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Efficacy and Safety of Janus Kinase Inhibitors for Chronic Hand Eczema: A Systematic Review of Randomized Controlled Trials

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Introduction & Objectives: Chronic hand eczema (CHE) is a recalcitrant skin condition often linked to filaggrin gene mutations and immune dysregulation involving both Type 1 and Type 2 pathways, with JAK/STAT signaling playing a key role in the immune alterations and skin barrier disruption. It typically persists for at least 3 months or recurs at least twice within 1 year. Recent studies show that CHE involves mixed Type 1/Type 2 pathway activation and immune dysregulation, with JAK/STAT signaling contributing to barrier damage. Treatment options are multiple and have more recently included topical and systemic Janus kinase inhibitors (JAKi) as a notable object of studies. This study aims to assess their effectiveness and potential adverse effects in CHE.

Materials & Methods: We conducted a systematic review on the efficacy of JAK inhibitors for hand eczema, searching PubMed, Embase, Cochrane Library, and Scopus for randomized controlled trials (RCTs) published up to March 28, 2025. Study selection and data extraction followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Cochrane recommendations.

Results: Five studies were included, comprising six RCTs and 1,260 participants, evaluating delgocitinib, gusacitinib, and ruxolitinib. Delgocitinib 20 mg demonstrated consistent improvements in Investigator's Global Assessment for Chronic Hand Eczema (IGA-CHE) response. In the DELTA 1 and DELTA 2 trials, responses rose from 15.4% at Week 4 to 22.8% at Week 8, with a slight decline by Week 16. Smaller studies supported these findings, with one reporting a response rate of 45.8% at Week 8 versus 13.3% for placebo. Another reported improvement from 24.5% to 37.7% between Weeks 8 and 16, with placebo groups maintaining low responses. Topical ruxolitinib 1.5% showed a progressive increase in IGA response, reaching 53.3% by Week 16 in a limited sample. Gusacitinib showed significant early efficacy based on the Physician's Global Assessment (PGA). At Week 2, 12.5% (80 mg) and 12.1% (40 mg) had clear or almost clear hands, compared to 0% in placebo. By Week 16, responses increased to 31.3% (80 mg) and 21.2% (40 mg) versus 6.3% with placebo. Regarding safety, gusacitinib 80 mg was associated with the highest frequency of adverse events (AEs), particularly infections, gastrointestinal, and nervous system disorders. Delgocitinib had a moderate AE profile, with nasopharyngitis and infections and infestations being the most reported. Serious AEs were rare across all studies. Ruxolitinib safety data were limited due to small sample size, though one serious AE was reported.

Conclusion: This systematic review underscores the potential of topical and systemic JAKi in management of CHE. Oral delgocitinib demonstrated sustained, consistent IGA-CHE improvements across multiple timepoints, while topical ruxolitinib also exhibited a progressive therapeutic response. Gusacitinib showed early and lasting efficacy based on PGA, with notable clinical responses as early as Week 2. The overall safety profile of JAKi was favorable, with serious adverse events infrequent. However, gusacitinib 80 mg was linked to a higher incidence of AEs, whereas delgocitinib showed a more moderate and manageable profile. These findings support the effectiveness

and safety of both topical and systemic JAKi in CHE, though further studies are needed to confirm efficacy, refine dosing, and assess long-term safety.