Baricitinib

We **recommend** baricitinib in AE patients, who are candidates for systemic treatment.	↑↑	**>75%** Evidence and consensus based, see Evidence Report

baricitinib in licence for for ≥ 2 years of age;
dosage age 2-18y: from 10kg<30kg: 2 mg per day; from 30kg: 4 mg per day
dosage adults: 4 mg per day
reduction to half dosage per day possible, depending on treatment response
dosage adults ≥ 65y: 2 mg per day

Certainty of evidence: Network meta-analysis from 2024[1, 2]:

Short term (up to 16 weeks) vs placebo (NMA medications used in clinical practice)

2 mg
⊕⊕⊕○ MODERATE for mean difference **EASI** -5.1 (-6.9, -3.4); **POEM** -3.8 (-4.9, -2.7); **peak pruritus NRS -1**.2 (-1.6, -0.9); **DLQI** -2.3 (-3.1, -1.4)

4 mg
⊕⊕⊕⊕ HIGH for mean difference **POEM** -5.4 (-6.6, -4.2); **peak pruritus NRS** -1.6 (-2, -1.3)
⊕⊕⊕○ MODERATE for mean difference **EASI** -7.5 (-9.4, -5.6); **DLQI** -3.5 (-4.4, -2.6)

For baricitinib versus other drugs, see Evidence Report

Mechanisms of action and efficacy

Baricitinib is an oral selective JAK1 and JAK2 Inhibitor. The drug has been tested in one phase 2 and several phase 3 trials in adults with moderate-to-severe AE at 1mg, 2mg and 4mg once daily against placebo, showing significant improvement with regard to EASI from baseline to 16 weeks, in particular in the two higher doses (2 mg daily (mean difference, 5.1-point reduction; 95% CI, -6.9, -3.4 [GRADE assessment: moderate certainty]) and 4 mg daily (mean difference, 7.5-point reduction; 95% CI, -9.4, -5.6 [GRADE assessment: moderate certainty]).[1] Similar efficacy has been shown in these studies with regard to the IGA and itch scores. The concomitant use of topical corticosteroids was allowed in one trial.[3]

In October 2023, baricitinib was approved by the EMA for the treatment of children (2 years and older) and adolescents with AE. Data from a phase 3 study (BREEZE-AD PEDS) had previously been published, in which 483 children and adolescents received baricitinib 0.5 mg or 1 mg or 2 mg or 4 mg or placebo over 16 weeks. The drug was convincing with regard to the primary endpoint Investigator Global Assessment of 0/1 with a ≥ 2-point improvement at week 16 as well as the secondary endpoints EASI-75, EASI-90, mean change from baseline in EASI score, SCORAD 75 and 4-point improvement in the Itch Numeric Rating scale.[4]

Dosage: acute flare, short term, long term

At present, Baricitinib data is available up to 68 weeks follow up[5,6], demonstrating sustained efficacy.

The recommended dose of baricitinib for adult patients is 4 mg once daily. A dose of 2 mg once daily should be considered for patients who have achieved sustained control of disease activity with 4 mg once daily and are eligible for dose tapering.

A dose of 2 mg once daily is recommended for patients at higher risk of venous thromboembolism, major adverse cardiovascular events and malignancy, as well as for patients aged ≥ 65 years and for patients with a history of chronic or recurrent infections.[7] A dose of 4 mg once daily may be considered for these patients who do not achieve adequate control of disease activity with 2 mg once daily dose.

For children and adolescents the recommended dose of baricitinib is 4 mg once daily for patients weighing 30 kg or more. For patients weighing 10-≤ 30 kg, the recommended dose is 2 mg once daily. A reduction to half the dose should be considered for patients who have achieved sustained control of disease activity with the standard recommended dose and are eligible for dose tapering.

Starting with the higher dose usually leads to a faster clinical response, better drug survival and adherence, and may therefore be advisable in younger, otherwise healthy patients.

Safety

The most common side effects with baricitinib in clinical trials include an increase in LDL cholesterol, upper respiratory tract infections, and headache. Acne is less common than with other JAK-Inhibitors. Infections reported with baricitinib include herpes simplex. However, the rate of these events reported in a recent combined safety study including 2531 patients with AE from 8 RCTs who were given baricitinib for 2247 patient-years (median duration 310 days) was overall low: eczema herpeticum (n = 11), cellulitis (n = 6) and pneumonia (n = 3). There were four opportunistic infections reported.[8] A transient increase of CPK may be seen, especially after extensive bodily exercise. No malignancies, gastrointestinal perforations, positively adjudicated cardiovascular events or tuberculosis were reported in the placebo-controlled period in baricitinib-treated patients. The frequency of herpes simplex was higher in the 4 mg group (6.1%) compared to the 2 mg (3.6%) and placebo groups (2.7%).[8] Analyses of long-term safety data are still pending in patients with AE. For use in rheumatoid arthritis, data is available from an integrated data base with 9 phase III/II/Ib and 1 long-term extension covering 3,770 patients for up to 9.3 years of baricitinib treatment (14 744 patient-years of exposure). Patients who received at least one dose of baricinib in the incorporated studies were included in the uncontrolled analysis set.[9] The incidence rate for serious infections was reported with 2.6 per 100 patient years, while the incidence rate for herpes zoster was reported with 3 per 100 patient years. The incidence rate for major cardiovascular events was 0.5 per 100 patient years, rising slightly to 0.77 in those patients over 50 with at least one cardiovascular risk factor. Incidence rates for deep vein thrombosis or pulmonary embolism were reported with 0.5 per 100 patient years.[9]

In the children and adolescents BREEZE-AD PEDS study abdominal pain, acne and headache were the most frequently reported adverse events. Few patients discontinued the study drug due to AEs (1.6% placebo and 0.6% baricitinib-treated).[4]

Screening and monitoring

For baseline screening, the manufacturer advises that patients with suspected hepatitis B consult a liver specialist for advice before initiation of treatment. Lipid and liver profiles need to be regularly monitored following treatment initiation. Screening for any haematological abnormalities is also advised.

In practice, the guideline group considers the same baseline screening and treatment monitoring investigations applicable to all JAK-Inhibitors. For baseline screening this is a full blood count, renal, liver and lipid profile and hepatitis B and C, HIV and TB screen.

For follow up monitoring we propose a full blood count, renal, liver and lipid profile at four weeks into treatment and then three-monthly while on therapy. The guideline group does not advocate for mandatory monitoring of creatinine phosphokinase levels in asymptomatic patients.

Combination with other treatments

We recommend combining baricitinib, as any systemic treatment, with emollients and, whenever needed, topical anti-inflammatory treatment in AE patients. No studies assessing the use of baricitinib with other systemic therapies in AE patients have been published to date, but the combination therapy with MTX is an established combination regimen in the management of rheumatoid arthritis.[10]

Special considerations

JAK-Inhibitors are also effective for certain other inflammatory diseases and are approved for their treatment in some cases.t. Therefore, patients with AE and with concomitant inflammatory diseases, such as AA, rheumatoid and juvenile idiopathic arthritis, ankylosing spondylitis and psoriatic arthritis and inflammatory bowel diseases are likely to experience additional beneficial effects for these concomitant diseases. Baricitinib is already licensed for most of these indications.

Please refer to the special considerations in the JAK-Inhibitor introduction chapter.

References

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