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Coverage Policy Number IP0453

Dupilumab

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Related Coverage Resources

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Overview

This policy supports medical necessity review for dupilumab (**Dupixent®**).

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

Medical Necessity Criteria

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

1. **Asthma.** Individual meets **ONE** of the following criteria (A or B):
    A. Initial Therapy. Individual meets **ALL** of the following criteria (i. ii, iii, iv, v, and vi)
        i. Individual is 6 years of age or older
        ii. Diagnosis of asthma is confirmed by **BOTH** of the following (a and b):
            a. Pre-bronchodilator FEV1 below the lower limits of normal for age in the setting of reduced FEV1/FVC (usually less than 80% in adults and 90% in children)

b. Variable expiratory airflow obstruction as documented by **ONE** of the following (1, 2 or 3):
    1. Increase of at least 12% AND 200 mL in FEV1 after the administration of 200 to 400 mcg albuterol or levalbuterol
    2. Increase of at least 12% AND 200 mL in FEV1 from baseline between visits or after 4 weeks of treatment
    3. Positive exercise or bronchial challenge testing

iii. Dupilumab (Dupixent) will be used as an add-on maintenance treatment for individuals with **ONE** of the following (a or b):
    a. Moderate to severe asthma with an eosinophilic phenotype and **ONE** of the following (1 or 2):
        1. Blood eosinophil level greater than or equal to 150 cells/mcl within the previous 6 weeks or within 6 weeks prior to treatment with Dupixent or another monoclonal antibody therapy that may lower blood eosinophil levels (for example, Adbry [tralokinumab], Cinqair [reslizumab], Fasenra [benralizumab], Nucala [mepolizumab], Tezspire [tezepelumab], or Xolair [omalizumab])
        2. History of blood eosinophil levels greater than or equal to 300 cells/mcl
    b. Oral (systemic) corticosteroid dependent asthma (for example, the individual has received a minimum daily dose of prednisone 5 mg or an equivalent corticosteroid for the previous 6 months)

iv. Individual has received at least 3 consecutive months of combination therapy with **BOTH** of the following (a and b):
    a. An inhaled corticosteroid
    b. At least one additional asthma controller or asthma maintenance medication (for example, inhaled long-acting beta$_2$-agonists, inhaled long-acting muscarinic antagonists, leukotriene receptor antagonists, theophylline, or monoclonal antibody therapies for asthma [e.g., Cinqair, Fasenra, Nucala, Tezspire, and Xolair]). Use of a combination inhaler containing both an inhaled corticosteroid and a long-acting beta$_2$-agonist would fulfill the requirement for both criteria [a] and [b].

v. Individual has asthma that is uncontrolled or was uncontrolled at baseline as defined by **ONE** of the following (a, b, c, or d):
"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, or Xolair
    a. Poor symptom control as defined by Asthma Control Questionnaire consistently greater than 1.5 or Asthma Control Test less than 20
    b. Individual experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year
    c. Individual experienced one or more asthma exacerbation(s) requiring hospitalization, an emergency department visit, or an urgent care visit in the previous year
    d. Daily or every other day oral corticosteroids are required to prevent asthma exacerbations

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

B. Individual is Currently Receiving Dupixent. Individual meets **ALL** of the following (i, ii, and iii):
An individual who has received less than 6 months of therapy or who is restarting therapy with Dupixent will be considered under criterion 1A (Asthma, Initial Therapy).

i. Individual has already received at least 6 months of therapy with dupilumab (Dupixent) and has documentation of beneficial clinical response.
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.

ii. Individual continues to receive therapy with one inhaled corticosteroid **OR** one inhaled corticosteroid-containing combination
iii. The medication is prescribed by or in consultation with an allergist, immunologist, or pulmonologist

2. **Atopic Dermatitis, Moderate to Severe.** Individual meets **ONE** of the following criteria (A or B):
   A. Initial Therapy. Individual meets **ALL** of the following (i, ii, and iii)
      i. Individual is 6 months of age or older
      ii. Documentation of **ONE** of the following (a, b, or c):
         a. Individual has had an inadequate response after at least 3 months of therapy with **ONE** conventional systemic immunomodulator used for the treatment of atopic dermatitis (for example, cyclosporine, azathioprine, methotrexate, mycophenolate mofetil)
         b. Individual has had an inadequate response to **ONE** prescription topical corticosteroid (medium-potency or higher) used for at least 28 days, unless contraindicated or intolerant
         c. Individual meets **BOTH** of the following criteria (1 and 2):
            1. Individual has atopic dermatitis affecting **ONLY** the following areas: face, skin folds, and/or genitalia
            2. Individual has had an inadequate response to **ONE** topical calcineurin inhibitor (pimecrolimus 1% cream [Elidel®], tacrolimus 0.03% or 0.1% ointment [Protopic®]) used for at least 28 days, unless contraindicated or intolerant
      iii. The medication is prescribed by or in consultation with an allergist, immunologist, or dermatologist
   B. Individual is Currently Receiving Dupixent. Individual meets **BOTH** of the following (i and ii): An individual who has received less than 4 months of therapy or who is restarting therapy with Dupixent will be considered under criterion 2A (Atopic Dermatitis, Initial Therapy).
      i. Individual has already received at least 4 months of therapy with dupilumab (Dupixent) and has documentation of beneficial response.
      Examples of beneficial 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.
      ii. The medication is prescribed by or in consultation with an allergist, immunologist, or dermatologist

