# PRIOR AUTHORIZATION POLICY

**POLICY:** Immunologicals – Dupixent Prior Authorization Policy
- Dupixent® (dupilumab subcutaneous injection – Regeneron/sanofi-aventis)

**REVIEW DATE:** 02/17/2021; selected revision 06/23/2021

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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 ≥ 12 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 years of age with moderate-to-severe disease whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.
- **Chronic rhinosinusitis with nasal polyposis (CRSwNP),** as an add-on maintenance treatment in adult patients with inadequately controlled disease.

## 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.[2,4] In atopic dermatitis, the majority of studies evaluated the efficacy of Dupixent at 16 weeks.[1,5,6] The pivotal studies involving patients with CRSwNP evaluated the primary efficacy endpoints following 24 weeks of treatment. Patients continued treatment with intranasal corticosteroids throughout the study.[1,8-10]

## Guidelines

*Asthma Guidelines*

The Global Initiative for Asthma (GINA) Global Strategy for Asthma Management and Prevention (2020) proposes a stepwise approach to asthma treatment.[11] The majority of patients can be managed with an ICS with or without a long-acting beta$_2$-agonist (LABA) and/or an additional controller. Dupixent is listed as an option for add-on therapy in patients ≥ 12 years of age with severe Type 2 asthma or asthma that requires treatment with an 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.[12,23] 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;
2) Frequent severe exacerbations: two or more bursts of systemic corticosteroids in the previous year;
3) Serious exacerbations: at least one hospitalization, intensive care unit stay, or mechanical ventilation in the previous year;
4) Airflow limitation: $FEV_1$ 80% predicted after appropriate bronchodilator witholding.

*Atopic Dermatitis Guidelines*

European consensus guidelines for the treatment of atopic dermatitis (2018) recommend Dupixent as a disease-modifying drug for patients with moderate-to-severe atopic dermatitis, in whom topical treatment does not produce a sufficient response and other systemic treatment is not advisable.[13] These guidelines note that daily emollients should be used with Dupixent and it may be combined with other topical anti-inflammatory medications as needed. US guidelines do not address Dupixent.[14-16] However, they reinforce that most patients with atopic dermatitis 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.

*Nasal Polyp Guidelines*

A 2014 Practice Parameter on the Diagnosis and Management of Rhinosinusitis, a 2020 Practice Parameter for the Management of Rhinitis from the Joint Task Force for Practice Parameters (JTFPP), and a 2015 Clinical Practice Guideline update on Adult Sinusitis from the American Academy of Otolaryngology (AAO) make similar recommendations regarding the diagnosis and management of CRSwNP.[17-20,24] 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. However, this requires confirmation of sinonasal inflammation, which can either be done via direct visualization or computed tomography (CT) scan. Nasal corticosteroids are recommended for the management of CRSwNP, as they decrease nasal polyp size, prevent regrowth of nasal polyps following surgical removal, and improve nasal symptoms. Short courses of oral corticosteroids are also recommended. Endoscopic surgical intervention may be considered as an adjunct to medical therapy in patients with chronic rhinosinusitis that is not responsive or is poorly responsive to medical therapy. Dupixent is listed as a treatment option in the JTFPP practice parameter, but with no specific recommendations for use. The AAO guidelines do not address Dupixent.

The European Forum for Research and Education in Allergy expert board on uncontrolled severe CRSwNP and biologics (2021) recommends that these agents, including Dupixent, only be used for severe uncontrolled CRSwNP when Type 2 inflammation is present.[28] Severe CRSwNP is defined as bilateral CRSwNP with a nasal polyp score $\geq 4$ and persistent symptoms (e.g., loss of smell/taste, nasal obstruction, secretion or postnasal drip, facial pain or pressure) with the need for add-on treatment to supplement intranasal corticosteroids. Severe CRSwNP is considered to be uncontrolled if the patient has received continuous treatment with an intranasal corticosteroid and has needed at least one course of systemic corticosteroids in the previous 2 years (or has a medical contraindication or intolerance) and/or has a previous sinonasal surgery.

