BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

NEMLUVIO® (nemolizumab-ilto) Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Nemluvio (nemolizumab-ilto) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Dermatologist

2. Individual has a confirmed diagnosis of **ONE** of the following:
   a. Individual 18 years of age or older with **prurigo nodularis (PN)**

   b. Individual 12 years of age or older with **moderate-to-severe atopic dermatitis (AD)** in combination with topical corticosteroids and/or calcineurin inhibitors when the disease is not adequately controlled with topical prescription therapies

3. Individual has **ONE** of the following:
    a. **For prurigo nodularis BOTH** of the following:
        i. A Worst Itch-Pruritus Numeric Rating Scale of 7 or more (see Definitions section)
        ii. At least 20 or more nodular/pruriginous lesions on both legs, and/or both arms and/or trunk which correspond to an IGA stage of 3 or more (see Definitions section)
    b. **For moderate to severe atopic dermatitis ALL** of the following: (see Definitions section)
        i. Body surface area (BSA) involvement of at least 10%
        ii. Investigator Global Assessment (IGA) score of at least 3
        iii. Eczema Area and Severity Index (EASI) score of at least 16
        iv. Peak Pruritus Numeric Scale (PP-NRS) score of qt least 4

4. Individual has received and completed **ALL** age-appropriate vaccinations recommended by current national guidelines as needed before initiation of treatment and with continued monitoring of the individual as clinically appropriate

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **ONE** the following:
    a. **For prurigo nodularis ONE** of the following:
        i. For limited number of nodular lesions there is a history of failing a 2-week course of very high potency topical corticosteroid (TCS) with or without intralesional corticosteroid injections or when TCS are not medically advisable (see Definitions section)
        ii. Widespread/recalcitrant disease with documented failure (used for 3 or more consecutive months), contraindication per FDA label, intolerance, or not a candidate for phototherapy with narrowband ultraviolet B (NBUVB)
    b. **For moderate to severe atopic dermatitis**
        i. At least a 2 consecutive month trial of **ONE** of the following **topical** treatments:
            1. Medium to high potency corticosteroid (such as triamcinolone acetonide 0.1%, mometasone furoate 0.1%, betamethasone dipropionate 0.05%, desoximetasone 0.05%, and others) choice of topical corticosteroid potency is based on the individual's age, body area involved, and degree of skin inflammation
            2. Calcineurin inhibitor (Protopic (tacrolimus) or Elidel (pimecrolimus))
            3. Phosphodiesterase 4 inhibitor (Eucrisa (crisaborole))
        ii. Individual has documented failure (used for > 3 consecutive months), contraindication per FDA label, intolerance, or is not a candidate for **Rinvoq** (upadacitinib) [adults & children 12 years or older]

7. **Request for use in prurigo nodularis or atopic dermatitis:** Individual has documented failure (used for > 3 consecutive months), contraindication per FDA label, intolerance, or is not a candidate for **Dupixent** (dupilumab)

8. Individual is not currently taking any other drugs that may cause a severe adverse reaction or a significant drug interaction that may require discontinuation

9. There is no concurrent use with Cinqair (reslizumab), Fasenra (benralizumab), Nucala (mepolizumab), Tezspire (tezepelumab), Xolair (omalizumab), Adbry (tralokinumab), Rinvoq (upadacitinib), Cibinqo (abrocitinib), or any other biologic therapy [e.g., rituximab (Rituxan and rituximab biosimilars), infliximab (Remicade and infliximab biosimilars), Enbrel (etanercept)]

10. Nemluvio is not being used concurrently with live vaccines

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Nemluvio (nemolizumab-ilto) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Dermatologist

