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Subject: Nemolizumab-ilto (Nemluvio) Injection

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DESCRIPTION:

Nemolizumab-ilto (Nemluvio) is an interleukin-31 (IL-31) receptor antagonist approved in August 2024 by the US Food and Drug Administration (FDA) for the treatment of adults with prurigo nodularis. IL-31 has been identified as a cytokine responsible for stimulating pruritus. Nemolizumab is the first IL-31 receptor antagonist to be approved by the FDA, and it is the second drug to be approved for the treatment of prurigo nodularis. Dupilumab (Dupixent) was the first drug to be approved for prurigo nodularis in September 2022. In December 2024, the FDA approved a second indication for the treatment of adults and pediatric patients 12 years of age and 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. Nemolizumab is the first IL-31 receptor antagonist to be approved for AD. Nemolizumab is also in Phase 3 development for chronic kidney disease-associated pruritus.

Atopic Dermatitis

Atopic dermatitis (AD), also known as atopic eczema, is a chronic, pruritic inflammatory dermatosis affecting up to 25% of children and approximately 7% of adults. AD follows a relapsing course and is associated with elevated serum immunoglobulin (IgE) levels and a personal or family history of type I allergies, allergic rhinitis, and/or asthma. Onset is most common between 3 and 6 months of age, with approximately 60% of patients developing the eruption in the first year of life and 90% by age 5. While the majority of affected individuals have resolution of disease by adulthood, 10 to 30% do not, and a smaller percentage first develop symptoms as adults. AD has a complex pathogenesis involving genetic, immunologic, and environmental factors, which lead to a dysfunctional skin barrier and dysregulation of the immune system. Clinical findings include erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and lichenification. These clinical findings vary by patient age and chronicity of lesions. Pruritus is a hallmark of the condition that is responsible for much of the disease burden borne by

patients and their families. Typical patterns include facial, neck and extensor involvement in infants and children, flexure involvement in any age group, with sparing of groin and axillary regions.

Goals of treatment are to reduce symptoms (pruritus and dermatitis), prevent exacerbations, and minimize therapeutics risks. Despite its relapsing and remitting nature, the majority of patients with AD can achieve clinical improvement and disease control with topical emollient/moisturizer use and conventional topical therapies (including corticosteroids and calcineurin inhibitors). Moisturizers reduce signs, symptoms, and inflammation in AD, and can improve severity while also increasing time between flares. Moisturizers are considered generally safe and are strongly recommended to be used as part of a treatment regimen for AD, either as monotherapy or as concurrent use with pharmacologic treatments.

Topical therapies remain the mainstay of treatment due to their proven track record and generally favorable safety profile. They can be utilized individually or in combination with other topical, physical, and/or systemic treatments; as different classes of treatment have different mechanisms of action, combining therapies allows for the targeting of AD via multiple disease pathways. The American Academy of Dermatology (AAD) strongly recommends the following topical agents:

- Topical corticosteroids (TCS)
- Calcineurin inhibitors (TCIs) (e.g., tacrolimus, pimecrolimus)
- Topical phosphodiesterase (PDE)-4 inhibitors (e.g., crisaborole) [mild to moderate AD]
- Topical Janus kinase (JAK) inhibitors (e.g., ruxolitinib) [mild to moderate AD]

TCS are the most commonly utilized FDA-approved therapies in AD and are commonly used as first-line treatment for mild-to severe dermatitis in all skin regions. TCS target a variety of immune cells and suppress the release of proinflammatory cytokines. High to very high (super) potency TCS can be used to control flares and treat severe disease, while medium potency TCS are utilized for longer courses and as maintenance therapy. Lower potency TCS may be used, and it is important to consider the anatomical site (i.e., using lower potency agents on the face, neck, genitals, and body folds) and severity of the disease when choosing a steroid potency. Clinical trials assessing efficacy generally had a duration of 2 to 6 weeks, and response to TCS therapy should be evaluated by week 4 in clinical practice. Most studies of TCS in AD management involve twice daily application, but some studies (particularly for potent TCS) suggest once daily use may be sufficient. Traditionally, TCS were stopped once AD signs and symptoms of an AD flare were controlled. Maintenance in between AD flares with once to twice weekly use of TCS is another approach.

