



Drug Coverage Policy

Effective Date8/1/2025

Coverage Policy Number.....IP0453

Policy Title..... Dupixent

Immunologicals – Dupixent

- Dupixent® (dupilumab subcutaneous injection – Regeneron/Sanofi-Aventis)

INSTRUCTIONS FOR USE

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OVERVIEW

Dupixent, an interleukin-4 receptor alpha antagonist, is indicated for the following uses:¹

- **Asthma**, as an add-on maintenance treatment in patients ≥ 6 years of age with moderate-to-severe disease with an eosinophilic phenotype or with oral corticosteroid-dependent asthma.

Limitation of Use: Dupixent is not indicated for the relief of acute bronchospasm or status asthmaticus.

- **Atopic dermatitis**, for the treatment of patients ≥ 6 months of age with moderate-to-severe disease not adequately controlled with topical prescription therapies or when those therapies are not advisable.
- **Chronic obstructive pulmonary disease (COPD)**, as add-on maintenance treatment in patients ≥ 18 years of age with inadequately controlled disease and an eosinophilic phenotype.

Limitation of Use: Dupixent is not indicated for the relief of acute bronchospasm.

- **Chronic rhinosinusitis with nasal polyposis (CRSwNP)** [i.e., nasal polyps], as an add-on maintenance treatment in patients ≥ 12 years of age with inadequately controlled disease.
- **Chronic spontaneous urticaria**, in patients ≥ 12 years of age who remain symptomatic despite H₁ antihistamine treatment.

Limitation of Use: Dupixent is not indicated for the treatment of other forms of urticaria.

- **Eosinophilic esophagitis**, in patients ≥ 1 year of age who weigh ≥ 15 kg.
- **Prurigo nodularis**, in patients ≥ 18 years of age.

Clinical Efficacy

Asthma

Timing of efficacy assessments varied by indication across the numerous pivotal studies in which Dupixent demonstrated benefit. In the asthma trials, efficacy with Dupixent was assessed as early as 24 weeks.²⁻⁵

Atopic Dermatitis

In atopic dermatitis, the majority of studies evaluated the efficacy of Dupixent at 16 weeks.^{1,6-10}

Chronic Obstructive Pulmonary Disease

Two pivotal studies evaluated Dupixent in adults with COPD.^{11,12} To be eligible for enrollment, patients had a blood eosinophil level ≥ 300 cells per microliter. Patients were required to have been receiving background triple inhaler therapy (i.e., an inhaled corticosteroid [ICS] with a long-acting muscarinic antagonist [LAMA] and a long-acting beta2-agonist [LABA]) or LAMA/LABA combination therapy if the patient had an ICS contraindication, for at least 3 months prior to randomization. Patients also had experienced at least two moderate COPD exacerbations (e.g., resulted in systemic corticosteroid treatment) or one severe COPD exacerbation (e.g., resulted in hospitalization for ≥ 24 hours) the year prior to screening. Overall, at least one of the patient's exacerbations had to have occurred while they were receiving ICS/LAMA/LABA therapy (or a LAMA/LABA if the patient had an ICS contraindication). Patients were randomized to receive either Dupixent or placebo in addition to background maintenance therapy (i.e., ICS/LAMA/LABA triple therapy or LAMA/LABA therapy if the patient had an ICS contraindication) for 52 weeks. While lung function parameters were improved as early as Week 12 (3 months), the other major efficacy endpoints were evaluated at Week 52 (e.g., exacerbations, dyspnea scores).

Chronic Rhinosinusitis with Nasal Polyps

The pivotal studies involving patients with CRSwNP evaluated the primary efficacy endpoints following 24 weeks of treatment.^{1,13-15} Patients continued treatment with intranasal corticosteroids throughout the studies.

Chronic Spontaneous Urticaria

The pivotal studies of Dupixent in patients with chronic spontaneous urticaria involved patients who were symptomatic despite H₁ antihistamine treatment at approved or higher doses.^{16,38} In both studies, patients were required to have experienced itch and hives for > 6 consecutive

weeks, despite treatment with an H₁ antihistamine up to 4 times a standard dose. The primary efficacy endpoints were evaluated following 24 weeks of treatment.

Eosinophilic Esophagitis

In Dupixent's eosinophilic esophagitis pivotal study, patients ≥ 12 years of age were required to have disease confirmed by baseline endoscopic biopsies with a demonstration of eosinophilic infiltration on central reading (peak cell count ≥ 15 eosinophils per high-powered field) that was unresponsive to an 8 week course of treatment with a high-dose proton pump inhibitor.¹⁷ Patients with other causes of eosinophilic esophagitis, such as hypereosinophilic syndrome and eosinophilic granulomatosis with polyangiitis, were excluded from the study. In the first portion of this study, efficacy, as measured by objective assessments (e.g., intraepithelial eosinophil count) and subjective assessments (e.g., dysphagia symptoms), was evaluated after 24 weeks (6 months) of Dupixent therapy. A very similarly designed pivotal study evaluated the efficacy of Dupixent for the treatment of eosinophilic esophagitis in patients 1 to 11 years of age.^{1,18} Endoscopic biopsy evidence of eosinophilic infiltration despite treatment with a proton pump inhibitor was again required for study enrollment.

