Pharmacy Policy Bulletin

Title: Dupilumab (Dupixent®)

Policy #: Rx.01.194

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **dupilumab (Dupixent®)** as provided under the member's prescription drug benefit. .

Description:

Atopic dermatitis (eczema) is a chronic, relapsing inflammatory skin disease characterized by redness, lesions, and intense pruritus. The cause of atopic dermatitis is a combination of genetics and environmental factors, such as allergies and irritants. Atopic dermatitis is prevalent worldwide and occurs most frequently in children, but also affects many adults. The onset of atopic dermatitis is most common between 3 to 6 months of age. Approximately 60% of patients develop atopic dermatitis within their first year of life and 90% by 5 years of age. More than 80% of children with atopic dermatitis have persistent symptoms into their adult years. More severe pruritus correlates to greater disease severity. Common features in infants include pruritic red, scaly and crusted lesions on the extensor surfaces and cheeks or scalp. In older children or adolescents, atopic dermatitis presents as lichenified plaques. In adults, it is more localized and lichenified. Atopic dermatitis associated with persistent pruritus could lead to sleep deprivation, symptoms of depression, anxiety, poor quality of life, and financial burden. Additionally, patients with atopic dermatitis are at increased risk for cutaneous bacterial, viral, and fungal infections due to persistent itching and scratching.

American Academy of Dermatology Association current treatment guidelines:

- Non-pharmacologic treatments
  - Topical moisturizers
  - Wet-wrap therapy
  - Bathing practices
- Pharmacologic treatments
  - 1ST line: Topical corticosteroids
    - Introduced after failure of lesions to respond to good skin care and regular use of emollients alone
    - Treatment is individualized due to multiple formulations, dosage forms, and potencies
    - Choice of potency is based on patient's age, body area involved, and degree of inflammation
      - Acute flares: short course of medium-high potency topical corticosteroid, followed by a quick taper in potency
      - Long-term management: lowest-potency initially, followed by an upward titration if failed
  - 2nd line: Topical calcineurin inhibitors
    - Pimecrolimus cream: mild-moderate atopic dermatitis
    - Tacrolimus ointment: moderate-severe atopic dermatitis
    - Clinical situations in which a topical calcineurin is preferred:
      - Sensitive areas (face, neck, skin folds, anogenital)
      - Recalcitrance to steroids

- Steroid-induced atrophy
- Long-term uninterrupted topical steroid use

Asthma is a chronic airway disorder that is characterized by reversible airflow obstruction due to air hyper responsiveness and airway inflammation. Generally, asthma starts in childhood in relation to sensitization to common inhaled allergens, which stimulates T helper type 2 cell proliferation, subsequently releasing cytokines (IL-4, IL-5, and IL-13) that induce airway inflammation. Chronic airway inflammation leads to airway remodeling by thickening the airway walls, which creates a narrower pathway for air to travel.

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a subtype of chronic rhinosinusitis (CRS), an inflammatory condition involving the paranasal sinuses and linings of the nasal passage, which persists for 12 weeks or longer. There is no cure for CRS, and therapy is intended to reduce symptoms and improve qualify of life. There is significant variability in the management of CRS which include saline washes and sprays, intranasal and systemic corticosteroids, antibiotics, and antileukotriene agents. Biologic agents are considered in patients with refractory disease when intranasal and oral corticosteroids failed to reduce polyp or to improve symptoms.

Eosinophilic esophagitis (EoE) is a chronic allergic/immune condition of the esophagus. In EoE, large number of eosinophils are found in the inner lining of the esophagus resulting in inflammation which causes symptoms such as chest pain ,heartburn, difficulty swallowing, or impaction.

Dupilumab (Dupixent®) is a fully human monoclonal IgG4 antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by binding to the IL-4 receptor alpha subunit shared by IL-4 and IL-13 receptor complexes. Dupilumab inhibits IL-4 signaling via the Type 1 receptor and both IL-4 and IL-13 signaling through the Type II receptor. IL-4 and IL-13 play a role in the pathogenesis of atopic dermatitis and asthma. Dupilumab reduces the release of pro-inflammatory cytokines. The mechanism of dupilumab (Dupixent®) action in asthma has not been definitively established.