TCIs are a safe anti-inflammatory option for mild-to-severe AD, particularly when there is concern for adverse events secondary to corticosteroid use. Both tacrolimus and pimecrolimus have been shown to be effective in treating AD, but pimecrolimus may be more appropriate for patients who have milder disease or are sensitive to local reactions. Prescribing information for pimecrolimus cream and tacrolimus ointment indicate evaluation after 6 weeks if symptoms of AD do not improve for adults and pediatrics.

When AD is more severe or refractory to topical treatment, advanced treatment with phototherapy or systemic medications can be considered. Phototherapy is conditionally recommended by the AAD as a treatment for AD based on low certainty evidence. The AAD strongly recommends the following systemic therapies:

- Monoclonal antibodies (biologics) (e.g., dupilumab, tralokinumab)
- JAK inhibitors (e.g., upadacitinib, abrocitinib, baricitinib)

In a change from the 2014 AAD AD guidelines, the use of systemic antimetabolites such as methotrexate, immunosuppressants such as systemic corticosteroids, mycophenolate mofetil, azathioprine, and cyclosporine are now conditionally recommended for AD only in a small number of select patients due to low or very low certainty of evidence and need for monitoring. The most favored first-line systemic is dupilumab.

There is no clear consensus on how to operationalize a definition of the FDA indication for treatment of patients with "moderate to severe" AD. The severity of AD can vary substantially over time and, from a patient's perspective, can include a complex combination of intensity of itch, location, body surface area (BSA) involvement, and degree of skin impairment. Given the variability of patient phenotype and lack of familiarity among clinicians with scoring systems used in clinical trials, it is advisable to create a broad clinically relevant definition inclusive of multiple specific measures of disease intensity for example:

- One of the following:
    - Affected BSA greater than or equal to 10%
    - Investigator Global Assessment (IGA) greater than or equal to 3
    - Eczema Area and Severity Index (EASI) greater than or equal to 16

    OR
- One of the following:
    - Affected BSA greater than or equal to 10%
    - Involvement of body sites that are difficult to treat with prolonged topical corticosteroid therapy (e.g., hands, feet, face, neck, scalp, genitals/groin, skin folds)
    - Severe itch that has been unresponsive to topical therapies

<u>Efficacy</u>

Two randomized, double-blind, placebo-controlled trials (ARCADIA 1 [NCT03985943] and ARCADIA 2 [NCT03989349]) 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 greater than or equal to 16, a minimum body surface area (BSA) involvement of greater than or equal to 10%, and a Peak Pruritus Numeric Rating Scale (PP-NRS) score of greater than or equal to 4. Seventy (70)% of subjects had a baseline IGA score of 3 (moderate AD), and 30% of subjects had a baseline IGA score of 4 (severe AD). The baseline mean EASI score was 27.5 and the baseline mean weekly average PP-NRS was 7.1. Overall, 63% of subjects received other previous systemic treatments for AD.

Subjects in the Nemluvio group received initial subcutaneous injections of Nemluvio 60 mg, followed by 30 mg injections every 4 weeks until Week 16. Concomitant low and/or medium potency topical corticosteroids (TCS) and/or topical calcineurin inhibitors (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.

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 greater than or equal to 2-point reduction from baseline) at Week 16
- Proportion of subjects with EASI-75 (greater than or equal to 75% improvement in EASI from baseline) at Week 16

The efficacy results for ARCADIA 1 and ARCADIA 2 evaluating the initial treatment period with Nemluvio over 16 weeks are presented in the table below.

	ARCADIA 1			**ARCADIA 2**		
	Nemluvio + TCS/TCI	Placebo + TCS/TCI	Difference from Placebo (95% CI)	Nemluvio + TCS/TCI	Placebo + TCS/TCI	Difference from Placebo (95% CI)
Number of subjects randomized	620	321		522	265	
Proportion of subjects with IGA 0 or 1	36%	25%	12% (6%, 17%)	38%	26%	12% (6%, 19%)
Proportion of subjects with EASI-75	44%	29%	15% (9%, 21%)	42%	30%	12% (6%, 19%)

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.

