

Depemokimab-ulaa (EXDENSUR) in Asthma National Drug Mini-Monograph

August 2026
VA Pharmacy Services and National Formulary Committee

The purpose of VA Pharmacy Services drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

SUMMARY OF PRESCRIBING INFORMATION¹²

Description / MOA	Depemokimab-ulaa is an interleukin-5 (IL-5) antagonist monoclonal antibody (humanized IgG1 kappa). It binds to IL-5, inhibiting it from binding to the alpha subunit of the IL-5 receptor complex expressed on the surface of eosinophils, thereby reducing eosinophilic inflammation. Depemokimab-ulaa contains a triple amino acid substitution (YTE) in the Fc region. This modification increases binding to the neonatal Fc receptor (FcRn), extending the elimination half-life to approximately 48 days, which is what enables the Q6 month dosing.
Indication Under Review	Depemokimab-ulaa is indicated for add-on maintenance treatment of severe asthma characterized by an eosinophilic phenotype in adult and pediatric patients aged 12 years and older.
Dosage Regimen	100 mg administered Q6 months by SC injection by a healthcare provider
Dosage Form(s)	100 mg/mL solution in a single-dose, prefilled syringe
Contraindications	None
Other Warnings	Hypersensitivity reactions, including anaphylaxis. Do not abruptly discontinue systemic or inhaled corticosteroids upon initiation. Treat pre-existing helminth infections prior to initiation. If infection occurs during therapy and is unresponsive to anti-helminthics, pause depemokimab-ulaa until resolution.
Most Common AEs	The most common adverse reactions (incidence $\geq 4\%$) include upper respiratory tract infection (9%), allergic rhinitis (6%), influenza (5%), arthralgia (4%), and pharyngitis (4%).
Drug Interactions	No drug interaction studies have been conducted. As a monoclonal antibody, depemokimab-ulaa is not expected to undergo CYP450-mediated metabolism or to affect CYP450 enzyme activity.
Pregnancy	Available human data are insufficient to identify a drug-associated risk of major birth defects or miscarriage. However, due to the YTE modification, there is a reasonable likelihood of increased and prolonged fetal exposure through placental transfer, particularly in the third trimester.
Lactation	There are no data on the presence of depemokimab-ulaa in human milk or its effects on the breastfed infant
Renal Impairment	No dosage adjustment
Hepatic Impairment	No dosage adjustment

CLINICAL EVIDENCE SUMMARY

Trial	SWIFT-1 and SWIFT 2 (Phase 3)³
Design	Two replicate, 52-week, global, randomized, double-blind, placebo-controlled, parallel-group trials
Primary Endpoint	The annualized rate of clinically significant asthma exacerbations over 52 weeks
Population	N=762 participants (SWIFT-1: n=382; SWIFT-2: n=380) aged ≥ 12 years with severe, uncontrolled eosinophilic asthma (blood eosinophils ≥ 300 cells/ μ L in past 12 months or ≥ 150 cells/ μ L at screening)
Interventions	Depemokimab-ulaa 100 mg SC Q26 weeks vs. matching placebo
Co-therapy	Background maintenance therapy consisting of medium- to high-dose inhaled corticosteroids (ICS) plus at least one additional asthma controller
Efficacy Results	Primary endpoint: Depemokimab-ulaa significantly reduced the annualized rate of clinically significant exacerbations versus placebo in both SWIFT-1 (rate ratio 0.56; 95% CI 0.38–0.82) and SWIFT-2 (rate ratio 0.44; 95% CI 0.30–0.64). Secondary endpoints: None of the secondary endpoints, including SGRQ, ACQ-5, and pre-bronchodilator FEV ₁ , demonstrated statistically significant improvement over placebo.

ADDITIONAL STUDIES - SUMMARY

Trial	NIMBLE (Phase 3)⁴
Design	52-week, global, multicenter, randomized, double-blind, double-dummy, parallel-group, phase 3A non-inferiority study
Primary Endpoint	The annualized rate of clinically significant asthma exacerbations over 52 weeks. The pre-defined non-inferiority margin was set at 1.28
Population	N=1,687 participants (depemokimab-ulaa: n=848; active comparator: n=839). Eligible participants were adults and adolescents (≥ 12 years) with severe eosinophilic asthma who were stable on and had documented clinical benefit from mepolizumab (100 mg SC Q4W) or benralizumab (30 mg SC Q8W) for ≥ 12 months prior to screening.
Interventions	Depemokimab-ulaa 100 mg SC every 26 weeks vs. continuation of prior active biologic (mepolizumab 100 mg SC Q4W or benralizumab 30 mg SC Q8W). Blinding was maintained using a double-dummy design with matching placebos for all active treatments

Co-therapy

All participants continued their baseline standard of care asthma maintenance therapy (typically medium- to high-dose ICS plus at least one additional controller)

