dupilumab (Dupixent®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO019

Description

Dupilumab (Dupixent) is a subcutaneously administered monoclonal antibody (IgG4 Kappa) that antagonizes interleukin-4 (IL-4) and interleukin-13 (IL-13).

Length of Authorization

- Initial: 12 months
- Renewal: 12 months

Quantity limits

Product Name	Indication	Dosage Form	Quantity Limit
dupilumab (Dupixent)	Asthma (moderate to severe)	200 mg/1.14mL pen injector or prefilled syringe	**Adult:** **First Month**: 4 (200mg OR 300mg) syringes/pens (4.56mL OR 8ml)/42 days **Maintenance:** 2 (200mg OR 300mg) syringes/pens (2.28mL OR 4ml)/28 days
			Pediatric (6-11 years of age): **No Loading Dose** **Maintenance:** • **15 to less than 30 kg:** 1 (200mg/1.14mL) syringes (2.28mL)/28 days; **OR** 1 (300mg/2mL) syringes/pens (2mL)/28days • **30 kg or more:** 2 (200mg/1.14mL) syringes/pens (2.28mL)/28 days
	Atopic Dermatitis (moderate to severe); Atopic Dermatitis (moderate to severe) and comorbid Asthma (Moderate to severe)	300 mg/2mL pen injector or prefilled syringe	**Adult:** **First Month:** 4 (300mg) syringes/pens (8 mL)/28 days **Maintenance:** 2 (300mg) syringes/pens (4 mL)/28 days
			Pediatric (6 – 17 years of age): **First Month:** • **15 to less than 30 kg:** 2 (300mg) syringes/pens (4 mL)/28 days • **30 to less than 60 kg:** 4 (200mg) syringes/pens (4.56 mL)/28 days • **60 kg or more:** 4 (300mg) syringes/pens (8 mL)/28 days **Maintenance:**

			• **15 to less than 30 kg:** 1 (300mg) syringes/pens (2 mL)/28 days • **30 to less than 60 kg:** 2 (200mg) syringes/pens (2.28 mL)/28 days • **60 kg or more:** 2 (300mg) syringes/pens (4 mL)/28 days
			Pediatric (6 months – 5 years of age): **No Loading Dose** **Maintenance:** • **5 to less than 15kg:** 2 (200mg) syringe/pen (2.28mL)/56 days • **15 to less than 30kg:** 2 (300mg) syringes/pens (4mL)/56 days
	Chronic rhinosinusitis with nasal polyposis	300 mg/2mL pen injector or prefilled syringe	2 (300mg) syringes/pens (4 mL)/28 days
	Prurigo Nodularis	300 mg/2mL pen injector or prefilled syringe	**First month:** 4 (300mg) syringes/pens (8 mL)/28 days **Maintenance:** 2 (300mg) syringes/pens (4 mL)/28 days
	Eosinophilic esophagitis	200 mg/1.14mL pen injector or prefilled syringe 300 mg/2mL pen injector or prefilled syringe	• **15 to less than 30kg:** 2 (200mg) syringes/pens (2.28 mL)/28 days • **30 to less than 40kg:** 2 (300mg) syringes/pens (4 mL)/28 days • **40kg and more**: 4 (300mg) syringes/pens (8mL)/28 days
	Chronic obstructive pulmonary disease (moderate to severe)	300 mg/2mL pen injector or prefilled syringe	2 (300mg) syringes/pens (4 mL)/28 days

