Biologics and Small Molecules for Inflammatory Nail Disorders: A Narrative Review

Carrie A. Forman, Shari R. Lipner

Department of Dermatology, Weill Cornell Medicine, New York, NY, USA

Abstract

Background: Inflammatory dermatological conditions, including psoriasis, lichen planus, eczema, and alopecia areata, are frequently accompanied by nail findings and can have a significant impact on quality of life. Biologic and small-molecule medications have been approved over the past several decades in treating patients with these inflammatory nail disorders. They may be used in conjunction with longstanding mainstays of treatment (topical and intralesional corticosteroids, topical vitamin D3 analogs). **Objectives:** Our objectives were to review biologic and small-molecule treatment efficacies for nail psoriasis and alopecia areata-associated nail dystrophy, including Janus kinase inhibitors, apremilast, tumor necrosis factor (TNF) inhibitors, interleukin (IL)-17 inhibitors, and IL-23 inhibitors. **Materials and Methods:** A comprehensive PubMed literature review of clinical research studies, narrative reviews, systematic reviews, and meta-analyses was performed. **Conclusion:** Many biologics and small molecules are effective in treating nail psoriasis and alopecia areata, with each requiring precautions for adverse events. Clinical trials for use of biologics and small molecules for nail lichen planus and atopic dermatitis have not been published to date.

Keywords: *Alopecia areata, atopic dermatitis, dermatology, interleukin-17, interleukin-23, Janus kinase inhibitors, lichen planus, nail diseases, nail psoriasis, TNF inhibitors*

Introduction

Several cutaneous and systemic disorders can manifest with nail changes including immunobullous disorders, connective tissue diseases, and sarcoidosis, as well as inflammatory autoimmune conditions, including psoriasis, lichen planus, atopic dermatitis, and alopecia areata [Figures 1-3]. When localized to the nail unit, the nail (s) may be painful and there can be difficulty performing daily activities, affecting quality of life and creating psychosocial challenges. Due to slow nail growth rates, improvements with treatment are gradual, and due to chronicity, treatment is often lifelong. However, recent advancements in development of small-molecules and biologic drugs for inflammatory nail disorders provide great promise for affected individuals.

Small molecules are low-molecular weight compounds and include Janus kinase (JAK) inhibitors, apremilast, and immunomodulators. Biologic drugs are large-molecule structures originating from living organisms that include antibodies targeting unique proteins and protein receptors, including interleukins, cytokines, and leukocytes. For the treatment of nail psoriasis (NP), they include anti-interleukin (IL)-17, anti-tumor necrosis factor (TNF), and IL-12/23 agents. Biologic and small-molecule drugs have emerged as effective treatments for NP and potentially for nail lichen planus (NLP), alopecia areata nail dystrophy (NAA), and atopic dermatitis nail dystrophy (NAD).

Materials and Methods

A PubMed online database literature search was performed on April 12, 2024 [Figure 4]. Clinical research studies, narrative reviews, systematic reviews, and meta-analyses written in English studying the efficacies of small-molecule drugs and biologic drugs on NP, NLP, NAA, and NAD, and their safety profiles, prior to April 12, 2024, were selected for review. Search filters included, but were not limited to, variations of an inflammatory nail disorder and a biologic or small molecule, such as "nail psoriasis AND adalimumab". Levels of Evidence (LoE) were attributed

How to cite this article: Forman CA, Lipner SR. Biologics and small molecules for inflammatory nail disorders: A narrative review. Indian Dermatol Online J 2025;16:50-8.

Received: 11-May-2024. **Revised:** 22-Sep-2024. **Accepted:** 13-Oct-2024. **Published:** 26-Dec-2024.

Address for correspondence:
Dr. Shari R. Lipner, 1305 York Avenue, NY, NY - 10021, USA. E-mail: shl9032@med.cornell.edu

Access this article online

Website: https://journals.lww.com/idoj

DOI: 10.4103/idoj.idoj_445_24

Quick Response Code:

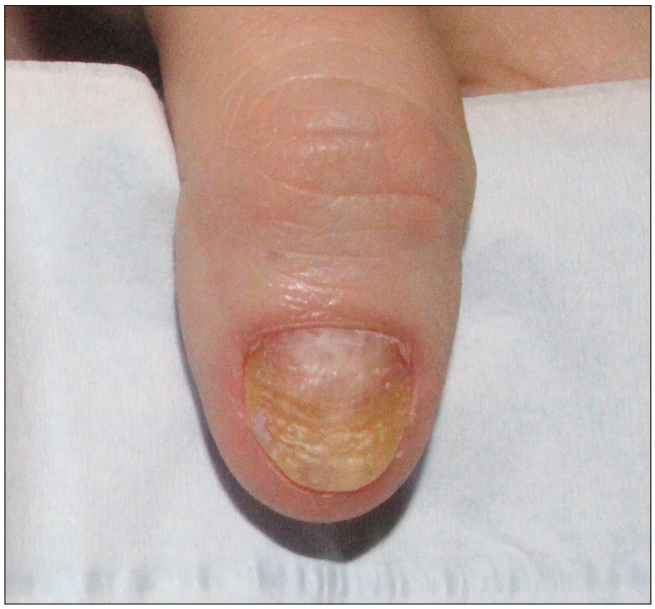

Figure 1: Nail psoriasis (NP): Patient with NP demonstrating pitting and onycholysis

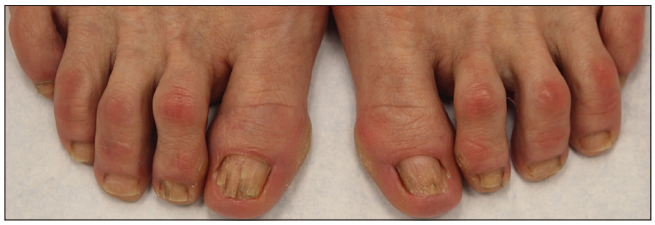

Figure 3: Lichen planus nail dystrophy (NLP): Patient with NLP demonstrates longitudinal ridging, splitting, and atrophy

based on the Oxford Centre for Evidence-Based Medicine's Oxford 2011 Levels of Evidence.[1] Case reports and case series were excluded. Studies without readily obtainable full text were excluded.

Nail psoriasis

NP affects approximately 80–90% of individuals with cutaneous plaque psoriasis in their lifetimes and may present with changes affecting the nail bed, including oil drop discoloration, onycholysis, and subungual hyperkeratosis, as well as changes to the nail matrix that include pitting, leukonychia, and red spots in the lunula.[2] NP is particularly comorbid with psoriatic arthritis (PsA), affecting up to 80% of PsA patients.[3] The exact etiology of psoriasis is not fully understood, but it is likely associated with immune dysregulation involving Th1, Th17, and Treg cell responses.[4]

Depending on number of nails involved, disease severity, comorbid conditions, and impact on quality of life, treatment typically includes topical and intralesional corticosteroids and topical vitamin D3 analogs.[5] Biologics and small-molecule agents [Supplementary Table 1][6-42] are recommended for patients with more than three nails

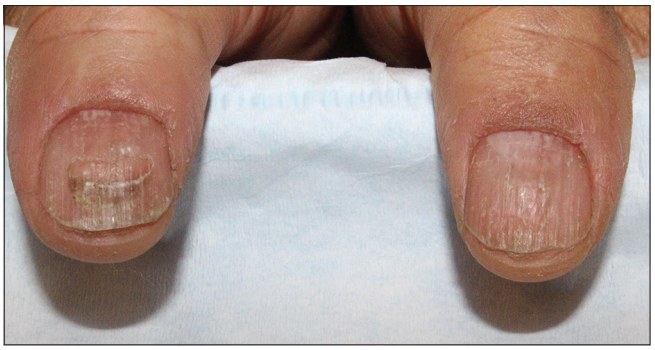

Figure 2: Alopecia areata nail dystrophy (NAA): Patient with NAA demonstrating onychorrhexis, nail plate thinning, and trachyonychia