## POLICY STATEMENT

Prior Authorization is recommended for prescription 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.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Dupixent is recommended in those who meet the following criteria:

**FDA-Approved Indications**

1. **Asthma.** Approve Dupixent for the duration noted if the patient meets one of the following conditions (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets the following criteria (i, ii, iii, iv and v):
     - **i.** Patient is ≥ 12 years of age; AND
     - **ii.** Patient meets ONE of the following criteria (a or b):
       - **a)** Patient has a blood eosinophil level ≥ 150 cells per microliter within the previous 6 weeks or within 6 weeks prior to treatment with any anti-interleukin therapy or Xolair; OR
         Note: Examples of anti-interleukin therapies include Dupixent, Nucala (mepolizumab injection for subcutaneous use), Cinqair (reslizumab injection for intravenous use), and Fasenra (benralizumab injection for subcutaneous use).
       - **b)** Patient has oral (systemic) corticosteroid-dependent asthma according to the prescriber (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)** An 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 $beta_2$-agonists, inhaled long-acting muscarinic antagonists, leukotriene receptor antagonists, anti-interleukin-5 therapies (e.g., Cinqair, Fasenra, Nucala), and theophylline. Use of a combination inhaler containing both an inhaled corticosteroid and a long-acting $beta_2$-agonist would fulfil the requirement for both criteria a and b.
     - **iv.** Patient has asthma that is uncontrolled or was uncontrolled at baseline as defined by ONE of the following (a, b, c, d or e):
       Note: "Baseline" is defined as prior to receiving any Dupixent or other anti-interleukin- 5 therapies (i.e., Cinqair, Fasenra, or Nucala).
       - **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 hospitalization or an Emergency Department visit in the previous year; OR
       - **c)** Patient has a forced expiratory volume in 1 second ($FEV_1$) < 80% predicted; OR
       - **d)** Patient has an $FEV_1$/forced vital capacity (FVC) < 0.80; OR
       - **e)** Patient has asthma that worsens upon tapering of oral corticosteroid therapy; AND
     - **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 criteria (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 or emergency department visits due to asthma; decreased requirement for oral corticosteroid therapy.

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

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

**i.** Patient is ≥ 6 years of age; AND

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

**a)** Patient has atopic dermatitis involvement estimated to be ≥ 10% of the body surface area according to the prescriber and meets ALL of the following criteria ([1], [2], and [3]):

**(1)** Patient has tried at least one medium-, medium-high, high-, and/or super-high-potency prescription topical corticosteroid; AND

**(2)** This topical corticosteroid was applied daily for at least 28 consecutive days; AND

**(3)** Inadequate efficacy was demonstrated with this topical corticosteroid therapy, according to the prescriber; OR

**b)** Patient has atopic dermatitis involvement estimated to be < 10% of the body surface area according to the prescriber and meets ALL of the following criteria ([1], [2], [3], and [4]):

**(1)** Patient has atopic dermatitis affecting ONLY the following areas: face, eyes/eyelids, skin folds, and/or genitalia; AND

**(2)** Patient has tried tacrolimus ointment; AND

**(3)** Tacrolimus ointment was applied daily for at least 28 consecutive days; AND

**(4)** Inadequate efficacy was demonstrated with tacrolimus ointment, according to the prescriber; AND

**iii.** 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 criteria (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. Nasal Polyps.** Approve Dupixent for the duration noted if the patient meets one of the following conditions (A or B):

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

**i.** Patient is ≥ 18 years of age; AND

**ii.** Patient has chronic rhinosinusitis with nasal polyposis 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 3 months 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 criteria (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 Rhinosinusitis with Nasal Polyposis, 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.

## CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Dupixent is not recommended in the following situations:

1. **Concurrent use of Dupixent with another Anti-Interleukin Monoclonal Antibody.** The efficacy and safety of Dupixent in combination with other anti-interleukin monoclonal antibodies (e.g., Cinqair, Nucala, Fasenra) have not been established.

2. **Concurrent use of Dupixent with Xolair® (omalizumab injection for subcutaneous use).** Xolair is a recombinant humanized immunoglobulin G (IgG)1κ monoclonal antibody with indications in severe asthma, idiopathic urticaria, and nasal polyps. The efficacy and safety of Dupixent used in combination with Xolair have not been established.

3. **Eosinophilic Esophagitis**. One small, phase II study (n = 45) evaluated the efficacy of Dupixent in patients with active eosinophilic esophagitis.[27] Compared with placebo, Dupixent was found to reduce dysphagia, histologic features of disease, and abnormal endoscopic features. There areongoing Phase III studies that are evaluating the use of Dupixent in pediatric and adult patients with eosinoiphilic esophagitis. Results are anticipated in 2022.[22] Guidelines for the management of eosinophilic esophagitis from the American Gastroenterological Association and the Joint Task Force on Allergy-Immunology Practice Parameters (2020) only recommend using Dupixent in the context of a clinical trial.[25]

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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