Prurigo Nodularis

Two pivotal studies, PRIME and PRIME2, evaluated Dupixent's efficacy in the treatment of prurigo nodularis.¹⁹ To enroll, patients were required to have ≥ 20 identifiable nodular lesions in total on both legs, and/or both arms, and/or trunk and to have failed a 2-week trial of a topical corticosteroid. Patients with prurigo nodularis secondary to medications or a medical condition such as neuropathy or psychiatric disease were excluded from the studies. The primary endpoint was evaluated at Week 24 in PRIME and initially at Week 12 and again at Week 24 in PRIME2.

Guidelines

Asthma Guidelines

The Global Initiative for Asthma Global Strategy for Asthma Management and Prevention (2025) proposes a stepwise approach to asthma treatment.²⁰ Dupixent is listed as an option for add-on therapy in patients ≥ 6 years of age with severe eosinophilic/Type 2 asthma or who require treatment with a maintenance oral corticosteroid. Severe asthma is defined as asthma that is uncontrolled despite adherence to optimized high-dose ICS/LABA therapy or that worsens when high-dose treatment is decreased. Higher blood eosinophil levels and higher fractional concentration of exhaled nitric oxide may predict a good asthma response to Dupixent. According to the European Respiratory Society/American Thoracic Society guidelines (2014; updated in 2020), severe asthma is defined as asthma which requires treatment with a high-dose inhaled corticosteroid (ICS) in addition to a second controller medication (and/or systemic corticosteroids) to prevent it from becoming uncontrolled, or asthma which remains uncontrolled despite this therapy.^{21,22} Uncontrolled asthma is defined as asthma that worsens upon tapering of high-dose ICS or systemic corticosteroids or asthma that meets one of the following four criteria:

- 1) Poor symptom control: Asthma Control Questionnaire consistently ≥ 1.5 or Asthma Control Test < 20; OR
- 2) Frequent severe exacerbations: two or more bursts of systemic corticosteroids in the previous year; OR
- 3) Serious exacerbations: at least one hospitalization, intensive care unit stay, or mechanical ventilation in the previous year; OR
- 4) Airflow limitation: forced expiratory volume in 1 second (FEV₁) < 80% predicted after appropriate bronchodilator withholding.

Atopic Dermatitis Guidelines

Guidelines for the care and management of atopic dermatitis (with topical therapies in adults [2022], with phototherapy and systemic agents [2023]) have been updated to address Dupixent.^{23,24} The guidelines note that despite the availability of newer, systemic therapies (e.g.,

Dupixent), topical agents remain the mainstay of treatment due to their proven track record and favorable safety profiles. Several topical agents are recommended, with topical corticosteroids commonly used first-line for mild to severe atopic dermatitis in all skin regions. If topical therapy and basic management (e.g., moisturizers, bathing modifications) have been optimized and the patient has not achieved adequate control, consider an alternative diagnosis or systemic therapy. In this setting, use of Dupixent is recommended in patients with moderate to severe disease (strong recommendation).

Chronic Obstructive Pulmonary Disease Guidelines

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2025) recommends triple inhaled therapy with an ICS/LAMA/LABA combination in patients with a history of exacerbations and elevated eosinophils.²⁵ However, guidelines note that ICS therapy increases the risk of pneumonia in patients with COPD, particularly those with severe disease. Dupixent is a recommended treatment option in patients who continue to have symptoms despite ICS/LAMA/LABA therapy and have eosinophils ≥ 300 cells/microliter and symptoms of chronic bronchitis.

Chronic Rhinosinusitis with Nasal Polyps Guidelines

The Joint Task Force on Practice Parameters (JTFPP) published a focused guideline update for the medical management of CRSwNP (2023), which updated recommendations regarding intranasal corticosteroids and biologic therapies.²⁶ Intranasal corticosteroids are recommended for the treatment of CRSwNP. Use of biologics (e.g., Dupixent) is also recommended. However, in patients who derived a sufficient benefit from other therapies such as intranasal corticosteroids, surgery, or aspirin therapy after desensitization, biologics may not be preferred. Conversely, biologics may be preferred over other medical treatment options in patients who continue to have a high burden of disease despite receiving at least 4 weeks of treatment with an intranasal corticosteroid.

The diagnosis of CRSwNP was not addressed in this focused guideline update, but previous guidelines have noted that the presence of two or more signs and symptoms of chronic rhinosinusitis (e.g., rhinorrhea, postnasal drainage, anosmia, nasal congestion, facial pain, headache, fever, cough, and purulent discharge) that persist for an extended period of time makes the diagnosis chronic rhinosinusitis likely.²⁷⁻³⁰ However, this requires confirmation of sinonasal inflammation, which can either be done via direct visualization or computed tomography (CT) scan. Oral corticosteroids and surgical intervention were not specifically addressed in this update, but prior guidelines recommend short courses of oral corticosteroid as needed and consideration of surgical removal as an adjunct to medical therapy in patients with CRSwNP that is not responsive or is poorly responsive to medical therapy.^{27,28,30}

Chronic Spontaneous Urticaria Guidelines

Guidelines for the definition, classification, diagnosis, and management of urticaria have been published by the European Academy of Allergy and Clinical Immunology/Global Allergy and Asthma European Network/European Dermatology Forum/Asia Pacific Association of Allergy, Asthma and Clinical Immunology (2022).³¹ The American Academy of Dermatology was involved in the development of these guidelines and endorses their recommendations. Chronic spontaneous urticaria is defined as the appearance of wheals, angioedema, or both for > 6 weeks due to known or unknown causes. Signs and symptoms may be present daily/almost daily or have an intermittent recurrent course. Second generation H₁-antihistamines taken regularly are the recommended first-line treatment for all types of urticaria following elimination of possible underlying causes. If standard doses do not eliminate urticaria signs and symptoms, the dose of the antihistamine should be increased up to 4-fold. Guidelines have not been updated since the approval of Dupixent. Short courses of rescue systemic corticosteroids are recommended for

treatment of patients with acute exacerbations of chronic urticaria. However, guidelines recommend against the long-term use of systemic steroids.