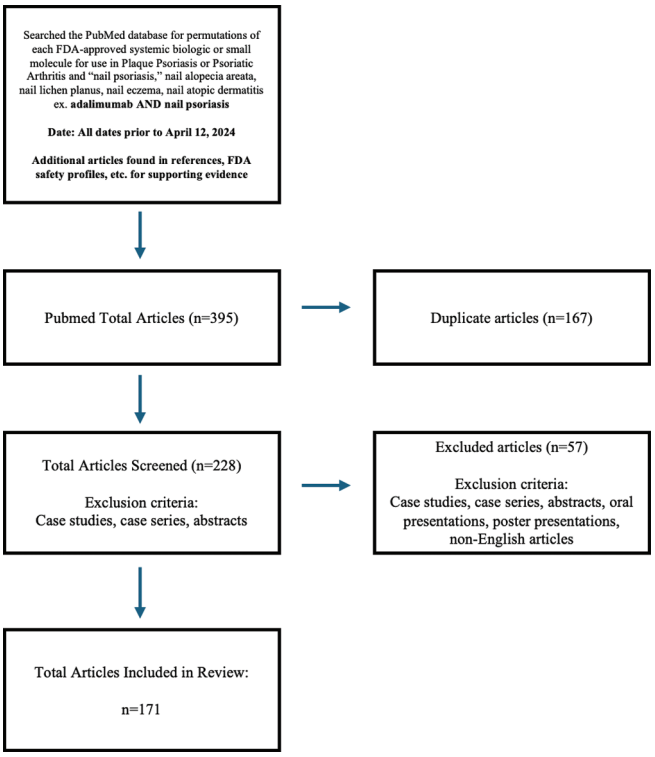

Figure 4: Methodology flowchart

involved and those with extensive skin or joint disease and/or with quality of life significantly affected.[5] The Nail Psoriasis Severity Index (NAPSI) is more often used in a clinical trial setting to determine response to treatment in patients with varying disease severities.

There are a few systematic reviews and meta-analyses on plaque psoriasis and PsA medications specific to NP; however, they have largely shown the superiority of IL-17 inhibitors, particularly IL-17 inhibitor ixekizumab, and JAK-inhibitor tofacitinib over other biologics and small-molecule medications for NP treatment. In a 2021 meta-analysis, the JAK-inhibitor tofacitinib was most effective at treating NP at week 16, showing a -1.08 point effect size or improvement in NP, compared to IL-17 inhibitors, IL-23 inhibitors, and TNF-inhibitors (-0.93 points, -0.88 points, and -0.62 points, respectively).[43] In

Reich *et al.*'s[44] 2022 meta-analysis, ixekizumab had the highest probability of complete NP resolution at weeks 24 to 26 compared to five other biologic drugs; however, JAK inhibitors were not included in this study. Ixekizumab has also outperformed adalimumab and ustekinumab in head-to-head trials.[45,46]

Despite these findings, randomized control trials consistently demonstrate that most approved TNF inhibitors and IL-23 inhibitors for plaque psoriasis and PsA also show statistically significant NP treatment benefits. These drugs may also have preferred safety profiles, insurance coverage benefits, or modes of administration compared to JAK inhibitors and IL-17 inhibitors for certain individuals based on their needs and comorbidities. Deucravacitinib, upadacitinib, and bimekizumab lack level 1 evidence support for NP treatment because they have not been analyzed in published reviews or have not proven efficacy in treating NP.

The Joint American Academy of Dermatology-National Psoriasis Foundation (AAD-NPF) and European League Against Rheumatism (EULAR) recommend the use of TNF inhibitors for patients with PsA. EULAR recommends IL-17 and IL-23 inhibitors for patients with concomitant plaque psoriasis or who do not tolerate TNF inhibitors. Furthermore, the US FDA requires that PsA patients fail a TNF-blocker before they are prescribed a JAK inhibitor due to a black box warning for heart-related events, infection, cancer, thrombosis, and death.[14,47]

Phosphodiesterase and Janus kinase inhibitors

Apremilast (LoE 1)

The efficacy of apremilast was demonstrated in the Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis 2016 phase III double-blind trials of 1255 plaque psoriasis patients (ESTEEM 1, ESTEEM 2). The apremilast-treated group of 558 NP patients improved in NAPSI by -22.5% versus +6.5% for placebo in ESTEEM 1 ($P < 0.0001$) and experienced a 60% NAPSI50 response at 32 weeks. A total of 266 apremilast-treated NP patients improved by -29% versus -7.1% for placebo in ESTEEM 2 ($P = 0.0052$).[48]

Deucravacitinib (LoE 5)

Evidence supporting deucravacitinib's efficacy for NP is sparse, and its efficacy does not have statistical significance. The Program to Evaluate the Efficacy and Safety of BMS-986165, a selective tyrosine kinase 2 inhibitor (POETYK PSO-1), a 52-week phase III trial comparing deucravacitinib with placebo and apremilast in 666 plaque psoriasis patients, showed that deucravacitinib-treated patients with moderate-to-severe finger NP [(Physician's Global Assessment (F-PGA) ≥ 3)] (n = 77) more often achieved f-PGA 0 or 1 at week 16 (20.9%) than placebo-treated patients (8.8%) (P value not reported). F-PGA in apremilast-treated patients was not reported.[49,50] A meta-analysis of three clinical trials including POETYK PSO-1 and POETYK PSO-2, a second 52-week phase III trial, did not show significant clinical improvement for NP.[51]

Tofacitinib (LoE 1)

The phase III Oral-treatment (OPT) Psoriasis Trial Pivotal 1 and 2 studies compared 745 plaque psoriasis patients treated with tofacitinib 5 mg, 741 patients treated with tofacitinib 10 mg, and 373 treated with placebo. A total of 1196 patients had NP. Patients treated with placebo were switched to tofacitinib after 16 weeks. At week 16, a greater proportion of NP patients in both tofacitinib groups achieved 50% improvement compared to baseline NAPSI (NAPSI50) versus the placebo group (32.8%, 44.2% vs 12.0%) ($P < 0.0001$), NAPSI75 (16.9%, 28.1% vs 6.8%) ($P < 0.0001$), and 100% improvement compared with baseline NAPSI (NAPSI100) (10.3%, 18.2% vs 5.1%) ($P < 0.0001$ and $P < 0.0099$, respectively). Benefits were maintained through week 52.[52]

Upadacitinib (LoE 3)

The UPJOINT 2023 observational study showed that after 12 weeks of treatment with upadacitinib, the proportion of PsA patients in a 296-patient cohort with NP (n = 86) decreased from 29.1% to 17.1%, which decreased to 12.5% after 24 weeks (P value not reported).[53]

TNF inhibitors

Adalimumab (LoE 1)

Adalimumab is the only biologic or small molecule US FDA-approved for NP. Adalimumab's efficacy was demonstrated in a 2019 52-week phase III trial of 217 patients with concomitant plaque psoriasis and NP. A greater proportion of patients treated with adalimumab achieved fingernail Modified Nail Psoriasis Severity Index (mNAPSI) with 75% improvement compared with baseline NAPSI (mNAPSI75) (46.6%) versus patients treated with placebo (3.4%) at week 26 ($P < 0.001$).[54,55] Another study of 267 plaque psoriasis patients with NP (with or without PsA) showed a correlation between percent reduction in Dermatology Life Quality Index (DLQI)[56] and improvement in NAPSI after 12 months of treatment (correlation coefficient, 0.343).[57]

Certolizumab pegol (LoE 1)

In RAPID-PsA, a phase III 24-week double-blind study of 409 patients with PsA (300 with NP), the mNAPSI decreased by 1.6 with certolizumab (CZP) 200 mg every 2 weeks and by 2.0 with CZP 400 mg every 4 weeks ($P = 0.003$ and $P < 0.001$ respectively) after 24 weeks of treatment. mNAPSI decreased by 1.1 with placebo.[58] A 4-year follow-up demonstrated a sustained decrease in mNAPSI and 65% resolution of NP after 4 years in 197 NP patients.[59]

Etanercept (LoE 1)

The multicenter NAIL study enrolled 136 plaque psoriasis patients with NP from four different countries who failed at least one type of systemic treatment for NP. The first group received etanercept 50 mg twice per week for 12 weeks, which then decreased to one time per week for 24 weeks. The second group received etanercept 50 mg one time per week for the full 24-week period. Both groups experienced similar improvements in NAPSI scores by 4.3 and 4.4, respectively ($P < 0.0001$), and DLQI scores at 24 weeks by 8.6% and 8.7%, respectively ($P < 0.0001$).[60]

Golimumab (LoE 1)

In the 24-week GO-VIBRANT study, 480 PsA patients were randomized to groups receiving golimumab or placebo. Patients with mNAPSI greater than zero at baseline (n = 367) improved by 9.6 points at week 14 versus 1.9 for placebo ($P < 0.0001$) and 11.4 versus 3.7 points at week 24. mNAPSI scores improved or were maintained at week 52. Similar responses were experienced by treatment-naïve patients and those receiving methotrexate at baseline.[61]

Infliximab (LoE 1)

Efficacy was shown in a 2005 phase III multicenter trial of 378 patients with plaque psoriasis. NAPSI improved for 235 NP patients in this cohort by 26.0% from baseline at 10 weeks and 56.3% for 233 NP patients at 24 weeks of treatment ($P < 0.0001$). Patients crossed over to infliximab from placebo at 24 weeks experienced a 38.9% improvement at 50 weeks.[62]

IL-17 inhibitors

Bimekizumab (LoE 2)

In the BE COMPLETE, a phase III, 92-site randomized clinical trial, 83 NP patients were treated with placebo compared with 159 patients who received bimekizumab 160 mg every 4 weeks.[63] After 16 weeks, 14% of placebo patients achieved mNAPSI 0, compared with 46% of patients taking bimekizumab (no *P* value reported).

