Research Article

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2025.62.009685

Monoclonal Antibodies for Prurigo Nodularis: Current Landscape and Future Directions

Calista Persson[1]*, Alisa Nguyen[1] and Akhil Gupta[2]

[1]*Nova Southeastern University Kiran Patel College of Osteopathic Medicine, United States*

[2]*Skin Center of Florida, North Palm Beach, United States*

***Corresponding author:** Calista Persson, Nova Southeastern University Kiran Patel College of Osteopathic Medicine, Davie, FL, United States

ARTICLE INFO

Received: May 07, 2025

Published: May 22, 2025

Citation: Calista Persson, Alisa Nguyen and Akhil Gupta. Monoclonal Antibodies for Prurigo Nodularis: Current Landscape and Future Directions. Biomed J Sci & Tech Res 62(1)-2025. BJSTR. MS.ID.009685.

ABSTRACT

Prurigo nodularis (PN) is a chronic skin condition that develops intensely itchy nodules, substantially reducing patients' quality of life. Immune system irregularities, neuroinflammation, and constant scratching damage the skin barrier to produce this condition. Corticosteroids and antihistamines, as traditional treatments, corticosteroids and antihistamines frequently fail to provide sufficient relief from symptoms, requiring specific biologic therapies. The latest progress in the field has led to the development of monoclonal antibodies that focus on essential pruritogenic pathways. This analysis examines dupilumab, nemolizumab, vixarelimab, and CDX-0159 (barzolvolimab) through information sourced from PubMed, Embase, Web of Science, and ClinicalTrials.gov between 2015 and 2025. Dupilumab demonstrated a 58.8% reduction in pruritus and a 46.4% increase in lesion clearance by week 24. Patients experienced a 56.3% reduction in itch severity with nemolizumab treatment by week 16. Patients recorded a 50.6% improvement with vixarelimab at week 8, while barzolvolimab remains in the initial testing stages. Safety profiles were generally favorable. Monoclonal antibodies provide targeted therapeutic solutions for patients suffering from refractory PN. There are still obstacles to overcome concerning treatment expenses as well as accessibility alongside patient safety and appropriate patient selection. Upcoming studies must target combination treatments while developing biomarker-based methods and evaluating long-term effectiveness.

Keywords: Prurigo Nodularis; Chronic Pruritus; Neuroinflammation; Targeted Therapy; Monoclonal Antibodies; Dupilumab; Nemolizumab; Vixarelimab; CDX-0159; Barzolvolimab

Abbreviations: PN: Prurigo Nodularis; AD: Alongside Atopic Dermatitis; RCTs: Randomized Controlled Trials; AEs: Adverse Events; SAEs: Serious Adverse Events; CGRP: Calcitonin Gene-Related Peptide; NGF: Nerve Growth Factor

Introduction

Prurigo nodularis is a persistent neuroinflammatory skin condition that produces intensely itchy, hyperkeratotic nodules on the extremities and trunk. The itch-scratch cycle that patients cannot control results in skin damage and thickening, severely affecting their sleep patterns, social well-being, and overall quality of life (Figure 1). The majority of PN patients are middle-aged and elderly adults, and approximately 87,000 people in the U.S. receive diagnoses each year. The condition develops through immune system and neural control issues that result in fibrosis and neurovascular changes accompanied by T cells, dendritic cells, mast cells, and eosinophils inflammatory infiltrates. The grouping of mast cells and eosinophils near peripheral nerve fibers demonstrates their role in neuroimmune interactions [1,2]. Th2 cytokines IL-4, IL-13, IL-17, and IL-22, along with neuroimmune pruritogen IL-31, drive inflammation in PN conditions, according to studies [3,4]. Neurotransmitters such as substance P and calcitonin gene-related peptides worsen itchiness by causing vasodilation and mast cell degranulation, which leads to persistent itch through immune-neural pathways activation [1,3,5]. PN occurs alongside atopic dermatitis (AD) because they share chronic dermatologic features, which include severe itching and eczematous lesions [6]. Clinical data shows that fifty percent of PN patients have previous atopic dermatitis or atopy, suggesting Th2-driven pathways are involved.

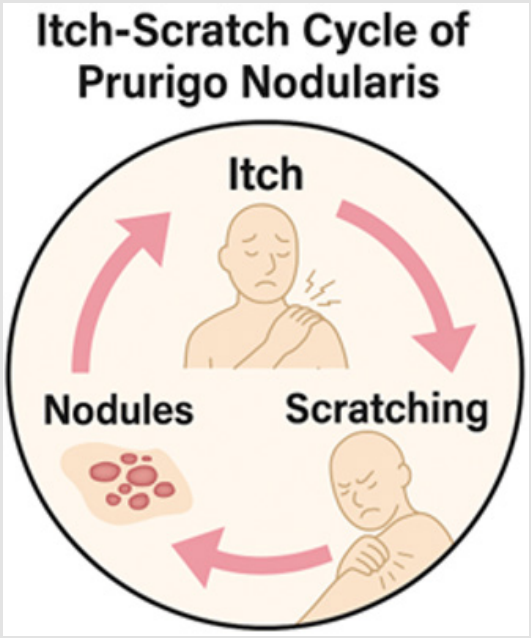

Figure 1: Itch-scratch Cycle of Prurigo Nodularis.

Transcriptomic research reveals that PN stands apart from AD by showing weaker Th2 patterns while demonstrating stronger fibrosis and neural dysregulation. The challenges faced by conventional atopic dermatitis therapies like topical steroids and antihistamines in managing PN demonstrate significant pathological distinctions. The severe and treatment-resistant character of PN demands therapeutic approaches that focus on its immune system drivers. Symptomatic treatment methods such as topical steroids, phototherapy, and systemic immunosuppressants like cyclosporine and methotrexate, alongside thalidomide and neuromodulators, formed the historic treatment approach but often delivered limited results and substantial side effects. The FDA had yet to approve any therapies for this condition before 2022. However, research into PN immunopathology and the roles of Th2 cytokines and IL-31 in pruritus led to the creation of new monoclonal antibodies. The FDA approved dupilumab as the first treatment option for PN in 2022 after its initial use for atopic dermatitis as an IL-4 receptor α antagonist. Nemolizumab was the first biologic drug explicitly created to treat PN when approved as an IL-31 receptor α antagonist in 2024. The investigational monoclonal antibody Vixarelimab targets oncostatin M receptor beta to disrupt IL-31 activity and inhibit OSMRβ, which is crucial in PN pathogenesis [7].

The emerging therapy CDX-0159 (barzolvolimab) functions by targeting the KIT (CD117) receptor tyrosine kinase, which is vital for mast cell survival to limit pruritogen release and inflammatory responses [5]. The emergence of these treatments marks a fundamental change in PN treatment. They deliver specific therapies that break the cycle of itching and scratching while aiding lesion repair. This review examines the development of monoclonal antibody treatments for PN by analyzing their mechanisms of action, evaluating their effectiveness and safety, and looking ahead to potential future developments.

Methods

Search Strategy

Our search covered all relevant research from 2015 to 2025 that studied monoclonal antibody treatment for prurigo nodularis. Our literature search covered PubMed/MEDLINE and Embase, Web of Science, and ClinicalTrials.gov as primary databases. Our search terms included "prurigo nodularis" and keywords including "biologics," "monoclonal antibody," "dupilumab," "nemolizumab," "IL-31," "IL-4," "IL-13," "mast cells," and "clinical trial" as well as specific drug names such as Dupixent, Nemolizumab, Vixarelimab, CDX-0159, Barzolvolimab. Filters restricted results to human studies from the last 10 years. Ongoing and recently completed trials were identified through ClinicalTrials.gov using "prurigo nodularis" as the condition and relevant intervention keywords (e.g., IL-31, biologic).