Efficacy Results

Primary endpoint: The annualized rate of clinically significant exacerbations over 52 weeks was 0.57 (95% CI: 0.50, 0.64) for depemokimab-ulaa (n = 848) compared to 0.49 (95% CI: 0.43, 0.55) for the active comparator group (aggregate of mepolizumab and benralizumab; n = 839), yielding a rate ratio of 1.16 (95% CI: 0.98, 1.38). Non-inferiority was not met, as the upper bound of the 95% CI (1.38) exceeded the pre-specified margin of 1.28. However, the low event rate in this well-controlled population caused individual events to carry disproportionate weight, reducing statistical power and widening the confidence interval. Notably, most participants in both treatment arms experienced no clinically significant exacerbations during the study period. Secondary endpoints: Health-related quality of life (SGRQ), asthma control (ACQ-5), and lung function (pre-bronchodilator FEV₁) remained stable in both treatment groups throughout the study.

THERAPEUTIC ALTERNATIVES ⁵⁶⁷						
DRUG	VANF	VA Restriction	FDA Indications	MOA	Dosage in Asthma	Guidelines in Asthma
Benralizumab	PA-F	CFU	Add-on maintenance treatment of severe asthma with an eosinophilic phenotype in patients ≥ 6 years; HES; EGPA	Anti-IL-5Rα; binds IL-5 receptor alpha subunit, inducing eosinophil apoptosis	30 mg SC Q4W x 3 doses, then Q8W; home self-injection	GINA: Step 5 option, eosinophilic asthma. CHEST: Rec for T2-high, AEC ≥300.
Mepolizumab	NF	No	Same as above for asthma; CRSwNP; COPD; EGPA; HES	Anti-IL-5; binds to circulating IL-5.	100 mg SC Q4W; home self-injection	GINA: Step 5 option, eosinophilic asthma. CHEST: Rec for T2-high, AEC ≥150.
Reslizumab	NF	No	Same as above for asthma; ≥ 18 years	Same as mepolizumab	3 mg/kg IV Q4W; in-clinic infusion	GINA: Step 5 option, eosinophilic asthma. CHEST: Rec for T2-high, AEC ≥400.
Depemokimab-ulaa	NF	No	Same as above; ≥ 12 years	Same as mepolizumab; extended half-life (YTE Fc modification)	100 mg SC Q6 months; healthcare provider-administered	GINA: Step 5 option, eosinophilic asthma. CHEST: Rec for T2-high (not explicitly named)
Omalizumab	PA-F	CFU	Moderate-to-severe persistent allergic asthma with a positive skin test or in vitro reactivity to a perennial aeroallergen, inadequately controlled with ICS; CRSwNP; IgE-mediated food allergy; CSU	Anti-IgE; binds to the Fc part of free IgE.	75 - 375 mg SC Q2-4W (weight/IgE-based); In-clinic initiation x3 doses → home self-injection eligible	GINA: Step 5 option, allergic asthma. CHEST: Rec for allergic phenotype.
Dupilumab	NF	No	Add-on maintenance treatment of moderate-to-severe asthma with an eosinophilic phenotype or OCS-dependent asthma in patients ≥ 6 years; CRSwNP; EoE; PN; COPD; urticaria; BP; AFRS; atopic dermatitis	Anti-IL-4Rα; blocks IL-4 and IL-13 signaling.	400/200 mg or 600/300 mg SC load, then Q2W; home self-injection	GINA: Step 5 option, eosinophilic/T2 or OCS-dependent. CHEST: Rec for T2-high, AEC ≥150 with OCS-dependence.
Tezepelumab	NF	CFU	Indication: Add-on maintenance treatment of severe asthma in patients ≥ 12 years (no phenotype limitation); CRSwNP	Anti-TSLP; binds circulating thymic stromal lymphopoietin	210 mg SC Q4W; home self-injection	GINA: Step 5 option, broad phenotype. CHEST: Rec for T2-low or high. Note: has not consistently demonstrated an OCS-sparing effect in trials