Brodalumab (LoE 1)

Brodalumab was superior to ustekizumab for treating NP in the multicenter, randomized, double-blind, placebo-controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Brodalumab in Patients with Moderate to Severe Plaque Psoriasis (AMAGINE-2 and AMAGINE-3). NAPSI was analyzed for 3712 plaque psoriasis patients with concomitant NP using brodalumab Q2W (n = 104), brodalumab Q2W after placebo (n = 194), or ustekinumab continuously for 52 weeks (n = 174). After 52 weeks, 63.8% of brodalumab-treated patients achieved NAPSI0, compared with 39.1% of ustekinumab-treated patients ($P < 0.05$).[64]

Ixekizumab (LoE 1)

Ixekizumab has consistently demonstrated efficacy and rapid resolution of NP in head-to-head studies with other biologics.[65] Superiority of ixekizumab to ustekinumab was shown in the Ixekizumab Observational Study in Participants with Moderate to Severe Plaque Psoriasis (IXORA-S) study of 189 plaque psoriasis patients with NP, which found that 57.4% of ixekizumab-treated patients with significant NP (n = 54) (defined as NAPSI $\geq$ 16 with $\geq$ 4 fingernails involved) achieved complete resolution by week 20, compared with 17.5% of the ustekinumab-treated group (n = 63) ($P < 0.001$).

Ixekizumab was also compared to adalimumab in Reich, *et al.*'s 52-week analysis from the SPIRIT Head-to-Head (SPIRIT-H2H) trial[46]. Complete clearance of fingernail NP was reported in 75.7% of ixekizumab-treated patients, compared with 51.2% of adalimumab-treated patients ($P = .035$). This trend continued to week 52.

Secukinumab (LoE 1)

Secukinumab's efficacy was demonstrated in (Trial to Evaluate the Efficacy and Safety of BI 655130 in Patients with Severe Plaque Psoriasis) TRANSFIGURE, a 2.5-year phase III study of 198 NP patients, the majority of which had 10-nail involvement. After 16 weeks, patients receiving secukinumab 300 mg (n = 66) experienced a 45.6% reduction in NAPSI, which continued to decrease to more than 70% after 64 weeks. This response was sustained through 132 weeks.[66]

IL-23 inhibitors

Guselkumab (LoE 1)

In the phase III VOYAGE 1 and VOYAGE 2 trials, 1049 plaque psoriasis patients with concomitant NP were randomized to guselkumab or adalimumab. Complete fingernail clearance (fingernail-PGA of 0) (27.4% vs 27.9%, respectively) ($P = 0.63$), improvements in NAPSI (52.9% vs 51.2%, $P = 0.96$), and a NAPSI score of 0 (30.6% vs 32.6% $P = 0.5$) were comparable between guselkumab-treated and adalimumab-treated groups at week 24. Guselkumab was superior to adalimumab at 48 weeks in VOYAGE 1 ($P = 0.038$).[67] Both treatments were superior to placebo at all timepoints. Patients taking guselkumab experienced longer-lasting NP improvements after withdrawal at 28 weeks (NAPSI 1.7 at week 28 vs 1.9 at week 48) compared with adalimumab (NAPSI 1.4 at week 28 vs 2.3 at week 48) (*P* value not reported).[68]

Risankizumab (LoE 1)

Risankizumab demonstrated efficacy in the KEEPsaKE-1 trial of 964 PsA patients, demonstrating a 9.8-point decrease in mNAPSI (n = 309) versus a 5.6-point decrease with placebo for the subset of patients affected by NP (n = 338) ($P < 0.001$) at week 24. In a 3-year retrospective study of 1084 plaque psoriasis

patients, 80.34% of risankizumab-treated patients with concomitant NP had clear or almost clear fingernails at 52 weeks (sample size of patients with NP unspecified).[69]

Tildrakizumab (LoE 1)

Evidence for tildrakizumab is less robust than for other biologics. The prospective cohort study TILOT was an observational study that analyzed 412 plaque psoriasis patients. At 52 weeks, nail-PGA improved by 72.7% (95% confidence interval, 63.9–81.6) in patients with NP (n = 182).[70]

Ustekinumab (LoE 1)

The efficacy for ustekinumab was demonstrated in the Psoriasis Hospital Outpatient Evaluations of Next Wave Innovations in Treatment (PHOENIX 1) phase III trial, which studied 545 plaque psoriasis patients with NP. Ustekinumab 45 mg (n = 255) and 90 mg (n = 256) treated groups had similar NAPSI improvement after 24 weeks compared to the placebo group that was crossed over at 12 and 16 weeks (46.5%, $P < 0.001$ and 48.7%, $P = 0.001$, respectively), and improvement continued for those who initially responded through week 52.[71]

Alopecia areata nail dystrophy

Alopecia areata is an autoimmune disorder causing inflammation of the hair follicles. Alopecia areata can manifest with pitting, trachyonychia, and red spotted lunulae. Nail changes may occur before or after hair loss presentation, and it is theorized that nail changes may be proportional to severity of hair loss.[72] Several studies have demonstrated efficacy for JAK inhibitors in treating NAA; however, baricitinib and ritlecitinib—the two U.S. Food and Drug Administration (US FDA)-approved JAK inhibitors for alopecia areata—have not been studied in clinical trials for their effects on NAA.

Tofacitinib has not been US FDA-approved for alopecia areata treatment; however, improvements in NAA were shown in smaller case control studies (LoE 4). In a retrospective study of 47 alopecia areata patients, 25.5% patients had concomitant 20-nail NAA at the start of treatment, which decreased to 3.4% of the cohort after 18 months ($P < 0.005$).[73] In another retrospective study of 33 patients with alopecia areata, 73.3% of 15 patients with concomitant NAA experienced improvement in pitting and red spotting of the lunula, at a median of 5 months after starting tofacitinib as measured by four categories (none, improved, no change, and worse).[74]

Nail lichen planus and atopic dermatitis

Lichen planus is an inflammatory condition presenting with pruritic violaceous papules and plaques on the skin and mucous membranes that can result in nail plate atrophy, onychorrhexis, longitudinal ridging, erythronychia, and if left untreated, pterygium and nail loss.[75,76] There have been no clinical trials on the use of biologics and small molecules for NLP; however, several case studies have demonstrated possible benefits.

