

LETTER TO THE EDITOR

First update of the living European guideline (EuroGuiDerm) on atopic eczema

Dear Editor,

The European guideline (EuroGuiDerm) on atopic eczema published in JEA DV on 18 August 2022 (part 1)¹ and 3 September 2022 (part 2)² was updated in October 2022 to reflect the most recent evidence on novel systemic medications by the European Medicines Agency (EMA) and the UK Medicines and Health care products Regulatory Agency (MHRA): Abrocitinib, an oral selective Janus kinase inhibitor, was approved by the EMA (adults) and MHRA (adults and adolescents). Tralokinumab, a human monoclonal antibody IL-13 inhibitor, received a licence for adolescents. In addition, the living network meta-analysis (NMA) 'Systemic Immunomodulatory Treatments for Atopic Dermatitis' by Drucker et al.³ was recently updated, which serves as the evidence base for the systemic treatment section of the European guideline.

The guideline development group (GDG) remained almost unchanged and comprised 28 members from 12 countries, including two patient representatives.

For the update, a new recommendation for the use of abrocitinib in patients with atopic eczema who are candidates for systemic treatment was voted on (Figure 1a). This recommendation was accepted unanimously receiving the highest recommendation strength 'we recommend'. Previously, abrocitinib had shown significantly better response on EASI-75 and IGA than placebo in several phase 3 trials of the Atopic Dermatitis Efficacy and Safety (JADE) global development programme.⁴⁻⁶ The 200 mg dose of abrocitinib also showed partially better results compared to dupilumab in a recent head-to-head trial.⁷ For treatment with abrocitinib, a starting dose of 200 mg once daily is recommended for adults. After a satisfactory response, the dose can be reduced to 100 mg daily. In patients aged 65 years and older, a starting dose of 100 mg once daily is recommended. The same is recommended for adolescents, even if currently licensed only for this age group in the UK. In clinical trials, the most common adverse events were nausea, headache, respiratory tract infections and acne. Herpesvirus infections, thrombocytopenia and elevation of serum creatinine phosphokinase occurred only rarely.⁸ Because of these potential side effects and based on experience with other Janus kinase inhibitors, the guideline recommends baseline safety screening before starting therapy (full blood count, renal, liver and lipid profile, creatinine phosphokinase level, as

well as hepatitis and tuberculosis screening, including a chest radiograph). During therapy with abrocitinib, repeat safety investigations (full blood count, renal, liver and lipid profile, and creatinine phosphokinase level) are recommended at 4 weeks into treatment and then every 3 months. To minimize the risk of serious side effects, the recently announced recommendations of the EMA's human medicines committee (CHMP) on Janus kinase inhibitors should also be followed.⁹

The previous recommendations from the first version of the evidence-based chapter on systemic treatments were re-voted, because new data were available from the updated NMA.³ However, all existing recommendations in this chapter were confirmed unchanged.

Furthermore, the stepped-care plans for children and adolescents as well as adults were adapted to reflect the new recommendation on abrocitinib and the new lower minimum age for dupilumab (6 months and above).

The stepped-care plan for children and adolescents now also recommends tralokinumab. EMA had previously approved tralokinumab from 12 years of age, as the drug showed significantly better efficacy than placebo in a phase 3 trial in adolescents aged between 12 and 17 years.^{10,11}

For severe atopic eczema in adult patients, six systemic drugs now received the strong recommendation 'we recommend': ciclosporin, the biologics dupilumab and tralokinumab, and the Janus kinase inhibitors abrocitinib, baricitinib and upadacitinib. The immunosuppressants azathioprine and methotrexate are used off-label and received the weaker recommendation 'we suggest', reflecting the lower strength of evidence available for the two medications. Systemic corticosteroids were suggested only as rescue therapy in exceptional cases with a weak recommendation strength (Figure 2a).

In children and adolescents, ciclosporin, dupilumab, tralokinumab (Figure 1b) and upadacitinib were strongly recommended for severe atopic eczema. In addition, abrocitinib was also strongly recommended. However, at present this drug has only been approved in the United Kingdom for those aged 12 and over. In the EU, this drug can only be used off-label in children and adolescents. As for adults, azathioprine and methotrexate received a weaker recommendation (Figure 2b).

The steps of baseline therapy and treatments for mild and moderate eczema remain unchanged.

