# INPLASY PROTOCOL

To cite: Ghirozi et al. Efficacy and safety of dupilumab for atopic dermatitis in children and adolescents. Inplasy protocol 202250160. doi: 10.37766/inplasy2022.5.0160

Received: 28 May 2022

Published: 28 May 2022

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**None reported.**

**Support:** **None.**

**Review Stage at time of this submission:** **Piloting of the study selection process.**

**Conflicts of interest:**
**None declared.**

# Efficacy and safety of dupilumab for atopic dermatitis in children and adolescents

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**Review question / Objective:** **Is dupilumab effective for treatment of children and adolescentes with moderate to severe atopic dermatitis? Does it improve SCORAD outomes? Does it reduce pruritus? Does it improve quality of life? Does improve sleep quality?**
**Condition being studied:** **Atopic dermatitis is a common and chronic skin disease characerized by inflammation, pruritus and dryness of the skin. Diminished quality of life, sleeping problems and intense chronic pruritus are among the consequences faced by patients with atopic dermatitis, especially those with moderate to severe presentations of the disease.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 May 2022 and was last updated on 28 May 2022 (registration number INPLASY202250160).

## INTRODUCTION

**Review question / Objective:** **Is dupilumab effective for treatment of children and adolescentes with moderate to severe atopic dermatitis? Does it improve SCORAD outomes? Does it reduce pruritus? Does it improve quality of life? Does improve sleep quality?**

**Rationale:** **Dupilumab is the drug of choice for treatment of adults with moderate to severe atopic dermatitis, but solid evidence about its efficacy and safety for children and adolescents is still lacking. Therefore,**

we aim to perform a systematic review and metanalysis examining the efficacy of dupilumab in children and adolescentes (aged 0 to 18) with moderate to severe atopic dermatitis, specifically interested in SCORAD outcomes, as well as in improvement of pruritus, quality of life and sleep quality.

**Condition being studied:** Atopic dermatitis is a common and chronic skin disease characerized by inflammation, pruritus and dryness of the skin. Diminished quality of life, sleeping problems and intense chronic pruritus are among the consequences faced by patients with atopic dermatitis, especially those with moderate to severe presentations of the disease.

## METHODS

**Search strategy:** Pubmed, EMBASE, Cochrane. Articles published from 2012 to 2022, searched on 22/05/2022.

**Participant or population:** Patients aged 0-18 years old with moderate to severe atopic dermatitis.

**Intervention:** Dupilumab.

**Comparator:** Placebo or non-use of dupilumab + topical corticosteroids.

**Study designs to be included:** Randomized controlled trials and observational studies will be included.

**Eligibility criteria:** We will include only studies with patients aged 0-18 years old with moderate to severe atopic dermatitis and that report any of the outcomes of interest.

**Information sources:** Electronic databases.

**Main outcome(s):** We will extract data for a pooled analysis on the following outcomes: (1) Eczema Area and Severity Index (EASI); (2), Investigator's Global Assessment Scale (IGA); (3) Patient Global Assessment of Disease Status (PGAD); (4) Scoring Atopic Dermatitis (SCORAD); (5) Pruritus Numerical Rating Scale (PNRS); (6) Dermatology Life Quality Index (DLQI); (7) EuroQol 5-Dimensions Questionnaire (ED-5D); (8) Patient-Oriented Eczema Measure (POEM).

**Additional outcome(s):** Sleep quality.

**Data management:** Two investigators will extract the data.

**Quality assessment / Risk of bias analysis:** We will use the Cochrane Collaboration's tool for assessing risk of bias in randomized trials for quality assessment of individual randomized studies qne 5h3 Risk of Bias of Non-randomized Studies of Interventions (ROBINS-I) for non-randomized studies.

**Strategy of data synthesis:** The systematic review and meta-analysis will be performed in line with recommendations from the Cochrane Collaboration and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement guidelines. We will extract the data from individual studies using hazard ratios (HR) to preserve time-to-event data from individual studies. Treatment effects for binary endpoints will be compared using pooled HR or odds-ratios (OR) with 95% confidence intervals. Weighted mean differences will be used to pool continuous outcomes. Heterogeneity will be evaluated with Cochran Q test and $I^2$ statistics; p values inferior to 0.10 and $I^2$>25% will be considered significant for heterogeneity. We will use a fixed-effect model for endpoints with $I^2$ < 25% (low heterogeneity). In pooled outcomes with high heterogeneity, DerSimonian and Laird random-effects model will be used. Review Manager 5.4 (Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) will be used for statistical analysis.

**Subgroup analysis:** Subgroup analyses were only performed if there were sufficient data.Subgroup analysis will be performed according to different ages and we will extract data and perform sub-analyses in the following subgroups: (1) male; (2) female.

**Sensitivity analysis:** Given considerable heterogeneity, random effect analysis will be used.

**Language:** English.

**Country(ies) involved:** United States, Brazil.

**Keywords:** Dupilumab ; atopic dermatitis ; children ; adolescents.

**Contributions of each author:**

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