NEMLUVIO® (nemolizumab-ilto) for injection 30mg

Atopic Dermatitis Prescribing Information

NEMLUVIO® (nemolizumab-ilto) for injection 30mg

Prurigo Nodularis Prescribing Information

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use NEMLUVIO safely and effectively. See full prescribing information for NEMLUVIO.

NEMLUVIO® (nemolizumab-ilto) for injection, for subcutaneous use
Initial U.S. Approval: 2024

----------INDICATIONS AND USAGE----------
NEMLUVIO is an interleukin-31 receptor antagonist 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. (1)

----------DOSAGE AND ADMINISTRATION----------
- Complete all age-appropriate vaccinations as recommended by current immunization guidelines prior to treatment with NEMLUVIO. (2.1)
- The recommended dosage is an initial dose of 60 mg (two 30 mg injections), followed by 30 mg given every 4 weeks. (2.2)
- After 16 weeks of treatment, for patients who achieve clear or almost clear skin, a dosage of 30 mg every 8 weeks is recommended. (2.2)
- Use NEMLUVIO with topical corticosteroids and/or topical calcineurin inhibitors. When the disease has sufficiently improved, discontinue use of topical therapies. (2.2)
- Administer NEMLUVIO by subcutaneous injection. (2.4)
- NEMLUVIO must be reconstituted prior to administration. (2.5)

----------DOSAGE FORMS AND STRENGTHS----------
For injection: single-dose pre-filled dual-chamber pen containing 30 mg of nemolizumab-ilto lyophilized powder and diluent, water for injection. (3)

----------CONTRAINDICATIONS----------
Known hypersensitivity to nemolizumab-ilto or to any of the excipients in NEMLUVIO. (4)

----------WARNINGS AND PRECAUTIONS----------
- Hypersensitivity: Hypersensitivity reactions have been reported with NEMLUVIO use. If a clinically significant hypersensitivity reaction occurs, immediately institute appropriate therapy and discontinue NEMLUVIO. (5.1)
- Vaccinations: Avoid use of live vaccines during treatment with NEMLUVIO. (5.2)

----------ADVERSE REACTIONS----------
Most common adverse reaction (incidence ≥1%) headache (including migraine), arthralgia, urticaria, and myalgia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Galderma Laboratories, L.P at 1-866-735-4137 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 12/2024

FULL PRESCRIBING INFORMATION: CONTENTS*

*** Sections or subsections omitted from the full prescribing information are not listed.**

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

NEMLUVIO is 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.

2 DOSAGE AND ADMINISTRATION

2.1 Vaccination Prior to Treatment

Complete all age-appropriate vaccinations as recommended by current immunization guidelines prior to treatment with NEMLUVIO *[see Warnings and Precautions (5.2)]*.

2.2 Recommended Dosage for Atopic Dermatitis

The recommended subcutaneous dosage of NEMLUVIO in adults and pediatric patients 12 years of age and older 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 subcutaneous dosage of 30 mg every 8 weeks is recommended.

Concomitant Topical Therapies:
Use NEMLUVIO with topical corticosteroids and/or topical calcineurin inhibitors. When the disease has sufficiently improved, discontinue use of topical therapies.

2.3 Missed Dose

If a dose is missed, administer the dose as soon as possible. Thereafter, resume dosing at the regular scheduled time.

2.4 Important Administration Instructions

- NEMLUVIO is administered by subcutaneous injection.

- 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 the preparation and administration of NEMLUVIO. Patients may self-inject NEMLUVIO 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 NEMLUVIO injections at different injection sites.

- Administer subcutaneous injection into the front upper thighs or abdomen except for the 2 inches (5 cm) around the navel. Injection in upper arm should only be performed by a caregiver or healthcare professional.

- Alternate the injection site with each injection. Do not inject NEMLUVIO into skin that is tender, inflamed, swollen, damaged or has bruises or scars or open wounds.

- Refer to the Instructions for Use for complete administration instructions with illustrations *[see Instructions for Use]*.

2.5 Preparation for Use of NEMLUVIO

- Before injection, remove NEMLUVIO carton from the refrigerator and allow to reach room temperature (30-45 minutes).

- Inspect NEMLUVIO visually prior to reconstitution. 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. Do not use if powder is not white, or if diluent is cloudy or contains visible particles.

