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Depemokimab-ulaa

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of care developed by: nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of

American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated, and coverage is not required for non-formulary drugs.

Coverage

Depemokimab-ulaa (Exdensur) **may be considered medically necessary** as an add-on maintenance treatment for moderate to severe eosinophilic asthma in individuals who meet the following criteria:

1. Individual is at least 12 years of age or older;
2. There is documented and current use of an inhaled corticosteroid (ICS) in combination with a long acting beta2-agonist (LABA), leukotriene receptor antagonist (LTRA), theophylline or long acting muscarinic antagonist (LAMA);
3. The individual has uncontrolled asthma while on control therapy as evidenced by two or more exacerbations requiring systemic glucocorticoids, frequent ER visits, or hospitalizations (see **NOTE 1**);
4. Blood eosinophil ≥ 150 cells/mcL at screening or ≥ 300 cells/mcL during the previous year.

NOTE 1: Individuals who do not meet the criteria for uncontrolled asthma, but whose asthma worsens on tapering off corticosteroids, will also meet this definition of moderate to severe asthma. For definition of uncontrolled asthma see Description section.

Depemokimab-ulaa (Exdensur) **is considered experimental, investigational and/or unproven** for all other non-Food and Drug Administration (FDA) approved indications.

Policy Guidelines

None.

Description

Asthma, a chronic respiratory disease, is characterized by symptoms like wheezing, chest tightness, coughing, and shortness of breath, resulting from factors including airway inflammation, bronchoconstriction, hyperresponsiveness, and airway remodeling. (2) Nearly 28 million people in the United States (U.S.) have asthma. (3)

Although the majority of asthma patients can be effectively treated with currently available medications, a substantial subset exists who remain difficult-to-treat. Much remains unclear regarding the best approaches to the management of these patients or concerning the underlying mechanisms driving this process. Severe asthma is a condition consisting of phenotypes such as eosinophilic asthma. (4) Asthma with an eosinophilic phenotype is a

subtype of asthma characterized by elevated levels of eosinophils (a type of white blood cell) in the airways and/or blood. (5)

Definition of Uncontrolled Asthma

At least one of the following:

- Poor symptom control: Asthma Control Questionnaire (ACQ) score consistently ≥1.5, Asthma Control Test (ACT) score <20 (or ''not well controlled'' by the National Asthma Education and Prevention Program (NAEPP) /Global Initiative for Asthma (GINA) guidelines);
- Frequent severe exacerbations: ≥2 bursts of systemic corticosteroids (CS) (≥3 days each) in the previous year;
- Serious exacerbations: at least 1 hospitalization, intensive care unit (ICU) stay, or mechanical ventilation in the previous year;
- Airflow limitation: after appropriate bronchodilator withhold, forced expiratory volume in 1 second (FEV_1) <80% predicted (in the face of reduced FEV_1/forced vital capacity [FVC] defined as less than the lower limit of normal). (4)

Depemokimab-ulaa

Depemokimab-ulaa is an interleukin-5 (IL-5) antagonist monoclonal antibody (humanized imunoglobulin G1 [IgG1] kappa). Depemokimab-ulaa is produced by recombinant DNA technology in Chinese hamster ovary cells. (1) Exdensur contains depemokimab-ulaa, an ultra-long-acting interleukin-5 (IL-5) antagonist that prevents IL-5 from activating its receptor on eosinophils, this in turn reduces eosinophil production, activation, and survival in the body. (5)

Regulatory Status

On December 17, 2025, the U. S. Food and Drug Administration (FDA) approved Exdensur as an add-on maintenance treatment of severe asthma characterized by an eosinophilic phenotype in adult and pediatric patients aged 12 years and older.

Exdensur is not indicated for the relief of acute bronchospasm or status asthmaticus.

Exdensur should be administered by a healthcare provider via subcutaneous injection.

The prescribing label for Exdensur includes the following Warnings and Precautions:

- Hypersensitivity reactions including anaphylaxis.
- Do not abruptly discontinue systemic or inhaled corticosteroids upon initiation of Exdensur therapy. Reductions in corticosteroid dose, if appropriate, should be gradual and performed under the supervision of a healthcare provider.
- Patients with pre-existing helminth infections should be treated for their infection prior to initiation of Exdensur therapy. If patients become infected while receiving treatment with Exdensur and do not respond to anti-helminth treatment, discontinue treatment with Exdensur until the infection resolves.

Rationale

This policy is based on the United States (U.S.) Food and Drug Administration (FDA) labeled indications for depemokimab-ulaa (Exdensur).

