

**Summary of Research: Mechanism of Action of Brodalumab May Correlate With Efficacy
in Patients With Inflammatory Skin Diseases**

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Journal: *Dermatology and Therapy*

Word count limit: Maximum of 4 PDF pages

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ABSTRACT

This is a summary of a review article that looked at how an injectable treatment called brodalumab may be effective in treating several inflammatory diseases, including plaque psoriasis. While several therapies are used to treat psoriasis, some do not work well for certain patients who need to switch therapies to manage their disease. Brodalumab is a therapy for adults with moderate-to-severe plaque psoriasis who are candidates for injections, pills, or light therapy and have not experienced adequate disease improvement with an injection or pill. Brodalumab works by blocking the receptor for a group of proteins from the interleukin-17 (IL-17) family, which play an important role in inflammation and the life cycle of skin cells. While there are several drugs that target certain IL-17 proteins, they do not work for all patients. By blocking the receptor for multiple IL-17 proteins, brodalumab has been shown to reduce the symptoms of psoriasis, even in people who have not had success with other treatments. In this summary article, we explain how brodalumab works in treating inflammatory skin conditions like psoriasis. We also describe how effective brodalumab is by analyzing data from controlled clinical trials as well as routine patient care in the real world. In addition, we discuss how brodalumab may help patients who had a poor response to other anti-IL-17 treatments with a different mechanism of action and lead to improvements in mental health and quality of life.

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This is a summary of the original review article “Mechanism of Action of Brodalumab May Correlate With Efficacy in Patients With Inflammatory Skin Diseases” [1].

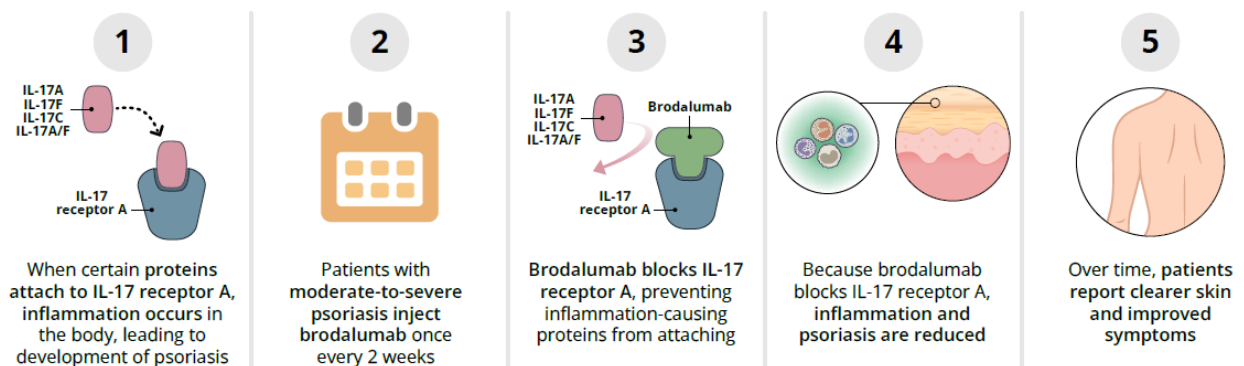
INTRODUCTION

Maintaining clear skin over a long period of time is a major treatment goal for people with psoriasis. For some patients, a treatment may not work well or may stop working, and effective options are needed for patients who have to switch treatments.

Brodalumab is an injectable treatment approved by the US Food and Drug Administration (FDA) to treat moderate-to-severe plaque psoriasis in adults who are candidates for injections or pills (systemic therapy) or light therapy and have tried other systemic treatments that did not work or stopped working. Brodalumab works by targeting a specific part of the immune system called the IL-17 receptor A. Certain inflammatory proteins (IL-17A, IL-17F, IL-17C, and IL-17A/F) can attach to the receptor and trigger inflammation that contributes to psoriasis. Similarly, brodalumab attaches to the IL-17 receptor A, thereby blocking the attachment of those inflammatory proteins. This blockage reduces inflammation and promotes disease control and improved psoriatic symptoms.

