

# Efficacy and Safety of Deucravacitinib in the Treatment of Psoriasis: A Systematic Review

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## Abstract

**Background:** Psoriasis, a chronic inflammatory skin disorder, poses substantial challenges to affected individuals, with plaque psoriasis being the most prevalent form. Despite advancements in treatment, including biologic drugs and oral small molecules, there remains a need for effective, accessible, and safe therapies for moderate-to-severe psoriasis. Deucravacitinib, a novel oral small molecule targeting Tyrosine Kinase 2 (TYK2), emerges as a promising option in psoriasis management. **Objective:** This study aims to evaluate the efficacy and safety of deucravacitinib in the treatment of psoriasis. **Method:** A comprehensive literature search was conducted across multiple databases, including PubMed, clinicaltrials.gov, Cochrane Skin, and Embase, up to February 16, 2023. Manuscripts were selected and analyzed following PRISMA guidelines. Relevant keywords such as "psoriasis," "oral small molecules," "deucravacitinib," "efficacy," and "safety" were used. Various types of manuscripts, including reviews, meta-analyses, clinical trials, and real-life experiences, were considered. Abstracts and full texts of selected articles were reviewed, and references were cross-checked. **Results:** A total of four completed trials and six ongoing studies were included in the review. Completed studies demonstrated the efficacy of deucravacitinib, with significant improvements in Psoriasis Area and Severity Index (PASI) scores compared to placebo and apremilast. Notably, deucravacitinib showed superiority in achieving PASI 75, 90, and 100 responses. Safety profiles were generally favorable, with common adverse events including nasopharyngitis, headache, diarrhea, and nausea. **Conclusion:** Deucravacitinib emerges as an innovative and valuable option for psoriasis management, offering promising efficacy and safety outcomes in clinical trials. While further research is warranted to validate its efficacy and compare it with existing therapies, deucravacitinib holds potential as a significant addition to the psoriasis treatment armamentarium.

**Keywords:** Psoriasis, deucravacitinib, oral small molecules, efficacy, safety, TYK2 inhibitor.

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## INTRODUCTION

Psoriasis, a persistent inflammatory skin condition affecting approximately 3% of the global population, primarily manifests as plaque psoriasis, which constitutes up to 90% of cases. This form is identifiable by distinct erythematous plaques covered with silvery-white scales. Psoriasis often accompanies various comorbidities such as metabolic syndrome, psoriatic arthritis, cardiovascular issues, nonalcoholic fatty liver disease, inflammatory bowel disease, and

depression, significantly impacting patients' well-being. While mild cases can be managed with topical treatments, moderate-to-severe forms necessitate systemic interventions. [1-3] However, traditional systemic therapies like cyclosporine, acitretin, methotrexate, and fumarates are frequently avoided due to contraindications or adverse effects. Phototherapy presents logistical challenges, and although recent advancements such as apremilast and biologic drugs targeting cytokines like TNF- $\alpha$ , IL-12/23, IL-17, and IL-23 have shown promising outcomes but they have

limitations and high costs. [4-6] Therefore, there persists a demand for accessible, efficient, and safe oral medications for moderate-to-severe psoriasis. [7-11] Deucravacitinib, a novel oral small molecule inhibiting Tyrosine Kinase 2 (TYK2), emerges as a potential solution in psoriasis management.

### Objective

In this study our main goal is to efficacy and safety of deucravacitinib in psoriasis.

### METHODOLOGY

A comprehensive literature search was conducted across PubMed, clinicaltrials.gov, Cochrane Skin, and Embase databases up to February 16, 2023. Manuscripts were identified, screened, and analyzed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The search utilized keywords such as "psoriasis," "oral small molecules," "deucravacitinib," "efficacy," and "safety." Various types of manuscripts

were included, such as reviews, meta-analyses, clinical trials, real-life experiences, case reports, and series, with a focus on relevance to the research objectives. Publications related to the use of deucravacitinib for dermatological conditions other than psoriasis were excluded. Abstracts and full texts of selected articles were meticulously reviewed, and references were cross-checked to ensure comprehensive coverage. Only articles in the English language were considered. It's important to note that this manuscript is a synthesis of previously conducted studies and does not involve any new research involving human or animal participants conducted by the authors.

### RESULTS

A total of 4 completed trials and 6 ongoing studies were considered in the current review. Among the completed studies with available results, two Phase II studies and two Phase III trials were identified. Main results in terms of effectiveness and safety are summarized in and, respectively.