Prurigo Nodularis

Prurigo nodularis (PN) is a skin disorder that is defined by the presence of chronic pruritus and multiple elevated, firm, and nodular lesions. PN is more common in older adults but can occur in children. The underlying cause of PN is unknown, but it appears neural and immunologic processes both play a role in its development. The nodules form in a subset of patients that have chronic pruritus, with the nodules forming in areas with continuous scratching over prolonged periods of time. There is significant disease burden associated with PN including sleep disruption, anxiety, and depression. The nodules are typically firm, dome-shaped, and itchy and range in size from millimeters to several centimeters. The nodules can range in color from flesh tones to brown/black and can range in number from a few to hundreds. The pruritis associated with PN can range from sporadic to continuous and generally the underlying cause is unknown. There are a number of conditions, both dermatologic and other diseases, that are associated with PN, such as atopic dermatitis, kidney disease, diabetes, and HIV.

The diagnosis of PN is generally one of exclusion. The American Academy of Dermatology (AAD) indicates that the diagnostic workup should include a clinical examination with a complete review of systems and assessment of PN severity, which should include both disease burden (e.g., quality of life, sleep disturbances) and pruritis intensity. The ADD notes three core features associated with PN:

- Presence of firm, nodular lesions
- Pruritus that lasts for at least 6 weeks
- History and/or signs of repeated scratching, picking, or rubbing

Management requires a multifaceted approach with a focus on reducing pruritis, interrupting the itch-scratch cycle, and healing lesions. General measures that should be used at baseline include gentle skin care, moisturizers, and antipruritic emollients. Treatment may need to address both the neural and immunologic components of pruritis based on patient signs and symptoms, and often involves the use of topical and systemic therapies. Most therapies for PN have not been adequately studied, and their evidence for use is based on small clinical trials, observational studies, and case reports.

Topical therapies are the initial treatment for limited disease. Topical corticosteroids (TCS) target the immunologic component of PN. The International Forum for the Study of Itch (IFSI) 2020 guideline on chronic prurigo including prurigo nodularis strongly recommends moderate to very potent topical corticosteroids on lesional skin. Intralesional corticosteroids may be directly injected into thicker lesions where required, but use should be limited to patients with less than 10 lesions. Topical calcineurin inhibitors and topical calcipotriol have also been used in patients who failed TCS therapy and a prolonged course of a topical immunomodulator is desired. Topical capsaicin, which targets the neural component of PN, has limited clinical evidence and tends to have short term efficacy.

Systemic therapies are used for widespread disease or disease refractory to topical therapy. Phototherapy is reasonably tolerated and addresses both the immunologic and neural components of PN. However, phototherapy combined with topical therapy will not be adequate for most patients, and the majority will require supplemental systemic therapy. Oral immunosuppressants, such as methotrexate and cyclosporine, have shown to reduce pruritis and heal lesions per limited data available. Methotrexate is generally preferred due to its more favorable side effect profile in comparison to cyclosporine, and cyclosporine should only be considered in more severe cases. Other systemic therapies that have shown to be less efficacious and treat the neural component of PN include thalidomide, gabapentin, pregabalin, antidepressants, aprepitant, and naltrexone. Since PN is a nonhistaminergic condition, antihistamines are unlikely to be effective and are not recommended.

Biologic agents are the first therapies to gain approval from the US Food and Drug Administration (FDA) for the treatment of PN. These immunomodulating drugs are believed to target molecules expressed by specific cell types that release a variety of itching mediators that directly or indirectly stimulate receptors on nerve endings in the skin. Biologic agents disrupt this cycle and have been proven to alleviate both pruritus and PN lesions.

<u>Efficacy</u>

Two randomized, double-blind, placebo-controlled trials (OLYMPIA 1 [NCT04501666] and OLYMPIA 2 [NCT04501679]) enrolled a total of 560 adult subjects with prurigo nodularis (PN). 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. 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 greater than or equal to 3, severe pruritus as defined by a weekly average of the PP-NRS score of greater than or equal to 7 on a scale of 0 to 10, and greater than or equal to 20 nodular lesions. Fifty-eight (58)% of subjects had a baseline IGA score of 3 (moderate PN), and 42% of subjects had a baseline IGA of 4 (severe PN). The baseline weekly average PP-NRS score was a mean of 8.5. Thirty-two (32)% of subjects had a history of atopy. In the OLYMPIA 2 trial, 78.5% of subjects had previously used topical corticosteroids for the treatment of PN.(5) In both trials, patients were prohibited from using other therapies for PN such as topical corticosteroids, topical calcineurin inhibitors, or systemic immunomodulators, unless they were required as a rescue medication at the discretion of the investigator.