Inclusion and Exclusion Criteria

We included original studies and reports with clinical data on monoclonal antibody treatments for prurigo nodularis. This encompassed randomized controlled trials (RCTs), open-label or uncontrolled clinical trials, extension studies, real-world observational studies, case series with at least five patients, and individual case

studies or small patient trials. Given the rarity of PN and the limited number of RCTs, we also included high-quality prospective cohort studies and post-hoc pooled analyses of trial data. Our focus was on literature published in peer-reviewed journals from 2015 onward. Non-English papers were excluded, along with review articles (however relevant reviews were referenced for background context). Preclinical studies were considered only if they provided mechanistic insights relevant to monoclonal therapy. Our objective was to capture all available human clinical evidence on FDA-approved and investigational monoclonal antibodies for PN while ensuring a comprehensive but focused selection of relevant studies.

Study Selection and Data Extraction

After conducting the searches, two reviewers (authors of this review) independently screened titles and abstracts to identify relevant studies. Full-text articles of potentially relevant citations were retrieved and reviewed for inclusion. Any discrepancies in study selection were resolved through consensus. For each included study, we extracted key data on study design (e.g., trial phase, sample size, randomized vs. open-label), patient characteristics (PN severity, prior treatments, comorbidities), intervention details (drug, dose, frequency, duration), and outcomes. The primary outcomes of interest were itch reduction (e.g., Worst Itch Numeric Rating Scale [WI-NRS], Peak Pruritus NRS) and lesion clearance (e.g., Investigator's Global Assessment [IGA] or nodule count). Secondary outcomes included sleep disturbance scores, quality-of-life indices, and patient-reported global impression of improvement. Safety data was also collected, including rates of common adverse events (AEs), serious adverse events (SAEs), and any reported lab abnormalities or immunogenicity concerns. For investigational therapies, we noted mechanisms of action and preliminary efficacy results from early trials.

Analysis and Interpretation

Due to the heterogeneity of data sources—ranging from RCTs to real-world studies—and the limited number of trials per agent, a formal meta-analysis was not conducted. Instead, we performed a qualitative synthesis of the available evidence, organizing results by drug and study type to summarize the efficacy and safety findings of each monoclonal antibody in PN. When multiple trials existed for the same agent, we compared their outcomes and incorporated pooled analyses where available (e.g., combined phase 3 dupilumab trial results) to derive more robust efficacy estimates [8]. Key efficacy endpoints, such as the proportion of patients achieving ≥4-point itch reduction or IGA 0/1 at weeks 16–24, were tabulated to facilitate indirect comparisons between therapies. A comparative analysis was conducted to evaluate whether specific targets (e.g., IL-4/13 vs. IL-31 vs. other pathways) demonstrated superior itch relief or lesion clearance, acknowledging the absence of head-to-head trials. Safety profiles were assessed qualitatively, highlighting differences in AE types and frequencies across agents. Throughout, we accounted for limitations in the data, including placebo response rates, short trial durations (most lasting 16–24 weeks), and the lack of long-term safety data for newer agents. We also recognized the inherent limitations of a narrative review; without formal meta-analytic pooling, our comparisons remain descriptive and may be subject to selection bias. To mitigate this, we included all available clinical trial data and clearly indicated the level of evidence (e.g., RCT vs. open-label study). In the Discussion section, we addressed gaps in knowledge and potential biases within the existing literature. By synthesizing current findings in a structured manner, this review aims to provide clinicians and researchers with a comprehensive yet accessible overview of monoclonal antibody therapy in PN while guiding future research directions.

Results

Monoclonal Antibodies Approved for PN

As summarized in Table 1, two monoclonal antibodies (dupilumab and nemolizumab) have completed Phase 3 trials with positive outcomes and are now approved for PN, whereas others (vixarelimab and barzolvolimab (CDX-0159)) remain in earlier stages of development.

Table 1: Summary of Key Clinical Trials of Monoclonal Antibodies in Prurigo Nodularis.

Monoclonal Antibody	Target Pathway	Trial Phase	Sample Size	Primary Outcome Achieved	FDA Approval
Dupilumab[1]	IL-4Rα	Phase 3	300	Yes	Yes (2022)
Nemolizumab[1]	IL-31RA	Phase 3	274	Yes	Yes (2024)
Vixarelimab[1]	OSMRβ	Phase 2a	49	Yes	No
Barzolvolimab[1] (CDX-0159)	KIT	Phase 2	20	Pending	No

Note: [1]Data from [20,12,17,22]

Nemolizumab (Anti–IL-31RA): Nemolizumab is a humanized monoclonal antibody that binds to the IL-31 receptor alpha to block IL-31 signaling pathways. Activated Th2 cells and additional immune cells generate IL-31, a primary pruritogenic cytokine. It acts on IL-31RA/OSMRβ receptors on sensory nerves and immune cells to drive itch and inflammation. By blocking the IL-31 pathway, nemolizumab directly targets the primary "itch cytokine" implicated in PN pathophysiology [9]. Nemolizumab was first evaluated in PN in a Phase 2 randomized trial published in 2020, demonstrating significant antipruritic effects [10]. A Phase II/III clinical trial demonstrated that

nemolizumab significantly reduced itch, with a -61.1% change in the Peak Pruritus Numerical Rating Scale (PP-NRS) observed in the 30 mg group and a -56.0% change in the 60 mg group, compared to a -18.6% change in the placebo group. The study also reported notable improvements in lesion count and overall quality of life [11]. Two subsequent Phase 3 trials (OLYMPIA 1 and 2) confirmed its efficacy [11-17], leading to FDA approval in 2024 under the brand name Nemluvio [18]. This made nemolizumab the first therapy specifically targeting IL-31 in PN. In the pivotal Phase 3 OLYMPIA 2 trial, 274 adults with moderate-to-severe PN were randomized to receive nemolizumab (monthly injections) or placebo for 16 weeks [11,13].

Nemolizumab led to a rapid and significant reduction in pruritus. By week 16, 56.3% of patients achieved a ≥4-point reduction in Peak Pruritus NRS compared to 20.9% on placebo, yielding a treatment difference of 37.4 percentage points [11-17]. This degree of itch improvement was accompanied by notable effects on skin lesions: 37.7% of nemolizumab-treated patients achieved clear or almost-clear skin (IGA 0/1) by week 16, versus 11.0% on placebo [11,13]. Sleep improvements were also evident within the first two weeks [11,15]. Nemolizumab has shown a favorable safety profile in clinical trials. In the Phase 3 studies, most AEs were mild, including headache (6.6% vs. 4.4% in placebo) and atopic dermatitis (5.5% vs. 0% in placebo) [12,13]. Injection site reactions and nasopharyngitis were also reported, but were generally mild. Importantly, no increase in serious infections or other serious AEs were observed with nemolizumab, and its use did not necessitate monitoring for systemic immunosuppression or lab abnormalities [11-17]. Its targeted mechanism makes it a promising long-term treatment option for patients suffering from refractory pruritus. Nemolizumab's approval has opened the door for targeted itch therapy in PN. It achieves substantial itch reduction by targeting IL-31, and many patients experience relief by the first or second dose. However, relatively short trial durations (16–24 weeks) and the lack of head-to-head comparisons with other biologics should be acknowledged [3,7]. Future research should focus on long-term safety, durability of response, and comparative effectiveness against other targeted therapies for PN.

Dupilumab (Anti–IL-4Rα): Dupilumab functions as a fully human monoclonal antibody by targeting the IL-4 receptor α subunit, which inhibits IL-4 and IL-13 signaling that contribute to type 2 inflammation in PN and related conditions [1,5]. Dupilumab targets IL-4 and IL-13 pathways to suppress Th2-related PN processes, including IgE production, eosinophil activation, and pruritic cytokine receptor upregulation [19]. IL-4 and IL-13 connect type 2 inflammation and PN itch mechanism by increasing IL-31 receptor levels in neurons [1]. Dupilumab's effectiveness in AD treatment, alongside the importance of type 2 inflammation in PN pathophysiology, led researchers to investigate dupilumab as a specific therapy option. Dupilumab received FDA approval as the first medication for adults with uncontrolled moderate-to-severe PN after successful Phase 3 trial results in September 2022 [8,18,20-25]. The two Phase 3 trials lasted 24 weeks. They were placebo-controlled studies involving adults with severe PN who experienced baseline itch levels of 7 or more out of 10, where dupilumab was administered at 300 mg subcutaneously biweekly after an initial 600 mg loading dose. The application of dupilumab led to significant improvements in itch relief and skin clearance compared to the placebo group [20,18].