Atopic dermatitis is an inflammatory skin disorder, characterized by pruritis and xerotic skin, that often starts in childhood and persists throughout life. Nail changes include pitting, trachyonychia, longitudinal, and transverse grooves. There has been a single case study supporting dupilumab, an IL-4 receptor alpha antagonist, for treatment of NAD.[77]

Considerations for patients with comorbidities

Use of small-molecule and biologic medications requires taking special precautions for certain patient populations. For example, cardiovascular disease and congestive heart failure (CHF) are correlated with severity of plaque psoriasis.[78] Infliximab specifically carries a US FDA-issued contraindication for use in moderate-to-severe CHF;[79] however, there is some evidence that biologics, including TNF-blockers, might help improve heart failure in psoriasis patients by decreasing systemic inflammation.[80,81]

A 2018 meta-analysis showed a 1.7-to-2.5-fold increase in the presence of inflammatory bowel disease (IBD) in patients with plaque psoriasis.[82] Brodalumab is contraindicated in patients with Crohn's disease due to possible disease worsening,[83] and all IL-17 inhibitors should be avoided in patients with IBD.[84]

Psoriasis is also associated with multiple sclerosis (MS), possibly due to an overly responsive immune system.[85] It is recommended that physicians exercise caution in prescribing TNF-a inhibitors to patients with MS or who have a first-degree relative with MS due to increased rates of demyelinating events in the central nervous system.[86] IL-17 inhibitors, such as secukinumab, may be beneficial for psoriasis patients with MS as there is some evidence that they could decrease lesion quantity.[87]

Tuberculosis risk may be elevated in all patients treated with small-molecule and biologic drugs due to immunosuppressive effects. TNF-a inhibitors, infliximab and adalimumab, may carry the highest risk.[88] Patients on all biologics should be screened prior to starting treatment.[89] Evidence for routine screening is controversial and may be stratified based on individual risk factors, such as working or dwelling in crowded facilities or living in tuberculosis-endemic areas.[90,91]

Dermatologists can consider TNF inhibitors, namely, certrolizumab pegol, for pregnant patients considering their generally longer established safety records.[92] Secukinumab and ustekinumab should be discontinued when planning for pregnancy or becoming pregnant.[93]

Emerging therapies

As the intracellular signaling pathways contributing to NP, NLP, NAA, and NAD become more well-defined, the

Table 1: Emerging biologic and small-molecule systemic therapies for plaque psoriasis, alopecia areata, lichen planus, and atopic dermatitis (includes drug classes that have undergone or are undergoing clinical trials)

Inflammatory Skin Disorder	Drug Class	Mechanism of Action	Investigatory Status
Plaque Psoriasis	JAK inhibitors	Inhibits JAK-STAT signaling pathway	Phase II and Phase III Clinical Trial[94]
	IL-23 Inhibitors	Binds to IL-23 receptor	Phase II Clinical Trial[95]
	IL-36 inhibitors	Bind to IL-36 receptor	Phase II and Phase III Clinical Trial[96]
	Retinoic acid receptor-related orphan receptor gamma t (RORγt) inhibitors	Binds to RORγt ligand-binding-domain destabilizing helix 12 and His479-Tyr502-Phe506	Phase I Trial[97]
	Rho-associated coiled-coil-containing protein kinase 2 (ROCK2) inhibitors	Binds to ATP-binding area of ROCK2	Preclinical and Phase II Trials
Alopecia Areata	JAK inhibitors	Inhibits JAK-STAT signaling pathway	Phase II and III Trials, Breakthrough Therapy Designation[98,99]
	IL-4 inhibitors	Binds to IL-4 receptor	Phase II Trial[100]
Lichen Planus	IL-17 inhibitors	Binds to IL-17 receptor	Compassionate use trial[101]
Atopic Dermatitis	IL-13 inhibitors	Binds to IL-13	Phase III Trial[102]
	IL-31 inhibitors	Binds to IL-31 or IL-31 receptor	Phase II and Phase III Trials[103]

treatment toolbox will expand to include emerging therapies such as retinoic-acid-receptor-related orphan receptor gamma-t (RORγt) inhibitors and rho-associated kinase inhibitors (ROCK2) [Table 1]. Biosimilar medications, which are nearly identical in structure and function with brand-name biologic treatments at a lower cost, are also becoming more commonly prescribed by providers as the patents on biologic drugs expire.

Conclusion

In summary, biologic and small-molecule medications are highly effective treatments for the nail manifestations of psoriasis and alopecia areata and are being studied for nail lichen planus and atopic dermatitis. It is important for physicians to educate patients on the benefits and risks of treating inflammatory nail disorders with these medications. Research in targeting various signaling pathways continues to advance rapidly.

Financial support and sponsorship

Dr. Lipner has served as a consultant for Ortho-Dermatologics, Eli Lilly, Moberg Pharmaceuticals, and BelleTorus Corporation.

Conflicts of interest

There are no conflicts of interest.

References

1. OCEBM Levels of Evidence Working Group. The Oxford 2011 Levels of Evidence. Oxford Centre for Evidence-Based Medicine. Available from: http://www.cebm.net/wp-content/uploads/2014/06/CEBM-Levels-of-Evidence-2.1.pdf. [Last accessed on 2024 Jul 10].
2. Conway J, Lipner S. A case of rapid fingernail growth associated with nail psoriasis: A case report. SAGE Open Med Case Rep 2023;11:2050313 231213149.
3. Williamson L, Dalbeth N, Dockerty JL, Gee BC, Weatherall R, Wordsworth BP. Extended report: Nail disease in psoriatic arthritis—clinically important, potentially treatable and often overlooked. Rheumatology (Oxford) 2004;43:790-4.
4. Furiati SC, Catarino JS, Silva MV. Th1, Th17, and treg responses are differently modulated by TNF-α inhibitors and methotrexate in psoriasis patients. Sci Rep 2019;9:7526.
5. Rigopoulos D, Baran R, Chiheb S, Daniel CR 3rd, Di Chiacchio N, Gregoriou S, Grover C, *et al*. Recommendations for the definition, evaluation, and treatment of nail psoriasis in adult patients with no or mild skin psoriasis: A dermatologist and nail expert group consensus. J Am Acad Dermatol 2019;81:228-40.
6. OTEZLA® (apremilast) tablets, for oral use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/205437s011lbl.pdf. [Last accessed on 2024 Jul 10].
7. Mease PJ, Hatemi G, Paris M, Cheng S, Maes P, Zhang W, *et al*. Apremilast long-term safety up to 5 years from 15 pooled randomized, placebo-controlled studies of psoriasis, psoriatic arthritis, and Behçet's syndrome. Am J Clin Dermatol 2023;24:809-20.
8. Vu A, Maloney V, Gordon KB. Deucravacitinib in moderate-to-severe psoriasis. Immunotherapy 2022;14:1279-90.
9. SOTYKTUTM (deucravacitinib) tablets, for oral use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/214958s000lbl.pdf. [Last accessed on 2024 Jul 10].
10. Furumoto Y, Gadina M. The arrival of JAK inhibitors: Advancing the treatment of immune and hematologic disorders. BioDrugs 2013;27:431-8.
11. XELJANZ® (tofacitinib) tablets, for oral use XELJANZ® XR (tofacitinib) extended-release tablets, for oral use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/203214s018lbl.pdf. [Last accessed on 2024 Jul 10].
12. RINVOQ® (upadacitinib) extended-release tablets, for oral use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/211675s003lbl.pdf. [Last accessed on 2024 Jul 10].
13. Burmester GR, Cohen SB, Winthrop KL, Nash P, Irvine AD, Deodhar A, *et al*. Safety profile of upadacitinib over 15 000 patient-years across rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and atopic dermatitis. RMD