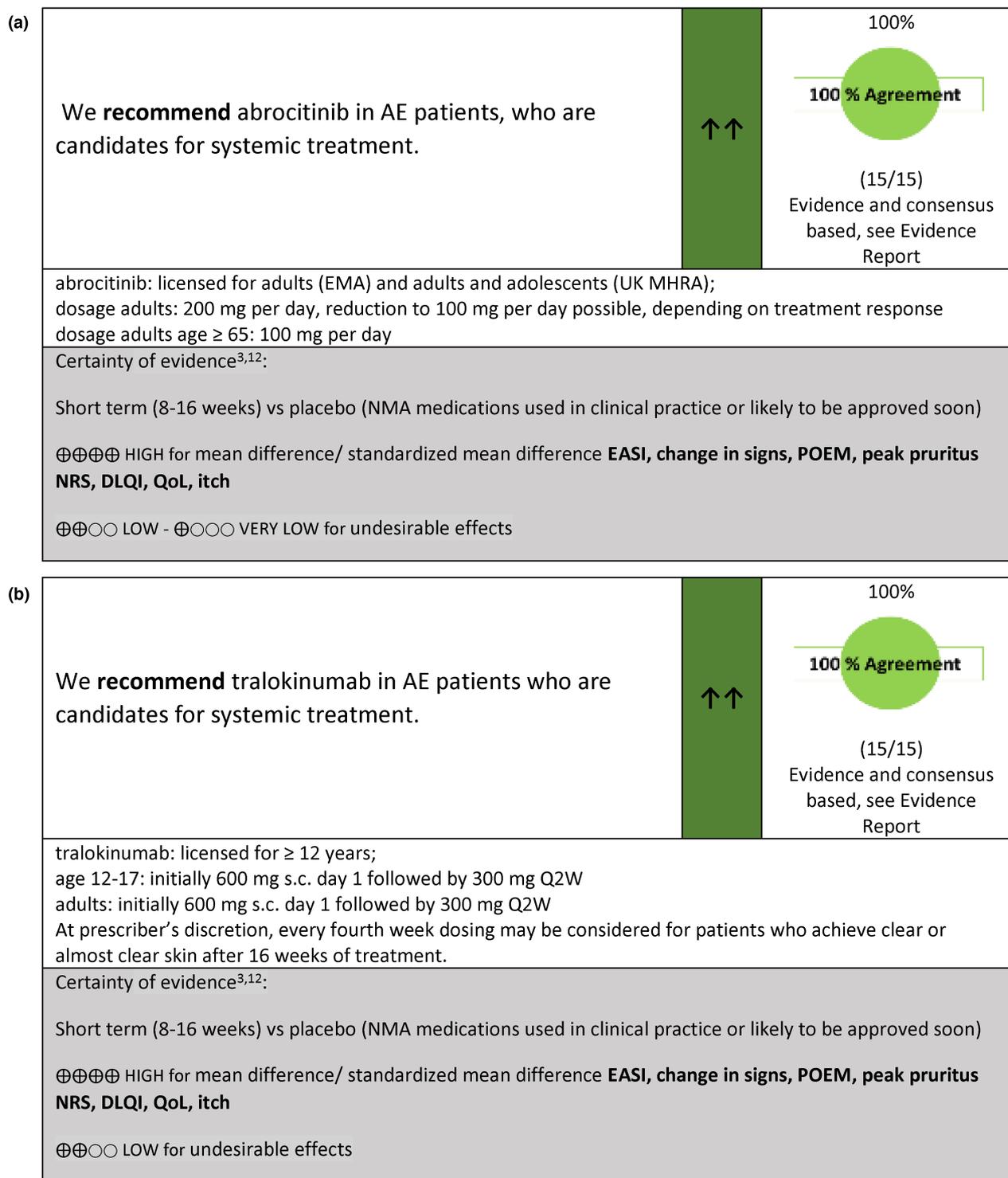


FIGURE 1 Recommendations: (a) on abrocitinib, (b) on tralokinumab.

FUNDING INFORMATION

This update of the EuroGuiDerm guideline was funded through the EuroGuiDerm Centre for Guideline Development. The European Dermatology Forum is responsible for fundraising and holds all raised funds in one account. The EuroGuiDerm Team is not involved in fundraising or in the decision making on which guideline (GL) or consensus statement (CS) development is funded. The decisions on which GL/CS is funded are