Clinical Studies (1)

The efficacy of Exdensur for the add-on maintenance treatment of severe asthma characterized by an eosinophilic phenotype was evaluated in 2 replicate, randomized (2:1 to Exdensur or placebo), double-blind, parallel-group, placebo-controlled, multicenter clinical trials (SWIFT-1 [NCT04719832] and SWIFT-2 [NCT04718103]) of 52 weeks duration. The trials enrolled adult and pediatric patients aged 12 years and older with asthma characterized by an eosinophilic phenotype, defined as a blood eosinophil count ≥150 cells/mcL at screening or ≥300 cells/mcL documented in the year prior to study entry. Patients were required to have 2 or more asthma exacerbations requiring treatment with systemic corticosteroids (SCS) in the prior year while on background asthma therapy consisting of a medium- to high-dose inhaled corticosteroid (ICS) plus at least one additional asthma controller with or without maintenance oral corticosteroids (OCS). Patients were also required to have reduced lung function at baseline (pre-bronchodilator forced expiratory volume in 1 second [FEV_1] <80% predicted normal in adults; FEV_1 <90% or FEV_1 to forced vital capacity ratio <0.8 in pediatric patients aged 12 years and older). Patients were enrolled without requiring a minimum baseline Asthma Control Questionnaire-5 (ACQ-5) score. In these trials, Exdensur 100 mg was administered SC once every 6 months for a total of 2 doses in addition to background asthma therapy. The efficacy population consisted of 762 patients who received at least 1 dose of Exdensur 100 mg or placebo in SWIFT-1 (N = 382) and SWIFT-2 (N = 380).

The demographics and baseline characteristics of the efficacy population in SWIFT-1 and SWIFT-2 are provided in Table 1**.**

Table 1. Demographics and Baseline Characteristics of Adult and Pediatric Patients Aged 12 Years and Older with Severe Asthma in SWIFT-1 and SWIFT-2

	SWIFT-1 N = 382	**SWIFT-2 N = 380**
Age (years), n (%)		
12-17	8 (2)	22 (6)
18-64	276 (72)	262 (69)
≥65	98 (26)	96 (25)
Mean (SD)	54 (14.2)	53 (16.2)
Female, n (%)	223 (58)	241 (63)
Race, n (%)		
White	316 (83)	272 (72)
Asian	58 (15)	75 (20)
Black or African American	8 (2)	28 (7)
Other	0	5 (1)
Hispanic or Latino, n (%)	23 (6)	65 (17)

Never smoked, n (%)	288 (75)	294 (77)
Duration of asthma (years), mean (SD)	22 (16.2)	25 (18.5)
Pre-bronchodilator % predicted FEV_1, mean (SD)	62 (15.2)	62 (15.9)
% reversibility, mean (SD)	17 (15.3)	18 (17.4)
Eosinophil count (cells/mcL), median (min; max)	310 (20; 2,360)	340 (10; 4,440)
Exacerbations in previous year, mean (SD)	2.2 (0.7)	2.7 (1.9)
High-dose ICS use, n (%)[a]	203 (53)	226 (59)
ICS + LABA + LAMA use, n (%)	95 (25)	127 (33)
Maintenance OCS use, n (%)	21 (5)	19 (5)
Total IgE (U/mcL), median (min; max)	185 (2; 12,142)	180 (2; 16,199)

FEV_1: forced expiratory volume in 1 second; ICS: inhaled corticosteroid; IgE: immunoglobulin E; LABA: long-acting beta agonist; LAMA: long-acting muscarinic antagonist; mcL: microliter; N: number of patients in the efficacy population; n: number of patients in the respective group; OCS: oral corticosteroid; SD: standard deviation; U: units.

[a] Medium ICS dose = 440 mcg fluticasone propionate (FP) daily or equivalent; High ICS dose >440 mcg FP daily or equivalent.

Exacerbations

The primary efficacy endpoint for SWIFT-1 and SWIFT-2 was the annualized rate of clinically significant exacerbations over the 52-week treatment period. A clinically significant exacerbation was defined as worsening of asthma requiring use of SCS such as intravenous (IV) or oral steroids for at least 3 days or a single intramuscular (IM) corticosteroid dose and/or hospitalization and/or Emergency Department visit. For patients on maintenance SCS, at least double the existing maintenance dose for at least 3 days was required. All patients experiencing an exacerbation were treated with SCS.

