Drug and Biologic Coverage Policy

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Dupilumab

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Related Coverage Resources

Benralizumab, Mepolizumab and Reslizumab - (1608)
Omalizumab - (4026)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer’s particular benefit plan document (Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document) may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer’s benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Coverage Policy

Dupilumab (Dupixent®) is considered medically necessary for ANY of the following:

- **Moderate to Severe Atopic Dermatitis** when ALL of the following are met:
  - Individual is 6 years of age or older
  - Dupixent is prescribed by, or in consultation with, an allergist, dermatologist, or immunologist
  - **EITHER** of the following:
    - Documented prior use of systemic immunomodulators for the treatment of atopic dermatitis (maintenance systemic corticosteroids, cyclosporine, azathioprine, methotrexate, mycophenolate mofetil, interferon gamma (Actimmune®))
    - **BOTH** of the following:
      - Documented failure/inadequate response after a 4 week trial (2 week trial for very high potency), contraindication per FDA label, intolerance, or not a candidate for at least ONE moderate to very high potency topical corticoid
      - Documented failure/inadequate response after a 6 week trial, contraindication per FDA label, intolerance or not a candidate for ONE topical calcineurin inhibitor (for example, tacrolimus 0.03% or 0.1% ointment, Elidel®)

- **Moderate to Severe Asthma** as add-on maintenance treatment when ALL of the following are met:
- Individual is 12 years of age or older
- Dupixent is prescribed by, or in consultation with, an allergist, immunologist, or pulmonologist
- Asthma diagnosis as evidenced by **ALL** of the following:
  - Pre-bronchodilator FEV1 ≤ 80% of predicted normal for adults and ≤ 90% of predicted normal for adolescents
  - Reversibility of at least 12% **AND** 200 mL in FEV1 after the administration of 200 to 400 mcg albuterol or levaterol
- **EITHER** of the following:
  - **Eosinophilic phenotype** and **ALL** of the following:
    - **EITHER** of the following blood eosinophil level conditions:
      - Blood eosinophils greater than or equal to 150 cells/mcl within the previous 6 weeks
      - History of blood eosinophils greater than or equal to 300 cells/mcl
    - History of 1 or more asthma exacerbations in the past 12 months that required treatment with systemic corticosteroids; an emergency department visit; or hospitalization for the treatment of asthma
    - Inadequately controlled with a medium-dose or high-dose inhaled corticosteroid (ICS) **AND** another controller therapy (for example, long-acting beta-agonist, leukotriene receptor) for at least 3 months
  - **Oral corticosteroid dependent asthma** and **BOTH** of the following:
    - Requiring a minimum daily dose of prednisone 5 mg (or an equivalent dose of another corticosteroid) for the previous 6 months
    - Inadequately controlled with a high-dose inhaled corticosteroid (ICS) **AND** another controller therapy (for example, long-acting beta-agonist, leukotriene receptor) for at least 3 months
    - Will not be used in combination with another antiasthmatic monoclonal antibody (for example, mepolizumab [Nucala®], benralizumab [Fasenra™], omalizumab [Xolair®], reslizumab [Cinqair®])
- **Chronic Rhinosinusitis with Nasal Polyposis (CRSwNP) as add-on maintenance treatment when ALL of the following are met:**
  - Individual is 18 years of age or older
  - Dupixent is prescribed by, or in consultation with, an allergist, immunologist, or otolaryngologist (ear, nose, and throat [ENT])
  - CRSwNP diagnosis as evidenced by **BOTH** of the following:
    - Symptoms (for example, nasal obstruction, rhinorrhea, or reduction/loss of smell) of CRS greater than or equal 12 weeks
    - Evidence of nasal polyposis by direct examination, endoscopy, or sinus CT scan
  - Inadequate response to intranasal corticosteroid therapy at appropriate doses to treat nasal polyposis
  - **ONE** of the following:
    - Individual has received treatment with a systemic corticosteroid within the previous two years or has a contraindication per FDA label to systemic corticosteroid therapy
    - Individual has had prior surgery for nasal polyps
  - Individual will continue intranasal corticosteroid therapy unless contraindicated per FDA label

*Initial authorization is up to 6 months.*

**Dupilumab (Dupixent) is considered medically necessary for continued use when the following are met:**
- Evidence of beneficial clinical response
- Pretreatment clinical condition met initial criteria
- For the treatment of moderate to severe asthma:
  - Continued use of an inhaled corticosteroid **AND** another controller therapy (for example, long-acting beta-agonist, leukotriene receptor)
  - Will not be used in combination with another antiasthmatic monoclonal antibody (for example, Cinqair, Fasenra, Nucala, Xolair)
- For the treatment of CRSwNP, continued use of intranasal corticosteroid therapy unless contraindicated per FDA label
Reauthorization for up to 12 months.