- NEMLUVIO must be reconstituted prior to administration.

- Following reconstitution, each prefilled pen delivers 30 mg/0.49 mL as a clear and colorless to slightly yellow solution. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if the reconstituted solution has discoloration or contains particles.

- Use NEMLUVIO pens within 4 hours after reconstitution. Discard unused reconstituted NEMLUVIO pens after 4 hours.

- Discard any unused portions after administration.

- Refer to the Instructions for Use for complete administration instructions with illustrations *[see Instructions for Use]*.

3 DOSAGE FORMS AND STRENGTHS

For injection: single-dose prefilled dual-chamber pen containing 30 mg of nemolizumab-ilto as a white lyophilized powder in one chamber and diluent, water for injection, in the other chamber.

4 CONTRAINDICATIONS

NEMLUVIO is contraindicated in patients who have known hypersensitivity to nemolizumab-ilto or to any of the excipients in NEMLUVIO *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity

Hypersensitivity reactions, such as facial angioedema, have been reported with use of NEMLUVIO. NEMLUVIO is contraindicated in patients with a known hypersensitivity to nemolizumab-ilto or to any of the excipients in NEMLUVIO. If a clinically significant hypersensitivity reaction occurs, immediately institute appropriate therapy and discontinue NEMLUVIO *[see Contraindications (4), Adverse Reactions (6.1)]*.

5.2 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.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail elsewhere in the labeling:

- Hypersensitivity *[see Warnings and Precautions (5.1)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

A total of 1148 subjects, including 180 subjects 12 to 17 years of age, with moderate-to-severe atopic dermatitis were treated with NEMLUVIO for at least 1 year during the development program.

The safety of NEMLUVIO was evaluated in a pool of two randomized, double-blind, placebo-controlled, multicenter phase 3 trials (ARCADIA 1, ARCADIA 2). In these two trials, 1135 adult and pediatric subjects 12 years of age and older with moderate-to-severe AD were treated with subcutaneous injections of NEMLUVIO, with concomitant topical corticosteroids (TCS) and/or topical calcineurin inhibitors (TCI) for up to 16 weeks (Initial Treatment Period) *[see Clinical Studies (14)]*.

After the Initial Treatment Period, subjects that responded to NEMLUVIO were re-randomized to every 4 weeks, every 8 weeks, or placebo dosing for the Maintenance Treatment Period (Week 16 through Week 48). The safety population during the Maintenance Treatment Period

had a mean age of 31 to 33 years (median age of 26 to 29 years) for the NEMLUVIO cohorts.

Week 0 to Week 16

In ARCADIA 1 and ARCADIA 2 trials through Week 16, the proportion of subjects who discontinued treatment because of adverse events was 2.3% in the NEMLUVIO 30 mg every 4 weeks group and 2.2% in the placebo groups. Table 1 summarizes the adverse reactions that occurred at a rate of at least 1% in the NEMLUVIO group, and for which the rate exceeds the rate in the placebo group during the first 16 weeks of treatment.

Table 1: Adverse Reactions Occurring in ≥1% of Adult and Pediatric Subjects 12 Years of Age and Older with Atopic Dermatitis in the NEMLUVIO Group and Greater than Placebo in ARCADIA 1 and ARCADIA 2 Trials through Week 16

Adverse reactions	NEMLUVIO (N = 1135) n (%)	Placebo (N=584) n (%)
Headache (incl. migraine)	52 (5)	22 (4)
Arthralgia	12 (1)	1 (0.2)
Urticaria	12 (1)	2 (0.3)
Myalgia	11 (1)	1 (0.2)

Assessment of the safety profile of NEMLUVIO in 505 subjects up through Week 48 in the ARCADIA 1 and ARCADIA 2 trials was generally consistent with the safety profile observed at Week 16.

Specific Adverse Reactions

Hypersensitivity reactions

Type 1 hypersensitivity reactions (Ig-E mediated reactions) were reported in subjects treated with NEMLUVIO. This included occurrence of mild urticaria that did not lead to discontinuation of treatment.

