PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 03/22/2023; selected revision 05/10/2023

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

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 ≥ 12 years of age who weigh ≥ 40 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 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] In total, 74.1% of patients had also previously received swallowed topical corticosteroids to treat their eosinophilic esophagitis. 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.

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 witholding.

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.

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.

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.[24-27] 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 ≥ 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.

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.

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.

- **Dupixent® (dupilumab subcutaneous injection – Regeneron/sanofi-aventis)**

is(are) covered as medically necessary when the following criteria is(are) met for fda-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Asthma.** Approve 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 ≥ 6 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 Dupixent or another monoclonal antibody therapy that may lower 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), Fasenra (benralizumab subcutaneous injection), Nucala (mepolizumab subcutaneous injection), Tezspire (tezepelumab subcutaneous injection), and Xolair (omalizumab subcutaneous injection).
- **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, and monoclonal antibody therapies for asthma (e.g., Cinqair, Fasenra, Nucala, Tezspire, and Xolair). Use of a combination inhaler containing both an inhaled corticosteroid and additional asthma controller/maintenance medication(s) 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 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 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 (systemic) 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, 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 conditions (A or B):

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

i. Patient is ≥ 6 months of age; AND

ii. Patient has atopic dermatitis involvement estimated to be ≥ 10% of the body surface area according to the prescriber; AND

iii. Patient meets ALL of the following criteria (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) Inadequate efficacy was demonstrated with this topical corticosteroid therapy, according to the prescriber; 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 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. **Eosinophilic Esophagitis**. Approve 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, vi and vii):

i. Patient is ≥ 12 years of age; AND

ii. Patient weighs ≥ 40 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 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 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.

4. **Nasal Polyps.** Approve 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 (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. **Prurigo Nodularis.** Approve 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 ≥ 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)** The patient has a secondary cause of prurigo nodularis that has been identified and adequately managed, according to the prescriber; AND

v. Patient meets ALL of the following criteria (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)** Inadequate efficacy was demonstrated with this topical corticosteroid therapy, according to the prescriber; 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 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 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.

CONDITIONS NOT COVERED

- **Dupixent® (dupilumab subcutaneous injection – Regeneron/sanofi-aventis)**

is(are) considered experimental, investigational or unproven for ANY other use(s) 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 (i.e., Adbry, Cinqair, Fasenra, Nucala, Tezspire, or Xolair).** The efficacy and safety of Dupixent in combination with other monoclonal antibody therapies have not been established.

2. **Concurrent Use of Dupixent with Janus Kinase Inhibitors (JAKis) [oral or topical].** Use of JAKis, such as Cibinqo® (abrocitinib tablets), Rinvoq® (upadacitinib tablets), and Opzelura™ (ruxolitinib cream), is not recommended for use in combination with other JAKis, biologic immunomodulators (e.g., Dupixent), or with other immunosuppressants.[30-32]

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	03/16/2022
Selected Revision	**Asthma:** Criteria for a blood eosinophil level ≥ 150 cells per microliter within the previous 6 weeks or within 6 weeks prior to any anti-interleukin therapy or Xolair was changed to prior to any treatment with Dupixent or another monoclonal antibody therapy that may lower blood eosinophil levels. Throughout criteria, updated notes to include examples of monoclonal antibody therapies to include Tezspire™ (tezepelumab subcutaneous injection), Adbry™ (tralokinumab-ldrm subcutaneous injection), and Xolair® (omalizumab subcutaneous injection). Criteria requiring the patient to have experienced one or more asthma exacerbation(s) requiring a hospitalization or an emergency department visit in the previous year, were updated to include an urgent care visit as well. **Eosinophilic Esophagitis:** New approval criteria for this indication were added. Initial approval criteria include an age requirement, a weight requirement, a confirmation of diagnosis, ruling out secondary causes of eosinophilic esophagitis, a previous trial of a proton pump inhibitor, a previous trial of either dietary modifications or a physician evaluation that dietary modifications are not appropriate, and specialist involvement. **Conditions Not Covered** **:** Criteria were updated to recommend against use of Dupixent with another monoclonal antibody therapy. Previously, criteria listed anti-interleukin monoclonal antibody therapies and Xolair separately. Eosinophilic esophagitis was removed as a Condition Not Recommended for Approval.	06/01/2022
Selected Revision	**Atopic Dermatitis:** The age of approval was reduced from ≥ 6 years of age to ≥ 6 months of age. Criteria providing initial approval for patients with < 10% body surface area involvement were removed.	06/15/2022
Selected Revision	**Prurigo Nodularis:** New approval criteria for this indication were added. Initial approval criteria include an age requirement, a nodular lesion threshold, a minimum duration of pruritus, a requirement that prurigo nodularis not have a secondary cause or if there is a secondary cause that it be adequately managed, a trial of a topical corticosteroid, and specialist involvement.	10/19/2022
Annual Revision	**Conditions Not Covered** **:** Criteria were updated to clarify that use of Dupixent with another monoclonal antibody therapy is specific to Cinqair, Fasenra, Nucala, Tezspire, Xolair, and Adbry.	03/22/2023
Selected Revision	**Conditions Not Covered** **:** Criteria were added for "Concurrent Use of Dupixent with Janus Kinase Inhibitors (JAKis) [oral or topical]".	05/10/2023