission. This Work is based on work by NSW Therapeutic Advisory Group Inc (TAG), funded by NSW Health.

Whilst the information contained in this document is considered to be true and correct at the date of publication, changes in circumstances after the time of publication may impact on the accuracy of the information. The information may change without notice and the State of New South Wales is not in any way liable for the accuracy of any information printed and stored or in any way interpreted and used by a user.
DRUG GUIDELINE
Use of baricitinib tablets for COVID-19

- eGFR = 15 - 30 mL/min/1.73m² – reduce dose to 1 mg orally once daily
- eGFR < 15 mL/min/1.73m² – use is not recommended
  - Patients taking strong OAT3 inhibitors, such as probenecid:
    - Halve the recommended dose. If the recommended baricitinib dose is 1 mg once daily, consider discontinuing probenecid.

For a dose of 1 mg baricitinib:

**Option 1:** A dose of 2 mg on alternate days has been used in clinical trials for the treatment of COVID-19 infection.

**Option 2:** Baricitinib tablets can be cut in half by pharmacy in a suitable powder containment cabinet (e.g., laminar flow hood).

**Option 3:** In areas where all staff are in full Personal Protective Equipment (PPE) and if local policies allow, the 2 mg tablet may be cut in half using a tablet cutter with a blade.

Staff who are pregnant should not cut or disperse baricitinib tablets as occupational exposure may be harmful.

Patients with enteral feeding tubes or swallowing difficulties – disperse the tablet in a suitable volume of water (see Table 1) and swirl gently until an even suspension is formed (tablet may take 5 minutes to completely disperse). Administer dose to patient. Rinse the container with a suitable volume of water (see Table 1) and then administer to patient to ensure the entire dose is given.

**Table 1: Dispersion instructions for 2 mg and 4 mg baricitinib tablets.**

<table>
<thead>
<tr>
<th>Administration via</th>
<th>Dispersion volume of water</th>
<th>Container rinse volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral dispersion</td>
<td>5 - 10 mL</td>
<td>At least 5 mL</td>
</tr>
<tr>
<td>Gastrostomy tube</td>
<td>15 mL</td>
<td>At least 15 mL</td>
</tr>
<tr>
<td>Nasogastric tube</td>
<td>30 mL</td>
<td>At least 15 mL</td>
</tr>
</tbody>
</table>

**Monitoring requirements**

- Monitor the patient for adverse effects (see Adverse effects section below). If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue, initiate appropriate medications and/or supportive care.
- Monitor:
  - for signs and symptoms of infection during and after treatment with baricitinib
  - baseline full blood count (with differential)
  - liver function tests
  - electrolytes, urea and creatinine
  - for adverse effects (see Adverse effects section below), interrupt treatment if:
    - absolute neutrophil count < 0.5 x 10⁹ cells/L
    - absolute lymphocyte count < 0.2 x 10⁹ cells/L
    - haemoglobin < 80 g/L
    - increases in ALT or AST are observed and drug-induced liver injury is suspected.

**Adverse effects**

It may be difficult to distinguish between adverse effects of baricitinib and signs and symptoms of COVID-19. As the proposed use is off-label, it is important to document and report all (from possible to confirmed) adverse effects experienced by the patient during treatment to inform its safety profile and future use. Refer to the Approved Product Information for complete list of possible adverse effects.

© 2022 – Clinical Excellence Commission. This Work is based on work by NSW Therapeutic Advisory Group Inc (TAG), funded by NSW Health.

Whilst the information contained in this document is considered to be true and correct at the date of publication, changes in circumstances after the time of publication may impact on the accuracy of the information. The information may change without notice and the State of New South Wales is not in any way liable for the accuracy of any information printed and stored or in any way interpreted and used by a user.

Updated by the Clinical Excellence Commission
July 2022, Version 1.5 – Page 3
• Very common (>10%):
  o Hepatic: increased serum alanine aminotransferase (≥ 3x ULN), increased serum aspartate aminotransferase (≥ 3x ULN)
• Common (≥ 1% to < 10%):
  o Cardiovascular: deep vein thrombosis, pulmonary embolism, venous thrombosis
  o Genitourinary: urinary tract infection
  o Haematological: thrombocythemia
  o Neuromuscular & skeletal: increased creatine phosphokinase in blood specimen (≥ 5x ULN)
• Frequency not defined:
  o Infection (including serious infection)

Reporting
• Healthcare professionals are asked to report any suspected adverse events to the TGA, Eli Lilly (drug sponsor) and via their facility’s incident management system.
• Drug and Therapeutics Committee oversight in the access process will enable appropriate medicines governance and ensure the collection and analysis of patient outcomes and systematic monitoring of medicine use. Baricitinib use and outcome reporting should occur as per local clinical governance processes.

Summary of changes made in version 1.5 – July 2022
• Added information about alternate day dosing regimen for patients on 1 mg dose.

References