Injection site reactions

The incidence of injection site reactions during initial period was reported for 1.2% of subjects treated with NEMLUVIO and 0.9% of subjects receiving placebo; during the maintenance period, the incidence was 0.6% with NEMLUVIO every 4 weeks, 0% with NEMLUVIO every 8 weeks, and 0% with placebo. None of these reactions led to discontinuation of treatment.

Herpes Zoster

During the initial treatment period herpes zoster infections were reported in 5 subjects (0.4%) treated with NEMLUVIO (including 1 case of ophthalmic herpes zoster) and no subjects receiving placebo. Cases of herpes zoster were mild to moderate in severity and did not lead to discontinuation of treatment.

Pediatric Subjects 12 Years of Age and Older with Atopic Dermatitis

The safety of NEMLUVIO was assessed in 176 subjects 12 to 17 years of age with moderate-to-severe atopic dermatitis enrolled in the ARCADIA 1 or ARCADIA 2 trials who received at least

one dose of NEMLUVIO from Week 0 to Week 16 in the primary safety population. The safety profile of NEMLUVIO in these subjects through Week 16 was consistent with the safety profile observed in adults with atopic dermatitis.

The safety profile of NEMLUVIO in 98 subjects 12 to 17 years of age followed through Week 48 was consistent with the safety profile observed at Week 16.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data on NEMLUVIO use in pregnant women exposed during clinical trials are insufficient to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Transport of human IgG antibody across the placenta increases as pregnancy progresses and peaks during the third trimester; therefore, NEMLUVIO may be transferred from the mother to the developing fetus (*see Clinical Considerations*). In an enhanced pre- and postnatal development study in cynomolgus monkeys, when nemolizumab-ilto was administered subcutaneously during organogenesis to parturition, an increase in early postnatal death was observed at a dose 50 times the maximum recommended human dose (MRHD) (see *Data*). The clinical significance of this nonclinical finding is unknown.

The background risk of major birth defects and miscarriage for the indicated populations are unknown. All pregnancies have a background risk of birth defects, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

Transport of endogenous IgG antibodies across the placenta increases as pregnancy progresses, and peaks during the third trimester. It is unclear whether nemolizumab-ilto may interfere with an infant's immune response to infections. Therefore, monitoring for the development of serious infection during the first 3 months of life in infants exposed in utero is recommended.

Data

Animal Data

In an enhanced pre- and postnatal development study, subcutaneous doses up to 25 mg/kg nemolizumab-ilto were administered to pregnant cynomolgus monkeys once every two weeks during organogenesis to parturition. No maternal or embryofetal toxicities were observed at doses up to 25 mg/kg (50 times the MRHD, based on AUC comparison). Early postnatal death occurred in the offspring of one control monkey and 3 monkeys at 25 mg/kg (50 times the MRHD, based on AUC comparison). The clinical significance of this nonclinical finding is unknown. Nemolizumab-ilto was administered subcutaneously to the offspring at doses up to 25 mg/kg (168 times the MRHD, based on AUC comparison), once every 2 weeks for 6 months,

starting from postnatal day 35. No adverse effects were noted in the remaining offspring.

8.2 Lactation

Risk Summary

There are no data on the presence of nemolizumab-ilto in human milk, the effects on the breastfed infant, or the effects on milk production. Nemolizumab-ilto was detected in breast milk of monkeys (*see Data*). Endogenous maternal IgG and monoclonal antibodies are transferred in human milk. The effects of local gastrointestinal exposure and limited systemic exposure in the breastfed infant to nemolizumab-ilto are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for NEMLUVIO and any potential adverse effects on the breastfed child from NEMLUVIO or from the underlying maternal condition.

Data

Nemolizumab-ilto was detected in breast milk of monkeys in the enhanced pre- and postnatal development study following subcutaneous doses up to 25 mg/kg once every two weeks during organogenesis to parturition. The mean nemolizumab-ilto concentrations in milk were approximately 0.3 – 0.5% of the maternal plasma levels from lactation day 7 to 63. The concentration of nemolizumab-ilto in animal milk does not necessarily predict the concentration of drug in human milk.

8.4 Pediatric Use

The safety and effectiveness of NEMLUVIO for the treatment of moderate-to-severe atopic dermatitis in combination with topical corticosteroids and/or calcineurin inhibitors have been established in pediatric patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies. Use of NEMLUVIO for this indication is supported by evidence from two randomized, double-blind, placebo-controlled trials. The safety and effectiveness were generally consistent between pediatric and adult subjects *[See Adverse Reactions (6.1) and Clinical Studies (14.1)]*.