POTENTIAL PLACE IN THERAPY

Summary of Evidence	<p>SWIFT-1/2 (N=762) demonstrated 54% pooled reductions in annualized exacerbations vs. placebo comparable to other agents; however, the first secondary endpoint (SGRQ) did not reach statistical significance in either trial, precluding formal inference on subsequent secondary endpoints (FEV₁, ACQ) per the hierarchical testing procedure; a subsequent 2026 pooled analysis⁸ suggested that numerical improvements in quality-of-life and symptom scores were enhanced in patients with uncontrolled symptoms at baseline (ACQ-5 ≥ 1.5), although these post-hoc results largely remained below established thresholds for clinical significance. In the NIMBLE switch trial, depemokimab-ulaa did not meet the prespecified noninferiority margin vs. continued mepolizumab/benralizumab. Exacerbation rates were low in both groups, and symptom control and lung function were maintained. Subgroup analyses suggested outcomes may differ by prior biologic, with the switch from mepolizumab appearing more seamless than the switch from benralizumab, where a numerically higher exacerbation rate was observed; however, the trial was not powered for subgroup-level conclusions. Phase 3 trials are ongoing for EGPA (NCT05263934), HES (NCT05334368), and COPD (VIGILANT, ENDURA-1/2); the CRSwNP indication (ANCHOR-1/2) was reviewed but not approved by the FDA (approved in UK/EU only).</p>
Place in Therapy	<p>Biologic selection in severe asthma is driven by the patient's clinical phenotype, biomarker profile (AEC, FeNO, IgE), comorbidities, OCS dependency, and practical factors including dosing frequency, route, and setting of administration. Anti-IL-5/IL-5R agents, including benralizumab, mepolizumab, reslizumab, and depemokimab-ulaa, are indicated for severe eosinophilic asthma and are not first-line options for patients whose disease is primarily driven by allergic (IgE-mediated) or non-eosinophilic mechanisms. Benralizumab (Q8W after induction) is the only anti-IL-5/IL-5R agent whose mechanism leads to near-complete direct eosinophil depletion; it demonstrates an OCS-sparing effect and offers the longest dosing interval among self-administered SC agents. Mepolizumab (Q4W, self-administered SC) may be considered as an alternative anti-IL-5 agent, offering the broadest range of FDA-approved eosinophilic indications in this class, which may be advantageous for patients with multiple eosinophilic comorbidities. Reslizumab (Q4W, in-clinic IV) is an option but may be reserved for patients who have not responded to SC anti-IL-5 options. Among anti-IL-5/IL-5R agents, depemokimab-ulaa's primary differentiator is its twice-yearly dosing schedule; this may provide an option for patients without other eosinophilic comorbidities who are routinely nonadherent to more frequently dosed biologics and who are able to make Q6-month in-clinic visits for administration by a healthcare provider. Dupilumab (anti-IL-4Rα; Q2W, self-administered SC) may also be considered for eosinophilic/Type 2 asthma, particularly when inflammation extends beyond eosinophilia (e.g., concurrent atopic dermatitis, CRSwNP), when FeNO ≥ 25 ppb, or in OCS-dependent patients; however, it is not suggested for patients with a pre-treatment AEC $>1,500$ cells/μL due to the risk of dupilumab-associated hypereosinophilia. Tezepelumab, the only biologic without a phenotype restriction, may be considered across T2-high and T2-low endotypes and may be suited for patients with overlapping allergic and eosinophilic features or those who have not responded to phenotype-directed biologics; however, it has not demonstrated an OCS-sparing effect. Omalizumab (anti-IgE; Q2–4W, weight/IgE-based dosing) remains a well-established option for moderate-to-severe allergic asthma characterized by elevated IgE and confirmed aeroallergen sensitization but is not indicated for eosinophilic asthma driven by non-IgE mechanisms.</p>

Contact person: Linda Tristani, PharmD, BCPS, National Program Manager, VA Pharmacy Services – Formulary Management

References

- EXDENSUR (depemokimab-ulaa) injection, [prescribing information online]. Philadelphia, PA: GlaxoSmithKline LLC; Revised December 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/761458Orig1s000lbl.pdf. Accessed 6/22/2026.
- Center for Drug Evaluation and Research (CDER). Multi-discipline review of EXDENSUR (depemokimab-ulaa) injection. Food and Drug Administration (FDA). December 2025.
- Pavord ID, Bel EH, Bourdin A, et al.; SWIFT-1 and SWIFT-2 Investigators. Depemokimab in severe eosinophilic asthma. *N Engl J Med*. 2024;391(24):2337-2347.
- Chupp G, Nagase H, Skowasch D, et al.; NIMBLE Study Investigators. Switching to twice-yearly depemokimab from mepolizumab/benralizumab in severe asthma: a multicenter, randomized, double-blind, phase 3A clinical trial (NIMBLE). *Am J Respir Crit Care Med*. 2026;212(5):921-935. doi:10.1093/ajrccm/aamag031.
- US Food and Drug Administration. Drugs@FDA: FDA Approved Drug Products. Available at: <https://www.accessdata.fda.gov/scripts/cder/daf/>. Accessed 6/18/26.
- Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2026. Updated May 2026. Available from: www.ginasthma.org
- Oberle AJ, Abbas F, Adrish M, et al. Biologic management in severe asthma for adults: an American College of Chest Physicians clinical practice guideline. *Chest*. 2026;169(2):336-348. doi:10.1016/j.chest.2025.08.042.
- Wechsler ME, Pavord ID, Panettieri RA, et al. Early and sustained efficacy of depemokimab in type 2 asthma: a pooled analysis of the SWIFT-1/-2 studies. *J Allergy Clin Immunol Pract*. 2026;14(6):1362.e1. doi:10.1016/j.jaip.2026.02.015.