Eosinophilic Esophagitis Guidelines

Guidelines for the diagnosis and management of EoE from the American College of Gastroenterology (2025) confirm that the diagnosis of EoE should be based on the presence esophageal dysfunction symptoms and ≥ 15 eosinophils per high-power field on esophageal biopsy.³² Treatment with a proton pump inhibitor is recommended. Dupixent is a recommended treatment for patients who are ≥ 1 year of age who are nonresponsive to proton pump inhibitor therapy. A food elimination diet is recommended. However, it is noted that patient preferences should be taken into account and that any decisions regarding diet should be agreed upon between the patient and the provider.

Prurigo Nodularis Guidelines

A United States Expert Panel Consensus provides a practical approach for the diagnosis and management of prurigo nodularis (2021).³³ The primary findings in patients with prurigo nodularis are the presence of firm, nodular lesions; pruritus lasting at least 6 weeks; and history or signs, or both, of repeated scratching, picking, or rubbing. Goals of treatment are to reduce pruritus, interrupt the itch-scratch cycle, and completely heal prurigo nodularis lesions.

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for benefit coverage of Dupixent. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Dupixent as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Dupixent to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Dupixent is considered medically necessary when ONE of the following is met (1, 2, 3, 4, 5, 6 or 7):

FDA-Approved Indications

1. Asthma. Approve for the duration noted if the patient meets one of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets the following (i, ii, iii, iv, v, and vi):

i. Patient is ≥ 6 years of age; AND

ii. Patient meets ONE of the following (a or b):

a) Patient meets ONE of the following (1 or 2):

(1) Patient has a blood eosinophil level ≥ 150 cells per microliter within the previous 6 weeks; OR

(2) Patient had a blood eosinophil level ≥ 150 cells per microliter prior to treatment with Dupixent or another monoclonal antibody therapy that may alter blood eosinophil levels; OR

Note: Examples of monoclonal antibody therapies that may lower blood eosinophil levels include Dupixent, Adbry (tralokinumab-ldrm subcutaneous injection), Cinqair (reslizumab intravenous infusion), Ebglyss (lebrikizumab-lbkz subcutaneous injection), Fasenra (benralizumab subcutaneous injection), Nemluvio (nemolizumab-ilito subcutaneous injection), Nucala (mepolizumab subcutaneous injection), Tezspire

- (tezepelumab subcutaneous injection), and Xolair (omalizumab subcutaneous injection).
- b)** According to the prescriber, the patient has oral (systemic) corticosteroid-dependent asthma (e.g., the patient has received ≥ 5 mg oral prednisone or equivalent per day for ≥ 6 months); AND
 - iii.** Patient has received at least 3 consecutive months of combination therapy with BOTH of the following (a and b):
 - a)** A medium- or high-dose inhaled corticosteroid; AND
 - b)** At least one additional asthma controller or asthma maintenance medication; AND
Note: Examples of additional asthma controller or asthma maintenance medications are inhaled long-acting beta₂-agonists, inhaled long-acting muscarinic antagonists, and monoclonal antibody therapies for asthma (e.g., Cinqair, Fasenra, Nucala, Tezspire, and Xolair). Use of a combination inhaler containing both a medium- or high-dose inhaled corticosteroid and additional asthma controller/maintenance medication(s) would fulfill the requirement for both criteria a and b.
 - iv.** Patient has a history of ONE of the following (a or b):
 - a)** Patient meets BOTH of the following (1 and 2):
 - (1)** Patient has a forced expiratory volume in 1 second (FEV₁) < 80% predicted; AND
Note: The reduced FEV₁ should not be due to smoking-related chronic obstructive pulmonary disease.
 - (2)** Patient has an FEV₁/forced vital capacity (FVC) < 0.80; OR
 - b)** Patient meets ONE of the following (1, 2, 3, 4, or 5):
 - (1)** Increase of > 12% and > 200ml in FEV₁ following administration of a standard dose of a short-acting bronchodilator; OR
 - (2)** Increase of > 12% and > 200ml in FEV₁ between prescriber visits; OR
 - (3)** Increase of > 12% and > 200ml in FEV₁ from baseline to after at least 4 weeks of asthma treatment; OR
 - (4)** Positive exercise challenge testing; OR
 - (5)** Positive bronchial challenge testing; AND
Note: The above lung function criteria may be met at any time prior to or during asthma treatment.
Note: Patients 6 to 11 years of age would only be required to have an increase of > 12% in FEV₁ in each of the respective criteria above (i.e., they would not be required to have an increase > 200 mL)
 - v.** Patient has asthma that is uncontrolled or was uncontrolled at baseline as defined by ONE of the following (a, b, or c):
 - Note: "Baseline" is defined as prior to receiving Dupixent or another monoclonal antibody therapy for asthma. Examples of monoclonal antibody therapies for asthma include Dupixent, Cinqair, Fasenra, Nucala, Tezspire, and Xolair.
 - a)** Patient experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year; OR
 - b)** Patient experienced one or more asthma exacerbation(s) requiring a hospitalization, an emergency department visit, or an urgent care visit in the previous year; OR
 - c)** Patient has asthma that worsens upon tapering of oral (systemic) corticosteroid therapy; AND
 - vi.** The medication is prescribed by or in consultation with an allergist, immunologist, or pulmonologist.
 - B) Patient is Currently Receiving Dupixent.** Approve for 1 year if the patient meets the following (i, ii, and iii):
 - i.** Patient has already received at least 6 months of therapy with Dupixent; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Dupixent should be considered under criterion 1A (Asthma, Initial Therapy).