The safety and effectiveness of NEMLUVIO have not been established in pediatric patients younger than 12 years of age.

8.5 Geriatric Use

Of the 1192 subjects with atopic dermatitis exposed to NEMLUVIO in the primary safety population, 72 (6.0%) subjects were 65 years of age or older. The long-term safety of NEMLUVIO was assessed in 78 (4.5%) subjects 65 years of age or older. Clinical studies of NEMLUVIO did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger adult subjects *[see Clinical Pharmacology (12.3)]*.

10 OVERDOSAGE

There is no specific treatment for NEMLUVIO overdose. In the event of overdosage, contact Poison Control (1-800-222-1222) for the latest recommendations and monitor the patient for any signs or symptoms of adverse reactions and institute appropriate symptomatic treatment immediately.

11 DESCRIPTION

Nemolizumab-ilto, an interleukin-31 receptor alpha (IL-31RA) antagonist, is a humanized monoclonal modified immunoglobulin G (IgG) antibody with a molecular weight of approximately 144 kDa. Nemolizumab-ilto is produced by recombinant DNA technology in Chinese Hamster Ovary cells.

NEMLUVIO (nemolizumab-ilto) for injection is a sterile, preservative-free, white lyophilized powder in a dual-chamber single-dose, prefilled pen. One chamber contains 30 mg of nemolizumab-ilto with inactive ingredients arginine hydrochloride (9.5 mg), poloxamer 188 (0.15 mg), sucrose (25.8 mg), trometamol (0.10 mg), and tris hydrochloride for pH adjustment. The diluent, water for injection, is in the other chamber. Following reconstitution, each prefilled pen delivers 30 mg/0.49 mL of nemolizumab-ilto with a pH of 6.7 to 7.3.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Nemolizumab-ilto is a humanized IgG2 monoclonal antibody that 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.

12.3 Pharmacokinetics

After a single dose, nemolizumab-ilto exposure increased dose proportionally over a dose range of 0.03 and 3 mg/kg following subcutaneous administration. After multiple doses, nemolizumab-ilto systemic exposure increased in an approximately dose-proportional manner across the subcutaneous dose range up to 30 mg. There was a decrease in bioavailability by 9% with the 60 mg subcutaneous dose and by 15% with the 90 mg subcutaneous dose.

Following multiple doses of NEMLUVIO in subjects with atopic dermatitis, the estimated mean (SD) steady-state trough concentrations of nemolizumab-ilto were 2.63 (1.27) µg/mL for 30 mg administered every 4 weeks and 0.74 (0.44) µg/mL for 30 mg administered every 8 weeks. Steady-state nemolizumab concentrations were achieved 4 weeks after the initial 60 mg loading dose.

Absorption

Following an initial subcutaneous dose of 60 mg, nemolizumab-ilto reached peak mean (SD) concentrations (C_{max}) of 7.5 (2.31) µg/mL by approximately 6 days post dose.

Distribution

The volume of distribution of nemolizumab-ilto was estimated to be 7.67 L.

Elimination

Nemolizumab-ilto is expected to be degraded in the same manner as endogenous IgG. The terminal elimination half-life (SD) of nemolizumab-ilto was estimated to be 18.9 (4.96) days and systemic clearance was estimated to be 0.263 L/day.

Metabolism

The metabolic pathway of nemolizumab-ilto has not been characterized. Nemolizumab-ilto is expected to be degraded into small peptides by catabolic pathways.

Specific Populations

Geriatric Populations

No clinically significant difference in the pharmacokinetics of nemolizumab-ilto was estimated based on age (subjects 18 to 65 years of age and older than 65 years of age). Dose adjustment in this population is not needed.

Pediatric Populations

No clinically significant difference in the pharmacokinetics of nemolizumab-ilto was estimated in pediatric subjects 12 to 17 years of age compared to adults. Dose adjustment in this population is not needed.

Renal or Hepatic Impairment

No clinically significant differences in the pharmacokinetics of nemolizumab-ilto were estimated based on mild to moderate renal or hepatic impairments. The effect of severe renal and severe hepatic impairments on the pharmacokinetics of nemolizumab-ilto is unknown.