2. Individual's condition has responded while on therapy with response defined as **ONE** of the following:
    a. **For prurigo nodularis TWO** of the following:
        i. Improvement (reduction) in WI-Pruritus NRS by ≥ 4 points
        ii. Achieved and maintains 0-5 nodules/pruriginous lesions which corresponds to an IGA stage of 0 or 1 and a ≥ 2-point improvement
        iii. Achieved and maintains both WI-Pruritus NRS and IGA as described in a & b
        iv. Achieved and maintains a WI-Pruritus of less than 2
    b. **For moderate to severe atopic dermatitis THREE** of the following:
        i. No evidence of disease progression
        ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use
        iii. Achieved and maintains a PGA score of "clear" or "almost clear" with at least a 2-grade or 30% improvement from baseline
        iv. Achieved and maintains at least 75% improvement in PASI (for plaque psoriasis) or EASI (for atopic dermatitis) over baseline
        v. Achieved and maintains a reduction in %BSA affected from baseline
        vi. Improvement in Numerical Rating Scale - Pruritus score for individual 12 years of age or older

3. Individual has been adherent with the medication

4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual is not currently taking any other drugs that may cause a severe adverse reaction or a significant drug interaction that may require discontinuation

6. There is no concurrent use with Cinqair (reslizumab), Fasenra (benralizumab), Nucala (mepolizumab), Tezspire (tezepelumab), Xolair (omalizumab), Adbry (tralokinumab), Rinvoq (upadacitinib), Cibinqo

(abrocitinib), or any other biologic therapy [e.g., rituximab (Rituxan and rituximab biosimilars), infliximab (Remicade and infliximab biosimilars), Enbrel (etanercept)]

7. Nemluvio is not being used concurrently with live vaccines

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Nemluvio (nemolizumab-ilto) is an interleukin-31 receptor antagonist, is a humanized monoclonal modified immunoglobulin G (IgG) antibody, indicated for the treatment of adults with prurigo nodularis. Nemluvio (nemolizumab-ilto) is also indicated 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.

Nemolizumab-ilto inhibits IL-31 signaling by binding selectively to IL-31 RA. IL-31 is a naturally occurring cytokine that is involved in pruritus, inflammation, epidermal dysregulation, and fibrosis. Nemolizumab-ilto inhibited IL-31-induced responses including the release of proinflammatory cytokines and chemokines.

Prurigo nodularis (PN) is an uncommon, chronic skin disorder affecting primarily older adults and is characterized by symmetrically distributed, multiple, firm, pruritic nodules. It occurs in patients with chronic severe pruritus and is frequently associated with a history of atopic dermatitis. PN is a distinctive reaction pattern that occurs from continuous scratching over a prolonged period of time. PN presents with firm, dome-shaped, itchy nodules that range in size from a few millimeters to several centimeters. They are often symmetrically distributed on the extensor surfaces of the arms and legs and on the trunk. The nodules can be flesh-colored, erythematous, or brown/black and range in number from few to hundreds. Pruritus is always severe and distressing. It can be paroxysmal, sporadic, or continuous and is worsened by heat, sweating, or irritation from clothing. Dupilumab is also indicated for the treatment of adult patients with prurigo nodularis (PN).

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by pruritus (itching), xerosis (skin dryness), and eczematous lesions whose features include erythema, infiltration/papulation, oozing with crusting, excoriations, and lichenification. AD may be managed with topical and systemic treatments, and phototherapy. Topical agents are the mainstay of AD therapy. Moisturizers are used to improve skin dryness and skin barrier dysfunction. Topical corticosteroids (TCS) are widely prescribed in adults and children for their anti-inflammatory effects. Topical calcineurin inhibitors (TCI) are effective for acute and chronic treatment in adults and children, particularly in selected sensitive anatomical areas. Crisaborole is a topical phosphodiesterase (PDE)-4 inhibitor with an acceptable safety profile in adults and children is most commonly used in the treatment of mild-to-moderate AD. Topical ruxolitinib (for adults & children older than 12 years) may be used for areas at high risk of

atrophy (e.g., face, skinfolds) may be an alternative to TCS. Topical roflumilast (for adults & children older than 6 years) and topical tapinarof (for adults & children older than 2 years) are also available.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Relative Potency of Selected Topical Corticosteroid Products:

Product	Dosage form	Strength
Category I – Very high potency		
Augmented betamethasone dipropionate	Gel, ointment	0.05
Clobetasol propionate	Ointment, gel, cream	0.05
Fluocinonide	Cream	0.1
Diflorasone diacetate	Ointment	0.05
Halobetasol propionate	Ointment, cream	0.05
Category II – High potency		
Amcinonide	Ointment, cream, lotion	0.1
Augmented betamethasone dipropionate	Cream, lotion	0.05
Betamethasone dipropionate	Ointment, cream	0.05
Betamethasone valerate	Ointment	0.1
Desoximetasone	Ointment, cream	0.25
Desoximetasone	Gel	0.05
Diflorasone diacetate	Ointment (emollient base), cream	0.05
Fluocinonide	Ointment, gel, cream	0.05
Halcinonide	Ointment, cream	0.1

Pruritus Numerical Rating Scale (NRS):
Numerical Rating Scale - Pruritus Resources (pruritussymposium.de) [Accessed October 09, 2021]

The NRS is comprised of one item and is represented by numbers 0 (“no itch”) to 10 (“worst imaginable itch”). Patients are asked to rate the intensity of their itch using this scale. It features high reliability and concurrent validity and is a popular choice for all patients due to its simple format. Time needed for completion: 1 minute. It has been validated in several languages.

- It can be interpreted as follows:
  - NRS 0 - no pruritus
  - NRS < 3 - mild pruritus
  - NRS ≥ 3 < 7 - moderate pruritus
  - NRS ≥ 7 < 9 - severe pruritus
  - NRS ≥ 9 - very severe pruritus

On a scale from 0 (no itch) to 10 (worst imaginable itch), how would you rate your itch overall (on average) during the past 24-hour? (Select number)										
0	1	2	3	4	5	6	7	8	9	10

Prurigo nodularis (PN):

Investigator Global Assessment (IGA) for stage of chronic prurigo (CPG), chronic nodular prurigo (CNPG) and signs of activity in chronic prurigo		
Score	Category	Description
IGA-NCPG stage		
0	Clear	No nodules (0 nodules)
1	Almost clear	Rare palpable pruriginous nodules (approximately 1–5 nodules)
2	Mild	Few palpable pruriginous nodules (approximately 6–19 nodules)
3	Moderate	Many palpable pruriginous nodules (approximately 20–100 nodules)
4	Severe	Abundant palpable pruriginous nodules (over 100 nodules)
IGA-CPG stage		
0	Clear	No pruriginous lesions (0 lesions)
1	Almost clear	Rare palpable pruriginous lesions (approximately 1–5 lesions)
2	Mild	Few palpable pruriginous lesions (approximately 6–19 lesions)
3	Moderate	Many palpable pruriginous lesions (approximately 20–100 lesions)
4	Severe	Abundant palpable pruriginous lesions (over 100 lesions)
IGA-CPG Activity		
0	Clear	No pruriginous lesions have excoriations or crusts
1	Almost clear	Very small proportion of pruriginous lesions have excoriations or crusts (up to approximately 10% of all pruriginous lesions)
2	Mild	Minority of pruriginous lesions have excoriations or crusts (approximately 11–25% of all pruriginous lesions)
3	Moderate	Many pruriginous lesions have excoriations or crusts (approximately 26–75% of all pruriginous lesions)
4	Severe	Majority of pruriginous lesions have excoriations or crusts (approximately 76–100% of all pruriginous lesions)

Investigator Global Assessment Scale (IGA):
Validated-Investigator-Global-Assessment-Scale_vIGA-AD_2017.pdf (eczemacouncil.org) [Accessed October 09, 2021]

The IGA score is selected using the morphologic descriptors that best describe the overall appearance of the lesions at a given time point. It is not necessary that all characteristics under Morphological Description be present.

Score	Morphological Description
0 – Clear	No inflammatory signs of atopic dermatitis (no erythema (reddening), no induration (hardening of soft tissue)/papulation, no lichenification (thick leathery skin), no oozing/crusting). Post-inflammatory hyperpigmentation and/or hypopigmentation may be present.