Open 2023;9:e002735. doi: 10.1136/rmdopen-2022-002735.
14. Qian J, Xue X, Shannon J. Characteristics of adverse event reporting of Xeljanz/Xeljanz XR, Olumiant, and Rinvoq to the US Food and Drug Administration. J Manag Care Spec Pharm 2022;28:1046-52.
15. Desai C. Meyler's side effects of drugs: The international encyclopedia of adverse drug reactions and interactions. Indian J Pharmacol 2016;48:224.
16. HUMIRA® (adalimumab) injection, for subcutaneous use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125057s410lbl.pdf. [Last accessed on 2024 Jul 10].
17. CIMZIA (certolizumab pegol) for injection, for subcutaneous use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125160s270lbl.pdf. [Last accessed on 2024 Jul 10].
18. Haraoui B, Bykerk V. Etanercept in the treatment of rheumatoid arthritis. Ther Clin Risk Manag 2007;3:99-105.
19. ENBREL® (etanercept) injection, for subcutaneous use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/103795s5556lbl.pdf. [Last accessed on 2024 Jul 10].
20. Esse S, Mason KJ, Green AC, Warren RB. Melanoma risk in patients treated with biologic therapy for common inflammatory diseases: A systematic review and meta-analysis. JAMA Dermatol 2020;156:787-94.
21. Mazumdar S, Greenwald D. Golimumab. MAbs 2009;1:422-31.
22. SIMPONI (gollmumab) Injection, solution for subcutaneous use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/125289s0064lbl.pdf. [Last accessed on 2024 Jul 10].
23. Kay J, Fleischmann R, Keystone E, Hsia EC, Hsu B, Mack M, *et al*. Golimumab 3-year safety update: An analysis of pooled data from the long-term extensions of randomised, double-blind, placebo-controlled trials conducted in patients with rheumatoid arthritis, psoriatic arthritis or ankylosing spondylitis. Ann Rheum Dis 2015;74:538-46.
24. Kavanaugh A, St Clair EW, McCune WJ, Braakman T, Lipsky P. Chimeric anti-tumor necrosis factor-alpha monoclonal antibody treatment of patients with rheumatoid arthritis receiving methotrexate therapy. The Journal of Rheumatology 2000;27:841-50.
25. INFLIXIMAB for injection, for intravenous use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/103772s5401lbl.pdf. [Last accessed on 2024 Jul 10].
26. Adams R, Maroof A, Baker T, Lawson ADG, Oliver R, Paveley R, *et al*. Bimekizumab, a novel humanized IgG1 antibody that neutralizes both IL-17A and IL-17F. Front Immunol 2020;11:1894. doi: 10.3389/fimmu.2020.01894.
27. BIMZELX® (bimekizumab-bkzx) injection, for subcutaneous use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761151s000lbl.pdf. [Last accessed on 2024 Jul 10].
28. Roman M, Chiu MW. Spotlight on brodalumab in the treatment of moderate-to-severe plaque psoriasis: Design, development, and potential place in therapy. Drug Des Devel Ther 2017;11:2065-75.
29. SILIQTM (brodalumab) injection, for subcutaneous use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761032lbl.pdf. [Last accessed on 2024 Jul 10].
30. Liu L, Lu J, Allan BW, Tang Y, Tetreault J, Chow CK. Generation and characterization of ixekizumab, a humanized monoclonal antibody that neutralizes interleukin-17A. J Inflamm Res 2016;9:39-50.
31. TALTZ (ixekizumab) injection, for subcutaneous use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125521s024lbl.pdf. [Last accessed on 2024 Jul 10].
32. Chatham WW, Rich RR, Fleisher TA, Shearer WT, Schroeder HW, Frew AJ, *et al*. 89-Biological modifiers of inflammatory diseases. Clinical Immunology. Philadelphia, PA: Elsevier; 2019. p. 1197-210.
33. COSENTYX® (secukinumab) injection, for subcutaneous use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125504s043lbl.pdf.
34. Al-Salama ZT, Scott LJ. Guselkumab: A review in moderate to severe plaque psoriasis. Am J Clin Dermatol 2018;19:907-18.
35. TREMFYA (guselkumab) injection, for subcutaneous use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761061s000lbl.pdf. [Last accessed on 2024 Jul 10].
36. Rutuja VN, Gowtham M, More PS, Shinde AS. Current and emerging prospects in the psoriatic treatment. International Immunopharmacology 2023;120:110331. doi: 10.1016/j.intimp. 2023.110331.
37. SKYRIZI® (risankizumab-rzaa) injection, for subcutaneous use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761105s014lbl.pdf. [Last accessed on 2024 Jul 10].
38. Kristensen LE, Keiserman M, Papp K, McCasland L, White D, Lu W, *et al*. Efficacy and safety of risankizumab for active psoriatic arthritis: 24-week results from the randomised, double-blind, phase 3 KEEPsAKE 1 trial. Ann Rheum Dis 2022;81:225-31.
39. Banaszczyk K. Tildrakizumab in the treatment of psoriasis-Literature review. Reumatologia 2019;57:234-8.
40. Scherl EJ, Kumar S, Warren RU. Review of the safety and efficacy of ustekinumab. Therap Adv Gastroenterol 2010;3:321-8.
41. Benson JM, Peritt D, Scallon BJ, Heavner GA, Shealy DJ, Giles-Komar JM, *et al*. Discovery and mechanism of ustekinumab: A human monoclonal antibody targeting interleukin-12 and interleukin-23 for treatment of immune-mediated disorders. MAbs 2011;3:535-45.
42. STELARA® (ustekinumab) injection, for subcutaneous or intravenous use. Food and drug administration. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/761044lbl.pdf. [Last accessed on 2024 Jul 10].
43. Zhang X, Xie B, He Y. Efficacy of systemic treatments of nail psoriasis: A systemic literature review and meta-analysis. Front Med (Lausanne) 2021;8:620562. doi: 10.3389/fmed.2021.620562.
44. Reich K, Conrad C, Kristensen LE, Smith SD, Puig L, Rich P, *et al*. Network meta-analysis comparing the efficacy of biologic treatments for achieving complete resolution of nail psoriasis. J Dermatolog Treat 2023;33:1652-60.
45. Wasel N, Thaçi D, French LE, Conrad C, Dutronc Y, Gallo G, *et al*. Ixekizumab and ustekinumab efficacy in nail psoriasis in patients with moderate-to-severe psoriasis: 52-week results from a phase 3, head-to-head study (IXORA-S). Dermatol Ther (Heidelb) 2020;10:663-70.
46. Reich K, Kristensen LE, Smith SD, Rich P, Sapin C, Leage SL, *et al*. Efficacy and safety of ixekizumab versus adalimumab in biologic-naïve patients with active psoriatic arthritis and moderate-to-severe psoriasis: 52-week results from

the randomized SPIRIT-H2H trial. Dermatol Pract Concept 2022;12:e2022104. doi: 10.5826/dpc. 1202a104.

