Table 1. Final recommendations after GRADE adolopment

Recommendations adopted from the source guideline

- 1. Clinicians managing atopic dermatitis cases should ensure the following good practice before any further treatment (12):
 - a. Ensure diagnosis and check any complication
 - b. Educate the patient about the disease
 - c. Emphasize avoidance of triggers
 - d. Emphasize adherence to treatment plan
 - e. Encourage symptomatic use of bland emollients as much as required

(strong recommendation, high certainty evidence)

2. In atopic dermatitis patients, use of a standard, fragrance-free and contact allergens-free moisturizer/emollient (white soft paraffin/aqueous cream) over a branded one is recommended (12).

(conditional recommendation, low certainty of evidence)

3. In uncontrolled atopic dermatitis unresponsive to moisturizer usage alone, the addition of a topical corticosteroid ointment (TCS) is recommended (10).

(strong recommendation, high-certainty evidence)

4. In uncontrolled atopic dermatitis unresponsive to moisturization alone at age ≥3 months, the addition of a topical calcineurin inhibitor (TCI) tacrolimus/pimecrolimus is recommended (12).

(strong recommendation, high certainty evidence)

5. In localised uncontrolled atopic dermatitis unresponsive to mid- to high-potency topical regime, the adoption of a "time and body area limited" application (ranging from 4–7 days a week; from minimum 1 hour to maximum overnight, once a day) trial of occlusive low- to mid-potency TCS; with or without wet dressings is recommended (12).

(conditional recommendation, very low certainty evidence)

6. In uncontrolled atopic dermatitis being managed with mid- to high-potency topical regimes, the once-a-day application, twice a day regime is preferrable and recommended (12).

(conditional recommendation, moderate certainty evidence)

7. In atopic dermatitis having frequent relapses, the use of proactive therapy, i.e. routine intermittent use of 2–3 times topical application a week to frequently flaring areas with a TCI or mid-potency TCS is recommended (12).

(strong recommendation, moderate-certainty evidence)

8. In moderate to severe atopic dermatitis, along with topical therapy, dilute bleach baths with complete written instructions to the patient based on their feasibility and tolerance due to fissuring in the eczematous skin are recommended (12).

(conditional recommendation, low-certainty evidence)

9. In moderate to severe atopic dermatitis not responding to mid-potency topical regimes, the addition of allergen immunotherapy (based on availability) to standard topical protocol is recommended (12,15)Click or tap here to enter text..

$(conditional\ recommendation, moderate-certainty\ evidence)$

10. In moderate to severe atopic dermatitis unresponsive to mid- to high-potency topical regime and systemic management options, the suggestion is against the use of oral azathioprine (12).

(conditional recommendation, low-certainty evidence)

11. In moderate to severe atopic dermatitis unresponsive to mid- to high-potency topical regime and systemic management options, adding oral cyclosporine (CsA) along with continued topical standard care is recommended (12).

(conditional recommendation, low-certainty evidence)

12. In moderate to severe atopic dermatitis unresponsive to mid- to high-potency topical regime and systemic management options, the panel suggests adding in-hospital narrow band ultraviolet B-light phototherapy in the outpatient department of the dermatology clinic (12).

(conditional recommendation, low-certainty evidence)

13. In adults with atopic dermatitis unresponsive to standard topical regimes and systemic treatment, replacing the systemic treatment with one of the oral JAK inhibitors, generally (abrocitinib, baricitinib, upadacitinib) is suggested.

(conditional recommendation, low-certainty evidence)

14. In mild to moderate atopic dermatitis refractory to moisturization alone, the panel suggests adding topical crisaborole 2% ointment over usual care alone.

(conditional recommendation, low-certainty evidence)

15. In adults with mild to moderate atopic dermatitis refractory to moisturization alone, the JTF panel suggests against adding topical ruxolitinib.

(conditional recommendation, low-certainty evidence)

Recommendations adapted from the source guideline

management options, the panel suggests against using mycophenolate mofetil (MMF).

Adapted version: Panel conditionally recommends MMF in place of CsA as a systemic treatment option for moderate to severe atopic dermatitis in patients who cannot tolerate or receive CsA due to medical reasons, but not in women who can or want to become pregnant (16). (conditional recommendation, low-certainty evidence)

Based on revised evidence for decision

Original recommendation: In atopic dermatitis, the use of elimination diets versus unrestricted diet is not recommended.