According to pooled analysis results involving approximately 151 dupilumab patients compared to 153 placebo patients, 58.8% of dupilumab participants showed a clinically significant drop in itch (≥4-point reduction in worst-itch NRS) at week 24 against 19.0% of those receiving placebo [8]. Patients who received dupilumab treatment reached 46.4% clear or almost-clear skin status (IGA-PN 0/1) compared to 17.1% of those who received placebo [8]. Dupilumab produced a fourfold higher response rate, where 35.3% of patients achieved both an itch reduction ≥4 and IGA 0/1 compared to 8.9% of patients receiving a placebo. The statistical analysis demonstrated highly significant findings with a p-value below 0.0001 [23]. Dupilumab's effects increased over time, with some patients showing itch improvement as early as weeks 4–8, though maximal responses—particularly in lesion clearance—were observed by six months [18,23]. These findings firmly establish IL-4/IL-13 blockade as an effective PN therapy, reducing itch severity and promoting nodule resolution where conventional treatments often fail. Real-world evidence supports these clinical trial findings [22] In a retrospective study of 16 PN patients treated with dupilumab, all patients experienced rapid and profound improvement, with mean itch scores decreasing from 8.7 at baseline to approximately 1.6 by week 6 and near 0 by week 32 [23]. Over 80% of patients achieved a ≥4-point itch NRS reduction by weeks 6–8 [23]. Many achieved complete itch and lesion resolution with continued dupilumab treatment for up to one year [23].

These data highlight dupilumab's durable efficacy, suggesting that sustained IL-4/IL-13 inhibition can maintain long-term disease remission in most PN patients. In terms of safety, dupilumab's profile in PN has been consistent with its extensive AD data. Treatment is generally well tolerated. The most common side effects include mild injection site reactions, such as transient erythema or swelling, and conjunctivitis [24]. While dupilumab-associated conjunctivitis has been more frequently reported in AD trials (~10–15% of patients), its incidence in PN trials was lower, though it remains a potential concern. These ocular effects are generally manageable with supportive care and rarely lead to discontinuation. Other less frequent AEs include transient eosinophilia and rare cases of "head and neck" dermatitis, a paradoxical erythema localized to these regions [25]. In real-world PN studies extending up to 84 weeks, no SAEs were reported, and patients did not experience increased infection risk [22]. This reassuring safety profile, combined with robust efficacy, positions dupilumab as a foundational therapy for PN.

Investigational Monoclonal Antibodies for PN

Vixarelimab (Anti–Oncostatin M Receptor β): The investigational monoclonal antibody vixarelimab targets the oncostatin M receptor beta subunit, which forms a crucial part of the receptor complex for both IL-31 and oncostatin M cytokines known to be involved in PN pathogenesis [3,7]. Vixarelimab functions by blocking OSMRβ to inhibit both IL-31 and oncostatin M signaling, which leads to reduced pruritus and potentially diminished skin inflammation and fibrosis [26]. The dual-action mechanism that distinguishes vixarelimab from nemolizumab presents a new strategy for IL-31 pathway inhibition. The drug vixarelimab (known previously as KPL-716) produced positive results during its Phase 2a randomized, placebo-controlled trial conducted by Kiniksa Pharmaceuticals. The study involved 49 moderate-to-severe PN patients administered either vixarelimab with a 720 mg initial dose followed by 320 mg weekly or placebo over 8 weeks [7]. The group of patients treated with vixarelimab exhibited a substantial 50.6% average decrease in itch (WI-NRS) by week 8, which was significantly higher than the 29.4% reduction observed in the placebo group ($p = 0.03$) despite the study's brief duration. Patients showed noticeable reductions in itch levels starting from the third week. Patients treated with vixarelimab reached a ≥4-point reduction in itch NRS at 52.2% by week 8. Still, this figure was higher than the 30.8% in placebo recipients without achieving statistical significance due to the limited sample size ($p = 0.11$) [7].

The treatment with vixarelimab demonstrated positive effects on skin lesions apart from providing itch relief. During week 8 of treatment, 30.4% of patients reached clear or almost-clear skin status (IGA 0/1), while placebo group patients only reached this outcome at 7.7% ($p = 0.03$) [7]. The evidence demonstrates that blocking OSMRβ can reduce itching while simultaneously helping resolve skin nodules quickly. Patients treated with vixarelimab demonstrated superior sleep quality and quality-of-life scores than placebo patients [3]. The trial established that vixarelimab brings quick relief from itching. Numerous patients noticed benefits in a 2–4 week period, and effectiveness further improved until week 8. The study's brief duration restricts long-term findings, but a longer Phase 2b trial extending to 12 weeks or more would clarify its full therapeutic capabilities. The Phase 2a study demonstrated that vixarelimab maintained a favorable safety profile. The study reported no occurrence of SAEs or treatment discontinuations related to adverse effects [7]. The safety profile of vixarelimab was demonstrated by the fact that 91% of patients experienced at least one adverse event as opposed to the 77% in the placebo cohort, even though these events remained mild, including injection site reactions and mild headaches as well as common cold symptoms [3].

Both blood count changes and liver enzyme alterations remained within normal limits, and dual IL-31/OSM inhibition showed no unexpected safety problems [26]. The results demonstrate proof-of-concept by showing that inhibiting IL-31 and OSM through OSMRβ targeting improves PN symptoms. Vixarelimab could deliver itch relief comparable to nemolizumab and enhance treatment outcomes due to its effect on OSM, contributing to broader inflammatory processes [27]. Further testing through Phase 2b and Phase 3 trials must establish the treatment's effectiveness, response longevity, and best dosage. Successful results from vixarelimab trials could establish it as a new option for IL-31 pathway inhibition when existing IL-4Rα or IL-31RA antagonists fail to work or cause patient intolerances.

CDX-0159 (Barzolvolimab, Anti-KIT): CDX-0159 (barzolvolimab) is a human monoclonal antibody that targets KIT (CD117), a receptor tyrosine kinase essential for mast cell survival and function. By binding to KIT, barzolvolimab induces mast cell depletion or functional silencing, thereby reducing mast cell–mediated release of pruritogens and inflammatory mediators in PN lesions [3,28]. This mechanism is distinct from the cytokine-targeting approaches of dupilumab and nemolizumab, representing a novel strategy focused on the cellular source of itch and inflammation. A Phase 2 trial is now underway, evaluating subcutaneous barzolvolimab injections over a 16-week period [27]. Safety data from other indications suggest that CDX-0159 is generally well tolerated. The most common AEs include mild-to-moderate infusion-related reactions, which can be managed with premedication, and transient hypoesthesia (numbness), possibly due to rapid mast cell mediator release. No serious drug-related AEs have been reported in other conditions treated with barzolvolimab, such as chronic urticaria [26]. By targeting the KIT pathway, barzolvolimab represents a novel approach to breaking the PN itch cycle. This mechanism makes it particularly promising for PN cases where mast cell–nerve interactions play a dominant role [2].

Early clinical observations in mast cell–driven diseases are encouraging. In chronic spontaneous urticaria, for example, around 60% of patients achieved complete symptom resolution with barzolvolimab in Phase 1b studies [28]. While PN data is not yet available, this dramatic effect in a similar pruritic condition suggests that CDX-0159 may offer meaningful itch reduction in PN as well. The ongoing Phase 2 trial will clarify its efficacy in PN, including effects on nodule count and itch scores. If CDX-0159 proves effective, it could be combined with cytokine inhibitors for a multi-targeted approach. Conceivably, depleting mast cells with barzolvolimab might enhance the efficacy of agents like dupilumab or nemolizumab by removing a key source of itch mediators [3]. Such combination therapy remains speculative and would require careful investigation given the potential for increased immunosuppression. Nonetheless, CDX-0159 expands the therapeutic landscape for PN by offering a non–cytokine-centric strategy.