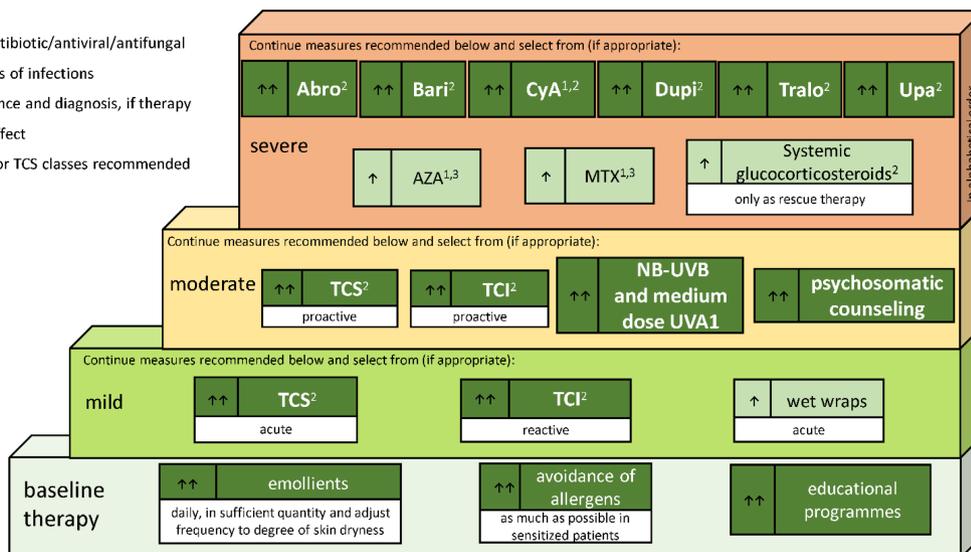
made by the EuroGuiDerm Board of Directors independently. The EDF or any other body supporting the EuroGuiDerm is never involved in the guideline development and had no say on the content or focus of the guideline.

CONFLICT OF INTEREST STATEMENT

This is a brief summary of the update of the EuroGuiDerm Guideline on Atopic Eczema. For the complete guideline,

(a)
EuroGuiDerm Guideline on Atopic Eczema
Stepped-care plan for adults with atopic eczema

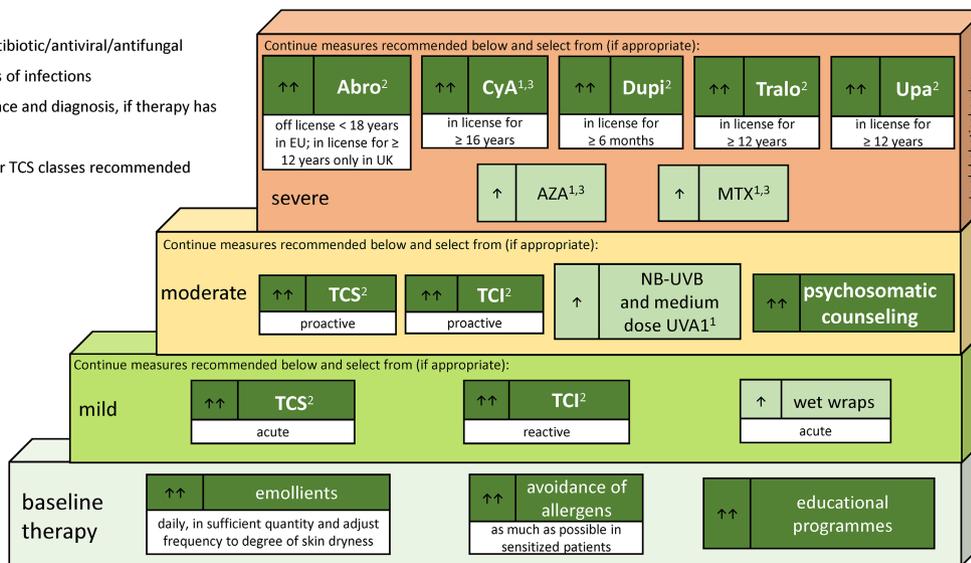
- Add antiseptic/antibiotic/antiviral/antifungal treatment in cases of infections
- Consider compliance and diagnosis, if therapy has insufficient effect
- Refer to table 3 for TCS classes recommended



¹ refer to guideline text for restrictions, ² licensed indication, ³ off-label treatment
 ↑↑ (dark green) strong recommendation for the use of an intervention / ↑ (light green) weak recommendation for the use of an intervention
 For definitions of disease severity, acute, reactive, proactive see section 'VII' and section 'Introduction to systemic treatment' of the EuroGuiDerm Atopic Eczema Guideline
 Abro= abrocitinib; AZA=azathioprine; Bari=baricitinib; CyA=ciclosporin; Dupi=dupilumab; MTX=metotrexate; TCI=topical calcineurin inhibitors; TCS= topical corticosteroids; Tralo=tralokinumab; Upa=upadacitinib; UVA1=ultraviolet A1; NB-UVB=narrow-band ultraviolet B

(b)
EuroGuiDerm Guideline on Atopic Eczema
Stepped-care plan for children and adolescents with atopic eczema

- Add antiseptic/antibiotic/antiviral/antifungal treatment in cases of infections
- Consider compliance and diagnosis, if therapy has insufficient effect
- Refer to table 3 for TCS classes recommended



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FIGURE 2 Stepped-care plans: (a) for adults with atopic eczema, (b) for children and adolescents with atopic eczema.

methods report (including COI disclosures) and evidence report see <https://www.guidelines.edf.one/guidelines/atopic-c-eczema>.

DATA AVAILABILITY STATEMENT
 Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

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