LOUISIANA BLUE

nemolizumab-ilto (Nemluvio™)

Policy # 00914
Original Effective Date: 03/01/2025
Current Effective Date: 03/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Prurigo Nodularis

Based on review of available data, the Company may consider nemolizumab-ilto (Nemluvio™)‡ for the treatment of prurigo nodularis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for nemolizumab-ilto (Nemluvio) for the treatment of prurigo nodularis will be considered when the patient selection criteria are met:

Initial

- Patient has a diagnosis of prurigo nodularis; AND
- Patient has greater than or equal to 20 prurigo nodularis nodular lesions; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient is 18 years of age or older; AND
- Patient has experienced pruritus for greater than or equal to 6 weeks; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient's pruritus is categorized as severe according to prescriber; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient meets one of the following:
  - Patient's prurigo nodularis is NOT medication induced or secondary to a non-dermatologic condition such as neuropathy or a psychiatric disease; OR
  - Patient has a secondary cause of prurigo nodularis that has been identified and adequately managed, yet symptoms of prurigo nodularis still persist; AND

  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

- Patient has tried and failed (e.g., intolerance or inadequate response) a GENERIC medium to very high potency topical corticosteroid product (e.g., betamethasone valerate, desoximetasone, fluocinolone acetonide, fluticasone propionate, hydrocortisone butyrate, mometasone furoate, prednicarbate, triamcinolone acetonide, trianex, triderm, amcinonide, augmented betamethasone dipropionate, apexicon E, betamethasone dipropionate, diflorasone diacetate, fluocinonide, fluocinonide E, clobetasol emollient, clobetasol propionate, clodan, cormax, diflorasone diacetate, and halobetasol propionate) for at least TWO consecutive weeks unless there is clinical evidence or patient history that suggest the use of these products will be ineffective or cause an adverse reaction to the patient; AND
- Patient has tried and failed (e.g., intolerance or inadequate response) dupilumab (Dupixent®)‡ unless there is clinical evidence or patient history that suggests the use of dupilumab (Dupixent) will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- The requested medication will NOT be used in combination with other monoclonal antibodies typically used for the treatment of prurigo nodularis (e.g., dupilumab [Dupixent]).

Continuation

- Patient has received an initial authorization; AND
- Patient has received at least 6 months of therapy with the requested drug; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has had a clinically meaningful beneficial response to Nemluvio therapy as compared to their baseline status (before Nemluvio therapy) as evidenced by ONE or more of the following:
  - Reduction in pruritus severity
  - Decrease in number of prurigo nodularis nodules
  - Reduced nodular size

  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

Atopic Dermatitis

Based on review of available data, the Company may consider nemolizumab-ilto (Nemluvio) for the treatment of atopic dermatitis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for nemolizumab-ilto (Nemluvio) for the treatment of atopic dermatitis will be considered when the patient selection criteria are met:

Initial

- Patient has a diagnosis of moderate to severe atopic dermatitis; AND
- Patient is 12 years of age or older; AND

- Patient has had chronic atopic dermatitis for at least 6 months; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has atopic dermatitis involvement estimated to be ≥ 10% of the body surface area (BSA) according to the prescribing physician; AND
  *(Note: This specific patient selection criterion is an additional Company requirement, based on clinical trials, for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has tried and failed (e.g., intolerance or inadequate response) at least ONE prescription GENERIC topical corticosteroid, unless there is clinical evidence or patient history that suggests the use of ONE prescription GENERIC topical corticosteroid will be ineffective or cause an adverse reaction to the patient; AND
- Patient has tried and failed (e.g., intolerance or inadequate response) GENERIC tacrolimus ointment OR GENERIC pimecrolimus cream, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
- Patient has tried and failed (e.g., intolerance or inadequate response) TWO of the following after at least 3 months of therapy with EACH product: dupilumab (Dupixent), tralokinumab-ldrm (Adbry™)‡, or upadacitinib (Rinvoq®)‡ unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Nemluvio will be used in combination with a topical corticosteroid and/or topical calcineurin inhibitor; AND
- Requested drug is NOT being used in combination with other monoclonal antibodies (e.g., tralokinumab-ldrm [Adbry]) or JAK (janus kinase) inhibitors (e.g., upadacitinib [Rinvoq], ruxolitinib [Opzelura™]‡, abrocitinib [Cibinqo™]‡) typically used to treat atopic dermatitis.