**Table-1: Effectiveness of Deucravacitinib for Psoriasis Management in Clinical Trials**

Author	Patients	Study Group	Efficacy			
			PASI75 n (%)	PASI90 n (%)	PASI100 n (%)	sPGA 0/1 n (%)
Papp <i>et al.</i> , [12]	267	Placebo:45 Deucravacitinib: 3mg QAD: 44 3mg QD: 44 3mg BID: 45 6mg BID: 45 12mg QD: 44	Placebo: 3 (6.7) Deucravacitinib: 3mg QAD: 4 (9.1) 3mg QD: 17 (38.6) 3mg BID: 31 (68.9) 6mg BID: 30 (66.7) 12mg QD: 33 (75.0)	Placebo: 1 (2.2) Deucravacitinib: 3mg QAD: 3 (6.8) 3mg QD: 7 (15.9) 3mg BID: 20 (44.4) 6mg BID: 20 (44.4) 12mg QD: 19 (43.2)	Placebo: 0 Deucravacitinib: 3mg QAD: 1 (2.3) 3mg QD: 0 (8.9) 3mg BID: 4 (17.8) 6mg BID: 8 (25.0) 12mg QD: 11 (25.0)	Placebo: 3 (6.7) Deucravacitinib: 3mg QAD: 9 (20.5) 3mg QD: 17(38.6) 3mg BID: 34 (75.6) 6mg BID: 29 (64.4) 12mg QD: 33 (75.0)
Armstrong <i>et al.</i> , [13]	666	Placebo: 166 Deucravacitinib 6mg QD: 332 Apremilast 30mg BID: 168	Placebo: 21 (12.7) Deucravacitinib: 194 (58.4) Apremilast: 59 (35.1)	Placebo: 7 (4.2) Deucravacitinib: 118 (35.5) Apremilast: 33 (19.6)	Placebo: 1 (0.6) Deucravacitinib: 47 (14.2) Apremilast: 5 (3.0)	Placebo: 12 (7.2) Deucravacitinib: 178 (53.6) Apremilast: 54 (32.1)
Strober <i>et al.</i> , [14]	1020	Placebo: 255 Deucravacitinib 6mg QD: 511 Apremilast 30mg BID: 254	Placebo: 24 (9.4) Deucravacitinib: 271 (53.0) Apremilast: 101 (39.8)	Placebo: 7 (2.7) Deucravacitinib: 138 (27.0) Apremilast: 46 (18.1)	Placebo: 3 (1.2) Deucravacitinib: 52 (10.2) Apremilast: 11 (4.3)	Placebo: 22 (8.6) Deucravacitinib: 253 (49.5) Apremilast: 86 (33.9)

**Table-2: Safety of Deucravacitinib for Psoriasis Management in Clinical Trials**

Author	Study Group	Any AEs n (%)	Serious AEs n (%)	Treatment-Related AEs n (%)	AEs Leading to Discontinuation n (%)	Most Common AEs n (%)
Papp <i>et al.</i> , [12]	Placebo: 45 Deucravacitinib: 3mg QAD: 44 3mg QD: 44 3mg BID: 45	AEs were collected in 51% of the subjects in the placebo cohort and 55 to 80%	Placebo: 1 (2.2) Deucravacitinib: 3mg QAD: 1 (2.3)	NR	Placebo: 2 (4.4) Deucravacitinib: 3mg QAD: 1 (2.3)	Nasopharyngitis, headache, diarrhea, and URTI were the

