VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

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

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OVERVIEW

Dupixent is and interleukin-4 receptor alpha (IL-4Rα) antagonist indicated:[1]

1) For the treatment of patients ≥ 6 years of age with moderate to severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.
2) As an add-on maintenance treatment in patients ≥ 12 years of age with moderate-to-severe asthma with an eosinophilic phenotype or with oral corticosteroid dependent asthma. Dupixent is not indicated for the relief of acute bronchospasm or status asthmaticus.
3) As an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP).

Dupixent is a human monoclonal antibody that binds to the IL-4Rα subunit shared by the interleukin (IL)-4 and IL-13 receptor complexes, thereby inhibiting IL-4 and IL-13 signaling.[1] This inhibition limits IL-4 and IL-13 cytokine-induced responses, including the release of proinflammatory cytokines, chemokines, and immunoglobulin (Ig)E involved in type 2 inflammation.

Clinical Efficacy

Asthma

The efficacy of Dupixent for the treatment of asthma was established in three randomized, double-blind, placebo-controlled, multicenter, pivotal studies in patients with persistent asthma.[2-4] Two of these studies included patients ≥ 12 years of age who had moderate to severe asthma that was uncontrolled despite treatment with a medium- to high-dose inhaled corticosteroid (ICS) and up to two additional controller medications.[2,4] In these studies, Dupixent significant reduced the annual exacerbation rate compared with placebo. Higher baseline eosinophil levels were correlated with larger asthma exacerbation reductions and greater increases in lung function parameters than were observed in patients with lower baseline blood eosinophil levels (i.e., < 150 cells/microliter). The third Dupixent pivotal trial included patients with severe asthma who were oral corticosteroid dependent.[3] Patients who received Dupixent were able to significantly reduce their oral corticosteroid doses compared with placebo. Dupixent was associated with a greater oral corticosteroid dose reduction regardless of baseline blood eosinoiphil count. Dupixent also reduced the rate of severe asthma exacerbations as well.

Atopic Dermatitis

The three pivotal Dupixent studies enrolled adult patients with moderate to severe chronic atopic dermatitis.[1,5,6] Patients' atopic dermatitis affected ≥ 10% of their body surface area (BSA) and had a recent history of an inadequate response to a sufficient course of topical therapy (e.g., corticosteroids and/or calcineurin inhibitors). The primary efficacy endpoint was a score of 0 (clear) or 1 (almost clear) on the Investigator's Global Assessment (IGA) and a reduction of ≥ 2 points from baseline to Week 16. Dupixent was found to be more effective in achieving the primary endpoint at Week 16 compared with placebo. The third study also found Dupixent to be more effective in achieving the primary endpoint at Week 52 compared with placebo. A fourth study evaluated the efficacy of Dupizent in patients 12 to 17 years of age with moderate to severe atopic dermatitis affecting ≥ 10% of their BSA.[1] Dupixent was

again found to be more effective in achieving an IGA score of 0 or 1 compared with placebo at Week 16 (primary endpoint). An additional trial evaluated the efficacy of Dupixent in patients 6 to 11 years of age with severe atopic dermatitis affecting ≥ 15% of their BSA.[1,22] Similar to other studies, a greater proportion of patients receiving Dupixent achieved an IGA score of 0 or 1 compared with placebo following 16 weeks of therapy.

Chronic Rhinosinusitis with Nasal Polyposis (CRSwNP)

Two randomized, double-blind, multicenter, placebo-controlled studies evaluated the efficacy of Dupixent in adult patients with CRSwNP.[1,17] Patients enrolled in these studies were also treated with intranasal corticosteroids and had failed treatment with sino-nasal surgery or systemic corticosteroids (or were ineligible or intolerant to). The co-primary efficacy endpoints were the change from baseline to Week 24 in bilateral endoscopic nasal polyp score (NPS) and the change from baseline in the nasal congestion/obstruction score (averaged over 28 days). Across both studies, Dupixent statistically significantly improved both primary endpoints when compared with placebo at Week 24. The reductions in the nasal polyp size (measure by the NPS) were sustained over a longer period of time (48 weeks in one study; 52 weeks in the other study). However, the treatment effect diminished over time. Dupixent was also found to positively impact several secondary outcomes, such as nasal congestion, loss of smell, and sino-nasal symptoms as well as reduce the need for systemic corticosteroid therapy and sino-nasal surgery.

Guidelines

Asthma Guidelines

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 beta$_2$-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 eospinophils, elevated fractional concentration of exhaled nitric oxide (FeNO), the need for maintenance oral corticosteroid therapy, or clinically allergen-driven asthma.

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 (AD) Guidelines

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.[9-11] 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) Guidelines

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.[18-20] 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 syptoms, 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).[21]

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Dupixent. 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, approval requires Dupixent to be prescribed by or in consultation with a physician who specializes in the condition being treated. Refer to criteria below for approval durations. All reviews will be forwarded to a Pharmacist or Medical Director.