Other Investigational Therapies

Additional IL-31 and Type 2 Pathway Inhibitors: Beyond nemolizumab and vixarelimab, other IL-31 targeted therapies are in early development. BMS-981164, an anti-IL-31 antibody, has been studied in chronic itch conditions, although not yet specifically for

PN. Given the success of nemolizumab, it is plausible that direct IL-31 ligand blockers or additional IL-31RA-targeting antibodies could yield similar favorable results [13,29]. Similarly, blocking upstream cytokines in the Th2 cascade, such as TSLP or IL-13, may provide therapeutic benefits. While dupilumab (an IL-4/IL-13 blocker) has been effective in PN, drugs like tralokinumab and lebrikizumab, both anti-IL-13 monoclonal antibodies, could be evaluated, particularly in patients with coexisting AD [17,24,30].

JAK-STAT Pathway Inhibitors: The JAK-STAT pathway is the signaling mechanism for multiple cytokines involved in PN, such as IL-4, IL-13, and IL-31 [3,5,8]. Small-molecule JAK inhibitors have entered evaluation for potential treatments. While not considered monoclonal antibodies, oral JAK inhibitors like abrocitinib (a JAK1 inhibitor) and povorcitinib (formerly ATI-1777, a pan-JAK inhibitor) have reached Phase 2 trials in PN research [3,30-33] Studies show that JAK inhibition produces quick pruritus relief through widespread cytokine signaling suppression. Targeted biologics may avoid systemic JAK inhibitors' immunosuppressive risks like heightened infection susceptibility and thrombotic complications.As an alternative treatment method, researchers explore topical JAK inhibition through ruxolitinib, which targets JAK1/2 and is presently undergoing Phase 3 testing for localized PN lesions [3,26]. Successful topical JAK inhibitors would treat targeted lesions while minimizing systemic risk factors. JAK inhibitors may serve as temporary treatment options alongside biologics to provide immediate symptom relief before monoclonal antibodies reach their complete therapeutic impact. The advancements presented emphasize JAK-STAT pathway regulation as a central factor in PN treatment and its therapeutic targeting potential.

Neuroimmune-Targeting Antibodies: The new treatment strategy for prurigo nodularis (PN) aims to disrupt neuroimmune pathways by focusing on substance P, which plays a role in the transmission of chronic itch. Serlopitant functions as a selective neurokinin-1 (NK1) receptor antagonist and has been researched because it blocks substance P signaling throughout the central and peripheral nervous systems [34]. However, it does not qualify as a monoclonal antibody. Research has shown that serlopitants produced significant antipruritic effects in early-stage clinical trials, including a Phase 2 study that demonstrated a substantial reduction of itch intensity in chronic pruritus patients. Study outcomes showed that this option might be an innovative treatment that avoids immunosuppression for chronic itch disorders like PN. Although Phase 2 trials showed promising results for serlopitant, the Phase 3 trials produced inconclusive evidence regarding its efficacy, halting its development for pruritic conditions and its inability to secure regulatory approval [34]. The interest in neuroimmune-targeted treatments continues to be substantial. Upcoming biologic treatments will target the modulation of neuroimmune mediators such as nerve growth factor (NGF) and calcitonin gene-related peptide (CGRP) to combat neuronal drivers of chronic itch in PN specifically. Research indicates that biologics targeting neuroimmune signaling pathways could transform PN patient treatment, primarily when their condition stems from excessive neuronal sensitivity or neurogenic inflammation [5,23,32].

Towards Personalized Therapy in PN

As our understanding of PN heterogeneity deepens, personalized treatment approaches may become a reality. PN likely consists of multiple endotypes, with some patients exhibiting a strong atopic/allergic Th2-driven component (elevated IgE, history of eczema), while others may have more neuropathic or Th1/Th17-driven disease with less overt atopy [1,3,4,32]. Identifying these subtypes could help optimize therapy selection in the future. Biomarkers serve as crucial tools for steering treatment choices. Dupilumab appears to be the most effective treatment for patients with atopic PN endotypes that show high levels of TARC/CCL17 or IgE [19]. In contrast, individuals with elevated IL-31 levels or genetic polymorphisms in the IL-31 pathway may derive greater benefit from nemolizumab [15,27,35,36]. Similarly, skin biopsy gene expression profiling could differentiate between lesions enriched for Th2 markers versus those showing greater fibrosis or neurotrophic alterations, suggesting whether an anti-cytokine biologic or a neural pathway modulator would be the most effective approach [3,4,33]. While precision medicine strategies have not yet been fully implemented in PN, ongoing research is investigating predictors of response to dupilumab and nemolizumab. Patient-specific factors, including chronic health conditions, age, and healthcare accessibility, will affect treatment decisions in conjunction with immunological profiling. A personalized strategy that integrates clinical data with molecular and genetic information will yield optimal patient results for PN treatment.

Mechanisms of Action and Pathway Targeting

IL-31 and Itch Modulation: The neuroimmune cytokine IL-31 plays a crucial role in prurigo nodularis and originates from activated Th2 cells along with Th17 cells and macrophages. The molecule exerts its biological function through interaction with a receptor made of IL-31RA and OSMRβ that exists on keratinocytes, macrophages, and sensory skin neurons [4,13]. The cytokine IL-31 receives the designation "itch cytokine" because of its powerful ability to trigger pruritus. Patients with PN exhibit elevated IL-31 concentrations in both skin tissue and blood serum, which directly correlates with the intensity of itching [13]. IL-31 receptor binding on skin nerves activates JAK-STAT and MAPK signaling pathways, which results in neuronal activation and itch signal transmission to the brain. IL-31 activates keratinocytes and immune cells to release additional pro-pruritic molecules, intensifying inflammation [29,30]. IL-31 fails to trigger histamine release, demonstrating antihistamines work poorly for PN-related itchiness. Monoclonal antibodies target this pathway at different points. Nemolizumab blocks IL-31 from activating its receptor by binding to IL-31RA [17,18,21,22,35,36], whereas vixarelimab blocks the OSMRβ subunit, preventing signaling from both IL-31 and oncostatin M. By interrupting IL-31-driven neural stimulation, these therapies effectively reduce itch in PN (Figure 2) [13].