1 – Almost clear	Barely perceptible erythema, barely perceptible induration/papulation, and/or minimal lichenification. No oozing or crusting.
2 – Mild	Slight but definite erythema (pink), slight but definite induration/papulation, and/or slight but definite lichenification. No oozing or crusting.
3 – Moderate	Clearly perceptible erythema (dull red), clearly perceptible induration/papulation, and/or clearly perceptible lichenification. Oozing and crusting may be present.
4 – Severe	Marked erythema (deep or bright red), marked induration/papulation, and/or marked lichenification. Disease is widespread in extent. Oozing or crusting may be present.
Notes: 1. In indeterminate cases, use extent to differentiate between scores. For example: • Patient with marked erythema (deep or bright red), marked papulation and/or marked lichenification that is limited in extent (instead of widespread), would be considered "3 – Moderate". 2. Excoriations should not be considered when assessing disease severity	

EASI score | DermNet NZ

What is an EASI score?
An EASI score is a tool used to measure the extent (area) and severity of atopic eczema (Eczema Area and Severity Index). It takes a few minutes and experience to calculate it accurately.
EASI score does not include a grade for dryness or scaling. Include only inflamed areas.

Body regions
There are four body regions:

- Head and neck
  - Face occupies 33% (17% each side), neck 33% (17% front and back) and scalp 33% of the head and neck region
- Trunk (including genital area)
  - Front occupies 55% and back 45% of the trunk
- Upper limbs
  - Each arm occupies 50% of the upper limbs region (front or back of one arm is 25%)
- Lower limbs (including buttocks)
  - Each leg occupies 45% (front or back of one leg is 22.5%) and buttocks 10% of the lower limbs region

Area score
Area score is recorded for each of the four regions of the body. The area score is the percentage of skin affected by eczema for each body region.

Area score	Percentage of skin affected by eczema in each region
0	No active eczema in this region
1	1-9
2	10-29
3	30-49
4	50-69

5	70-89
6	90-100: the entire region is affected by eczema

Severity score
Severity score is recorded for each of the four regions of the body. The severity score is the sum of the intensity scores for four signs. The four signs are:

1. Redness (erythema, inflammation)
2. Thickness (induration, papulation, swelling—acute eczema)
3. Scratching (excoriation)
4. Lichenification (lined skin, furrowing, prurigo nodules—chronic eczema).

The *average* intensity of each sign in each body region is assessed as: none (0), mild (1), moderate (2) and severe (3).

Half scores are allowed. It may be difficult to assess redness in dark skin. If in doubt, increase the average redness score by one level. The 16 images below have been chosen as typical examples of different intensities of each sign.

Score	Intensity of redness, thickness/swelling, scratching. lichenification
0	None, absent
1	Mild (just perceptible)
2	Moderate (obvious)
3	Severe

Calculations
For each region, record the intensity for each of four signs and calculate the severity score.

- Severity score = redness intensity + thickness intensity + scratching intensity + lichenification intensity

For each region, multiple the severity score by the area score and by a multiplier. The multiplier is different for each body site.

- Head and neck: severity score x area score x 0.1 (in children 0–7 years, x 0.2)
- Trunk: severity score x area score x 0.3
- Upper limbs: severity score x area score x 0.2
- Lower limbs: severity score x area score x 0.4 (in children 0–7 years, x 0.3)

Add up the total scores for each region to determine the final EASI score. The minimum EASI score is 0 and the maximum EASI score is 72. A higher EASI score represents more severe disease.

IGAxBSA Severity Evaluation

- A practice-friendly alternative to the Eczema Area and Severity Index to (EASI) assess atopic dermatitis severity in children
- Studies have shown high and consistent agreement between IGA×BSA and EASI
- Suggested severity strata for IGA×BSA are:
    - Mild: 0-30
    - Moderate: >30-130

- Severe: >130-400

Numerical Rating Scale - Pruritus Resources (pruritussymposium.de)

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  NRS ≥ 7< 9 - severe pruritus
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Resources:

Nemluvio (nemolizumab-ilto) product information, revised by Galderma Laboratories, L.P. 08-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 21, 2024. **Prurigo nodularis**

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ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT03989349: A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Nemolizumab in Subjects With Moderate-to-Severe Atopic Dermatitis. Available from: http://clinicaltrials.gov. Last update posted August 14, 2024. Last verified August 2024. Accessed April 29, 2025.