	6mg BID: 45 12mg QD: 44	patients in the deucravacitinib groups, with the highest percentage in the 6mg BID dose.	3mg QD: 1 (2.3) 3mg BID: 1 (2.2) 6mg BID: 0 12mg QD: 0		3mg QD: 2 (4.5) 3mg BID: 1 (2.2) 6mg BID: 3 (6.7) 12mg QD: 1 (2.3)	most common AEs.
Armstrong <i>et al.</i> , [13]	Placebo: 166 Deucravacitinib 6mg QD: 332 Apremilast 30mg BID: 168	Placebo: 70 (42.4) Deucravacitinib: 176 (53.0) Apremilast: 93 (55.4)	Placebo: 9 (5.5) Deucravacitinib: 7 (2.1) Apremilast: 4 (2.4)	Placebo: 20 (12.1) Deucravacitinib: 65 (19.6) Apremilast: 36 (21.4)	Placebo: 7 (4.2) Deucravacitinib: 6 (1.8) Apremilast: 10 (6.0)	<b>Placebo:</b> nasopharyngitis (7, 4.2%) – URTI and diarrhea (6, 3.6%) – headache (5, 3.0%) <b>Deucravacitinib:</b> nasopharyngitis and URTI (21, 6.3%) – headache (16, 4.8%) – diarrhea (13, 3.9%) <b>Apremilast:</b> nausea (19, 11.3%) – headache and diarrhea (17, 10.1%) – nasopharyngitis (14, 8.3%)
Strober <i>et al.</i> , [14]	Placebo: 255 Deucravacitinib 6mg QD: 511 Apremilast 30mg BID: 254	Placebo: 138 (54.3) Deucravacitinib: 293 (57.5) Apremilast: 150 (59.1)	Placebo: 3 (1.2) Deucravacitinib: 8 (1.6) Apremilast: 1 (0.4)	Placebo: 45 (17.7) Deucravacitinib: 99 (19.4) Apremilast: 73 (28.7)	Placebo: 9 (3.5) Deucravacitinib: 14 (2.7) Apremilast: 12 (4.7)	<b>Placebo:</b> nasopharyngitis (29, 11.4%) – diarrhea (19, 7.5%) – headache (14, 5.5%) <b>Deucravacitinib:</b> nasopharyngitis (55, 10.8%) – URTI (25, 4.9%) – diarrhea (24, 4.7%) <b>Apremilast:</b> diarrhea (33, 13.0%) – headache (28, 11.0%) – nasopharyngitis and nausea (23, 9.1%)

## DISCUSSION

Managing psoriasis, especially its moderate-to-severe forms, poses significant challenges. While the advent of biologic drugs and oral small molecules

(OSMs) has transformed treatment options, providing promising results in efficacy and safety, the ongoing COVID-19 pandemic has added further complexities to clinical practice. Despite these advancements, there remains a need for novel therapies to tailor treatment more precisely to individual patients and sustain long-term effectiveness, as traditional systemic treatments are often avoided due to contraindications or adverse effects, and logistical concerns limit phototherapy [6-7].

Among OSMs, apremilast stands out as the sole innovative drug with oral administration, functioning by inhibiting the phosphodiesterase-4 enzyme and modulating the immune system. However, its efficacy, though safe for patients with conditions like hepatitis or cancer, falls short compared to biologics, especially in achieving PASI 90 and 100 responses. Similarly, while biologics demonstrate effectiveness and safety, their parental administration and associated limitations may restrict their usage [12-13].

In this landscape, advancements in understanding psoriasis pathogenesis have led to the development of selective therapies. Notably, TYK2, a kinase pivotal in signaling IL-23 and other cytokines implicated in psoriasis, emerged as a promising target for novel treatments. Unlike Janus Kinase (JAK) inhibitors, deucravacitinib selectively inhibits TYK2, minimizing the risk of adverse events associated with direct JAK inhibition [14].

Deucravacitinib's efficacy and safety have been evidenced in clinical trials, positioning it as a valuable addition to the psoriasis treatment arsenal. Phase 2 and 3 trials demonstrated its superiority over placebo and apremilast, maintaining clinical response over extended periods. However, considerations regarding infections, malignancies, and laboratory parameter monitoring are warranted [13].

While current therapeutic options offer alternatives for psoriasis management when conventional systemic treatments are unsuitable, the trend towards personalized medicine underscores the importance of introducing innovative, safe, and effective treatments like deucravacitinib. Real-world data are yet to emerge, but its potential to address unmet needs in psoriasis treatment is promising.

## CONCLUSION

In summary, deucravacitinib emerges as an innovative and valuable option for psoriasis management, supported by promising efficacy and safety outcomes from clinical trials. The clinical trials demonstrate its potential to provide better skin clearance for patients compared to existing oral options. Its mechanism of action represents a novel approach in psoriasis treatment. This selectivity may offer a more targeted therapy with potentially fewer systemic side effects. The oral route of administration presents a

significant advantage for patients who prefer not to use injectable options, thus improving treatment adherence and patient satisfaction. While these initial findings are encouraging, further research is necessary to validate and compare deucravacitinib against biologic drugs, clarifying its precise role in the treatment paradigm for psoriasis. Cost-effectiveness analyses will also be essential to determine deucravacitinib's value proposition compared to existing therapies, especially considering the high costs associated with biologic treatments.

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