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 greater than or equal to 4 from baseline in PP-NRS, the proportion of subjects with an IGA of 0 (Clear) or 1 (Almost Clear) and a greater than or equal to 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 less than 2.

	OLYMPIA 1			**OLYMPIA 2**		
	Nemluvio (n=190)	Placebo (n=96)	Difference from Placebo (95% CI)	Nemluvio (N=183)	Placebo (n=91)	Difference from Placebo (95% CI)
Proportion of subjects with both an improvement (reduction) of greater than or equal to 4 from baseline in PP-NRS and IGA 0 or 1	22%	2%	15% (8%, 21%)	25%	4%	22% (14%, 30%)
Proportion of subjects with IGA 0 or 1	26%	7%	15% (7%, 23%)	38%	11%	29% (19%, 38%)
Proportion of subjects with an improvement (reduction) of greater than or equal to 4 from baseline in PP-NRS	56%	16%	38% (27%, 48%)	49%	16%	34% (23%, 45%)
Proportion of subjects with PP-NRS less than 2	32%	4%	28% (20%, 36%)	31%	7%	26% (18%, 34%)

In both OLYMPIA 1 and OLYMPIA 2, statistically significant improvements in itch and PN skin lesions were observed at Week 16, with some subjects achieving this as early as Week 4. Examination of weight,

age, gender, race, history of atopy, and prior treatment did not identify meaningful differences in response to Nemluvio among these subgroups at Week 16.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of nemolizumab-ilto (Nemluvio) **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "6"):

1. **ONE** of the following ("a", "b", or "c"):
    a. The member has been treated with nemolizumab (starting on samples is not approvable) within the past 90 days
    b. The prescriber states the member has been treated with nemolizumab (starting on samples is not approvable) within the past 90 days **AND** is at risk if therapy is changed
    c. **BOTH** of the following ('i" and "ii"):
        i. Nemolizumab will be used for the treatment of an indication listed in the Table, and **ALL** of the indication-specific criteria are met
        ii. **EITHER** of the following if the member has an FDA-approved indication ("I" or "II"):
            I. The member's age is within FDA labeling for the requested indication for nemolizumab
            II. The prescriber has provided information in support of using nemolizumab for the member's age for the requested indication
2. If the member has a diagnosis of atopic dermatitis, then **ALL** of the following ("a", "b", and "c"):
    a. **BOTH** of the following ("i" and "ii"):
        i. The member is currently treated with topical emollients and practicing good skin care
        ii. The member will continue the use of topical emollients and good skin care practices in combination with nemolizumab
    b. **ONE** of the following ("i", "ii", or "iii"):
        i. **BOTH** of the following:
            - The member is currently treated with at least a low-potency topical corticosteroid **OR** a topical calcineurin inhibitor therapy (e.g., Elidel/pimecrolimus, Protopic/tacrolimus)
            - The member will continue topical corticosteroid **OR** topical calcineurin inhibitor therapy in combination with nemolizumab
        ii. The member has been treated with nemolizumab for at least 16 consecutive weeks, **AND BOTH** of the following:
            - The member's atopic dermatitis has sufficiently improved

- Based on disease activity, concurrent topical therapies (e.g., topical corticosteroid, topical calcineurin inhibitor) have been tapered and discontinued

iii. The member has an intolerance, hypersensitivity, or FDA labeled contraindication to **ALL** topical corticosteroids **AND** topical calcineurin inhibitors

c. **ONE** of the following:

i. The member is initiating therapy with nemolizumab

ii. The member has been treated with nemolizumab for less than 16 consecutive weeks

iii. The member has been treated with nemolizumab for at least 16 consecutive weeks, **AND EITHER** of the following:

- The requested dose is 30 mg every 8 weeks
- The requested dose is 30 mg every 4 weeks, **AND EITHER** of the following:
  - The member has **NOT** achieved clear or almost clear skin
  - There is support for continued therapy at the requested dose of 30 mg every 4 weeks