Initial Evaluation

I. **Dupilumab (Dupixent)** may be considered medically necessary when the following criteria below are met:
   A. Medication is prescribed by, or in consultation with, a dermatologist or a physician specializing in allergy, pulmonology, gastroenterology, immunology, or ENT (ear, nose, throat); **AND**
   B. Must not be used in combination with another monoclonal antibody (e.g., benralizumab, mepolizumab, omalizumab, reslizumab, ensifentrine, etc.); **AND**
   C. A diagnosis of one of the following:
      1. **Atopic dermatitis (moderate to severe); AND**
         i. Member is six months of age or older; **AND**
            a. Body surface area (BSA) involvement of at least 10%; **OR**
               i. Involves areas of the face, ears, hands, feet, or genitalia; **AND**
         ii. Treatment with at least two of the following groups has been ineffective or not tolerated, unless ALL are contraindicated:
            a. Group 1: Topical corticosteroids of at least medium/moderate potency (e.g., clobetasol, betamethasone, halobetasol)
            b. Group 2: Topical calcineurin inhibitors (e.g. pimecrolimus cream, tacrolimus ointment)
            c. Group 3: Topical PDE-4 inhibitors (e.g. crisaborole [Eucrisa]); **OR**
      2. **Asthma (moderate to severe)**; **AND**
         i. Member is 6 years of age or older; **AND**
         ii. Member has **MODERATE** asthma as defined by one of the following:
            a. Daily symptoms
            b. Nighttime awakenings > 1x/week but not nightly
            c. SABA (e.g. albuterol, levalbuterol) use for symptom control occurs daily
            d. Some limitation to normal activities
            e. Lung function (percent predicted FEV1) >60%, but <80%
            f. Exacerbations requiring oral systemic corticosteroids are generally more frequent and intense relative to mild asthma; **OR**
         iii. Member has **SEVERE** asthma as defined by one of the following:
            a. Symptoms throughout the day
            b. Nighttime awakenings, often 7x/week
            c. SABA (e.g. albuterol, levalbuterol) use for symptom control occurs several times per day
            d. Extremely limited normal activities

e. Lung function (percent predicted FEV1) <60%
f. Exacerbations requiring oral systemic corticosteroids are generally more frequent and intense relative to moderate asthma; **AND**

iv. Member must have asthma with an eosinophilic phenotype defined as blood eosinophils ≥150 cells/µL within the last 12 months; **AND**
   a. Member must have two or more exacerbations in the previous year requiring daily oral corticosteroids for at least 3 days (in addition to the regular maintenance therapy defined below); **OR**

v. Member is dependent on oral corticosteroids for asthma control; **AND**

vi. Member is currently being treated with:
   a. A medium- to high-dose, or maximally tolerated inhaled corticosteroid (ICS) [e.g., budesonide, fluticasone, mometasone]; **AND**
      i. One additional asthma controller medication (e.g., long-acting beta-2 agonist [LABA] {e.g., Serevent Diskus}, long-acting muscarinic antagonist [LAMA] {e.g., Spiriva Respimat}, leukotriene receptor antagonist [e.g., Singular], or theophylline); **OR**
   b. A maximally tolerated ICS/LABA combination product (e.g., Advair, Airduo, Breo, Dulera, Symbicort); **AND**

vii. Background controller medications (e.g., Advair, Airduo, Breo, Dulera, Symbicort) will be continued with the use of dupilumab (Dupixent), unless contraindicated; **OR**

3. **Chronic rhinosinusitis with nasal polyposis (CRSwNP); AND**

i. Member is 12 years of age or older; **AND**

ii. Provider attests that the member has ALL of the following:
   a. Diagnosis of bilateral sinonasal polyposis as evidenced by an endoscopy or computed tomography (CT); **AND**
   b. Member has impaired Health-Related Quality of Life due to ongoing nasal congestion, blockage, or obstruction with moderate to severe symptom severity; **AND**
   c. Member has at least <u>one</u> of the following symptoms:
      i. Nasal discharge
      ii. Facial pain or pressure
      iii. Reduction or loss of smell; **AND**

iii. Member has current persistent symptomatic nasal polyps despite maximal treatment with an intranasal corticosteroid, unless ineffective, not tolerated, or contraindicated; **AND**

iv. Background intranasal corticosteroid (e.g., beclomethasone [Qnasl], budesonide [Rhinocort], ciclesonide [Omnaris; Zetonna], flunisolide, fluticasone [Flonase], mometasone [Nasonex], triamcinolone [Nasacort]) will be continued with the use of dupilumab (Dupixent), unless contraindicated; **OR**