[Infographic showing brodalumab’s mechanism of action]

Brodalumab blocks IL-17 receptor A

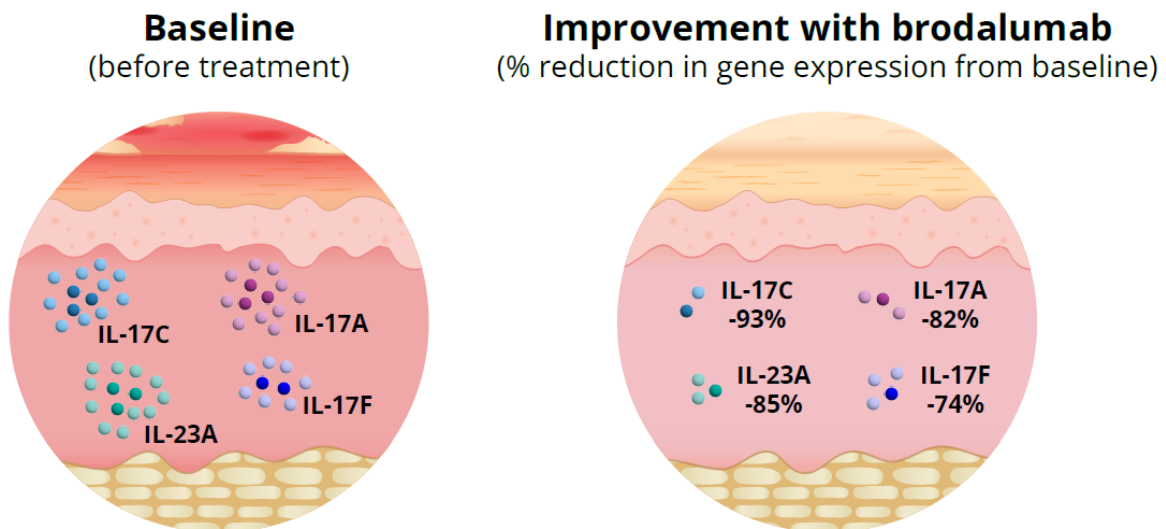


WHAT DID THIS REVIEW SHOW?

Brodalumab blocks inflammatory proteins that contribute to psoriasis

Brodalumab greatly reduced inflammatory proteins in psoriatic plaques at 12 weeks, including IL-17A, IL-17F, IL-17C, and IL-23A, compared with baseline (levels determined before treatment was initiated). The levels of inflammatory proteins decreased with brodalumab treatment but not a placebo (a treatment with no active ingredient).

[Infographic showing percent cytokine reduction from baseline in lesional skin treated with brodalumab]



Additionally, unlike a biologic that only targeted IL-17A (ixekizumab), brodalumab was able to return psoriasis-associated genes to a normal state in human skin cells. These genes were activated by IL-17A, IL-17F, and IL-17C. This means that brodalumab may reduce inflammation by targeting more inflammatory proteins than other medicines.