Body Weight

The exposure of nemolizumab-ilto decreases with increasing body weight. With the recommended dose, the steady state mean exposure parameters (AUC_{ss}, C_{maxss} and C_{trough}) of subjects with body weight of above 87 kg is expected to be 1.7-fold lower than that of subjects weighing below 62 kg.

The difference in systemic exposure due to body weight had no clinically meaningful impact on efficacy in subjects with atopic dermatitis. Dose adjustment based on body weight is not needed.

Drug Interaction Studies

The effects of nemolizumab on the pharmacokinetics of midazolam (CYP3A4/5 substrate), warfarin (CYP2C9 substrate), omeprazole (CYP2C19 substrate), metoprolol (CYP2D6 substrate), and caffeine (CYP1A2 substrate) were evaluated in a study in 14 subjects with

moderate to severe AD receiving an initial SC dose of 60 mg followed by 30 mg SC every four weeks for 12 weeks. No clinically significant changes in the exposure of CYP450 substrates before and after multiple nemolizumab injections were observed, with Cmax and AUC ratios ranging from 88.2 to 107.8%. The concomitant use of nemolizumab-ilto is unlikely to influence the PK profiles of CYP substrates.

12.6 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the trials described below with the incidence of anti-drug antibodies in other trials, including those of nemolizumab-ilto or other nemolizumab products.

In the phase 3 trials (ARCADIA 1, ARCADIA 2) up to 16 weeks, the incidence of treatment-emergent ADAs was 5.6% (33/593) and 6.8% (34/499), respectively. Among subjects who continued treatment from week 16 through week 48 in the two studies, the ADA incidence was 11.2% (10/89) and 16.9% (13/77) for those received 30 mg every 4 weeks, and 12.8% (11/86) and 8% (6/75) for those received 30 mg every 8 weeks. Neutralizing antibody incidence was 6% (2/33) and 2.9% (1/34) among the ADA+ subjects throughout 48 weeks in ARCADIA 1 and ARCADIA 2, respectively.

Antibodies to nemolizumab-ilto were associated with reduced serum nemolizumab-ilto concentrations beyond Week 16. In the phase 3 trials, NEMLUVIO treated subjects who developed ADAs had nemolizumab-ilto concentrations that were 20% to 70% lower compared to subjects who did not develop ADAs. There was no clinically significant effect of anti-drug antibodies on safety or efficacy of nemolizumab-ilto over the treatment duration of 48 weeks.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been conducted to evaluate the carcinogenic or mutagenic potential of NEMLUVIO.

No effects on fertility parameters as reproductive organ morphology, menstrual cycle length, or sperm/testicular analysis were observed in male or female sexually mature cynomolgus monkeys that were administered nemolizumab-ilto at subcutaneous doses up to 25 mg/kg once every two weeks for 6 months (72 times the MRHD, based on AUC comparison). The monkeys were not mated to evaluate fertility.

14 CLINICAL STUDIES

14.1 Atopic Dermatitis

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 ≥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.

In these trials, at baseline, 51% of subjects were male, 80% were White, 13% were Asian, and 6% were Black or African American; for ethnicity, 9% of subjects identified as Hispanic or Latino. Fifteen (15)% of subjects were 12-17 years of age. 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.

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 AD. EASI scores range from 0 to 72 points and reflect the severity and extent of AD. EASI-75 indicates at least a 75% improvement in EASI score from baseline. The 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.

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

PP-NRS improvement ≥ 4 from baseline at Week 16 was a key secondary outcome in both trials.

Clinical Response at Week 16 (ARCADIA 1 and ARCADIA 2)

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

Table 2: Efficacy Results of NEMLUVIO (30 mg Every 4 Weeks) with Concomitant TCS/TCI at Week 16 in Adult and Pediatric Subjects 12 Years of Age and Older with Moderate to Severe AD in ARCADIA 1 and ARCADIA 2

	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[a]	36%	25%	12% (6%, 17%)	38%	26%	12% (6%, 19%)
Proportion of subjects with EASI-75[a]	44%	29%	15% (9%, 21%)	42%	30%	12% (6%, 19%)
Proportion of subjects with an improvement (reduction) of ≥4 from baseline in PP-NRS[a]	33%	15%	18% (13%, 23%)	36%	15%	21% (15%, 27%)

[a] Subjects who received rescue treatment or had missing data (fewer than 4 PP-NRS daily diary entries in a 7-day period) were considered non-responders.