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 Dupixent 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.** Dupixent is prescribed by or in consultation with an allergist, immunologist, or pulmonologist; AND
     - **iii.** Patient meets ONE of the following criteria (a or b):
       - **a)** Patient has a blood eosinophil level of ≥ 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, Cinqair, and Fasenra.
       - **b)** Patient has oral (systemic) corticosteroid-dependent asthma per the prescriber (e.g., the patient has received ≥ 5 mg oral prednisone or equivalent per day for ≥ 6 months); AND
     - **iv.** 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/maintenance medication; AND

       Note: An exception to the requirement for a trial of one additional asthma controller/maintenance medication (criterion b) can be made if the patient has already received anti-interleukin-5 therapy (e.g., Cinqair, Fasenra, Nucala) or Xolair used concomitantly with an inhaled corticosteroid for at least 3 consecutive months. Examples of additional asthma controller/maintenance medications are inhaled long-acting $beta_2$-agonists, inhaled long-acting muscarinic antagonists, leukotriene receptor antagonists, 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.
     - **v.** Patient's asthma is uncontrolled or was uncontrolled prior to starting any anti-interleukin therapy or Xolair as defined by ONE of the following (a, b, c, d or e):
       - **a)** The patient experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year; OR
       - **b)** The patient experienced one or more asthma exacerbation requiring hospitalization or an Emergency Department (ED) 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)** The patient's asthma worsens upon tapering of oral corticosteroid therapy.

       Note: Examples of anti-interleukin therapies include Dupixent, Nucala, Cinqair, and Fasenra.
   - **B)** Patients Continuing Dupixent Therapy. Approve Dupixent for 1 year if the patient meets the following criteria (i, ii, and iii):
     - **i.** The patient has already received at least 6 months of therapy with Dupixent; AND
       Note: Patients who have received < 6 months of therapy or those who are 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.** The patient has responded to Dupixent 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 (ED) 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. Dupixent is prescribed by or in consultation with an allergist, immunologist, or dermatologist; AND

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

a) Patient has atopic dermatitis involvement estimated to be ≥ 10% of the body surface area (BSA) 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 BSA 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 (Protopic®, generics); AND

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

(4) Inadequate efficacy was demonstrated with tacrolimus ointment (Protopic, generics), according to the prescriber.

B) Patients Continuing Dupixent Therapy. Approve for 1 year if the patient meets the following criteria (i and ii):

i. The patient has already received at least 4 months of therapy with Dupixent; AND
Note: Patients who have received < 4 months of therapy or those who are restarting therapy with Dupixent should be considered under criterion 2A (Atopic Dermatitis, Initial Therapy).

ii. The patient has responded to Dupixent 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 (BSA) affected with atopic dermatitis; or other responses observed.

3. Chronic Rhinosinusitis with Nasal Polyposis. 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 ≥ 18 years of age; AND

ii. Dupixent is prescribed by or in consultation with an allergist, immunologist, or an otolaryngologist (ear, nose and throat [ENT] physician specialist); AND

iii. Patient is currently receiving therapy with an intranasal corticosteroid; AND

iv. Patient is experiencing significant rhinosinusitis symptoms such as nasal obstruction, rhinorrhea, or reduction/loss of smell according to the prescriber; AND

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

a) Patient has received treatment with a systemic corticosteroid within the previous 2 years or has a contraindication to systemic corticosteroid therapy; OR

b) Patient has had prior surgery for nasal polyps.

B) Patients Continuing Dupixent Therapy. Approve for 1 year if the patient meets the following criteria (i, ii and iii):

- **i.** The patient has already received at least 6 months of therapy with Dupixent; AND
  Note: Patients who have received < 6 months of therapy or those who are 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.** The patient has responded to Dupixent 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 sino-nasal symptoms, improved sense of smell.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Dupixent has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Concurrent use of Dupixent with another Anti-Interleukin (IL) Monoclonal Antibody.** The efficacy and safety of Dupixent in combination with any other anti-IL monoclonal antibody (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 indicated for use in patients ≥ 6 years of age with moderate to severe persistent asthma and who have a positive skin test or *in vitro* reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with ICSs.[14] Xolair is also indicated for chronic idiopathic urticaria in adults and adolescents 12 years of age and older who remain symptomatic despite H_1 antihistamine treatment. The efficacy and safety of Dupixent used in combination with Xolair have not been established.

3. **Eosinophilic Esophagitis**. A Phase II study has been conducted evaluating Dupixent for the treatment of eosinophilic esophagitis.[13] Results are not yet available. There is an additional Phase III study that is currently underway in patients with eosinoiphilic esophagitis. Results are anticipated in 2022. The efficacy and safety of Dupixent for the treatment of eosinophilic esophagitis have not been established.

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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