Continuation

- Patient has received and initial authorization; AND
- Patient has received at least 6 months of therapy with the requested drug; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has been adherent to the requested drug and other medications for the condition being treated; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

- Patient has had a clinically meaningful beneficial response to Nemluvio therapy as compared to their baseline status (before Nemluvio therapy) as evidenced by TWO or more of the following:
    - Reduction in disease severity (e.g., erythema, dryness, edema/papulation, excoriations, lichenification, oozing/crusting)
    - Reduction in the frequency or intensity of pruritus
    - Reduction in the frequency of disease exacerbations/flares
    - Reduction in the BSA with atopic dermatitis involvement (a 20% reduction in percent BSA involved over baseline)
    - Improvement in overall patient quality of life (e.g., improved sleep, less depression or anxiety, etc.); AND

  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT being used in combination with other monoclonal antibodies (e.g., tralokinumab-ldrm [Adbry]) or JAK inhibitors (e.g., upadacitinib [Rinvoq], ruxolitinib [Opzelura], abrocitinib [Cibinqo]) typically used to treat atopic dermatitis.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of nemolizumab-ilto (Nemluvio) when ANY of the following criteria for the requested diagnosis are NOT met to be **not medically necessary**:**

- Prurigo Nodularis
    - Patient has greater than or equal to 20 prurigo nodularis nodular lesions
    - Patient has experienced pruritus for greater than or equal to 6 weeks
    - Patient's pruritus is categorized as severe
    - Patient's prurigo nodularis is NOT medication induced or secondary to a non-dermatologic condition such as neuropathy or a psychiatric disease, OR Patient has a secondary cause of prurigo nodularis that has been identified and adequately managed, yet symptoms of prurigo nodularis still persist
    - Patient has tried and failed a GENERIC medium to very high potency topical corticosteroid product (e.g., betamethasone valerate, desoximetasone, fluocinolone acetonide, fluticasone propionate, hydrocortisone butyrate, mometasone furoate, prednicarbate, triamcinolone acetonide, trianex, triderm, amcinonide, augmented betamethasone dipropionate, apexicon E, betamethasone dipropionate, diflorasone diacetate, fluocinonide, fluocinonide E, clobetasol emollient, clobetasol propionate, clodan, cormax, diflorasone diacetate, and halobetasol propionate) for at least TWO consecutive weeks
    - Patient has tried and failed dupilumab (Dupixent)
    - For continuation requests: Patient has received at least 6 months of therapy with the requested drug

    - For continuation requests: Patient has had a clinically meaningful beneficial response to Nemluvio therapy as compared to their baseline status (before Nemluvio therapy) as evidenced by ONE or more of the following:
        - Reduction in pruritus severity
        - Decrease in number of prurigo nodularis nodules
        - Reduced nodular lesion size
- Atopic Dermatitis
    - Patient has had chronic atopic dermatitis for at least 6 months
    - Patient has atopic dermatitis involvement estimated to be ≥ 10% of the BSA according to the prescribing physician
    - Patient has tried and failed (e.g., intolerance or inadequate response) TWO of the following after at least 3 months of therapy with EACH product: dupilumab (Dupixent), tralokinumab-ldrm (Adbry), or upadacitinib (Rinvoq)
    - For continuation requests: Patient has received at least 6 months of therapy with the requested drug
    - For continuation requests: Patient has been adherent to the requested drug and other medications for the condition being treated
    - For continuation requests: Patient has had a clinically meaningful beneficial response to Nemluvio therapy as compared to their baseline status (before Nemluvio therapy) as evidenced by TWO or more of the following:
        - Reduction in disease severity (e.g., erythema, dryness, edema/papulation, excoriations, lichenification, oozing/crusting)
        - Reduction in the frequency or intensity of pruritus
        - Reduction in the frequency of disease exacerbations/flares
        - Reduction in the BSA with AD involvement (a 20% reduction in percent BSA involved over baseline)
        - Improvement in overall patient quality of life (e.g., improved sleep, less depression or anxiety, etc.)

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of nemolizumab-ilto (Nemluvio) when the patient selection criteria are not met (EXCEPT those denoted as **not medically necessary****) to be **investigational.***

Based on review of available data, the Company considers the use of nemolizumab-ilto (Nemluvio) for any non-FDA approved indication to be **investigational.***

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Background/Overview

Nemluvio is an interleukin-31 receptor antagonist indicated for the treatment of adults with prurigo nodularis and for the treatment of adults and pediatric patients 12 years of age and older with moderate to severe atopic dermatitis in combination with topical corticosteroids and/or topical calcineurin inhibitors. Nemluvio is available in a single-dose prefilled pen containing 30 mg of nemolizumab-ilto. The recommended dose for prurigo nodularis for adult patients weighing less than 90 kg is an initial dose of 60 mg subcutaneously, followed by 30 mg given subcutaneously every 4 weeks. For adult patients weighing more than 90 kg, the recommended dose is 60 mg subcutaneously, followed by 60 mg given subcutaneously every 4 weeks. For atopic dermatitis, the recommended dose is an initial dose of 60 mg, followed by 30 mg given every 4 weeks. Nemluvio can be self-injected by the patient after receiving proper training on preparation and administration.