47. Ytterberg. Cardiovascular and cancer risk with tofacitinib in rheumatoid arthritis. N Engl J Med 2022;386:316.
48. Rich P, Gooderham M, Bachelez H, Goncalves J, Day RM, Chen R, *et al*. Apremilast, an oral phosphodiesterase 4 inhibitor, in patients with difficult-to-treat nail and scalp psoriasis: Results of 2 phase III randomized, controlled trials (ESTEEM 1 and ESTEEM 2. J Am Acad Dermatol 2016;74:134-42.
49. Hudgens S, Rich P, Geng Z, Williams D, Fleischer A, Ganguli A. Development and validation of the physician's global assessment of fingernail psoriasis. J Eur Acad Dermatol Venereol 2021;35:2324-30.
50. Armstrong AW, Gooderham M, Warren RB, Papp KA, Strober B, Thaçi D, *et al*. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: Efficacy and safety results from the 52-week trial. J Am Acad Dermatol 2023;88:29-39.
51. Jin JQ, Spencer RK, Reddy V, Bhutani T, Liao W. Clinical utility of deucravacitinib for the management of moderate to severe plaque psoriasis. Ther Clin Risk Manag 2023;19:413-23.
52. Merola JF, Elewski B, Tatulych S, Lan S, Tallman A, Kaur M. Efficacy of tofacitinib for the treatment of nail psoriasis: Two 52-week, randomized, controlled phase 3 studies in patients with moderate-to-severe plaque psoriasis. J Am Acad Dermatol 2017;77:79-87.e1.
53. Werner SG, Baraliakos X, Reckert S, Bohl-Bühler M, Laliberté MC, Girard T, *et al*. Treatment with upadacitinib in active psoriatic arthritis: Efficacy and safety data of the first 192 patients from the UPJOINT study, a multicentre, observational study in clinical practice. Rheumatol Ther 2023;10:1503-18.
54. Cassell SE, Bieber JD, Rich P, Tutuncu ZN, Lee SJ, Kalunian KC, *et al*. The modified Nail Psoriasis Severity Index: Validation of an instrument to assess psoriatic nail involvement in patients with psoriatic arthritis. J Rheumatol 2007;34:123-9.
55. Elewski BE, Baker CS, Crowley JJ, Poulin Y, Okun MM, Calimlim B, *et al*. Adalimumab for nail psoriasis: Efficacy and safety over 52 weeks from a phase-3, randomized, placebo-controlled trial. J Eur Acad Dermatol Venereol 2019;33:2168-78.
56. Finlay AY, Khan GK. Dermatology life quality index (DLQI)-a simple practical measure for routine clinical use. Clin Exp Dermatol 1994;19:210-6.
57. Kokolakis G, Bachmann F, Wolk K, Sabat R, Philipp S. Efficacy of adalimumab for nail psoriasis during 24 months of continuous therapy. Acta Derm Venereol 2020;100:adv00214. doi: 10.2340/00015555-3545.
58. Mease PJ, Fleischmann R, Deodhar AA, Wollenhaupt J, Khraishi M, Kielar D, *et al*. Effect of certolizumab pegol on signs and symptoms in patients with psoriatic arthritis: 24-week results of a Phase 3 double-blind randomised placebo-controlled study (RAPID-PsA). Ann Rheum Dis 2014;73:48-55.
59. van der Heijde D, Deodhar A, FitzGerald O, Fleischmann R, Gladman D, Gottlieb AB, *et al*. 4-year results from the RAPID-PsA phase 3 randomised placebo-controlled trial of certolizumab pegol in psoriatic arthritis. RMD Open 2018;4:e000582. doi: 10.1136/rmdopen-2017-000582.
60. Ortonne JP, Paul C, Berardesca E, Marino V, Gallo G, Brault Y, *et al*. A 24-week randomized clinical trial investigating the efficacy and safety of two doses of etanercept in nail psoriasis. Br J Dermatol 2013;168:1080-7.
61. Mease P, Elaine Husni M, Chakravarty SD, Kafka S, Parenti D, Kim L, *et al*. Evaluation of improvement in skin and nail psoriasis in bio-naïve patients with active psoriatic arthritis treated with golimumab: Results through week 52 of the GO-VIBRANT study. ACR Open Rheumatol 2020;2:640-7.
62. Reich K, Nestle FO, Papp K, Ortonne JP, Evans R, Guzzo C, *et al*. Infliximab induction and maintenance therapy for moderate-to-severe psoriasis: A phase III, multicentre, double-blind trial. Lancet 2005;366:1367-74.
63. Merola JF, Landewé R, McInnes IB, Mease PJ, Ritchlin CT, Tanaka Y, *et al*. Bimekizumab in patients with active psoriatic arthritis and previous inadequate response or intolerance to tumour necrosis factor-α inhibitors: A randomised, double-blind, placebo-controlled, phase 3 trial (BE COMPLETE. Lancet 2023;401:38-48.
64. Elewski B, Rich P, Lain E, Soung J, Lewitt GM, Jacobson A. Efficacy of brodalumab in the treatment of scalp and nail psoriasis: Results from three phase 3 trials. J Dermatolog Treat 2022;33:261-5.
65. Elewski BE, Blauvelt A, Gallo G, Wolf E, McKean-Matthews M, Burge R, *et al*. Simultaneous nail and skin clearance in ixekizumab head-to-head trials for moderate-to-severe psoriasis and psoriatic arthritis. Dermatol Ther (Heidelb) 2022;12:911-20.
66. Reich K, Sullivan J, Arenberger P, Jazayeri S, Mrowietz U, Augustin M, *et al*. Secukinumab shows high and sustained efficacy in nail psoriasis: 2.5-year results from the randomized placebo-controlled TRANSFIGURE study. Br J Dermatol 2021;184:425-36.
67. Foley P, Gordon K, Griffiths CEM, Wasfi Y, Randazzo B, Song M, *et al*. Efficacy of guselkumab compared with adalimumab and placebo for psoriasis in specific body regions: A secondary analysis of 2 randomized clinical trials. JAMA Dermatol 2018;154:676-83.
68. Tillett W, Egeberg A, Sonkoly E, Gorecki P, Tjärnlund A, Buyze J, *et al*. Nail psoriasis dynamics during biologic treatment and withdrawal in patients with psoriasis who may be at high risk of developing psoriatic arthritis: A post hoc analysis of the VOYAGE 2 randomized trial. Arthritis Res Ther 2023;25:169.
69. Gargiulo L, Ibba L, Malagoli P, Amoruso F, Argenziano G, Balato A, *et al*. Effectiveness, tolerability, and drug survival of risankizumab in a real-world setting: A three-year retrospective multicenter study-IL PSO (ITALIAN LANDSCAPE PSORIASIS. J Clin Med 2024;13:495. doi: 10.3390/jcm13020495.
70. Tsianakas A, Schwichtenberg U, Pierchalla P, Hinz T, Diemert S, Korge B. Real-world effectiveness and safety of tildrakizumab in long-term treatment of Plaque Psoriasis: Results from the non-interventional, prospective, multicentre study TILOT. J Eur Acad Dermatol Venereol 2023;37:85-92.
71. Rich P, Bourcier M, Sofen H, Fakharzadeh S, Wasfi Y, Wang Y, *et al*. PHOENIX1 investigators. Ustekinumab improves nail disease in patients with moderate-to-severe psoriasis: Results from PHOENIX1. Br J Dermatol 2014;170:398-407.
72. Gandhi V, Baruah MC, Bhattacharaya SN. Nail changes in alopecia areata: Incidence and pattern. Indian J Dermatol Venereol Leprol 2003;69:114-5.
73. Asilian A, Mohammadian P, Shahmoradi Z. Effectiveness of oral tofacitinib treatment on patients with moderate-to-severe alopecia areata in Iran. J Cosmet Dermatol 2024;23:886-90.
74. Lee JS, Huh CH, Kwon O, Yoon HS, Cho S, Park HS. Nail involvement in patients with moderate-to-severe alopecia areata treated with oral tofacitinib. J Dermatolog Treat 2018;29:819-22.
75. Grover C, Kharghoria G, Baran R. Nail lichen planus: A review of clinical presentation, diagnosis and therapy. Ann Dermatol Venereol 2022;149:150-64.
76. Wechsuruk P, Bunyaratavej S, Kiratiwongwan R, Suphatsathienkul P, Wongdama S, Leeyaphan C. Clinical features