Adapted version: In atopic dermatitis, our panel suggests the use of elimination diets versus unrestricted diet based on specific IgE to food allergens test report and positive history.

(conditional recommendation, low-certainty evidence)

UVB, the use of systemic corticosteroids is not recommended.

Adapted version: In atopic dermatitis, the panel suggests using systemic corticosteroids reserved exclusively for acute, severe disease flares and as a short-term bridge option (less than 30 days) between other systemic, corticosteroid-sparing drugs.

(conditional recommendation, low-certainty evidence)

New recommendations

In pregnant females with atopic dermatitis, the panel recommends the use of TCS of lowest effective potency, i.e. preferably of classes 6 & 19. 7, with precautions in body areas prone to striae formation, e.g. breasts, abdomen and thighs. Classes 1 & 2 TCS should be avoided during pregnancy due to the risk of systemic absorption and side-effects, but can be used in localised chronic and lichenified lesions and as occasional rescue management option (17,18)Click or tap here to enter text..

(strong recommendation, moderate-certainty evidence)

20. In pregnant and lactating females with atopic dermatitis the panel recommends conditional off-label use of TCI. Tacrolimus use is recommended as the preferred TCI during pregnancy due to the large available existing data in published literature. It is only conditionally recommended for use in areas prone to striae formation due to topical steroids like face, flexures, thighs, abdomen and breast or for localized resistant disease not responding to moisturizers alone (18).

(conditional recommendation, low-certainty evidence)

21. In pregnant and lactating females with atopic dermatitis the panel recommends conditional use of phototherapy especially NB-UVB as second line treatment option in settings where this facility is available. Folate supplementation should be done. Face should be covered with mask during NB-UVB to avoid melasma (18).

(conditional recommendation, low-certainty evidence)

In pregnant and lactating females with atopic dermatitis not responding to topical treatment and phototherapy, the use of AZA vs CsA 22. is not recommended. CsA is regarded as the default but off-label immunosuppressive therapeutic option in atopic dermatitis during pregnancy when continuous treatment is required, abiding by all the precautions for non-pregnant cases. AZA may be used as off-label treatment alternative for continuation therapy in atopic dermatitis cases already on AZA at the time of conception (18).

(strong recommendation, moderate-certainty evidence)

- 23. The panel recommends that systemic corticosteroids use for atopic dermatitis be limited to moderate to severe cases not responding to topical treatment and phototherapy after 1st trimester. Prednisolone, but not dexamethasone, must be used if required in atopic dermatitis patients with pregnancy, and only for shorter periods of time, generally less than 2-3 weeks and 0.5 mg/kg/day. Children born to mothers receiving > 35 mg/day prednisolone at the time of delivery should be observed for a 48-hour period in NICU. Treatment with systemic TCS during lactation is safe, since <0.1% of maternal dosage is secreted in breast milk (18). (conditional recommendation, low-certainty evidence)
- In patients with atopic dermatitis, the panel suggests multidisciplinary treatment approach involving educational training for patients 24. and families of patients, including input from paediatricians, dermatologists, pulmonologists, allergists and psychologists. (The Pakistan Association of Dermatology will develop a standardized educational programme for atopic dermatitis patients and conduct training for atopic dermatitis patients and families monthly at teaching hospitals without additional payments). (strong recommendation, moderate-certainty evidence)
- Panel suggests the use of probiotics as alternative treatment for moderate to severe atopic dermatitis in children and adults either alone 25. or in combination with prebiotics but not in infants (19,20).

(conditional recommendation, low-certainty evidence)

- In patients with moderate to severe atopic dermatitis requiring systemic immunosuppressant, our panel recommends ciclosporin for 26. short-term quicker disease control and methotrexate in the long-term for maintaining remission (21). Both CsA and MTX are effective, well-tolerated treatment options for moderate to severe atopic dermatitis in children and adults not responding to topicals and phototherapy. MTX must be avoided in pregnant women and should be stopped 6 months before conception in men and women. (conditional recommendation, moderate-certainty evidence)
- In moderate to severe atopic dermatitis requiring systemic therapy not responding to, or unable to receive, systemic corticosteroids, CsA, 27. MTX or MMF can be given as a trial of biologic i.e. omalizumab in special instances for disease control, as dupilumab is not available

(conditional recommendation, low-certainty evidence)