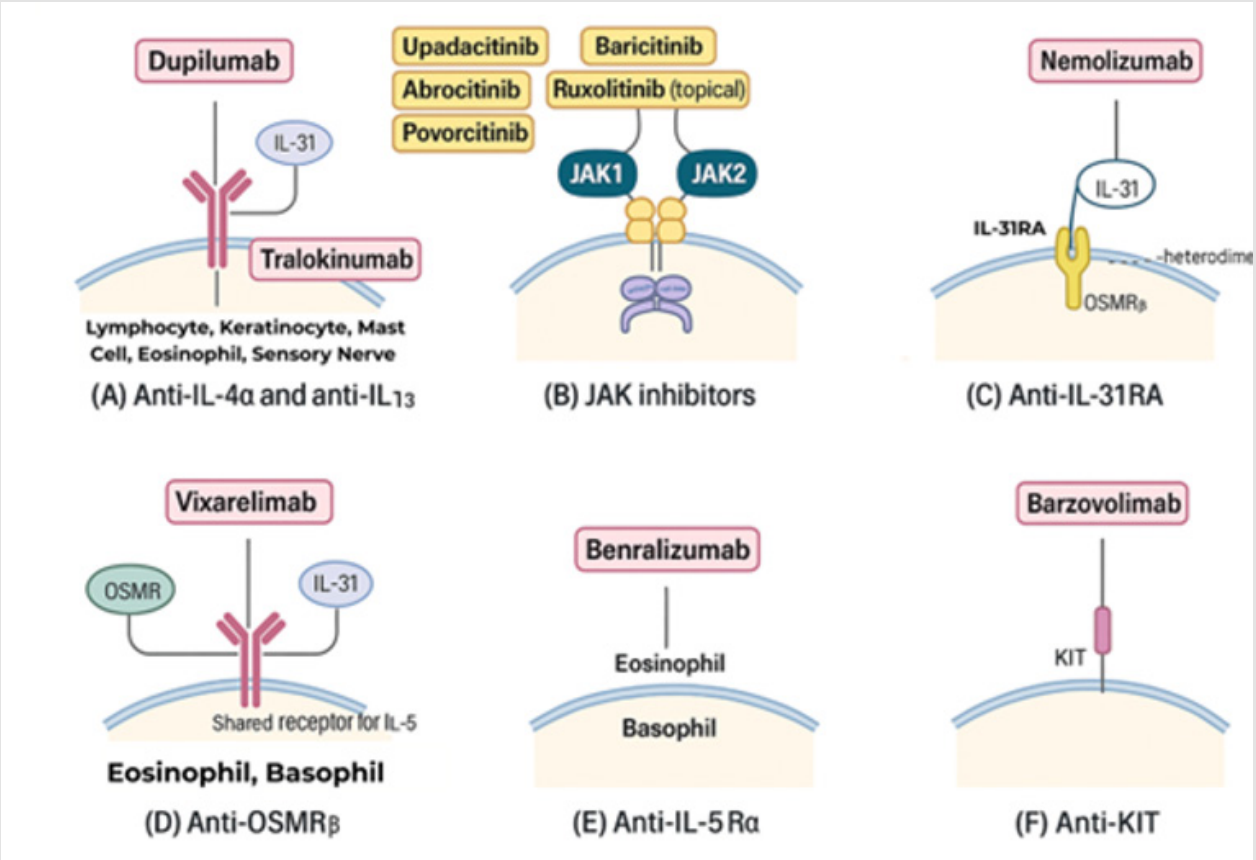

Figure 2: Mechanisms of Action of Monoclonal Antibodies in PN.

IL-4/IL-13 and Type 2 Inflammation: The Type 2 helper T-cell cytokine axis operates as a major pathway in PN, focusing on the cytokines IL-4 and IL-13. Patients with PN exhibit Th2-skewed immune profiles comparable to chronic atopic inflammation as their skin shows increased IL-4/IL-13 activity, generating chronic itch and skin lesions. IL-4 and IL-13 generate pruritus by recruiting eosinophils and mast cells, stimulating IgE production, and activating itch-related mediators such as IL-31 [1,8,30]. Medical treatments that target this pathway show high effectiveness. Dupilumab functions as an IL-4 receptor α subunit blocker, which disables IL-4 and IL-13 signaling pathways, resulting in major decreases in PN itch and nodule severity [1]. The positive clinical results with dupilumab for PN demonstrate IL-4/IL-13–mediated inflammation as a crucial factor in the disease's development process.

Mast Cells and the KIT Pathway: In addition to T-cell cytokines, the mast cell–neuronal pathway (often termed the KIT pathway) is an important target in PN. Mast cells are increased in PN lesions and release pruritogenic mediators (e.g. histamine, tryptase) that activate cutaneous nerves and sustain inflammation [26]. Mast cell survival and activation depend on stem cell factor binding to the KIT (c-Kit) receptor, and this pathway has emerged as a therapeutic interest. In fact, early studies suggest that inhibiting c-Kit signaling can reduce mast cell numbers and itch – for example, novel anti-KIT monoclonal antibodies (such as CDX-0159) are being explored to interrupt this mast cell–driven itch cycle [2,3,23]. While KIT pathway inhibitors are not yet approved for PN, their development reflects the broader strategy of targeting neuroimmune interactions in the disease. By disrupting IL-31, IL-4/IL-13, and KIT-mediated signaling, these biologic therapies directly address the pathogenic pathways of PN, offering more effective relief from chronic itch and nodular skin lesions [5,23].

Discussion

Monoclonal antibody therapies have transformed the treatment landscape for PN in recent years, providing effective relief for a patient population that previously had limited options [3]. Dupilumab became the first FDA-approved treatment for PN in 2022 [20,32-34], followed by nemolizumab's approval in 2024 [18]. These two biologics have demonstrated comparable efficacy in clinical trials despite targeting different pathways [8,13,35]. Both therapies achieve approximately a threefold increase in responder rates compared to placebo for itch reduction and lesion clearance endpoints [8,13]. Around

55–60% of patients experience a ≥4-point reduction in itch severity with either agent by the primary endpoint at 16–24 weeks, while skin clearance (IGA 0/1) is achieved in roughly 38–46% of treated patients [8,13]. In contrast, placebo response rates remain relatively low (8–20%), reinforcing the robustness of these biologic effects in the treatment of PN. Although direct comparisons between these biologics are limited by differences in trial design—dupilumab's Phase 3 trials lasted 24 weeks, whereas nemolizumab's Phase 3 study concluded at 16 weeks—nemolizumab had already approached dupilumab's 24-week efficacy by week 16 [36]. This suggests IL-31 blockade may reach peak effect more quickly, while IL-4/13 blockade might provide continued lesion improvement over 24 weeks [35]. Open-label studies and real-world data indicate that dupilumab continues to improve PN beyond 24 weeks, with some patients achieving full lesion clearance at 6–12 months [18,21-25].

The long-term efficacy of nemolizumab beyond 16 weeks is less documented in published literature, though an ongoing Phase 3 extension study will provide additional insights [35]. At present, no head-to-head trial exists to determine whether dupilumab or nemolizumab is superior. In clinical practice, treatment selection may depend on patient-specific factors such as comorbid atopic disease, cost, and availability. A hypothesis emerging from clinical experience suggests that patients with strong atopic features (elevated IgE, history of eczema) may respond particularly well to dupilumab due to its broader suppression of type 2 inflammation [1,3,18,21-25]. Conversely, patients with predominantly neurogenic itch and minimal eczema may benefit more directly from nemolizumab's focused inhibition of IL-31 [18]. Additionally, nemolizumab's rapid onset—often achieving significant itch reduction within two weeks [10-18]—could make it a preferable option for patients in need of quick relief, whereas dupilumab typically demonstrates substantial effects by 4–6 weeks [19].

Emerging Biologic Therapies in PN

Beyond dupilumab and nemolizumab, investigational biologics such as vixarelimab have demonstrated promising efficacy. In a Phase 2a study, vixarelimab led to a 50% reduction in itch within eight weeks [7]. While early-stage, this level of efficacy is comparable to that of nemolizumab, which is unsurprising given that both therapies target the IL-31 pathway. An interesting observation from the vixarelimab study was that approximately 30% of patients achieved clear or almost-clear skin (IGA 0/1) by week 8 [7]. This appears to be an earlier lesion response than what is typically observed with dupilumab at the same time point, potentially due to vixarelimab's additional inhibition of the oncostatin M pathway, which may influence fibrosis and inflammation. If ongoing Phase 3 trials confirm these findings, vixarelimab could provide an alternative IL-31 pathway inhibitor, particularly for patients who cannot access or have lost response to nemolizumab over time [12] (see Table 2). For CDX-0159 (barzolvolimab), efficacy in PN has yetto be fully quantified. However, given its dramatic effects in chronic spontaneous urticaria—where approximately 60% of patients achieved complete symptom resolution in early trials—CDX-0159 may offer meaningful itch reduction in PN as well [2,5].

Table 2: Comparative efficacy of monoclonal antibodies in prurigo nodularis.