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.

Dupilumab (Dupixent) is considered experimental, investigational or unproven for ANY other use.

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

FDA Approved Indications

FDA Approved Indication
Atopic Dermatitis
Dupixent is indicated for the treatment of patients aged 6 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent can be used with or without topical corticosteroids.

Asthma
Dupixent is indicated as an add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older 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.

Chronic Rhinosinusitis with Nasal Polyposis
Dupixent is indicated as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP).

Recommended Dosing

FDA Recommended Dosing
Dupixent is administered by subcutaneous injection.

Dupixent is intended for use under the guidance of a healthcare provider. A patient may self-inject Dupixent after training in subcutaneous injection technique using the pre-filled syringe. Provide proper training to patients and/or caregivers on the preparation and administration of Dupixent prior to use according to the "Instructions for Use".

Atopic Dermatitis
Dosing in Adults
The recommended dose of Dupixent for adult patients is an initial dose of 600 mg (two 300 mg injections), followed by 300 mg given every other week (Q2W).

Dosing in Pediatric Patients (6 to 17 years of Age)
The recommended dose of Dupixent for patients 6 to 17 years of age is specified in Table 1.

Table 1: Dose of Dupixent for Subcutaneous Administration in Pediatric Patients (6 to 17 Years of Age)

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Initial Dose</th>
<th>Subsequent Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 to less than 30 kg</td>
<td>600 mg (two 300 mg injections)</td>
<td>300 mg every 4 weeks (Q4W)</td>
</tr>
<tr>
<td>30 to less than 60 kg</td>
<td>400 mg (two 200 mg injections)</td>
<td>200 mg every other week (Q2W)</td>
</tr>
<tr>
<td>60 kg or more</td>
<td>600 mg (two 300 mg injections)</td>
<td>300 mg every other week (Q2W)</td>
</tr>
</tbody>
</table>

Concomitant Topical Therapies
Dupixent can be used with or without topical corticosteroids. Topical calcineurin inhibitors may be used, but should be reserved for problem areas only, such as the face, neck, intertriginous and genital areas.

**Asthma**
The recommended dose of Dupixent for adults and adolescents (12 years of age and older) is:
- an initial dose of 400 mg (two 200 mg injections) followed by 200 mg given every other week or
- an initial dose of 600 mg (two 300 mg injections) followed by 300 mg given every other week
- For patients with oral corticosteroids-dependent asthma, or with co-morbid moderate-to-severe atopic dermatitis for which Dupixent is indicated, start with an initial dose of 600 mg followed by 300 mg given every other week

**Chronic Rhinosinusitis with Nasal Polyposis**
The recommended dose of Dupixent for adult patients is 300 mg given every other week.

**General Background**

**Pharmacology**
Dupilumab is a human monoclonal IgG4 antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by specifically binding to the IL-4Ra subunit shared by the IL-4 and IL-13 receptor complexes. Dupilumab inhibits IL-4 signaling via the Type I receptor and both IL-4 and IL-13 signaling through the Type II receptor. (PI, 2019)

Blocking IL-4Ra with dupilumab inhibits IL-4 and IL-13 cytokine-induced responses, including the release of proinflammatory cytokines, chemokines, nitric oxide, and IgE; however, the mechanism of dupilumab action in asthma has not been definitively established. (PI, 2019)

**Professional Societies/Organizations**

**Asthma**
Guidelines do not advocate one antiasthmatic monoclonal antibody treatment over another, but do provide treatment recommendations according to asthma phenotype (allergic asthma, eosinophilic asthma).

**Global Initiative for Asthma (GINA)**
The 2019 Global Initiative for Asthma (GINA) Global Strategy for Asthma Management and Prevention proposes a step-wise approach to asthma treatment.7 Patients with persistent symptoms or exacerbations despite a medium-dose ICS/long-acting beta2-agonist (LABA) combination with or without an additional controller, GINA recommends referral of the patient to a specialist with expertise in the management of severe asthma for phenotypic assessment and add-on treatment. Dupixent is listed as an option for add-on therapy in patients ≥ 12 years of age with severe Type 2 asthma or oral corticosteroid-dependent asthma. Evidence of Type 2 inflammation can include elevated sputum or blood eosinophils, elevated fractional concentration of exhaled nitric oxide (FeNO), the need for maintenance oral corticosteroid therapy, or clinically allergen-driven asthma.(GINA, 2019b)

**European Respiratory Society/American Thoracic Society (ERS/ATS)**
According to the European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines (2014), 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.8 Uncontrolled asthma is defined as asthma that meets one of the following four criteria: poor symptom control, frequent severe exacerbations, serious exacerbations, or airflow limitation. Additionally, patients may also have severe asthma if their asthma worsens upon tapering of corticosteroids.