and treatment outcomes of nail lichen planus: A retrospective study. JAAD Case Rep 2021;17:43-8.
77. Zubek AE, Vesely MD. Onychodystrophy associated with dupilumab therapy for atopic dermatitis. JAAD Case Rep 2020;7:20-22.
78. Kan J, Chen Q, Tao Q, Wu L, Wang D, Jiang Z, Du X, Gu Y, *et al*. Prospective evaluation of cardiovascular risk and mortality in patients with psoriasis: An American population-based study. Exp Dermatol 2024;33:e15010. doi: 10.1111/exd.15010.
79. Chung ES, Packer M, Lo KH, Fasanmade AA, Willerson JT, Anti-TNF Therapy Against Congestive Heart Failure Investigators. Randomized, double-blind, placebo-controlled, pilot trial of infliximab, a chimeric monoclonal antibody to tumor necrosis factor-alpha, in patients with moderate-to-severe heart failure: Results of the anti-TNF therapy against congestive heart failure (ATTACH) trial. Circulation 2003;107:3133-40.
80. Han JH, Park HE, Kim YH, Jung JH, Lee JH, Park YM, *et al*. Comparison of the risk of heart failure in psoriasis patients using anti-TNF α inhibitors and ustekinumab. ESC Heart Fail 2022;9:1502-4.
81. Terui H, Asano Y. Biologics for reducing cardiovascular risk in psoriasis patients. J Clin Med 2023;12:1162. doi: 10.3390/jcm12031162.
82. Fu Y, Lee CH, Chi CC. Association of psoriasis with inflammatory bowel disease: A systematic review and meta-analysis. JAMA Dermatol 2018;154:1417-23.
83. Targan SR, Feagan B, Vermeire S, Panaccione R, Melmed GY, Landers C, *et al*. Placebo-controlled phase 2 study of brodalumab in patients with moderate-to-severe Crohn's disease. Am J Gastroenterol 2016;111:1599-607.
84. Thatiparthi A, Martin A, Liu J, Egeberg A, Wu JJ. Biologic treatment algorithms for moderate-to-severe psoriasis with comorbid conditions and special populations: A review. Am J Clin Dermatol 2021;22:425-42.
85. Silfvast-Kaiser AS, Homan KB, Mansouri B. A narrative review of psoriasis and multiple sclerosis: Links and risks. Psoriasis (Auckl) 2019;9:81-90.
86. Fromont A, De Seze J, Fleury MC, Maillefert JF, Moreau T. Inflammatory demyelinating events following treatment with anti-tumor necrosis factor. Cytokine 2009;45:55-7.
87. Havrdová E, Belova A, Goloborodko A, Tisserant A, Wright A, Wallstroem E, *et al*. Activity of secukinumab, an anti-IL-17A antibody, on brain lesions in RRMS: Results from a randomized, proof-of-concept study. J Neurol 2016;263:1287-95.
88. Esmail H, Wilkinson RJ. Minimizing tuberculosis risk in patients receiving anti-TNF therapy. Ann Am Thorac Soc 2017;14:621-23.
89. Doherty SD, Van Voorhees A, Lebwohl MG, Korman NJ, Young MS, Hsu S. National psoriasis foundation consensus statement on screening for latent tuberculosis infection in patients with psoriasis treated with systemic and biologic agents. J Am Acad Dermatol 2008;59:209-17.
90. Dobler CC. Biologic agents and tuberculosis. Microbiol Spectr 2016;4. doi: 10.1128/microbiolspec.TNMI7-0026-2016.
91. Megna M, Ferrillo M, Ruggiero A, Cinelli E, Gallo L, Fabbrocini G. QuantiFERON TB-gold conversion rate among psoriasis patients under biologics: A 9-year retrospective study. Int J Dermatol 2021;60:352-7.
92. Porter ML, Lockwood SJ, Kimball AB. Update on biologic safety for patients with psoriasis during pregnancy. Int J Womens Dermatol 2017;3:21-5.
93. Owczarek W, Walecka I, Lesiak A, Czajkowski R, Reich A, Zerda I, *et al*. The use of biological drugs in psoriasis patients prior to pregnancy, during pregnancy and lactation: A review of current clinical guidelines. Postepy Dermatol Alergol 2020;37:821-30.
94. Megna M, Potestio L, Ruggiero A, Cacciapuoti S, Maione F, Tasso M, *et al.* JAK inhibitors in psoriatic disease. Clin Cosmet Investig Dermatol 2023;16:3129-45.
95. Bissonnette R, Pinter A, Ferris LK, Gerdes S, Rich P, Vender R, *et al.* An oral interleukin-23-receptor antagonist peptide for plaque psoriasis. N Engl J Med 2024;390:510-21.
96. Bernardo D, Thaçi D, Torres T. Spesolimab for the treatment of generalized pustular psoriasis. Drugs 2024;84:45-58.
97. Mohamed MF, Qian Y, D'Cunha R, Sligh T, Ferris LK, Eldred A, *et al.* Pharmacokinetics, safety, and efficacy of cedirogant from phase I studies in healthy participants and patients with chronic plaque psoriasis. Clin Transl Sci 2024;17:e13682. doi: 10.1111/cts. 13682.
98. King BA, Craiglow BG. Janus kinase inhibitors for alopecia areata. J Am Acad Dermatol 2023;89:S29-S32.
99. Jain NK, Tailang M, Jain HK, Chandrasekaran B, Sahoo BM, Subramanian A, *et al*. Therapeutic implications of current Janus kinase inhibitors as anti-COVID agents: A review. Front Pharmacol 2023;14:1135145. doi: 10.3389/fphar. 2023.1135145.
100. Guttman-Yassky E, Renert-Yuval Y, Bares J, Chima M, Hawkes JE, Gilleaudeau P, *et al.* Phase 2a randomized clinical trial of dupilumab (anti-IL-4Rα) for alopecia areata patients. Allergy 2022;77:897-906.
101. Solimani F, Pollmann R, Schmidt T, Schmidt A, Zheng X, Savai R, *et al.* Therapeutic targeting of Th17/Tc17 cells leads to clinical improvement of lichen planus. Front Immunol 2019;10:1808. doi: 10.3389/fimmu. 2019.01808.
102. Lytvyn Y, Gooderham M. Targeting interleukin 13 for the treatment of atopic dermatitis. Pharmaceutics 2023;15:568. doi: 10.3390/pharmaceutics15020568.
103. Orfali RL, Aoki V. Blockage of the IL-31 pathway as a potential target therapy for atopic dermatitis. Pharmaceutics 2023;15:577. doi: 10.3390/pharmaceutics15020577.

Supplementary Table 1: Biologics and small molecules for nail psoriasis (NP) and alopecia areata nail dystrophy (NAA)*,†

Name	Drug Class	Mechanism of Action	US FDA Approval for Dermatologic Indications	Evidence for Inflammatory Nail Disease	Highest LoE for Inflammatory Nail Disorder Treatment	US FDA Administration/ Dosage/Frequency	US FDA Most Common Adverse Reactions	US FDA Warnings and Precautions
Apremilast	Small Molecule	Phosphodiesterase-4 Inhibitor	Plaque psoriasis, psoriatic arthritis (PsA)[6]	NP	Level 1 – systematic review and crossover	Oral/18+/30 mg BID after day 6; renal dosing advised	(<5%) Diarrhea, nausea, headache, upper respiratory tract infection (URTI)[7]	Hypersensitivity, depression, weight decrease, drug interactions, severe diarrhea, nausea, vomiting
Deucravacitinib	Small Molecule	Allosterically inhibits tyrosine kinase 2 in the JAK-STAT pathway[8]	Plaque psoriasis[9]	NP	Level 5 – no significance in meta-analysis	Oral/18+/6 mg daily	(≥1%) URTI, elevated blood creatinine phosphokinase (CPK), herpes simplex, mouth ulcers, folliculitis, acne	Hypersensitivity, infections, tuberculosis, malignancy, rhabdomyolysis and elevated CPK, laboratory abnormalities, immunization interactions, higher rates of all-cause mortality related to JAK inhibition
Tofacitinib	Small Molecule	Targets JAK1, JAK2, and JAK3 enzymes, inhibiting the JAK-STAT signaling pathway[10]	PsA[11]	NP, NAA	NP: Level 1 – systematic review NAA: Level 4 – case control study	Oral/18+/Tofacitinib 5 mg BID or Tofacitinib extended release XR 11 mg once daily; renal and hepatic dosing advised	(≥5%) URTI, nasopharyngitis, diarrhea, headache	Serious infections, tuberculosis, malignancy, gastrointestinal perforations, laboratory abnormalities and immunization interactions Black box warning for heart-related events, cancer, thrombosis, and death Contraindicated in breastfeeding; Combination with potent immunosuppressants not recommended
Upadacitinib	Small Molecule	Selective JAK1 inhibitor	PsA, atopic dermatitis[12]	NP	Level 3 – observational study without dramatic effect	Oral/12+/15mg once daily; pediatric, renal and co-usage of CYP3A4 inhibitor dosing may be advised	PsA(≥1%):URTI, herpes zoster, herpes simplex, bronchitis, nausea, cough, pyrexia, acne and headache Atopic Dermatitis (≥1%): URTI, acne, herpes simplex, headache, increased, CPK, cough, hypersensitivity, folliculitis, nausea, abdominal pain, pyrexia, increased weight, herpes zoster, influenza, fatigue, neutropenia, myalgia, and influenza-like illness[13]	Hypersensitivity, gastro intestinal perforations, laboratory abnormalities, embryo-fetal toxicity Black box warning for serious infections, mortality, malignancy, cardiovascular death, and thrombosis[14] Contraindicated in severe hepatic impairment; use with immunosuppressants or JAK inhibitors, live vaccines, and strong cytochrome P450 3A4 (CYP3A4) inhibitors not recommended

Contd...

Supplementary Table 1: Contd...