Monoclonal Antibody	≥4-point WI-NRS Improvement (%)	IGA 0/1 (%)	Onset of Itch Relief (weeks)	Peak Efficacy (weeks)
Dupilumab	58.8	46.4	4	24
Nemolizumab	56.3	37.7	2	16
Vixarelimab	50.6	30.4	3	8

Note: [1]WI-NRS = Worst Itch Numeric Rating Scale; IGA 0/1 = proportion of patients achieving clear or almost-clear skin. Data from [20,12,17,22]

Its mechanism of action, which depletes or functionally silences mast cells, provides a distinct therapeutic approach compared to cytokine blockade [2]. A speculative but intriguing possibility is that combining a mast cell suppressor like CDX-0159 with a cytokine-targeting biologic could yield additive benefits, effectively addressing both the immune cells and the inflammatory mediators driving PN [17]. While this combination has yet to be formally studied, it represents a promising direction for future PN treatment strategies. Table 3 and Figure 3 outlines the comparative timeline of each therapy's onset of itch relief, time to significant improvement, peak efficacy, and sustained benefit.

Table 3: Comparative onset of action and efficacy timeline of monoclonal antibodies in PN.

Monoclonal Antibody	Itch Reduction Starts (weeks)	Significant Improvement (weeks)	Peak Efficacy Achieved (weeks)	Sustained Benefit (months)
Dupilumab[1]	4	8	24	12+
Nemolizumab[1]	2	4	16	Ongoing data
Vixarelimab[1]	2	3	12	Unknown
Barzolvolimab[1] (CDX-0159)	Unknown	Unknown	Unknown	Unknown

Note: [1]Timeline based on clinical trial endpoints and follow-up data: Dupilumab and nemolizumab from Phase 3 trials [12,14,16,19,22] vixarelimab from Phase 2a results [7], and CDX-0159 from preliminary reports [27].

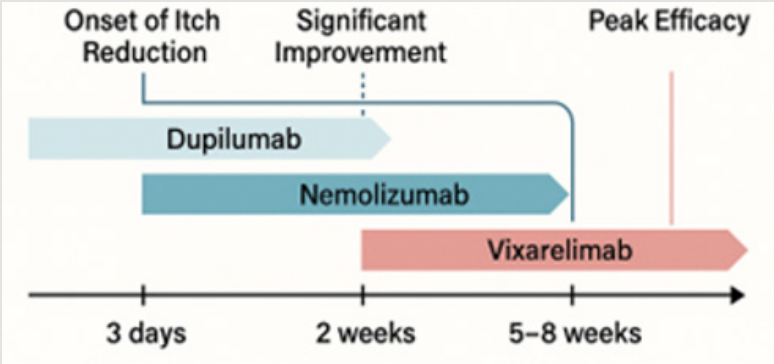

Figure 3: Timeline of Therapeutic Effect Onset for Monoclonal Antibodies.

Safety Profile of Targeted Biologics in PN

Monoclonal antibody treatments for PN are safer than traditional systemic immunosuppressants such as corticosteroids and thalidomide. The newer biologic treatments maintain safety profiles without significant immunosuppressive effects. Patients receiving dupilumab and nemolizumab show no increased serious infection rates compared to placebo across six months of treatment [13,22]. Dupilumab has proven to be safe through its widespread application in treating AD. Patients commonly experience mild injection site reactions, including localized redness or swelling. Conjunctivitis occurs less often in PN trials, but clinicians continue to monitor it closely as a potential side effect [22]. Researchers have yet to fully understand conjunctivitis's underlying mechanism that may involve IL-13's function in maintaining ocular surface balance. Most instances of this condition remain treatable and do not require stopping the therapy. Dupilumab treatment for AD has been linked to rare dermatologic conditions, including facial erythema, psoriasis, or arthritis, which seem idiosyncratic since no such cases were reported in PN studies [22]. AD trial data shows that dupilumab can be administered safely for over four to five years. This suggests that PN patients could also use long-term therapy with minimal safety risks. Researchers continue to collect long-term data to establish Nemolizumab's safety profile.

The Phase 3 trials produced no significant safety issues, while some participants reported mild headaches and occasional increases in eczema symptoms [13]. IL-31 participates in specific immune functions, yet no immune-associated side effects have appeared after IL-31 blockade. The Phase 2a study of vixarelimab showed no serious adverse events, with injection site reactions and mild headaches being the most common side effects reported [7]. The urticaria-focused CDX-0159 treatment has demonstrated mild-to-moderate infusion reactions and transient hypoesthesia as primary AEs [5] while maintaining an acceptable safety profile. Overall, these biologics have shown a marked improvement in safety profile compared to traditional immunosuppressive therapies in PN. In accordance with the above, Table 4 summarizes common and serious AEs reported for each monoclonal antibody and the available long-term safety data.

Table 4: Comparative onset of action and efficacy timeline of monoclonal antibodies in PN.

Monoclonal Antibody	Common AEs (%)	Serious AEs	Long-Term Safety Data
Dupilumab[1]	Injection site reactions (5–10%), conjunctivitis (5–15%)	None significant	Available (>5 years in AD)
Nemolizumab[1]	Headache (6.6%), eczema flare (5.5%)	None significant	Ongoing (1-year data reported)
Vixarelimab[1]	Injection site reactions (mild), mild headache	None reported	Not yet available
Barzolvolimab[1] (CDX-0159)	Infusion reactions, mild hypoesthesia	Infusion-related reactions in some cases	Not yet available

Note: [1]Long-term data for dupilumab are derived from its use in atopic dermatitis. Data compiled from published trials and reports [7,23,29,31].

Challenges in Access and Implementation

Despite the efficacy and safety of these therapies, practical considerations impact their use. In general, biologics are expensive, and insurance coverage can be a significant hurdle [14] (Galderma, 2023). Many patients face prior authorization requirements, with some insurers requiring evidence of inadequate response to dupilumab before approving nemolizumab or vice versa [18]. Such requirements can delay treatment initiation. Manufacturer-sponsored patient assistance programs may help some uninsured or underinsured patients,

but broad accessibility remains an issue [28]. Availability is another concern. Dupilumab is widely accessible globally, but nemolizumab's rollout may be slower, particularly outside of the U.S., as it was initially developed in Japan before being licensed internationally [29]. These biologics also require administration by injection, meaning patients must be able to self-administer or visit a clinic for treatment. Dupilumab's every-two-week dosing with a prefilled pen allows for at-home use, while nemolizumab's once-monthly dosing may improve adherence—though missing doses could lead to itch flares [10,22,34]. Ensuring that elderly PN patients or those with limited dexterity can administer these medications or receive assistance is essential. Physician awareness also presents a challenge. PN has historically been regarded as difficult to treat, and many healthcare providers, particularly non-dermatologists, may be unaware of the availability and efficacy of biologics [3].

Increasing awareness through education and clinical guidelines is critical to improving referrals and patient access. Health disparities could further complicate access, as PN disproportionately affects older individuals and, according to some studies, African American patients [3]. These populations often face greater healthcare access challenges, making equitable distribution of biologics a priority. Beyond access to treatment, patients with PN often have long-standing disease with associated comorbidities, including depression and chronic pain from neuropathy [35]. While biologics effectively alleviate itch and skin lesions, comprehensive management should also include mental health support and over-the-counter topical treatments to address residual scratch-induced injuries [3].

Potential Future Combinations and Adjunctive Therapies

With multiple pathways now targetable in PN, the question arises whether combination therapy could enhance outcomes or provide solutions for refractory cases. While combining biologics is uncommon in other inflammatory diseases like psoriasis or rheumatoid arthritis due to infection risk and cost, sequential or adjunctive use may have a role in PN [9]. For instance, a patient who experiences partial itch relief with dupilumab but continues to struggle with residual symptoms may benefit from adding nemolizumab to directly block IL-31 signaling [34,36]. Given their overlapping mechanisms—both reducing itch but through distinct pathways—there is potential for synergy. However, no formal studies have explored this approach, and the cost of dual therapy remains a significant limitation [13]. Another potential strategy is using a JAK inhibitor as a short-term adjunct while initiating a biologic. Oral JAK inhibitors, such as upadacitinib, can reduce itch within days and might serve as a bridge until dupilumab's effects manifest over several weeks [37]. This approach has occasionally been employed by dermatologists for severe AD—starting a JAK inhibitor to provide rapid symptom control, then tapering it once a biologic reaches full efficacy [2,5]. In PN, this could be a viable strategy for patients experiencing an unbearable itch crisis during the early course of biologic therapy. Combination therapy with antihistamines or sedatives is also commonly used. While histamine does not play a major role in IL-31-driven itch, some PN patients have coexisting dermatographism or urticarial papules where histamine contributes to symptoms.