3. The prescriber is a specialist in the area of the member's diagnosis (e.g., dermatologist, allergist, or immunologist for AD and prurigo nodularis), **OR** the prescriber has consulted with a specialist in the area of the member's diagnosis
4. The member does **NOT** have any FDA labeled contraindications to Nemluvio
5. The member will **NOT** be using nemolizumab in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
6. **ONE** of the following ("a", "b", or "c"):

a. The requested quantity (dose) does **NOT** exceed the following based on the member's indication and weight:

- Atopic dermatitis:
  - Initiation of therapy or less than 16 weeks of therapy: 60 mg subcutaneously for one dose, followed 30 mg subcutaneously every 4 weeks (28 days)
    - QL: 30 mg prefilled pen – 1 pen per 28 days*
  - At least 16 weeks of therapy - 30 mg subcutaneously every 4 weeks (28 days)
    - QL: 30 mg prefilled pen – 1 pen per 28 days
- Prurigo nodularis:
  - 90 kg or greater: 60 mg subcutaneously every 4 weeks (28 days)
    - QL: 30 mg prefilled pen – 2 pens per 28 days
  - Less than 90 kg: 60 mg subcutaneously for one dose, followed 30 mg subcutaneously every 4 weeks (28 days)
    - QL: 30 mg prefilled pen – 1 pen per 28 days*

**2 pens are permitted for the initial 28-day supply (i.e., loading dose)*

b. The requested quantity (dose) exceeds the program quantity limit but does **NOT** exceed the maximum FDA labeled dose for the requested indication, **AND** there is support for why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does **NOT** exceed the program quantity limit

c. The requested indication does **NOT** have a maximum FDA labeled dose, **AND** there is support for therapy with a higher dose for the requested indication

Approval duration: 6 months for atopic dermatitis (AD) and prurigo nodularis (PN); 12 months for all other indications

Table 1

Indications and Specific Criteria	
Indication	**Specific Criteria**
Moderate-to-severe atopic dermatitis (AD	When **BOTH** of the following are met ("1" and "2"): 1. **ONE** of the following ("a", "b", "c", or "d"): a. The member has at least 10% body surface area involvement **OR** b. The member has involvement of body sites that are difficult to treat with prolonged topical corticosteroid therapy (e.g., hands, feet, face, neck, scalp, genitals/groin, skin folds) **OR** c. The member has an Eczema Area and Severity Index (EASI) score greater than or equal to 16 **OR** d. The member has an Investigator Global Assessment (IGA) score greater than or equal to 3 **AND** 2. **EITHER** of the following ("a" or "b"): a. **BOTH** of the following ("i" and "ii"): i. **ONE** of the following: • The member has tried and had an inadequate response to **ONE** at least medium-potency topical corticosteroid used in the treatment of AD after at least a 4-week duration of therapy **OR**

	• The member has an intolerance or hypersensitivity to **ONE** at least medium-potency topical corticosteroid used in the treatment of AD **OR** • The member has an FDA labeled contraindication to **ALL** medium-, high-, and super-potency topical corticosteroids used in the treatment of AD **AND** ii. **ONE** of the following: • The member has tried and had an inadequate response to **ONE** topical calcineurin inhibitor (e.g., Elidel/pimecrolimus, Protopic/tacrolimus) used in the treatment of AD after at least a 6-week duration of therapy **OR** • The member has an intolerance or hypersensitivity to **ONE** topical calcineurin inhibitor used in the treatment of AD **OR** • The member has an FDA labeled contraindication to **ALL** topical calcineurin inhibitors used in the treatment of AD **OR** b. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of AD
Prurigo nodularis (PN)	When **BOTH** of the following are met ("1" and "2"): 1. The member has **ALL** of the following features associated with PN: a. Presence of greater than or equal to 20 firm, nodular lesions **AND** b. Pruritus that has lasted for at least 6 weeks **AND** c. History and/or signs of repeated scratching, picking, or rubbing **AND** 2. **EITHER** of the following ("a" or "b"): a. **ONE** of the following: i. The member has tried and had an inadequate response to **ONE** at least medium-potency topical corticosteroid used in the treatment of PN after at least a 2-week duration of therapy