In SWIFT-1 and SWIFT-2, the annualized rate of asthma exacerbations was significantly lower in patients receiving Exdensur compared to placebo (Table 2). During the 52-week treatment period, fewer patients experienced exacerbations in the Exdensur group (32% and 32%) compared to the placebo group (46% and 50%) in SWIFT-1 and SWIFT-2, respectively.

Table 2. Annualized Rate of Clinically Significant Asthma Exacerbations Over 52 Weeks in SWIFT-1 and SWIFT-2

	SWIFT-1		**SWIFT-2**	
	Exdensur N = 250	Placebo N = 132	Exdensur N = 252	Placebo N = 128
Annualized rate of clinically significant asthma exacerbations	0.46	1.11	0.56	1.08
Rate ratio (95% CI)	0.42 (0.30, 0.59)		0.52 (0.36, 0.73)	
P-value	<0.001		<0.001	

CI: confidence interval; N: number of patients in the efficacy population.

Note: Results obtained from a negative binomial model with an offset term for years in study and fixed effects for treatment group, asthma exacerbation history, baseline ICS dose, geographical region, and baseline pre-bronchodilator % predicted FEV_1.

The percentage of patients with exacerbations requiring hospitalization and/or Emergency Department visit was numerically lower for patients treated with Exdensur (1% and 4%) compared with placebo (8% and 10%) in SWIFT-1 and SWIFT-2, respectively.

In SWIFT-1 and SWIFT-2, the time to first clinically significant exacerbation was longer for Exdensur compared to placebo.

Lung Function

In SWIFT-1 and SWIFT-2, the mean change from baseline in pre-bronchodilator FEV_1 for Exdensur was 160 mL and 240 mL, respectively, compared to 160 mL and 184 mL for placebo. The treatment difference in SWIFT-1 and SWIFT-2 relative to placebo was -1 mL (95% CI (confidence interval): -89, 88) and 56 mL (95% CI: -43, 154), respectively.

Patient-Reported Outcome

In SWIFT-1 and SWIFT-2, the proportion of ACQ-5 responders (clinically meaningful improvement defined as a decrease in score of 0.5 or more) at Week 52 was 54% for Exdensur in both studies compared to 55% and 53%, respectively, for placebo.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J2361

*Current Procedural Terminology (CPT®) ©2025 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Label:

1. Prescribing Label: Exdensur (depemokimab-ulaa) injection, for subcutaneous use. December 2025. Available at <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm> (accessed July 1, 2026).

Other:

2. Hussain M, Liu G. Eosinophilic Asthma: Pathophysiology and Therapeutic Horizons. Cells. Feb 23 2024; 13(5):384. PMID 38474348
3. Asthma and Allergy Foundation of America. Asthma. Available at <https://aafa.org> (accessed July 1, 2026).
4. Chung KF, Wenzel SE, Brozeh JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. Eur Respir J. Feb 2014; 43(2):343-373. PMID 24337046
5. Exdensur (depemokimab-ulaa) FDA Approval History. Available at <https://www.drugs.com> (accessed July 1, 2026).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
09/01/2026	Document updated. The following change was made to Coverage: Removed criteria 5 and 6 addressing adult and pediatric lung function parameters. No new references added.
07/01/2026	New medical document. Depemokimab-ulaa (Exdensur) may be considered medically necessary as an add-on maintenance treatment for moderate to severe eosinophilic asthma in individuals who meet the following criteria: Individual is at least 12 years of age or older; There is documented and current use of an inhaled corticosteroid (ICS) in combination with a long acting beta2-agonist (LABA), leukotriene receptor antagonist (LTRA), theophylline or long acting muscarinic antagonist (LAMA); The individual has uncontrolled asthma while on control therapy as evidenced by two or more exacerbations requiring systemic glucocorticoids, frequent ER visits, or hospitalizations (see NOTE 1); Blood eosinophil ≥ 150 cells/mcL at screening or ≥ 300 cells/mcL during the previous year; Adults: Reduced lung function demonstrated by pre-bronchodilator forced expiratory volume in 1 second (FEV_1) < 80% of predicted; Pediatrics: Reduced lung function demonstrated by one of the following: FEV_1 <90%, OR FEV_1 to forced vital capacity ratio < 0.8. NOTE 1: Individuals who do not meet the criteria for uncontrolled asthma, but whose asthma worsens on tapering off corticosteroids, will also

	meet this definition of moderate to severe asthma. For definition of uncontrolled asthma see Description section. Depemokimab-ulaa (Exdensur) is considered experimental, investigational and/or unproven for all other non-Food and Drug Administration (FDA) approved indications.