Dupilumab (Dupixent®) is indicated in adults and children 6 months of age or older for the treatment of moderate to severe atopic dermatitis not adequately controlled with topical prescription therapy or when those therapies are inadvisable, and as an add-on maintenance treatment in patients with moderate-to-severe asthma aged 6 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma. It is also indicated as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis. Dupixent ® can be used with or without topical corticosteroids. It should not be used for the relief of acute bronchospasm or status asthmaticus. It is also used for the treatment of adult and pediatric patients aged 12 and older, weighing at least 40 kg, with eosinophilic esophagitis (EoE).

Policy:

Atopic Dermatitis

INITIAL CRITERIA Dupilumab (Dupixent®) is approved ALL of the following are met:

1. Member is 6 months of age or older; and
2. Diagnosis of moderate-severe atopic dermatitis; and
3. Prescribed by or in consultation with a dermatologist, allergist, or immunologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate ONE of the following:
    a. Topical steroids, medium potency or higher; or
    b. Topical tacrolimus; or
    c. Topical pimecrolimus; or
    d. Eucrisa®; and
5. No concurrent therapy with any other biologic agents; and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration:2 years

REAUTHORIZATION CRITERIA Dupilumab (Dupixent®) is re-approved when ALL of the following are met:

1. Documentation of positive clinical response to therapy (e.g., reduction in body surface area involvement, reduction in pruitus severity); and
2. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Reauthorization duration: 2 years

	DOSE

Adults	Initial dose: 600 mg (two 300mg injections) Maintenance: 300 mg given every other week
Pediatric patients 6 months to 5 years of age	5 to less than 15 kg: 200 mg (one 200 mg injection) every 4 weeks 15 to less than 30 kg: 300 mg (one 300 mg injection) every 4 weeks
Pediatric patients 6 years to 17 years of age	15 to less than 30 kg: 600 mg (two 300 mg injections) initially, followed by 300 mg every 4 weeks 30 to less than 60 kg: 400 mg (two 200 mg injections) initially, followed by 200 mg every 2 weeks 60 kg or more: 600 mg (two 300 mg injections) initially, followed by 300 mg every 2 weeks

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Moderate to severe asthma

INITIAL CRITERIA Dupilumab (Dupixent®) is approved when ALL of the following are met:

1. Member is 6 years of age or older; and
2. One of the following:
    a. Submission of documentation (e.g., chart notes) confirming a diagnosis of Moderate to severe asthma with an eosinophilic phenotype defined as blood eosinophil levels of at least 150 cells/mcL at baseline or at least 300 cells/mcL within the past 12 months; or
    b. Submission of documentation (e.g., chart notes) confirming a diagnosis of Moderate to severe oral corticosteroid-dependent asthma; and
3. Paid claims or submission of documentation (e.g., chart notes) confirming member is currently being treated with ONE of the following or is unable to tolerate these medications:
    a. Medium to high dose inhaled corticosteroid (e.g., greater than or equal to 500mcg fluticasone propionate equivalent/day); and ONE additional controller medication; or
    b. One maximally dosed combination ICS/LABA product (e.g., Advair (fluticasone propionate/salmeterol), Dulera (mometasone/formoterol), Symbicort (budesonide/formoterol); and
4. Prescribed by or in consultation with a pulmonologist or allergy/ immunology specialist; and
5. No concurrent therapy with any other biologic agents; and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Dupilumab (Dupixent®) is re-approved when ALL of the following are met:

1. Documentation of a positive clinical response to therapy (e.g., reduction in exacerbations, improvement in FEV1, decreased use of rescue medications); and
2. Paid claims or submission of documentation (e.g., chart notes) confirming member is currently being treated with ONE of the following or is unable to tolerate these medications:
    a. Medium to high dose inhaled corticosteroid (e.g., greater than or equal to 500mcg fluticasone propionate equivalent/day); and ONE additional controller medication; or
    b. One maximally dosed combination ICS/LABA product (e.g., Advair (fluticasone propionate/salmeterol), Dulera (mometasone/formoterol), Symbicort (budesonide/formoterol); and
3. Prescribed by or in consultation with a pulmonologist or allergy/immunology specialist; and
4. No concurrent therapy with any other biologic agents; and
5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Reauthorization duration: 2 years