Using a non-sedating antihistamine during the day and a sedating antihistamine like hydroxyzine or doxepin at night may provide symptomatic relief [2]. Likewise, phototherapy, particularly narrowband UVB (NB-UVB), has modest efficacy in PN as monotherapy but may serve as an adjunct to speed lesion resolution when used alongside biologics [38]. Once biologic therapy controls itch, targeted phototherapy could accelerate nodule shrinkage [10]. Topical treatments such as capsaicin or steroid tapes may also be continued for residual lesions [38]. Long-term follow-up studies will provide insight into the durability of biologic therapy in PN. It remains unclear whether PN can "burn out" with prolonged treatment—potentially allowing for a drug holiday—or if maintenance therapy will be required indefinitely. Some case reports suggest that PN recurs when biologics are discontinued, implying that ongoing treatment may be necessary, similar to AD [8]. Future research will clarify whether remission can be sustained after prolonged itch suppression and lesion resolution. As the PN treatment landscape continues to expand, ongoing studies will help optimize the use of biologics and emerging therapies, refining treatment algorithms and identifying the best approaches for sustained disease control. Combination trials, biomarker-driven studies, and head-to-head comparisons between agents such as dupilumab and nemolizumab will be particularly valuable in shaping the future of PN management [5].

Conclusion

Monoclonal antibody therapies have transformed prurigo nodularis treatment by turning a once untreatable disease into a manageable condition for numerous patients. Dupilumab and nemolizumab target IL-4/IL-13 and IL-31 pathways to achieve precise immune regulation that breaks the itch-scratch cycle and facilitates the healing of chronic nodules, greatly enhancing patients' quality of life. The effectiveness of these biologics demonstrates that the complex and elusive pathogenesis of PN can be effectively managed by targeting key mechanisms like type 2 inflammation and neuroimmune pathways. Real-world clinical cases reinforce findings from trials. Individuals suffering from PN for extended periods of years to decades now experience improved sleep quality, a near-total reduction of itching symptoms, and the elimination of persistent skin lesions. The treatment effects reach past dermatological symptoms, providing relief from the anxiety, depression, and social isolation that commonly follow PN's persistent itch. Biologic therapy restores physical comfort and improves psychological well-being, highlighting PN's extensive systemic impact and illustrating the importance of successful treatment methods. Although progress has been made, these discoveries still leave research gaps and issues with treatment access and extended disease management. Dupilumab and nemolizumab show high effectiveness, but complete remission remains unattainable for certain patients.

The partial improvement observed in some patients indicates that disease persistence may involve additional mechanisms like neuropathic pathways. Some patients remain unresponsive to treatment because of their genetic makeup or unique immune system characteristics [3]. The future course of PN treatment with biologics remains uncertain as it's unknown whether patients can stop therapy after prolonged remission without relapsing or if they need permanent treatment to avoid disease recurrence. Patients face considerable difficulties when trying to obtain these treatments. The high cost of biologic therapies means they can reach tens of thousands of dollars annually, and many patients from less-developed healthcare systems struggle to get these medications for extended periods. Optimal treatment remains inaccessible for patients in high-income nations due to insurance restrictions. Wider access through formulary inclusion, patient support programs, and future biosimilar development can help lessen these disparities. Health equity challenges need immediate attention since PN affects older adults and African American patients more severely, and these groups already encounter numerous systemic healthcare obstacles. Research must conduct head-to-head clinical trials and combination therapy studies to determine effective treatment strategies [39,40].

The medical question persists whether combining an IL-31 inhibitor with an IL-4/IL-13 blocker will lead to additional therapeutic advantages compared to using a single pathway inhibitor. Research focused on biomarkers takes precedence because finding predictive markers allows clinicians to assign patients to the best therapies while minimizing treatment delays and expenses. Further investigation is needed to understand adjunctive therapies like neuropathic itch treatments and physical interventions to decrease nodule fibrosis. Long-term safety monitoring remains crucial. The current safety profile for IL-31 and IL-4/IL-13 blockade treatment appears acceptable, but long-term application may expose unusual or unforeseen adverse effects. Chronic IL-31 suppression may affect mood pathways and immune function, yet no problems have emerged. Continuous pharmacovigilance and post-marketing research activities are vital for maintaining drug safety and therapeutic effectiveness. The potential of biologic therapy in dermatology and PN stands as exceptionally promising. Future therapeutic options may include several approved biologics, like anti-OSMRβ agents and KIT inhibitors, which will enable patient-specific treatment decisions based on their unique disease characteristics.

Early biologic treatment holds the promise of disease modification by controlling symptoms and preventing the progression and chronicity of PN, which stops the itch-scratch cycle before permanent neuroplastic changes develop. Future research may lead to the subdivision of PN into specific endotypes, which will benefit from targeted treatments following the personalized protocols established for asthma and chronic urticaria. Understanding treatments for PN will shape how other persistent itching conditions like lichen simplex chronicus and non-PN chronic prurigo are managed, pushing forward advancements in itch medicine. The treatment landscape of PN has undergone a significant transformation through monoclonal antibodies, which allow many patients to remission from a previously debilitating condition. Research initiatives combined with clinical advances and expanded access programs must continue to develop practical treatment approaches to benefit every patient from these medical developments. Recent advancements in treatment indicate that PN will transition from an "untreatable" disease to a "well-controlled" condition as precision medicine advances dermatology.

Author Contributions

Conceptualization, C.P.; methodology, C.P.; software, C.P.; validation, C.P., A.H., and A.G.; formal analysis, C.P. and A.H.; investigation, C.P. and A.H.; resources, C.P.; data curation, C.P.; writing—original draft preparation, C.P. and A.H.; writing—review and editing, A.G. and C.P..; visualization, C.P.; supervision, A.G.; project administration, C.P. All authors have read and agreed to the published version of the manuscript.

Funding

This research received no external funding.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Data is contained within the article.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. Shao Y, Wang D, Zhu Y, Xiao Z, Jin T, et al. (2023) Molecular mechanisms of pruritus in prurigo nodularis. Front Immunol 14: 1301817.
2. Zeidler C, Ständer S (2016) The pathogenesis of Prurigo nodularis – 'Super-Itch' in exploration. Eur J Pain 20(1): 37-40.
3. Liao V, Cornman HL, Ma E, Kwatra SG (2024) Prurigo nodularis: new insights into pathogenesis and novel therapeutics. Br J Dermatol 190(6): 798-810.
4. Girolomoni G, Maurelli M, Gisondi P (2022) The emerging role of the neuroimmune cytokine interleukin-31 in chronic inflammatory skin diseases. Ital J Dermatol Venerol 157(4): 306-312.
5. Labib A, Ju T, Vander Does A, Yosipovitch G (2022) Immunotargets and therapy for prurigo nodularis. Immunotargets Ther 11: 11-21.
6. Sonkoly E (2022) Reversal of the disease signature in prurigo nodularis by blocking the itch cytokine. J Allergy Clin Immunol 149(4): 1213-1215.