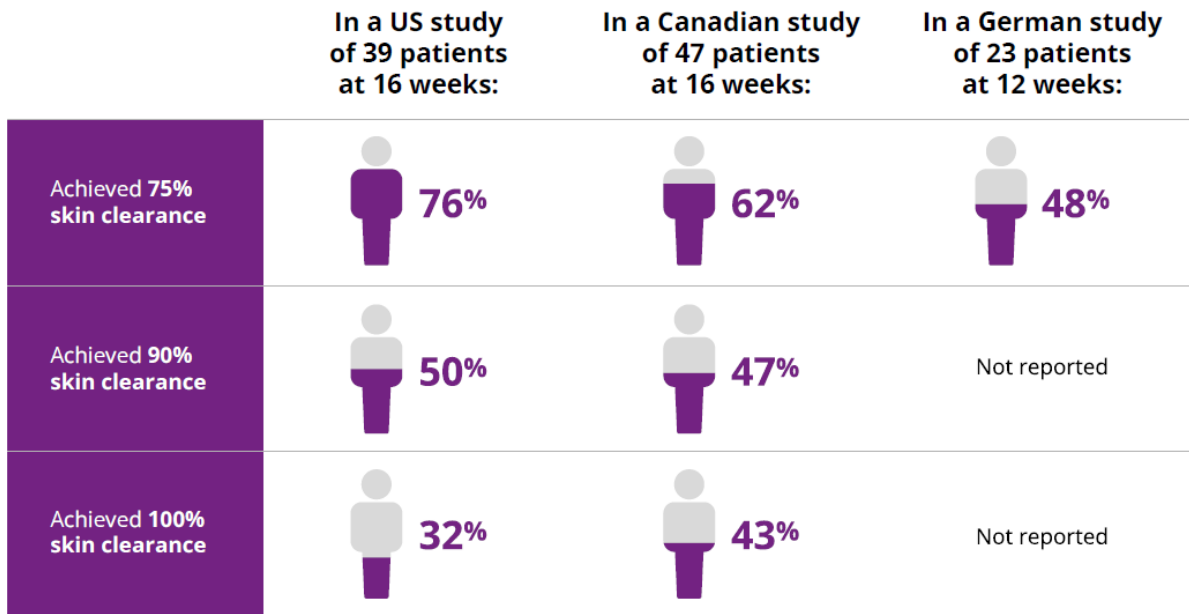
Brodalumab in patients whose disease did not respond to IL-17 therapy

Several biologics target a specific protein, IL-17A, to treat psoriasis. However, some patients may not respond well or may stop responding to these treatments over time. This might happen because there are multiple types of IL-17 proteins that can cause inflammation in the

body. Because brodalumab blocks the receptor that all IL-17 proteins attach to, it can stop the inflammation caused by various IL-17 proteins, not just IL-17A. Real-world studies have shown that brodalumab can be effective for patients who did not respond well to other IL-17A–targeting medications.

[Efficacy in patients who failed IL-17 biologics]

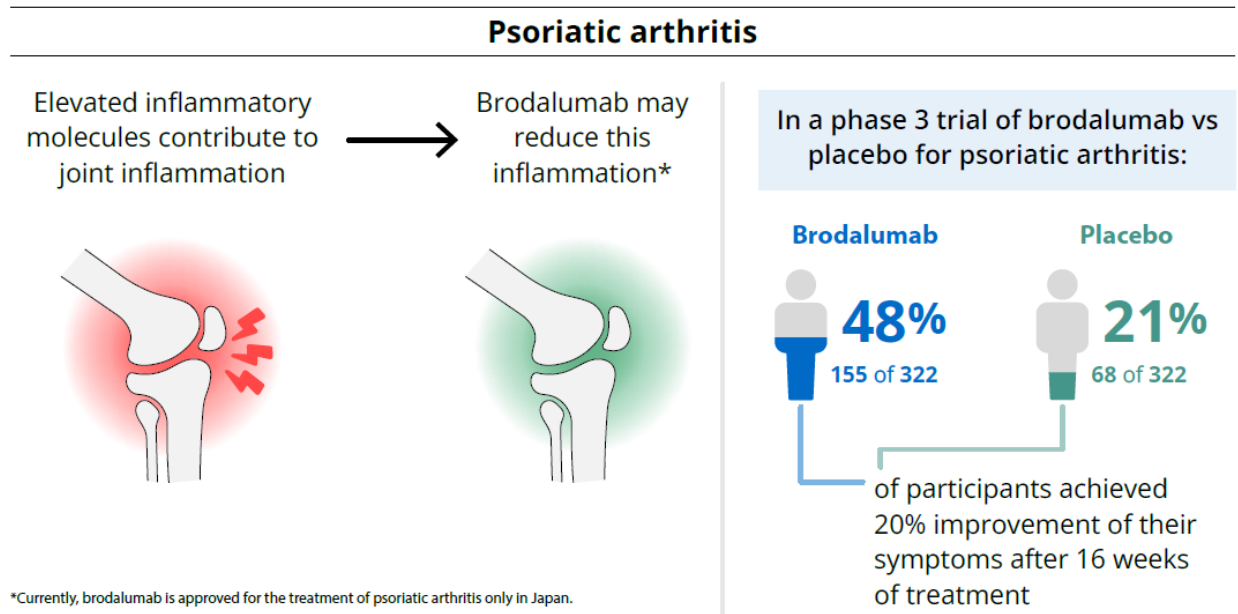
Psoriasis improvement in patients whose disease did not respond to anti-IL-17 biologics