	OR ii. The member has an intolerance or hypersensitivity to **ONE** at least a medium-potency topical corticosteroid used in the treatment of PN **OR** iii. The member has an FDA-labeled contraindication to **ALL** medium-, high-, and super-potency topical corticosteroid used in the treatment of PN **OR** b. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of PN
Other indications	The member has another FDA labeled indication or an indication supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a

Continuation of nemolizumab-ilto (Nemluvio) **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "6"):

1. An authorization or reauthorization for nemolizumab has been previously approved by Florida Blue [Note: members not previously approved for the requested agent will require initial evaluation review]
2. The member has had clinical benefit with nemolizumab
3. **ALL** of the following if the member has diagnosis of atopic dermatitis ("a", "b", and "c"):
    a. The member will continue standard maintenance therapies (e.g., topical emollients, good skin care practices) in combination with nemolizumab
    b. **ONE** of the following ("i", "ii", or "iii"):
        i. The member will continue topical corticosteroid **OR** topical calcineurin inhibitor therapy in combination with nemolizumab
        ii. The member has been treated with nemolizumab for at least 16 consecutive weeks **AND BOTH** of the following:
            - The disease has sufficiently improved
            - Based on disease activity, concurrent topical therapies (e.g., topical corticosteroid, topical calcineurin inhibitor) have been tapered and discontinued
        iii. The member has an intolerance, hypersensitivity, or FDA labeled contraindication to **ALL** topical corticosteroids **AND** topical calcineurin inhibitors
    c. **ONE** of the following ("i", "ii", or "iii"):
        i. The member is initiating therapy with nemolizumab
        ii. The member has been treated with nemolizumab for less than 16 consecutive weeks

iii. The member has been treated with nemolizumab for at least 16 consecutive weeks, **AND EITHER** of the following ("1" or "2"):

1. The requested dose is 30 mg every 8 weeks
2. The requested dose is 30 mg every 4 weeks, **AND EITHER** of the following:
    - The member has **NOT** achieved clear or almost clear skin
    - There is support for continued therapy at the requested dose of 30 mg every 4 weeks

3. The prescriber is a specialist in the area of the member's diagnosis (e.g., dermatologist, allergist, or immunologist for AD and prurigo nodularis), **OR** the prescriber has consulted with a specialist in the area of the member's diagnosis
4. The member does **NOT** have any FDA labeled contraindications to Nemluvio
5. The member will **NOT** be using nemolizumab in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
6. **ONE** of the following ("a", "b", or "c"):
    a. The requested quantity (dose) does **NOT** exceed the following based on the member's indication and weight:
        - Atopic dermatitis: 30 mg subcutaneously every 4 weeks (28 days)
            - QL: 30 mg prefilled pen – 1 pen per 28 days
        - Prurigo nodularis:
            - 90 kg or greater: 60 mg subcutaneously every 4 weeks (28 days)
                - QL: 30 mg prefilled pen – 2 pens per 28 days
            - Less than 90 kg: 30 mg subcutaneously every 4 weeks (28 days)
                - QL: 30 mg prefilled pen – 1 pen per 28 days

    b. The requested quantity (dose) exceeds the program quantity limit but does **NOT** exceed the maximum FDA labeled dose for the requested indication, **AND** there is support for why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does **NOT** exceed the program quantity limit

    c. The requested indication does **NOT** have a maximum FDA labeled dose, **AND** there is support for therapy with a higher dose for the requested indication