7. Sofen H, Bissonnette R, Yosipovitch G, Silverberg JI, Tyring S, et al. (2023) Efficacy and safety of vixarelimab, a human monoclonal oncostatin M receptor β antibody, in moderate-to-severe prurigo nodularis: a randomised, double-blind, placebo-controlled, phase 2a study. EClinicalMed 57: 101826.
8. Ju T, Labib A, Nattkemper L, Sarah Engle, Autum Auxier, et al. (2023) Serum interleukin-13 and caspase 8 are elevated in prurigo nodularis. Acta Derm Venereol 103: adv00861.
9. Chen CH, Hu SCS (2024) Recent advances in treatment of prurigo nodularis. Dermatol Sin 42(3): 183-193.
10. Bader K (2025) FDA Approves Nemolizumab for the Treatment of Prurigo Nodularis. Available online: https://www.dermatologytimes.com/view/fda-approves-nemolizumab-for-the-treatment-of-prurigo-nodularis.
11. Yokozeki H, Murota H, Matsumura T, Komazaki H (2024) Efficacy and safety of nemolizumab and topical corticosteroids for prurigo nodularis: results from a randomized double-blind placebo-controlled phase II/III clinical study in patients aged ≥13 years. Br J Dermatol 191(2): 200-208.
12. Yosipovitch G, Ständer S, Metz M, Pink AE, Silverberg JI, et al. (2024) Nemolizumab monotherapy improves itch, sleep disturbance, and skin lesions in patients with moderate-to-severe prurigo nodularis: pooled analyses from OLYMPIA 1 and OLYMPIA 2 phase 3 studies. Br J Dermatol 191(2): ljae266.046.
13. Nilforoushzadeh MA, Heidari N, Ghane Y, Heidari A, Hajikarim-Hamedani A, et al. (2024) A systematic review of interleukin-31 inhibitors in the treatment of prurigo nodularis. Inflammopharmacol 32(2): 991-1003.
14. Ständer S, Yosipovitch G, Legat FJ, Reich A, Paul C, et al. (2023) 436 Nemolizumab monotherapy was associated with significant improvements in prurigo activity score in adult patients with moderate-to-severe prurigo nodularis: results from a phase 3 trial (OLYMPIA 2). Br J Dermatol 188(3).
15. Ständer S, Yosipovitch G, Lacour JP, Legat FJ, Paul C, et al. (2022) Nemolizumab efficacy in prurigo nodularis: onset of action on itch and sleep disturbances. J Eur Acad Dermatol Venereol 36(10): 1820-1825.
16. Ständer S, Yosipovitch G, Legat FJ, Reich A, Paul C, et al. (2025) Efficacy and Safety of Nemolizumab in Patients With Moderate to Severe Prurigo Nodularis: The OLYMPIA 1 Randomized Clinical Phase 3 Trial. JAMA Dermatol 161(2): 147-156.
17. Kwatra SG, Yosipovitch G, Legat FJ, Reich A, Paul C, et al. (2023) Phase 3 Trial of Nemolizumab in Patients with Prurigo Nodularis. N Engl J Med 389(17): 1579-1589.
18. Brooks SG, Yosipovitch G (2024) A critical evaluation of nemolizumab for prurigo nodularis. Expert Rev Clin Immunol 20(6): 577-587.
19. Yosipovitch G, Kim BS, Kwatra SG, Mollanazar NK, Ständer S, et al. (2024) Dupilumab improves pruritus and skin lesions in patients with prurigo nodularis: Pooled results from 2 phase 3 trials (LIBERTY-PN PRIME and PRIME2). JAAD Int 16: 163-174.
20. (2025) US Food and Drug Administration. FDA approves first treatment for prurigo nodularis. Available online: https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-first-treatment-prurigo-nodularis (accessed on March 18, 2025).
21. Harb H, Chatila TA (2020) Mechanisms of Dupilumab. Clin Exp Allergy 50(1): 5-14.
22. Yosipovitch G, Mollanazar N, Ständer S, Kwatra SG, Kim BS, et al. (2023) Dupilumab in patients with prurigo nodularis: two randomized, double-blind, placebo-controlled phase 3 trials. Nat Med 29: 1180-1190.
23. Paganini C, Talamonti M, Maffei V, Di Raimondo C, Bianchi L, et al. (2024) Dupilumab for Treatment of Prurigo Nodularis: Real-Life Effectiveness for up to 84 Weeks. J Clin Med 13(3): 878.
24. Silverberg JI, Irvine AD, Foley P, Del Rosso JQ, Puig L, et al. (2025) Comparative efficacy of lebrikizumab, dupilumab, and tralokinumab in maintaining treatment response in atopic dermatitis at varying treatment continuance rates. Skin 9(1): s519.
25. Honigman AD, Oo HP, Macdonell R, Kern JS (2024) The safety and efficacy of dual biological therapy: dupilumab and fremanezumab. Australas J Dermatol 65(3): e63-e65.
26. Yook HJ, Lee JH (2024) Prurigo Nodularis: Pathogenesis and the Horizon of Potential Therapeutics. Int J Mol Sci 25(10): 5164.
27. Akhtar S, Ahmad F, Alam M, Ansari AW, Uddin S, et al. (2024) Interleukin-31: the inflammatory cytokine connecting pruritus and cancer. Front Biosci 29(9): 312.
28. Metz M, Ständer S, Moiin A, Nattkemper L, Bloom BJ, et al. (2024) Barzolvolimab demonstrates safety and clinically meaningful activity as early as two weeks in moderate to severe prurigo nodularis. J Am Acad Dermatol 91: AB140.
29. Labib A, Ju T, Yosipovitch G (2022) Managing atopic dermatitis with lebrikizumab – the evidence to date. Clin Cosmet Investig Dermatol 15: 1065-1072.
30. Armstrong AW, Augustin M, Bauer AS, Bissonnette R, Blauvelt A, et al. (2024) Advances in atopic dermatitis and chronic hand eczema: delgocitinib and tralokinumab. Dermatol Am J, p. 2-12.
31. Kwatra SG, Bordeaux ZA, Parthasarathy V, Kollhoff AL, Alajmi A, et al. (2024) Efficacy and Safety of Abrocitinib in Prurigo Nodularis and Chronic Pruritus of Unknown Origin: A Nonrandomized Controlled Trial. JAMA Dermatolog 160(7): 717-724.
32. Kwatra SG, Ständer S, Yosipovitch G, Kim BS, Levit NA, et al. (2025) Pathophysiology of Prurigo Nodularis: Neuroimmune Dysregulation and the Role of Type 2 Inflammation. J Invest Dermatol 145(2): 249-256.
33. Hughes JDM, Woo TE, Belzberg M, Khanna R, Williams KA, et al. (2020) Association between Prurigo Nodularis and Etiologies of Peripheral Neuropathy: Suggesting a Role for Neural Dysregulation in Pathogenesis. Medicines 7(1): 4.
34. Ständer S, Spellman MC, Kwon P, Yosipovitch G (2019) The NK1 receptor antagonist serlopitant for treatment of chronic pruritus. Expert Opin Investig Drugs 28(8): 659-666.
35. Ständer S, Yosipovitch G, Legat FJ, Lacour JP, Paul C, et al. (2020) Trial of Nemolizumab in Moderate-to-Severe Prurigo Nodularis. N Engl J Med 382(8): 706-716.
36. Ma F, Gharaee-Kermani M, Tsoi LC, Plazyo O, Chaskar P, et al. (2024) Single-cell profiling of prurigo nodularis demonstrates immune-stromal crosstalk driving profibrotic responses and reversal with nemolizumab. J Allergy Clin Immunol 153(1): 146-160.
37. Gil-Lianes J, Morgado-Carrasco D, Riquelme-Mc Loughlin C (2024) Treatment of chronic prurigo with upadacitinib: A case series. J Eur Acad Dermatol Venereol 38(1): e106-e109.
38. Müller S, Bieber T, Ständer S (2022) Therapeutic potential of biologics in prurigo nodularis. Expert Opin Biol Ther 22(1): 47-58.
39. Li W, Pi Y, Xu J (2025) Association between atopic dermatitis and prurigo nodularis: a systematic review and meta-analysis. Int J Dermatol 64(2): 282-286.
40. Ranpariya M, Zaino ML, McCampbell LE, Patel T, Feldman SR, et al. (2024) Non-systemic medication for the treatment of prurigo nodularis: a systematic review. J Cutan Med Surg 28(2): 173-177.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2025.62.009685

Calista Persson. Biomed J Sci & Tech Res

Submission Link: https://biomedres.us/submit-manuscript.php