Prurigo Nodularis

Prurigo nodularis (PN) is an uncommon skin disorder that is characterized by symmetrically distributed multiple, firm, pruritic nodules. The exact pathogenesis of the disorder is unclear. PN typically presents with firm, dome-shaped nodules that range in size and can be flesh-colored, erythematous, brown, or black. They often range in number from just a few to hundreds of lesions. Another core symptom of PN is pruritus lasting greater than or equal to 6 weeks that has led to signs of repeated scratching, picking, or rubbing. PN can occur all over the body, but the face, palms of the hand, soles of the feet, and genitalia are rarely affected. PN has a profound impact on a patient's quality of life, often due to sleep deprivation, depression, and anxiety. Several medical conditions are associated with PN such as atopic dermatitis, chronic kidney disease, diabetes, heart failure, hepatitis B or C virus, HIV, and non-Hodgkin lymphoma. When diagnosing PN, it is recommended for clinicians to do a full review of systems, especially in patients who do not have a history of a pruritic skin condition, to assess if there is a systemic disease or malignancy possibly causing PN. Treatment goals for PN include reducing pruritus, interrupting the itch-scratch cycle, and completely healing PN lesions. Several recommended therapies are off-label treatments that include gentle skin care, antipruritic emollients, topical corticosteroids, topical calcineurin inhibitors, topical capsaicin, neuromodulators, antidepressants, phototherapy, and immunosuppressants. Nemluvio is the second agent, after Dupixent, to be approved for PN.

Atopic Dermatitis

Atopic dermatitis, the most common type of a group of conditions known as eczema, is a chronic skin condition that causes dry, inflamed, and itchy skin. It commonly affects both children and adults. There are various treatment options for atopic dermatitis, including first line agents such as topical corticosteroids (many of which are in generic form) and topical immunomodulatory agents such as generic tacrolimus and generic pimecrolimus. For those that are refractory to topical therapies, systemic immunomodulatory agents are an option for therapy.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Nemluvio is indicated for the treatment of adults with prurigo nodularis and for the treatment of adults and pediatric patients 12 years of age and older with moderate to severe atopic dermatitis in combination with topical corticosteroids and/or calcineurin inhibitors when the disease is not adequately controlled with topical prescription therapies.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Prurigo Nodularis

Nemluvio was studied in two randomized, double-blind, placebo-controlled trials (OLYMPIA 1 and OLYMPIA 2) that enrolled a total of 560 adult subjects with prurigo nodularis (PN). Disease severity was defined using an Investigator's Global Assessment (IGA) in the overall assessment of prurigo nodularis nodules on a severity scale of 0 to 4. The IGA is a 5-category scale, including "0 = clear", "1 = almost clear", "2 = mild", "3 = moderate" or "4 = severe" indicating the investigator's overall assessment of the pruriginous nodules. The peak pruritus numeric rating scale (PP-NRS) score is a weekly average of daily PP-NRS scores on an 11-point scale from 0-10 that assesses the maximal intensity of pruritus in the last 24 hours with 0 being no itch and 10 being worst itch imaginable. Subjects enrolled in these two trials had an IGA score ≥ 3, severe pruritus as defined by a weekly average of a PP-NRS score of ≥ 7 on a scale of 0 to10, and greater than or equal to 20 nodular lesions. OLYMPIA 1 and OLYMPIA 2 assessed the effect of Nemluvio on the signs and symptoms of PN, targeting improvement in skin lesions and pruritus over 16 weeks. In OLYMPIA 1, subjects were extended up to 24 weeks of treatment.

Subjects weighing less than 90 kg in the Nemluvio group received subcutaneous injections of Nemluvio 60 mg at week 0, followed by 30 mg injections every 4 weeks. Subjects weighing 90 kg or more in the Nemluvio group received subcutaneous injections of Nemluvio 60 mg at week 0 and every 4 weeks.

Efficacy was assessed with the proportion of subjects with an improvement of ≥ 4 from baseline in PP-NRS, the proportion of subjects with an IGA of 0 (Clear) or 1 (Almost Clear) and a ≥ 2-point improvement from baseline, the proportion of subjects who achieved a response in both PP-NRS and IGA per the criteria described above, and the proportion of subjects with PP-NRS < 2.