Brodalumab for the treatment of other conditions

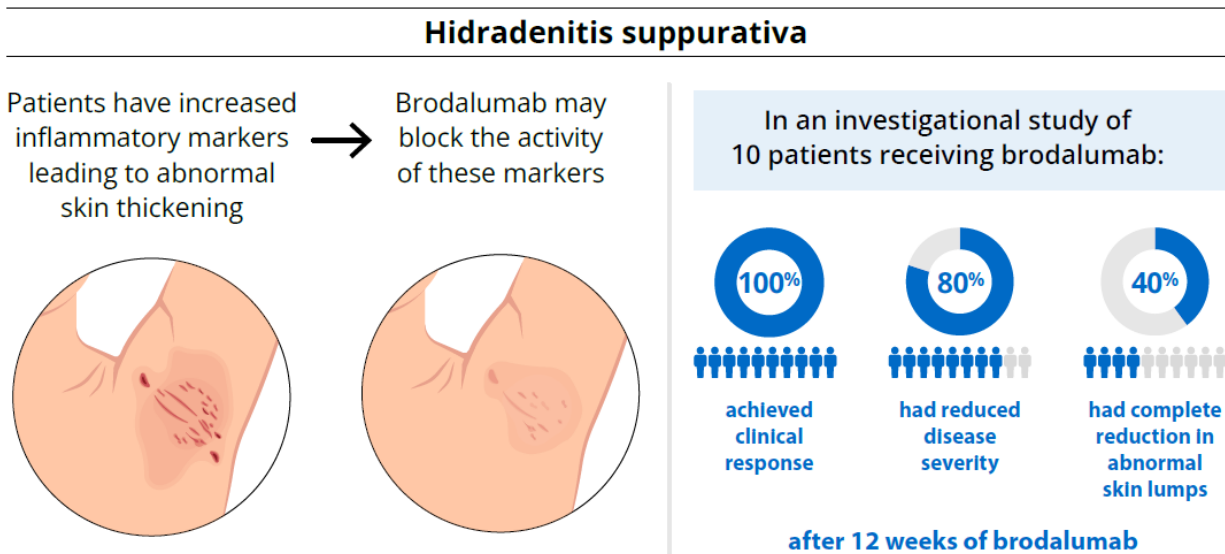
Other inflammatory conditions like psoriatic arthritis and hidradenitis suppurativa (HS) are also associated with IL-17 activity. Although brodalumab is only approved to treat psoriatic arthritis in Japan and is not approved for HS anywhere, researchers have studied how well it works for both conditions. Two phase 3 studies of patients with psoriatic arthritis (AMVISION-1 and AMVISION-2) found that brodalumab improved symptoms compared with a placebo. Brodalumab was also associated with better skin clearance and improvement in other measures of arthritis compared with a placebo.

[Infographic for brodalumab efficacy in psoriatic arthritis]



A small study of 10 patients with HS found that brodalumab improved HS symptoms and severity, with no serious side effects. In this study, patients had previously used other biologic therapies similar to brodalumab.