**Atopic Dermatitis**
The American Academy Dermatology (AAD) guidelines of care for the management of AD (2014) and the Joint Task Force AD practice parameter (from the American Academy of Allergy, Asthma, and Immunology [AAAAI],
the American College of Allergy, Asthma, and Immunology (ACAAI), and the Joint Council of Allergy, Asthma, and Immunology (JCAAI) [2012] make similar recommendations for AD therapy. (Schneider, 2013, Sidbury 2014, Eichenfield, 2018) Dupixent is not addressed. It is noted that the majority of patients with AD can achieve disease control with non-pharmacologic interventions (e.g., emollients), standard topical anti-inflammatory therapies (e.g., topical corticosteroids, topical calcineurin inhibitors), and elimination of exacerbating factors (e.g., allergens, irritants, and emotional stress). A patient who does not respond to first-line therapy should be referred to a provider who specializes in the treatment of AD. If topical regimens and/or phototherapy continue to inadequately control the signs and symptoms of AD, systemic immunomodulatory therapies are indicated, particularly if the patient’s disease has significant negative physical, psychological, or social effects. European consensus guidelines for the treatment of AD (2018) from multiple European dermatology associations, including the European Dermatology Forum (EDF), the European Academy of Dermatology and Venereology (EADV), and the European Academy of Allergy and Clinical Immunology (EAACI), recommend Dupixent as a disease-modifying drug for patients with moderate to severe AD, in whom topical treatment does not produce a sufficient response and other systemic treatment is not advisable.12 These guidelines note that daily emollients should be used with Dupixent and it may be combined with other topical anti-inflammatory medications as needed.

Chronic Rhinosinusitis with Nasal Polyposis (CRSwNP)
Dupixent is not addressed in current guidelines. A 2014 Joint Practice Parameter on the Diagnosis and Management of Rhinosinusitis and a 2008 (evidence update in 2017) Joint Practice Parameter for the Management of Rhinitis recommend nasal corticosteroids be used in patients with CRSwNP.(Peters, 2014, Joint Task Force, 2008, Dykewicz, 2017) Data demonstrate that nasal corticosteroids decrease nasal polyp size and prevent regrowth of nasal polyps following removal. Additionally, these agents improve nasal patency, reduce nasal symptoms, and improve quality of life. Short courses of oral corticosteroids are also recommended in CRSwNP, because they can decrease polyp size and alleviate symptoms. Endoscopic surgical intervention may be considered as an adjunct to medical therapy in patients with CRS that is not responsive or is poorly responsive to medical therapy. A 2015 Clinical Practice Guideline update on Adult Sinusitis from the American Academy of Otolaryngology makes similar recommendations, stating that clinicians should recommend saline nasal irrigation, topical intranasal corticosteroids, or both for symptom relief in patients with CRS (with or without nasal polyps). (Rosenfield, 2015)

The American Board of Internal Medicine’s (ABIM) Foundation Choosing Wisely® Initiative
No recommendations are available for antiasthmatic monoclonal antibodies.

Centers for Medicare & Medicaid Services - National Coverage Determinations (NCDs)
There are no CMS National Coverage Determinations for dupilumab (Dupixent).

Other Uses with Supportive Evidence
AHFS Drug Information 2019 Edition does not support any off-label uses of dupilumab (Dupixent).

Other Uses without Supportive Evidence
The FDA product information notes that these agents are not indicated for the relief of acute bronchospasm and status asthmaticus.

Coding/Billing Information

Note: Dupilumab is typically covered under pharmacy benefit plans. Certain prescription drugs require an authorization for coverage to ensure that appropriate treatment regimens are followed. Medical drug coding and diagnosis codes, however, are generally not required for pharmacy claims submissions, therefore, this section is not in use.

References


7. Joint Task Force on Practice Parameters: American Academy of Allergy, Asthma and Immunology; the American College of Allergy, Asthma and Immunology; and the Joint Council of Allergy, Asthma and Immunology. The diagnosis and management of rhinitis: An updated practice parameter. J Allergy Clin Immunol. 2008;122(2):S1-S84.