In OLYMPIA 1, 22% of patients experienced improvement by 4 or more points from baseline in PP-NRS and concurrently achieved an IGA score of 0 or 1 compared to 2% of patients receiving

placebo. In OLYMPIA 2, the results were 25% for the Nemluvio group and 4% in the placebo group, respectively. The proportion of patients who achieved an IGA score of 0 or 1 was 26% of patients in OLYMPIA 1 and 38% of patients in OLYMPIA 2 who received Nemluvio, compared to 7% of patients receiving placebo in OLYMPIA 1 and 11% of patients receiving placebo in OLYMPIA 2. In OLYMPIA 1, 56% of patients receiving Nemluvio achieved an improvement by 4 or more points from baseline in the PP-NRS score compared to 16% of patients receiving placebo. In OLYMPIA 2, 49% of patients receiving Nemluvio achieved an improvement by 4 or more points from baseline in the PP-NRS score compared to 16% of patients receiving placebo. In OLYMPIA 1 and OLYMPIA 2, the proportion of patients with a PP-NRS less than 2 was 32% and 31%, respectively, of those receiving Nemluvio compared 4% and 7%, respectively, of those receiving placebo.

Atopic Dermatitis
Nemluvio was studied in two randomized, double-blind, placebo-controlled trials (ARCADIA 1 and ARCADIA 2) that enrolled a total of 1728 subjects 12 years of age and older with moderate-to-severe atopic dermatitis not adequately controlled by topical treatments. Disease severity was defined by an Investigator's Global Assessment (IGA) score of 3 (moderate) and 4 (severe) in the overall assessment of atopic dermatitis, an Eczema Area and Severity Index (EASI) score of ≥ 16, a minimum body surface area (BSA) involvement of ≥ 10%, and a Peak Pruritus Numeric Rating Scale (PP-NRS) score of ≥ 4.

Subjects in the Nemluvio group received initial subcutaneous injections of Nemluvio 60 mg, followed by 30 mg injections every 4 weeks. Concomitant low and/or medium potency TCS and/or TCI were administered for at least 14 days prior to baseline and continued during the trial. Based on disease activity, these concomitant therapies could be tapered and/or discontinued at investigator discretion.

After 16 weeks, subjects achieving either EASI-75 or IGA success continued into the trial maintenance period for another 32 weeks to evaluate the maintenance of response achieved at Week 16. Nemluvio responders were re-randomized to either Nemluvio 30 mg every 4 weeks, Nemluvio 30 mg every 8 weeks, or placebo every 4 weeks (all groups continued background TCS/TCI). Subjects randomized to placebo in the initial treatment period who achieved the same clinical response at Week 16 continued to receive placebo every 4 weeks.

Both ARCADIA 1 and ARCADIA 2 assessed the co-primary endpoints of:
- Proportion of subjects with an IGA success (defined as an IGA of 0 [clear] or 1 [almost clear] and a ≥ 2-point reduction from baseline) at Week 16
- Proportion of subjects with EASI-75 (≥ 75% improvement in EASI from baseline) at Week 16

In ARCADIA 1, 36% of patients who received Nemluvio achieved an IGA score of 0 (clear) or 1 (almost clear) versus 25% with placebo at Week 16; 38% of patients who received Nemluvio

achieved IGA scores of 0 or 1 in ARCADIA 2 versus 26% with placebo at Week 16. Also at Week 16, the percentage of patients who achieved ≥ 75% improvement in the EASI-75 was 44% and 42% for those receiving Nemluvio in ARCADIA 1 and ARCADIA 2, respectively, compared with 29% and 30% of patients receiving placebo. In both trials, of the number of patients who were IGA responders at Week 16, 63% of patients receiving a maintenance dose of Nemluvio every 4 weeks and 64% of patients receiving Nemluvio every 8 weeks maintained an IGA score of 0 or 1 at Week 48 compared to 55% of patients receiving placebo. In both trials, of the number of patients who were EASI-75 responders at Week 16, 75% of patients receiving a maintenance dose of Nemluvio every 4 weeks and 77% of patients receiving Nemluvio every 8 weeks maintained an EASI-75 at Week 48 compared to 65% of patients receiving placebo.

References

1. Nemluvio [package insert]. Galderma Laboratories, L.P. Dallas, Texas. Updated December 2024.
2. Nemluvio Drug Evaluation. Express Scripts. Updated August 2024.
3. Prurigo nodularis. UpToDate. Accessed February 2023.
4. Elmariah S, Kim B, Berger T, et al. Practical approaches for diagnosis and management of prurigo nodularis: United States expert panel consensus. J Am Acad Dermatol. 2021;84(3):747-760.
5. Treatment of atopic dermatitis (eczema). UpToDate. Accessed January 2025.

Policy History

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02/06/2025 Medical Policy Committee review
02/12/2025 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 02/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.