- ii. Patient continues to receive therapy with one inhaled corticosteroid or one inhaled corticosteroid-containing combination inhaler; AND
- iii. Patient has responded to therapy as determined by the prescriber.
Note: Examples of a response to Dupixent therapy are decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, emergency department visits, or urgent care visits due to asthma; decreased requirement for oral corticosteroid therapy.

2. Atopic Dermatitis. Approve for the duration noted if the patient meets one of the following (A or B):

A) Initial Therapy. Approve for 4 months if the patient meets the following (i, ii, iii, and iv):

- i. Patient is ≥ 6 months of age; AND
- ii. According to the prescriber, patient has atopic dermatitis involvement estimated to be $\geq 10\%$ of the body surface area; AND
- iii. Patient meets ALL of the following (a, b, and c):
 - a) Patient has tried at least one medium-, medium-high, high-, and/or super-high-potency prescription topical corticosteroid; AND
 - b) This topical corticosteroid was applied daily for at least 28 consecutive days; AND
 - c) According to the prescriber, inadequate efficacy was demonstrated with this topical corticosteroid therapy; AND
- iv. The medication is prescribed by or in consultation with an allergist, immunologist, or dermatologist.

B) Patient is Currently Receiving Dupixent. Approve for 1 year if the patient meets the following (i and ii):

- i. Patient has already received at least 4 months of therapy with Dupixent; AND
Note: A patient who has received < 4 months of therapy or who is restarting therapy with Dupixent should be considered under criterion 2A (Atopic Dermatitis, Initial Therapy).
- ii. Patient has responded to therapy as determined by the prescriber.
Note: Examples of a response to Dupixent therapy are marked improvements in erythema, induration/papulation/edema, excoriations, and lichenification; reduced pruritus; decreased requirement for other topical or systemic therapies; reduced body surface area affected with atopic dermatitis; or other responses observed.

3. Chronic Obstructive Pulmonary Disease (COPD). Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, and v):

- i. Patient is ≥ 18 years of age; AND
- ii. Patient meets ONE of the following (a or b):
 - a) Patient has a blood eosinophil level ≥ 300 cells per microliter within the previous 6 weeks; OR
 - b) Patient had a blood eosinophil level ≥ 300 cells per microliter prior to treatment with Dupixent or another monoclonal antibody therapy that may alter blood eosinophil levels; AND
Note: Examples of monoclonal antibody therapies that may alter blood eosinophil levels include Dupixent, Adbry (tralokinumab-ldrm subcutaneous injection), Cinqair (reslizumab intravenous infusion), Ebglyss (lebrikizumab-lbkz subcutaneous injection); Fasenra (benralizumab subcutaneous injection), Nemluvio (nemolizumab-ilto subcutaneous injection); Nucala (mepolizumab subcutaneous injection), Tezspire (tezepelumab subcutaneous injection), and Xolair (omalizumab subcutaneous injection).
- iii. Patient meets ONE of the following (a or b):

- a) Patient has received at least 3 consecutive months of combination therapy with ALL of the following (1, 2, and 3):

(1) Inhaled long-acting beta₂-agonist (LABA); AND

(2) Inhaled long-acting muscarinic antagonist (LAMA); AND

(3) Inhaled corticosteroid (ICS); OR

Note: Use of single-entity inhalers or a combination inhaler containing multiple agents from the medication classes listed would fulfill the requirement.

- b) Patient meets BOTH of the following (1 and 2):

(1) Patient has received at least 3 consecutive months of combination therapy with an inhaled LABA and an inhaled LAMA; AND

Note: Use of single-entity inhalers or a combination inhaler containing multiple agents from the medication classes listed would fulfill the requirement.

(2) According to the prescriber, the patient has a contraindication to the use of an inhaled corticosteroid; AND

- iv. Patient meets ONE of the following (a or b):

a) Patient experienced two or more COPD exacerbations requiring treatment with a systemic corticosteroid with or without an antibiotic in the previous 12 months; OR

b) Patient experienced one or more COPD exacerbation(s) requiring a hospitalization in the previous 12 months; AND

Note: A hospitalization includes a hospital admission or an emergency medical care visit with observation lasting > 24 hours.

- v. The medication is prescribed by or in consultation with an allergist, immunologist, or pulmonologist.

- B) Patient is Currently Receiving Dupixent.** Approve for 1 year if the patient meets the following (i, ii, and iii):

- i. Patient has already received at least 6 months of therapy with Dupixent; AND

Note: A patient who has received < 6 months of therapy or who is restarting therapy with Dupixent should be considered under criterion 3A (Chronic Obstructive Pulmonary Disease, Initial Therapy).

- ii. Patient continues to receive combination therapy with an inhaled LABA and LAMA; AND

Note: Use of single-entity inhalers or a combination inhaler containing multiple agents from the medication classes listed would fulfill the requirement.

