Ciclosporin

We recommend using ciclosporin to achieve disease control in AE patients who are candidates for systemic treatment.

<table>
<thead>
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<th>Ciclosporin: in licence for ≥ 16 years</th>
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<td>standard dosage adults: 2.5-5 mg/kg per day in two single doses</td>
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<td>commonly used dosage children: 2.5-5 mg/kg per day in two single doses</td>
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Certainty of evidence\(^1,2\):
- Short term (8-16 weeks) vs placebo (NMA medications used in clinical practice or likely to be approved soon)
- \(\oplus\oplus\oplus\) MODERATE for standardized mean difference change in signs
- \(\oplus\oplus\oplus\) MODERATE - \(\oplus\bigcirc\) LOW for standardized mean difference QoL
- \(\oplus\bigcirc\) LOW for standardized mean difference itch

For ciclosporin versus other drugs, see Evidence Report

We recommend to start with higher ciclosporin dosages in order to achieve a more rapid response in AE patients who are candidates for systemic treatment.

Mechanisms of action and efficacy

Ciclosporin inhibits T cell activation and proliferation by blocking nuclear factor of activated T cells (NFAT)-dependent cytokine production.

Ciclosporin has been approved for treatment of AE in adults in many European countries and is considered as first line option for patients with severe disease if other, novel therapies are not available or indicated. Ciclosporin is very effective for AE in both children and adults with a better tolerability in children.\(^3,4\) Although similarly effective in the above NMA meta-analysis evaluating trials up to 16 weeks, real life data reveal a longer drug survival of dupilumab compared to CyA after 16 months.\(^5,6\)
In head-to-head trials ciclosporin was superior to MTX, prednisolone, IVIG, UVA and UVB, and similarly efficacious as enteric-coated mycophenolate sodium (EC-MPS). In the short-term treatment of AE, higher ciclosporin dosages (5 mg/kg per day) lead to a more rapid response and are more efficacious than lower dosages (2.5-3 mg/kg per day). Long-term use of ciclosporin up to 1 year can be recommended based on several trials, however, their evidence is limited because of the open-label design and high dropout rates.

**Dosage: acute flare, short term, long term**

- in licence for ≥ 16 years
- standard dosage adults: 2.5-5 mg/kg per day in two single doses
  - Acute flare, short-term: 4-5 mg/kg body weight per day
  - Long-term: 2.5-3 mg/kg body weight per day
- commonly used dosage children: 2.5-5 mg/kg per day in two single doses
  - We recommend combining CyA, as any systemic treatment, with emollients and, whenever needed, topical anti-inflammatory treatment in AE patients.

**Safety**

Ciclosporin has a narrow therapeutic index and requires a close follow-up for blood pressure and signs of renal impairment. To note, clinically relevant increase of creatinine seems less common than expected.

**Monitoring**

- Blood pressure, full blood count, renal and liver profile (including GGT) according to national guidelines (e.g. at baseline, 4 weeks and then 3-monthly).
- Screening for hepatitis B/C and HIV before therapy should be considered.

**Combination with other treatments**

Concomitantly to ciclosporin, topical therapy with corticosteroids and/or calcineurin inhibitors can be applied.

Because of a potentially increased risk to develop skin cancer, ciclosporin should not be combined with UV light (UVA, UVB, PUVA).

**Special considerations**

Ciclosporin has been shown to be effective, safe and well tolerated in children and adolescents.

Ciclosporin can be considered in pregnant woman with severe AE. So far, no increased risk of congenital malformations or fetal death compared to the background populations have been reported. An increased risk of low birthweight cannot be ruled out. Where systemic therapy is likely to be needed throughout pregnancy, ciclosporin is first choice therapy.
References