Name	Drug Class	Mechanism of Action	US FDA Approval for Dermatologic Indications	Evidence for Inflammatory Nail Disease	Highest LoE for Inflammatory Nail Disorder Treatment	US FDA Administration/ Dosage/Frequency	US FDA Most Common Adverse Reactions	US FDA Warnings and Precautions
Adalimumab	Biologic	TNF-inhibitor (recombinant human IgG1 (Immunoglobulin G) monoclonal antibody)[15]	Plaque psoriasis, PsA, NP, Hidradenitis Suppurativa[16]	NP	Level 1 – systematic review	2+/Subcutaneous/ PsA: 40 mg every other week Plaque Psoriasis: 40 mg every other week starting one week after initial dose	(>10%): infections, injection site reactions, headache, rash	Serious infections, tuberculosis, malignancy, invasive fungal infection, hypersensitivity reaction, Hepatitis B reactivation, demyelinating disease, cytopenia, heart failure, and lupus-like syndrome
Certolizumab Pegol	Biologic	TNF-inhibitor (humanized Fab' antibody fragment that binds to and blocks TNF-alpha)	Plaque psoriasis, PsA[17]	NP	Level 1 – systematic review	18+/Subcutaneous/ Plaque Psoriasis: 400 mg (given as 2 subcutaneous injections of 200 mg each) every other week. Dosing for body weight advised. PsA: 200 or 400 mg every other week after week 4	(>7%): URTI, rash, urinary tract infection	Serious infections, tuberculosis, invasive fungal infections, malignancy, heat failure, hypersensitivity reaction, Hepatitis B reactivation, demyelinating disease, cytopenias, lupus-like syndrome
Etanercept	Biologic	TNF-inhibitor (human dimeric fusion protein that competitively binds to and inhibits TNF-alpha and TNF-beta[18])	Plaque psoriasis, PsA[19]	NP	Level 1 – systematic review	2+/Subcutaneous/ Plaque Psoriasis: 50 mg once weekly after 3 months Pediatric dosing advised. PsA: 50 mg once weekly with or without methotrexate (MTX)	(>5%): infections and injection site reactions	Serious infection, tuberculosis, malignancy, invasive fungal infection, demyelinating disease, congestive heart failure, pancytopenia or aplastic anemia, Hepatitis B reactivation, hypersensitivity reaction, lupus-like syndrome Use with live vaccines, anakinra, abatacept, and cyclophosphamide not recommended[20]
Golimumab	Biologic	TNF-Inhibitor (human IgG1 monoclonal antibody that blocks TNF-alpha)[21]	PsA[22]	NP	Level 1 – crossover and systematic review	18+/Subcutaneous or IV infusion/ Subcutaneous 50 mg once per month; IV infusion 2 mg/kg at weeks 0 and 4, and every 8 weeks thereafter	(>5%): URTI, nasopharyngitis[23]	Serious infections, invasive fungal infections, Hepatitis B reactivation, malignancy, heart failure, demyelinating disease, hypersensitivity reactions

Contd...

Supplementary Table 1: Contd...

Name	Drug Class	Mechanism of Action	US FDA Approval for Dermatologic Indications	Evidence for Inflammatory Nail Disease	Highest LoE for Inflammatory Nail Disorder Treatment	US FDA Administration/ Dosage/Frequency	US FDA Most Common Adverse Reactions	US FDA Warnings and Precautions
Infliximab	Biologic	TNF-inhibitor (recombinant humanized monoclonal TNF-alpha antibody[24])	Plaque psoriasis, PsA	NP	Level 1 – systematic review	6+/Intravenous/5 mg/kg every 8 weeks after week 6	(>10%): infections (ex. URTI, sinusitis, pharyngitis), infusion-related reactions, headache, abdominal pain[25]	Serious infections, invasive tuberculosis, fungal infections, malignancy, Hepatis B reactivation, hepatotoxicity, heart failure, cytopenias, hypersensitivity, cardiovascular and cerebrovascular reactions, demyelinating disease, lupus-like syndrome Use with live vaccines not recommended Doses >5 mg/kg contraindicated in patients with moderate-to-severe heart failure
Bimekizumab	Biologic	IL-17 Inhibitor (binds the IL-17A, IL-17F, and the IL-17A & F heterodimer[26]	Plaque psoriasis[27]	NP	Level 2- randomized control	18+/ Subcutaneous/320 mg (two 160 mg injections) every 8 weeks after week 16. Weight based dosing advised.	(≥1%): URTI, oral candidiasis, headache, injection site reactions, tinea, gastroenteritis, herpes simplex, acne, folliculitis, other candida infections, fatigue	Suicidal ideation and behavior, serious infections, tuberculosis, liver enzyme abnormalities, IBD
Brodalumab	Biologic	IL-17 Inhibitor (fully human monoclonal IgG2 antibody[28])	Plaque psoriasis[29]	NP	Level 1- systematic review	18+/ Subcutaneous/210 mg every 2 weeks after week 2	(≥1%): arthralgia, headache, fatigue, diarrhea, oropharyngeal pain, nausea, myalgia, injection site reactions, influenza, neutropenia, tinea	Serious infections, tuberculosis, Crohn's disease Black box warning for suicidal ideation and behavior. Contraindicated in Crohn's Disease Use with live vaccines not recommended
Ixekizumab	Biologic	IL-17 Inhibitor (humanized IgG4 monoclonal antibody[30])	Plaque psoriasis, PsA[31]	NP	Level 1 – systematic review	6+/Subcutaneous/ Plaque Psoriasis: 80 mg every 4 weeks after week 12 PsA: 80 mg every 4 weeks after initial dose	(≥1%): injection site reactions, URTI, nausea, tinea	Serious infections, tuberculosis, IBD Use with live vaccines not recommended

Contd...

Supplementary Table 1: Contd...

Name	Drug Class	Mechanism of Action	US FDA Approval for Dermatologic Indications	Evidence for Inflammatory Nail Disease	Highest LoE for Inflammatory Nail Disorder Treatment	US FDA Administration/ Dosage/Frequency	US FDA Most Common Adverse Reactions	US FDA Warnings and Precautions
						Pediatric and concomitant Plaque Psoriasis and PsA dosing advised.		
Secukinumab	Biologic	IL-17 inhibitor (human IgG1[32])	Plaque psoriasis, PsA[33]	NP	Level 1- systematic review	6+/ Subcutaneous (plaque psoriasis), Subcutaneous or Intravenous (PsA)/ Plaque psoriasis: 150 or 300 mg every 4 weeks after week 4. PsA: Subcutaneous: With a loading dose: 150 mg every 4 weeks after week 4 Without loading dose: 150 mg every 4 weeks Dosage of 300 mg every 4 weeks can be considered for continued active PsA Intravenous: With a loading dosage: 1.75 mg/kg every 4 weeks after loading dose Without a loading dosage: 1.75 mg/kg every 4 weeks Dosing for pediatric and concomitant plaque psoriasis and PsA advised.	(>1%): nasopharyngitis, diarrhea, URTI	Serious infections, tuberculosis, IBD, hypersensitivity reactions Use with live vaccines not recommended

Contd...

Supplementary Table 1: Contd...

Name	Drug Class	Mechanism of Action	US FDA Approval for Dermatologic Indications	Evidence for Inflammatory Nail Disease	Highest LoE for Inflammatory Nail Disorder Treatment	US FDA Administration/ Dosage/Frequency	US FDA Most Common Adverse Reactions	US FDA Warnings and Precautions
Guselkumab	Biologic	IL-23 Inhibitor (human immunoglobulin G1 lambda (IgG1λ) monoclonal antibody[34])	Plaque psoriasis	NP	Level 1 – systematic review and crossover	18+/ Subcutaneous/100 mg every 8 weeks after week 4	(>1%): nasopharyngitis, diarrhea, URTI[35]	Serious infections, tuberculosis, IBD, hypersensitivity reactions Use with live vaccines not recommended
Risankizumab	Biologic	IL-23 Inhibitor (humanized IgG monoclonal antibody that selectively inhibits the p19 subunit[36])	Plaque psoriasis, PsA[37]	NP	Level 1- systematic review	18+/ Subcutaneous/150 mg every 12 weeks after week 4	(≥1%): URTI, headache, fatigue, injection site reactions, tinea[38]	Hypersensitivity reactions, serious infections, tuberculosis Use with live vaccines not recommended
Tildrakizumab	Biologic	IL-23 Inhibitor (humanized monoclonal IgG1κ antibody that selectively binds the p19 subunit[39])	Plaque psoriasis	NP	Level 1 - systematic review	18+/ Subcutaneous/100 mg every twelve weeks after week 4	(≥1%): URTI, injection site reactions, diarrhea	Hypersensitivity, serious infections, tuberculosis
Ustekinumab	Biologic	IL-23 Inhibitor (human monoclonal antibody that binds to IL-12Rβ1, which inhibits IL-12 and IL-23[40])	Plaque psoriasis and PsA[41]	NP	Level 1 – systematic review and crossover	6+/Subcutaneous/45 mg every 12 weeks after week 4 Pediatric and concomitant plaque psoriasis dosing advised.	(>3%): nasopharyngitis, URTI, headache, fatigue[42]	Serious infections, tuberculosis, malignancy, hypersensitivity reactions, Reversible Posterior Leukoencephalopathy Syndrome

*Note that hypersensitivity reactions can occur with all biologic and small-molecule drugs for inflammatory nail disease. †This table contains limited information. Details about dosing, including loading dosages, indications, and side effects should be obtained from trained physicians and US FDA-approved sources