- iii. Patient has experienced a beneficial clinical response, defined by ONE of the following (a, b, c, d, or e):

a) Reduced COPD symptoms; OR

b) Reduced COPD exacerbations; OR

c) Reduced COPD-related hospitalizations; OR

d) Reduced emergency department or urgent care visits; OR

e) Improved lung function parameters.

- 4. Chronic Rhinosinusitis with Nasal Polyps.** Approve for the duration noted if the patient meets one of the following (A or B):

- A) Initial Therapy.** Approve for 6 months if the patient meets the following (i, ii, iii, iv, v, and vi):

- i. Patient is ≥ 12 years of age; AND

- ii. Patient has chronic rhinosinusitis with nasal polyps as evidenced by direct examination, endoscopy, or sinus computed tomography (CT) scan; AND

- iii. Patient has experienced two or more of the following symptoms for at least 6 months: nasal congestion, nasal obstruction, nasal discharge, and/or reduction/loss of smell; AND

- iv. Patient meets BOTH of the following (a and b):

- a) Patient has received at least 4 weeks of therapy with an intranasal corticosteroid; AND
 - b) Patient will continue to receive therapy with an intranasal corticosteroid concomitantly with Dupixent; AND
 - v. Patient meets ONE of the following (a, b, or c):
 - a) Patient has received at least one course of treatment with a systemic corticosteroid for 5 days or more within the previous 2 years; OR
 - b) Patient has a contraindication to systemic corticosteroid therapy; OR
 - c) Patient has had prior surgery for nasal polyps; AND
 - vi. The medication is prescribed by or in consultation with an allergist, immunologist, or an otolaryngologist (ear, nose, and throat [ENT] physician specialist).
- B) Patient is Currently Receiving Dupixent.** Approve for 1 year if the patient meets the following (i, ii, and iii):
- i. Patient has already received at least 6 months of therapy with Dupixent; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Dupixent should be considered under criterion 3A (Nasal Polyps, Initial Therapy).
 - ii. Patient continues to receive therapy with an intranasal corticosteroid; AND
 - iii. Patient has responded to therapy as determined by the prescriber.
Note: Examples of a response to Dupixent therapy are reduced nasal polyp size, improved nasal congestion, reduced sinus opacification, decreased sinonasal symptoms, improved sense of smell.

5. Chronic Spontaneous Urticaria (Chronic Idiopathic Urticaria). Approve Dupixent for the duration noted if the patient meets ONE of the following (A or B):

- A) Initial Therapy.** Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):
- i. Patient is ≥ 12 years of age; AND
 - ii. Patient has/had urticaria for > 6 weeks (prior to treatment with Dupixent), with symptoms present > 3 days per week despite daily non-sedating H₁ antihistamine therapy with doses that have been titrated up to a maximum of four times the standard FDA-approved dose; AND
Note: Examples of non-sedating H₁ antihistamine therapy are cetirizine, desloratadine, fexofenadine, levocetirizine, and loratadine.
 - iii. The medication is prescribed by or in consultation with an allergist, immunologist, or dermatologist; OR
- B) Patient is Currently Receiving Dupixent.** Approve Dupixent for 1 year if the patient meets BOTH the following criteria (i and ii):
- i. Patient has already received at least 6 months of therapy with Dupixent; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Xolair should be considered under criterion 5A (Chronic Spontaneous Urticaria [Chronic Idiopathic Urticaria], Initial Therapy).
 - ii. Patient has experienced a beneficial clinical response, defined by ONE of the following (a, b, or c):
 - a) Decreased itch severity; OR
 - b) Decreased number of hives; OR
 - c) Decreased size of hives

6. Eosinophilic Esophagitis. Approve for the duration noted if the patient meets one of the following (A or B):

- A) Initial Therapy.** Approve for 6 months if the patient meets the following (i, ii, iii, iv, v, vi and vii):
- i. Patient is ≥ 1 year of age; AND
 - ii. Patient weighs ≥ 15 kg; AND

- iii. Patient has a diagnosis of eosinophilic esophagitis as confirmed by an endoscopic biopsy demonstrating ≥ 15 intraepithelial eosinophils per high-power field; AND
- iv. Patient does not have a secondary cause of eosinophilic esophagitis; AND
Note: Examples of secondary causes of eosinophilic esophagitis are hypereosinophilic syndrome, eosinophilic granulomatosis with polyangiitis, and food allergy.
- v. Patient has received at least 8 weeks of therapy with a proton pump inhibitor; AND
- vi. Patient meets ONE of the following (a or b):
 - a) Patient has tried dietary modifications to treat/manage eosinophilic esophagitis; OR
 - b) The provider has determined that the patient is not an appropriate candidate for dietary modifications; AND
Note: Examples of dietary modifications to treat eosinophilic esophagitis include an elemental diet or an elimination diet.
- vii. The medication is prescribed by or in consultation with an allergist or gastroenterologist.

B) Patient is Currently Receiving Dupixent. Approve for 1 year if the patient meets the following (i and ii):

- i. Patient has already received at least 6 months of therapy with Dupixent; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Dupixent should be considered under criterion 3A (Eosinophilic Esophagitis, Initial Therapy).
- ii. Patient has experienced a beneficial clinical response, defined by ONE of the following (a, b, or c):
 - a) Reduced intraepithelial eosinophil count; OR
 - b) Decreased dysphagia/pain upon swallowing; OR
 - c) Reduced frequency/severity of food impaction.