	DOSE
Adults and pediatric patients 12 years and older	Initial dose: 400 mg (two 200 mg injections) Maintenance: 200 mg every 2 weeks OR Initial dose: 600 mg (two 300 mg injections) Maintenance dose: 300 mg every 2 weeks
Dosage for patients with oral corticosteroid-	Initial dose: 600 mg (two 300 mg injections) Maintenance dose: 300 mg every 2 weeks

dependent asthma or with co-morbid moderate-to-severe atopic dermatitis or adults with co-morbid chronic rhinosinusitis with nasal polyposis	
Pediatric patients 6 years to 11 years of age	15 to less than 30 kg: 100 mg every other week OR 300 mg every 4 weeks ≥ 30 kg: 200 mg every other week

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Chronic rhinosinusitis with nasal polyposis (CRSwNP)

INITIAL CRITERIA Dupilumab (Dupixent®) is approved when ALL of the following are met:

1. Submission of documentation (e.g., chart notes) confirming diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with an allergist, immunologist, or Ear Nose Throat specialist; and
4. Paid claims or submission of documentation (e.g., chart notes) confirming an inadequate response or inability to tolerate at least a 2-month treatment with intranasal corticosteroid (e.g., fluticasone); and
5. Used in combination with another agent for CRSwNP; and
6. No concurrent therapy with any other biologic agents; and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial Authorization duration: 2 years

REAUTHORIZATION CRITERIA Dupilumab (Dupixent®) is re-approved when ALL of the following are met:

1. Documentation of a positive clinical response to therapy (e.g., reduction in nasal polyps score [NPS; 0-8 scale], improvement in nasal congestion/obstruction score [NC; 0-3 scale]); and
2. Prescribed by allergist, immunologist or Ear Nose Throat specialist; and
3. Used in combination with another agent for CRSwNP; and
4. No concurrent therapy with any other biologic agents and
5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Reauthorization duration: 2 years

	DOSE
Adults	300 mg every other week

Eosinophilic Esophagitis (EoE)

INITIAL CRITERIA Dupilumab (Dupixent®) is approved when ALL of the following are met:

1. Submission of documentation (e.g., chart notes) confirming diagnosis of eosinophilic esophagitis (EoE); and
2. Member has symptoms of esophageal dysfunction (e.g., dysphagia, food impaction, gastroesophageal reflux disease [GERD]/heartburn symptoms, chest pain, abdominal pain); and
3. Member has at least 15 intraepithelial eosinophils per high power field (HPF); and
4. Other causes of esophageal eosinophilia have been ruled out; and
5. Both of the following:
    a. Member is 12 years of age or older; and
    b. Member weighs at least 40 kg; and
6. Paid claims or submission of documentation (e.g., chart notes) confirming an inadequate response or inability to tolerate at least an 8-week trial of one of the following:
    a. Proton Pump Inhibitors (e.g., pantoprazole, omeprazole); or
    b. Topical (esophageal) corticosteroids (e.g., budesonide, fluticasone); and

7. Prescribed by or in consultation with gastroenterologist or allergist/immunologist; and
8. No concurrent therapy with any other biologic agents; and
9. Dose and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Dupilumab (Dupixent®) is re-approved when ALL of the following are met:

1. Documentation of a positive clinical response to therapy as evidenced by improvement of at least one of the following from baseline:
    a. Symptoms (e.g., dysphagia, food impaction, heartburn, chest pain); or
    b. Histologic measures (e.g., esophageal intraepithelial eosinophil count); or
    c. Endoscopic measures (e.g., edema, furrows, exudates, rings, strictures); and
2. No concurrent therapy with any other biologic agents; and
3. Dose and frequency does not exceed maximum FDA recommendation per indication requested

Reauthorization duration: 2 years

	DOSE
Adults and pediatric patients 12 years of age and older, weighing at least 40 kg	300 mg every week

Black Box Warning as shown in the drug Prescribing Information:

N/A

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

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Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Dupixent®	dupilumab

Cross References:

Off-Label Use Rx.01.33

Policy Version Number:	16.00
P&T Approval Date:	September 15, 2022
Policy Effective Date:	January 01, 2023
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