Approval duration: 12 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL

PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Indicated for the treatment of adults with prurigo nodularis
    - Adult patients weighing <90 kg: The recommended subcutaneous dosage is an initial dose of 60 mg (two 30 mg injections), followed by 30 mg given every 4 weeks.
    - Adult patients weighing ≥90 kg: The recommended subcutaneous dosage is an initial dose of 60 mg (two 30 mg injections), followed by 60 mg given every 4 weeks.
- 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
    - The recommended subcutaneous dosage is an initial dose of 60 mg (two 30 mg injections), followed by 30 mg given every 4 weeks. After 16 weeks of treatment, for patients who achieve clear or almost clear skin, a dosage of 30 mg every 8 weeks is recommended.
    - Use Nemluvio with topical corticosteroids and/or topical calcineurin inhibitors. When the disease has sufficiently improved, discontinue use of topical therapies.
- Nemluvio is intended for use under the guidance of a healthcare provider. Prior to the first injection, provide patients and/or caregivers with proper training on preparation and administration. Patients may self-inject after receiving training on subcutaneous injection techniques. In pediatric patients 12 years of age and older, administer Nemluvio by or under the supervision of a trained adult or caregiver. For the initial dose, administer each of the two injections at different injection sites. Administer subcutaneous injection into the front upper thighs or abdomen except for the 2 inches around the navel. Injection in upper arm should only be performed by a caregiver or healthcare professional.
- Nemluvio is supplied in a single-dose prefilled dual-chamber pen with white powder in one chamber and a clear diluent in the other chamber. Nemluvio must be reconstituted prior to administration. Use Nemluvio pens within 4 hours after reconstitution. Refer to the product labeling for more information.

Dose Adjustments

- Hepatic impairment – Specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed.
- Renal impairment - Specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed.

Drug Availability

- Available in a single-dose, dual chamber prefilled pen containing 30 mg of nemolizumab in one chamber and the diluent, water for injection, in the other chamber. Following reconstitution, each prefilled pen delivers 30 mg/0.49 mL of nemolizumab.
- Store the dual chamber prefilled pen in a refrigerator at 36°F to 46°F (2°C to 8°C) in the original carton to protect from light until the expiration date. Do not freeze. Do NOT expose to heat or direct sunlight. Alternatively, the carton containing the unused dual chamber prefilled pen may be stored at room temperature [up to 77°F (25°C)] for up to 90 days.

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Known hypersensitivity to nemolizumab or to any of the excipients in Nemluvio

Precautions/Warnings

- **Hypersensitivity**: Hypersensitivity reactions, such as facial angioedema, have been reported with Nemluvio use. If a clinically significant hypersensitivity reaction occurs, immediately institute appropriate therapy and discontinue Nemluvio.
- **Vaccinations**: Complete all age-appropriate vaccinations as recommended by current immunization guidelines prior to treatment with Nemluvio. Avoid use of live vaccines in patients during treatment with Nemluvio. It is unknown if administration of live vaccines during Nemluvio treatment will impact the safety or effectiveness of these vaccines. No data are available on the response to non-live vaccines.

BILLING/CODING INFORMATION:

HCPCS Coding

J3590	Unclassified biologics

ICD-10 Diagnosis Codes That Support Medical Necessity

L20.0	Besnier's prurigo
L20.81	Atopic neurodermatitis
L20.82	Flexural eczema
L20.84	Intrinsic (allergic) eczema
L20.89	Other atopic dermatitis
L20.9	Atopic dermatitis, unspecified
L28.1	Prurigo nodularis

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

Eczema Area Severity Index score (EASI) - assesses severity (severity score) and body surface area affected by erythema, induration/papulation/edema, excoriations, and lichenification (area score), which are graded systematically for each of 4 anatomical regions (head and neck, trunk, upper limbs, lower limbs) and assembled in a composite score, with a score range of 0 to 72.

- EASI 50 - a percentage improvement of EASI score from baseline that is ≥50%
- EASI 75 - a percentage improvement of EASI score from baseline that is ≥75%
- EASI 90 - a percentage improvement of EASI score from baseline that is ≥90%

Pruritus – itching

RELATED GUIDELINES:

Abrocitinib (Cibinqo), 09-J4000-27

Dupilumab (Dupixent) Injection, 09-J2000-80

Lebrikizumab-lbkz (Ebglyss) Injection, 09-J5000-00

Thalidomide (Thalomid) Capsules, 09-J1000-56

Tralokinumab (Adbry), 09-J4000-20

Upadacitinib (Rinvoq), 09-J3000-51

OTHER:

The "**Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy**" list can be found at the following link **–** Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/12/25.

GUIDELINE UPDATE INFORMATION:

01/01/25	New Medical Coverage Guideline.
07/01/25	Revision to guidelines consisting of update to the description section, position statement, dosage/administration, definitions, related guidelines, billing/coding, and references. New indication of moderate-to-severe atopic dermatitis added.
01/01/26	Review and revision to guidelines consisting of update to the description section, position statement, and references.