7. Prurigo Nodularis. Approve for the duration noted if the patient meets one of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets the following (i, ii, iii, iv, v, and vi):

- i. Patient is ≥ 18 years of age; AND
- ii. Patient has ≥ 20 identifiable nodular lesions in total on both arms, and/or both legs, and/or trunk; AND
- iii. Patient has experienced pruritus for ≥ 6 weeks; AND
- iv. Patient meets ONE of the following (a or b):
 - a) Patient's prurigo nodularis is NOT medication-induced or secondary to a non-dermatologic condition such as neuropathy or a psychiatric disease; OR
 - b) According to the prescriber, the patient has a secondary cause of prurigo nodularis that has been identified and adequately managed; AND
- v. Patient meets ALL of the following (a, b, and c):
 - a) Patient has tried at least one high- or super-high-potency prescription topical corticosteroid; AND
 - b) This topical corticosteroid was applied daily for at least 14 consecutive days; AND
 - c) According to the prescriber inadequate efficacy was demonstrated with this topical corticosteroid therapy; AND
- vi. The medication is prescribed by or in consultation with an allergist, immunologist, or dermatologist.

B) Patient is Currently Receiving Dupixent. Approve for 1 year if the patient meets the following (i and ii):

- i. Patient has already received at least 6 months of therapy with Dupixent; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Dupixent should be considered under criterion 5A (Prurigo Nodularis, Initial Therapy).

- ii. Patient has experienced a beneficial clinical response, defined by ONE of the following (a, b, or c):
 - a) Reduced nodular lesion count; OR
 - b) Decreased pruritus; OR
 - c) Reduced nodular lesion size.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Dupixent for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

- 1. Concurrent Use of Dupixent with another Monoclonal Antibody Therapy.** The efficacy and safety of Dupixent in combination with other monoclonal antibody therapies have not been established.
Note: Monoclonal antibody therapies are Adbry® (tralokinumab-ldrm subcutaneous injection), Cinqair® (reslizumab intravenous injection), Ebglyss® (lebrikizumab-lbkz subcutaneous injection), Fasenra® (benralizumab subcutaneous injection), Nemludio® (nemolizumab-ilto subcutaneous injection), Nucala® (mepolizumab subcutaneous injection), Tezspire® (tezepelumab-ekko subcutaneous injection), or Xolair® (omalizumab subcutaneous injection).
- 2. Concurrent Use of Dupixent with Janus Kinase (JAK) Inhibitors (oral or topical).** Use of JAK inhibitors is not recommended for use in combination with other JAK inhibitors, biologic immunomodulators (e.g., Dupixent), or with other immunosuppressants.²⁹⁻³¹
Note: Examples of JAK inhibitors are Cibinqo® (abrocitinib tablets), Leqselvi™ (deuruxolitinib tablets), Rinvoq®/Rinvoq® LQ (upadacitinib tablets and oral solution), and Opzelura™ (ruxolitinib cream)
- 3. Peanut Allergy.** Dupixent is not indicated for the management of patients with peanut allergy.¹ One phase II, single-arm, open-label study evaluated Dupixent in children and adolescents with peanut allergy (n = 24).³⁹ Following 24 weeks of therapy, Dupixent monotherapy did not improve desensitization to peanut exposure after food challenge. Only 2 patients (8.3%) were able to achieve the primary endpoint of passing the 24-week double-blind placebo-controlled food challenge (DBPCFC) [≥ 444 mg {cumulative} of peanut protein]. Another 8 patients (33.3%) experienced a grade 2 allergic reaction at the 24-week DBPCFC, and 10 patients (41.7%) used epinephrine rescue medication. An additional study (n = 128) evaluated whether Dupixent enhances the efficacy and safety of an oral immunotherapy product, Palforzia® (peanut [*Arachis hypogaea*] allergen powder-dnfp for oral administration), in patients 6 to ≤ 17 years of age with peanut allergy.⁴⁰ Patients received either Dupixent + Palforzia or placebo + Palforzia during a 28- to 40-week up-dosing period. Then, patients in the Dupixent + Palforzia group were re-randomized to receive Dupixent + Palforzia or placebo + Palforzia during a 24-week maintenance period. Following the up-dosing period, Dupixent + Palforzia resulted in a modest increase in efficacy vs. placebo + Palforzia (20.2% increase in the number of patients who passed a DBPCFC [2,044 mg peanut protein {cumulative}] with Dupixent +

Palforzia vs. placebo + Palforzia). Similarly, during the maintenance period, Dupixent + Palforzia increased the number of patients who passed the DBPCFC (2,044 mg peanut protein [cumulative]) vs. placebo + Palforzia (16.6% treatment difference). However, Dupixent was not found to provide protection against Palforzia-related anaphylaxis, which occurred in 5.1% of patients receiving Dupixent + Palforzia and 4.0% of patients receiving placebo + Palforzia. Additional studies are needed to establish the efficacy of Dupixent for peanut allergy.