[Infographic for brodalumab efficacy in HS]

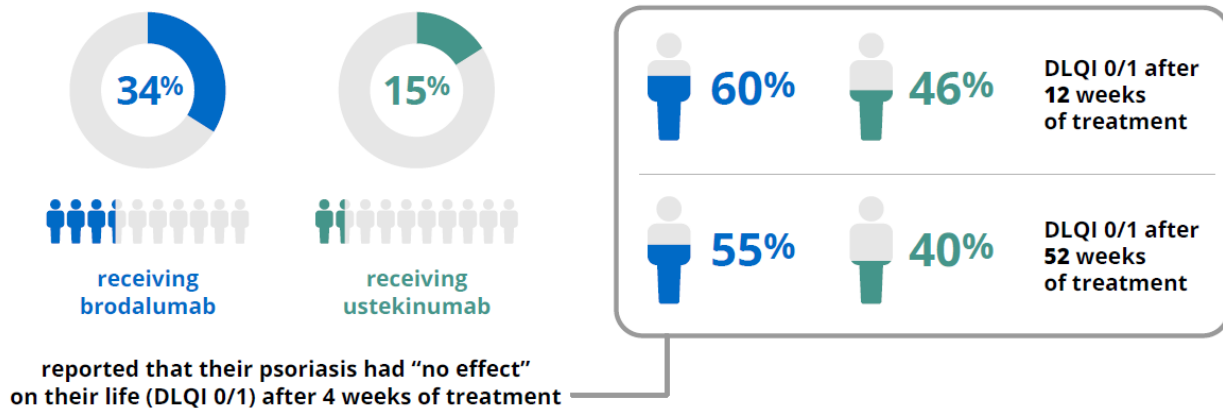


Improvements in quality of life and mental health

In two phase 3 trials (AMAGINE-2/-3), brodalumab was associated with a significantly greater improvement in quality of life, as measured by the dermatology life quality index (DLQI), compared with ustekinumab, another psoriasis treatment.

[Infographic for quality of life with brodalumab treatment]

Of patients who reported at the start of the AMAGINE-2/-3 trials that psoriasis had a negative effect on their life (DLQI >1):



In another trial (AMAGINE-1), more patients receiving brodalumab experienced significant improvements in mental health measures compared with those receiving a placebo.

Although no direct link between brodalumab and suicidal thoughts or behaviors was found during the main trials, brodalumab has a boxed warning about this potential risk. Real-world safety data from various sources, including US safety reports, clinical experience summaries, and case reports, have shown that brodalumab's safety profile is consistent with that of long-term clinical studies.

CONCLUSIONS

Brodalumab, which works differently from other biologics, blocks multiple forms of IL-17, especially IL-17A, IL-17C, and IL-17F. This may explain why brodalumab works in patients whose disease did not respond well to medications that only target IL-17A. Clinicians should be aware of the previously demonstrated effectiveness of brodalumab in the management of inflammatory conditions such as psoriatic arthritis and HS. These clinical improvements are linked to enhanced quality of life. More research is needed to better understand the burden on patients who do not respond well to biologic therapy and the effects of switching treatment.

ACKNOWLEDGMENTS

Funding

Funding for this summary and the journal's Rapid Service Fee was provided by Ortho Dermatologics (a division of Bausch Health Companies Inc). The original article was funded by Ortho Dermatologics.

Medical Writing and Editorial Assistance

Writing and editorial support for this summary was provided under the direction of the authors by MedThink SciCom and funded by Ortho Dermatologics (a division of Bausch Health Companies Inc). Plain language content was generated in part by artificial intelligence technology.

Author Contributions

April Armstrong, Richard Fried, John Koo, and Abby Jacobson, authors of the original article, reviewed and approved the summary.

Conflict of Interest

Please see original article for full author disclosures.

Ethical Approval

This article is based on previously conducted work and does not contain any new studies with human participants or animals.

Data Availability

Data sharing is not applicable to this summary article as no datasets were generated or analyzed.

Prior Publication

This is a summary of a peer-reviewed article previously published in the *Journal of Drugs in Dermatology*. 2023;22(10):994-1000.

[[REFERENCE TO BE EDITED AND STYLED AFTER APPROVAL OF FINAL DRAFT.]]

REFERENCE

1. Armstrong A, Fried R, Koo J, Gottlieb A, Jackson A. Mechanism of Action of Brodalumab May Correlate With Efficacy in Patients With Inflammatory Skin Diseases. *J Drugs Dermatol.* 2023;22(10):994-1000.