Examination of weight, age, gender, race, and prior treatment did not identify meaningful difference in response to NEMLUVIO among these subgroups at Week 16.

Maintenance and Durability of Response (Week 16 to Week 48)

The clinical response in NEMLUVIO responders (IGA 0/1 or EASI-75 at Week 16) was evaluated between Week 16 and Week 48 in ARCADIA 1 and ARCADIA 2 trials. For the maintenance treatment period, NEMLUVIO responders were re-randomized to NEMLUVIO 30 mg every 4 weeks, NEMLUVIO 30 mg every 8 weeks or placebo every 4 weeks (NEMLUVIO withdrawal) with concomitant TCS/TCI. The results are presented in Table 3.

Table 3: Efficacy Results of NEMLUVIO with Concomitant TCS/TCI at Week 48 in Adult and Pediatric Subjects 12 Years of Age and Older with Moderate to Severe AD in ARCADIA 1 and ARCADIA 2

	NEMLUVIO Every 4 Weeks + TCS/TCI	**NEMLUVIO Every 8 Weeks + TCS/TCI**	**Placebo + TCS/TCI**
Number of subjects who were IGA Responders[a] at Week 16	**142**	**142**	**131**
Proportion of subjects with IGA 0 or 1[b] at Week 48	63%	64%	55%
Number of subjects who were EASI-75 Responders at Week 16	**163**	**163**	**157**
Proportion of subjects with EASI-75[b] at Week 48	75%	77%	65%

[a] Responder was defined as a subject with an IGA of 0 (clear) or 1 (almost clear) and a ≥2-point reduction from baseline.

[b] Subjects who received rescue treatment or with missing data were considered non-responders.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

NEMLUVIO (nemolizumab-ilto) for injection is a sterile, preservative-free, white lyophilized powder available in single-dose, dual-chamber prefilled pen containing 30 mg of nemolizumab-ilto 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-ilto.

Each carton contains 1 single-dose prefilled pen.

Presentation	**Pack size**	**NDC #**
Pre-filled Pen	Pack of 1 pen	0299-6220-15

Storage and Handling

Store the NEMLUVIO 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 NEMLUVIO 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. Write the date the NEMLUVIO dual chamber prefilled pen is first removed from the refrigerator in the space provided on the inner partition for the pen. Do not use the NEMLUVIO dual chamber prefilled pen beyond the expiration date or 90 days after the date it was first removed from the refrigerator (whichever is earlier).

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Hypersensitivity

Advise patients to seek immediate medical attention and discontinue NEMLUVIO if they experience any symptoms of hypersensitivity reactions *[see Warnings and Precautions (5.1)]*.

Vaccinations

Instruct patients to inform their healthcare provider that they are taking NEMLUVIO prior to a potential vaccination *[see Warnings and Precautions (5.2)]*.

Administration Instructions:

- Instruct patients and/or caregivers to receive proper training in subcutaneous injection technique prior to self-injection *[see Dosage and Administration (2.4)]*. Inform patients and/or caregivers that Galderma Customer Support may be called for assistance at 1-866-735-4137.

- Inform patients that NEMLUVIO must be reconstituted prior to administration. Advise patients/caregivers to refer to the Instructions for Use that accompany the NEMLUVIO pen

for complete mixing and administration instructions with illustrations *[see Dosage and Administration (2.4, 2.5), Instructions for Use]*.

- Inform patients and/or caregivers of proper pen disposal and caution against any reuse of needles. Instruct patients and/or caregivers to discard used pens in an appropriate sharps disposal container following safe needle disposal practices *[see Instructions for Use]*.

- Advise patients and/or caregivers of the importance of complying with dosing schedule. If a dose is missed, instruct patients/caregivers to administer the injection as soon as possible, and thereafter, resume dosing at the regular scheduled time. *[see Dosage and Administration (2.3)]*.

Manufactured by:
Galderma Laboratories, L.P., Dallas, TX 75201
U.S. License No. 2289
NEMLUVIO® is a trademark of Galderma.