Coding Information

Note:

- 1) This list of codes may not be all-inclusive.
- 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J3490	Unclassified drug
J3590	Unclassified biologic

References

1. Dupixent® subcutaneous injection [prescribing information]. Tarrytown, NY: Regeneron/Sanofi-Aventis; September 2024.
2. Castro M, Corren J, Pavord ID, et al. Dupilumab efficacy and safety in moderate-to-severe uncontrolled asthma. *N Engl J Med*. 2018;378(26):2486-2496.
3. Wenzel S, Castro M, Corren J, et al. Dupilumab efficacy and safety in adults with uncontrolled persistent asthma despite use of medium-to-high-dose inhaled corticosteroids plus a long-acting β_2 agonist: a randomised double-blind placebo-controlled pivotal phase 2b dose-ranging trial. *Lancet*. 2016;388(10039):31-44.
4. Rabe KF, Nair P, Brusselle G, et al. Efficacy and safety of dupilumab in glucocorticoid-dependent severe asthma. *N Engl J Med*. 2018;378(26):2475-2485.
5. Bacharier LB, Maspero JF, Katelaris CH, et al. Dupilumab in children with uncontrolled moderate-to-severe asthma. *N Engl J Med*. 2021;385(24):2230-2240.
6. Simpson EL, Bieber T, Guttman-Yassky E, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med*. 2016;375(24):2335-2348.
7. Blauvelt A, de Bruin-Weller M, Gooderham M, et al. Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial. *Lancet*. 2017;389:2287-2303.
8. Simpson EL, Paller AS, Siegfried EC, et al. Efficacy and safety of dupilumab in adolescents with uncontrolled moderate to severe atopic dermatitis: a phase 3 randomized clinical trial. *JAMA Dermatol*. 2020;156(1):44-56.
9. Paller AS, Siegfried EC, Thaci D, et al. Efficacy and safety of dupilumab with concomitant topical corticosteroids in children 6 to 11 years old with severe atopic dermatitis: a randomized, double-blinded, placebo-controlled phase 3 trial. *J Am Acad Dermatol*. 2020;83(5):1282-1293.

10. Paller AS, Simpson EL, Siegfried EC, et al. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2022;400:908-919.
11. Bhatt SP, Rabe KF, Hanania NA, et al. Dupilumab for COPD with type 2 inflammation indicated by eosinophil counts. *N Engl J Med*. 2023;289(3):205-214.
12. Bhatt SP, Rabe KF, Hanania NA, et al. Dupilumab for COPD with blood eosinophil evidence of type 2 inflammation. *N Engl J Med*. 2024;390(24):2274-2283.
13. Bachert C, Han JK, Desrosiers M, et al. Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): results from two multicenter, randomized, double-blind, placebo-controlled, parallel-group phase3 trials. *Lancet*. 2019;394(10209):1638-1650.
14. Bachert C, Mannent L, Naclerio RM, et al. Effect of subcutaneous dupilumab on nasal polyp burden in patients with chronic sinusitis and nasal polyposis: a randomized clinical trial. *JAMA*. 2016;315(5):469-479.
15. Jonstam K, Swanson BN, Mannent L, et al. Dupilumab reduces local type 2 pro-inflammatory biomarkers in chronic rhinosinusitis with nasal polyposis. *Allergy*. 2019;74(4):743-752.
16. Maurer M, Casale TB, Saini SS, et al. Dupilumab in patients with chronic spontaneous urticaria (LIBERTY_CSU CUPID): two randomized, double-blind, placebo-controlled phase 3 trials. *J Allergy Clin Immunol*. 2024;154(1):184-194.
17. Dellon ES, Rothenberg ME, Collins MH, et al. Dupilumab in adults with adolescents with eosinophilic esophagitis. *N Engl J Med*. 2022;387(25):2317-2330.
18. Chehade M, Dellon ES, Spergel JM, et al. Dupilumab for eosinophilic esophagitis in patients 1 to 11 years of age. *N Engl J Med*. 2024;390(24):2239-2251.
19. Yosipovitch G, Mollanazar N, Stander S, et al. Dupilumab in patients with prurigo nodularis: two randomized, double-blind, placebo-controlled phase 3 trials. *Nat Med*. 2023;29(5):1180-1190.
20. Global Initiative for Asthma. Global strategy for asthma management and prevention. Updated 2024. Available at: <http://www.ginasthma.org>. Accessed on March 29, 2025.
21. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2014;43:343-373.
22. Holguin F, Cardet JC, Chung KF, et al. Management of severe asthma: a European Respiratory Society/American Thoracic Society Guideline. *Eur Respir J*. 2020;55:1900588.
23. Davis DMR, Drucker AM, Alikhan A, et al. Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies. *J Am Acad Dermatol*. 2024;90(2):e43-e56.
24. Sidbury R, Alikhan A, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis in adults with topical therapies. *J Am Acad Dermatol*. 2023;89(e1-e20).
25. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. National Institutes of Health, National Heart, Lung, and Blood Institute; 2025. Available at: <https://goldcopd.org/gold-reports/>. Accessed on April 8, 2025.
26. Rank MA, Chu DK, Bognanni A, et al. Joint Task Force on Practice Parameters GRADE guidelines for the medical management of chronic rhinosinusitis with nasal polyposis. *J Allergy Clin Immunol*. 2023;151(2):386-398.
27. Peters AT, Spector S, Hsu J, et al. Diagnosis and management of rhinosinusitis: a practice parameter update. *Ann Allergy Asthma Immunol*. 2014;347-385.
28. Dykewicz MS, Wallace DV, Baroody F, et al. Treatment of seasonal allergic rhinitis: an evidenced-based focused 2017 guideline update. *Ann Allergy Asthma Immunol*. 2017;119(6):489-511.
29. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical practice guideline (update): adult sinusitis. *Otolaryngol Head Neck Surg*. 2015;152(2S):S1-S39.