3. **Chronic Rhinosinusitis with Nasal Polyps (CRSwNP).** Individual meets **ONE** of the following criteria (A or B):
   A. Initial Therapy. Individual meets **ALL** of the following (i, ii, iii, iv, and v) :
      i. Individual is 18 years of age or older
      ii. Dupilumab (Dupixent) will be used as an add-on maintenance treatment for individuals with **BOTH** of the following (a and b)
         a. Evidence of nasal polyps by direct examination, endoscopy, or sinus CT scan
         b. Individual 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
      iii. Individual meets **BOTH** of the following (a and b):
         a. Individual has received at least 4 weeks of therapy with an intranasal corticosteroid
         b. Individual will continue intranasal corticosteroid therapy concomitantly with Dupixent, unless contraindicated or intolerant
      iv. Individual meets **ONE** of the following (a or b):
         a. Individual has received at least one course of treatment with a systemic corticosteroid within the previous two years or has a contraindication or intolerance to systemic corticosteroid therapy

b. Individual has had prior surgery for nasal polyps

v. The medication is prescribed by, or in consultation with, an allergist, immunologist, or otolaryngologist (ear, nose, and throat [ENT])

B. Individual is Currently Receiving Dupixent. Individual meets **ALL** of the following (i. ii, and iii) An individual who has received less than 6 months of therapy or who is restarting therapy with Dupixent will be considered under criterion 4A (Nasal Polyps, Initial Therapy).

i. Individual has already received at least 6 months of therapy with dupilumab (Dupixent) and has documentation of beneficial clinical response
Examples of beneficial response to Dupixent therapy are reduced nasal polyp size, improved nasal congestion, reduced sinus opacification, decreased sinonasal symptoms, improved sense of smell

ii. Continued concomitant therapy with an intranasal corticosteroid

iii. The medication is prescribed by, or in consultation with, an allergist, immunologist, or otolaryngologist (ear, nose, and throat [ENT] specialist)

4. **Eosinophilic Esophagitis (EoE)**. Individual meets **ONE** of the following criteria (A or B):

A. Initial Therapy. Individual meets **ALL** of the following (i. ii, iii, iv, v, vi, vii, and viii) :

i. Individual is 1 year of age or older

ii. Individual weighs at least 15 kg

iii. Individual has symptomatic eosinophilic esophagitis (for example, dysphagia, pain upon swallowing, food impaction)

iv. Documented diagnosis confirmed by an endoscopic biopsy demonstrating 15 or more intraepithelial eosinophils per high-power field

v. Individual does not have a secondary cause of eosinophilic esophagitis
Examples of secondary causes of eosinophilic esophagitis are hypereosinophilic syndrome, eosinophilic granulomatosis with polyangiitis, and food allergy.

vi. Individual has had an inadequate response after at least 8 weeks of therapy with a proton pump inhibitor, unless contraindicated or intolerant.

vii. Individual has had an inadequate response to dietary modifications to treat/manage eosinophilic esophagitis **OR** the provider has determined that the individual is not an appropriate candidate for dietary modifications
Examples of dietary modifications to treat eosinophilic esophagitis include an elemental diet or an elimination diet.

viii. The medication is prescribed by or in consultation with an allergist or gastroenterologist.

B. Individual is Currently Receiving Dupixent. Individual meets **BOTH** of the following (i and ii):
An individual who has received less than 6 months of therapy or who is restarting therapy with Dupixent will be considered under criterion 3A (Eosinophilic Esophagitis, Initial Therapy).

i. Individual has already received at least 6 months of therapy with dupilumab (Dupixent) and has documentation of beneficial clinical response defined by **ONE** of the following (a or b):

a. Reduced intraepithelial eosinophil count (for example, 6 or less eosinophils per high-power field)

b. Documented reduction in eosinophilic esophagitis associated symptoms (for example, a decrease in dysphagia symptom questionnaire [DSQ] score, reduced frequency/severity of dysphagia, pain upon swallowing or food impaction)

ii. The medication is prescribed by or in consultation with an allergist or gastroenterologist.