30. Joint Task Force on Practice Parameters: American Academy of Allergy, Asthma and Immunology and the American College of Allergy, Asthma and Immunology. Rhinitis 2020: a practice parameter update. *J Allergy Clin Immunol*. 2020;146:721-767.
31. Zuberbier T, Abdul Latiff AH, Abuzakouk M, et al. The international EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy*. 2022;73:734-766.
32. Dellon ES, Muir AB, Katzka DA, et al. ACG Clinical Guideline: Diagnosis and Management of Eosinophilic Esophagitis. *Am J Gastroenterol*. 2025;120(1):31-59.
33. Elmariah S, Kim B, Berger T, et al. Practical approaches for diagnosis and management of prurigo nodularis: United States expert panel consensus. *J Am Acad Dermatol*. 2021;84(3):747-760.
34. Cibinqo[®] tablets [prescribing information]. New York, NY: Pfizer; December 2023.
35. Rinvoq[®] extended-release tablets/Rinvoq[®] LQ oral solution [prescribing information]. North Chicago, IL: AbbVie; March 2025.
36. Opzelura[®] cream [prescribing information]. Wilmington, DE: Incyte; January 2023.
37. Leqselvi[™] tablets [prescribing information]. Whippany, NJ: Sun/Halo; July 2024.
38. Casale T, Saini S, Bernstein J, et al. Dupilumab significantly improves itch and hives in patients with chronic spontaneous urticaria (CUPID Study C) [abstract LBA002]. Presented at: 2024 Annual Scientific Meeting American College of Allergy, Asthma, & Immunology; Boston, MA; October 24-28, 2024.
39. Sindher SB, Nadeau C, Chinthrajah RS, et al. Efficacy and safety of dupilumab in children with peanut allergy: a multicenter, open-label, phase II study. *Allergy*. 2025;80(1):227-237.
40. Chinthrajah RS, Sindher SB, Nadeau KC, et al. Dupilumab as an adjunct to oral immunotherapy in pediatric patients with peanut allergy. *Allergy*. 2025;80(3):827-842.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	<p>Policy Name Change: Updated from “Dupilumab” to “Immunologicals – Dupixent.”</p> <p>Asthma: Updated diagnostic criteria requirements for confirmation of asthma.</p> <p>Atopic Dermatitis: Updated diagnostic criteria requirements for confirmation of atopic dermatitis.</p> <p>Chronic Rhinosinusitis with Nasal Polyps: Added the requirement for systemic steroid use for at least 5 days.</p> <p>Currently Receiving Dupixent: Removed requirement for prescription by or in consultation with a specialist for all indications.</p> <p>Authorization Duration: Updated initial therapy duration from 12 months to 4 months for atopic dermatitis and 6 months for all other indications.</p>	09/01/2024
Selected Revision	<p>Asthma: Eosinophil level requirements were clarified to require a level ≥ 150 cells/microliter either within the previous 6 weeks OR prior to treatment with a monoclonal antibody that may alter eosinophil levels. Previously, criteria required a level ≥ 150 cells/microliter either within the previous 6 weeks OR within 6 weeks prior to treatment with a monoclonal antibody that may lower eosinophil levels.</p>	12/15/2024

	<p>Throughout the policy, Ebglyss (lebrikizumab-lbkz subcutaneous injection) and Nemluvio (nemolizumab-ilto subcutaneous injection) were added to notes as examples of monoclonal antibody therapies.</p> <p>Chronic Rhinosinusitis with Nasal Polyps: The age of approval was changed from ≥ 18 years of age to ≥ 12 years of age.</p> <p>Chronic Obstructive Pulmonary Disease: This condition and criteria for approval were added to the policy. New approval criteria for this indication were added that include an age requirement, an eosinophil requirement, a trial of inhaled therapies, a history of chronic bronchitis signs or symptoms, a history of COPD exacerbations, and specialist involvement.</p> <p>Conditions not Recommended for Approval, Concurrent Use of Dupixent with Janus Kinase (JAK) Inhibitors (oral or topical): Leqselvi™ (deuruxolitinib tablets) and Rinvoq® LQ (upadacitinib oral solution) were added as examples of JAK inhibitors.</p>	
Annual Revision	<p>Chronic Spontaneous Urticaria (Chronic Idiopathic Urticaria): This condition and criteria for approval were added to the policy. New approval criteria for this indication were added that include an age requirement, a duration of symptom requirement, a trial of H₁ antihistamine therapy, and specialist involvement.</p> <p>Conditions Not Covered, Peanut Allergy: Peanut allergy was added to the "Conditions Not Covered" section.</p> <p>Coding Information Added C9399, J3490 and J3590</p>	7/15/2025
Selected Revision	<p>Chronic Obstructive Pulmonary Disease: Criteria requiring the patient to have signs and symptoms of chronic bronchitis were removed. Exacerbation criteria were simplified to require the patient to have experienced two or more COPD exacerbations requiring treatment with a systemic corticosteroid with or without an antibiotic in the previous 12 months or one or more COPD exacerbations requiring a hospitalization in the previous 12 months. Previously, these criteria required that the patient experienced two or more COPD exacerbations requiring treatment with a systemic corticosteroid and/or an antibiotic in the</p>	8/1/2025

	previous 12 months and one or more of these exacerbations required treatment with a systemic steroid and one or more of these exacerbations occurred while the patient was receiving combination inhaled therapy. Previous criteria also required that one or more COPD exacerbations requiring a hospitalization in the previous 12 months had occurred while the patient was receiving combination inhaled therapy.	
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The policy effective date is in force until updated or retired.

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