5. **Prurigo Nodularis.** Individual Meets **ONE** of the following conditions: (A or B):

A. Initial Therapy. Meets **ALL** of the following criteria:

i. 18 years of age or older

ii. Has greater than or equal to 20 identifiable nodular lesions in total

iii. Has experienced pruritus for at least 6 weeks

iv. If prurigo nodularis is from a secondary cause, then that secondary cause has been identified and adequately managed, according to the prescriber

v. Has had an inadequate response to **ONE** prescription topical corticosteroid (high-potency or higher) used for at least 14 consecutive days, unless contraindicated or intolerant
vi. Medication is prescribed by or in consultation with an allergist, immunologist, or dermatologist

B. Currently Receiving Dupixent. Individual meets **ALL** of the following criteria:
An individual who has received less than 6 months of therapy or who is restarting therapy with Dupixent should be considered under criterion 5A (Prurigo Nodularis, Initial Therapy).
i. Has already received at least 6 months of therapy with dupilumab (Dupixent) and has documentation of beneficial clinical response
Examples of beneficial response to Dupixent therapy are reduced nodular lesion count, decreased pruritus, reduced nodular lesion size
ii. Medication is prescribed by or in consultation with an allergist, immunologist, or dermatologist

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.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

1. **Concurrent Use with Another Monoclonal Antibody Therapy (i.e., Adbry, Cinqair, Fasenra, Nucala, Tezspire, or Xolair).** The efficacy and safety of Dupixent in combination with other monoclonal antibody therapies (for example, Adbry, Cinqair, Fasenra, Nucala, Tezspire, Xolair) has not been established.[1]

2. **Concurrent Use with Janus Kinase Inhibitors (oral or topical).** Janus Kinase inhibitors (for example, Cibinqo, Olumiant, Opzelura, Rinvoq, Xeljanz/XR) are not recommended in combination with biologic immunomodulators such as Dupixent.[1]

Background

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 rhinosinusitis with nasal polyposis (CRSwNP)** [i.e., nasal polyps], as an add-on maintenance treatment in adults with inadequately controlled disease.
- **Eosinophilic esophagitis**, in patients ≥ 1 year of age who weigh ≥ 15 kg.
- **Prurigo nodularis**, in patients ≥ 18 years of age.

Clinical Efficacy
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] In atopic

dermatitis, the majority of studies evaluated the efficacy of Dupixent at 16 weeks.[1,6-10] The pivotal studies involving patients with CRSwNP evaluated the primary efficacy endpoints following 24 weeks of treatment.[1,11-13] Patients continued treatment with intranasal corticosteroids throughout the studies.

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.[14] 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] Endoscopic biopsy evidence of eosinophilic infiltration despite treatment with a proton pump inhibitor was again required for study enrollment.

Two pivotal studies, PRIME and PRIME2, evaluated Dupixent's efficacy in the treatment of prurigo nodularis.[15,16] 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 (2022) proposes a stepwise approach to asthma treatment.[17] The majority of patients can be managed with an inhaled corticosteroid (ICS) with or without a long-acting beta$_2$-agonist and/or an additional controller. Dupixent is listed as an option for add-on therapy in patients ≥ 6 years of age with severe eosinophilic/Type 2 asthma or for patients ≥ 12 years of age who require treatment with a maintenance oral corticosteroid. 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 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.[18,19] 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: FEV_1 < 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 [2014]) do not address Dupixent.[10,21] However, the guidelines note that topical therapies remain the cornerstone of treatment for atopic dermatitis due to their efficacy and generally favorable safety profiles. If patients fail topical therapy, use of systemic therapy may be considered. European guidelines on atopic eczema (2022) have been updated to address Dupixent.[22] Candidates for systemic treatment (i.e., Dupixent) are patients with severe, highly symptomatic disease, patients who have failed topical therapy, or patients who are unable to participate in normal daily life activities with their non-systemic treatment regimen.

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.[33] 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.[24-27] 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.[24,25,27]

Eosinophilic Esophagitis Guidelines
Guidelines for the management of eosinophilic esophagitis from the American Gastroenterological Association and the Joint Task Force on Allergy-Immunology Practice Parameters (2020) have not been updated since the FDA approval of Dupixent for this indication.[23] In patients with symptomatic disease, use of a proton pump inhibitor is recommended over no treatment, as is treatment with topical corticosteroids. Guidelines recommend diet modifications, such as an elemental diet (amino-acid based formulas) or an elimination diet, over no treatment. However, it is noted that patients who put a higher value on avoiding the challenges of adherence to these diets and the prolonged process of dietary reintroduction may reasonably decline this treatment option.

Prurigo Nodularis Guidelines
A United States Expert Panel Consensus provides a practical approach for the diagnosis and management of prurigo nodularis (2021).[29] 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.

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