4. **Eosinophilic Esophagitis (EoE); AND**
   i. Member is one year of age or older; **AND**
   ii. Member weighs at least 15kg (33 lbs); **AND**
   iii. Provider attests that the member has ALL of the following:
      a. Symptoms consistent with eosinophilic esophagitis (e.g., dysphagia, food impaction, vomiting, central chest and upper abdominal pain, etc.); **AND**
      b. Eosinophil-predominant inflammation, consisting of a peak value of ≥15 eos/hpf or ~60 eosinophils/mm^2, as confirmed by endoscopic biopsy; **AND**
      c. Underlying cause of the member's condition is NOT considered to be any other allergic condition(s) or other form(s) of esophageal eosinophilia; **AND**
   iv. Member has experienced persistent EoE symptoms during or following an adequate trial of dietary restriction (e.g., empiric elimination diet); **AND**
   v. Treatment with at least one agent in each of the following classes has been ineffective, contraindicated, or not tolerated:
      a. Proton pump inhibitors (PPIs) for at least eight weeks; **AND**
      b. Swallowed topical corticosteroids (e.g., fluticasone, budesonide); **OR**

5. **Prurigo nodularis (moderate to severe); AND**
   i. Member is 18 years of age or older; **AND**
   ii. Member has a confirmed diagnosis of moderate to severe prurigo nodularis based on all of the following:
      a. Presence of nodules for at least 3 months; **AND**
      b. Disease is moderate to severe in severity (e.g., Worst-Itch Numeric Rating Scale (WI-NRS) score of at least 7, Investigator Global Assessment (IGA) score of 3 or 4; presence of at least 20 lesions on the body); **AND**
      c. Provider attests underlying cause of prurigo nodularis is not considered to be drug-induced or caused by other medical conditions, such as dermatillomania; **AND**
   iii. Treatment with at least one medium to very high potency topical corticosteroid has been ineffective, not tolerated, or contraindicated; **AND**

i. Treatment with at least one of the following has been ineffective or not tolerated, unless ALL are contraindicated:
   a. Topical calcineurin inhibitors (e.g. pimecrolimus cream, tacrolimus ointment)
   b. Topical vitamin D analogue (e.g., calcipotriene)
   c. Phototherapy (UVA or PUVB)
   d. Systemic immunosuppressants (e.g. methotrexate or cyclosporine); **OR**

6. **Chronic obstructive pulmonary disease (COPD); AND**
   i. Member is 18 years of age or older; **AND**
   ii. Member has a confirmed diagnosis of moderate to severe COPD with an eosinophilic phenotype defined by all of the following:
      a. Post-bronchodilator FEV1/FVC ratio of <0.7; **AND**
      b. Post-bronchodilator FEV1 % predicted ≥30% and <80%; **AND**
      c. Documentation of blood eosinophils ≥300 cells/µL within the last 12 months; **AND**
   iii. Member is in COPD treatment Group E defined by one of the following:
      a. ≥2 moderate (e.g., treated with short-acting bronchodilators and oral corticosteroids ± antibiotics); **OR**
      b. ≥1 severe (e.g., required hospitalization or emergency room visit) exacerbation(s) within the last 12 months; AND
   iv. Member is currently being treated with:
      a. A triple therapy inhaler regimen comprising of a long-acting beta-2 agonist [LABA], a long-acting muscarinic antagonist [LAMA], and an inhaled corticosteroid (ICS), unless ICS is contraindicated, such as:
         i. LABA/LAMA/ICS combination product (e.g., Trelegy Ellipta, Breztri Aerosphere); **OR**
         ii. LABA/LAMA combination product (e.g., Anoro Ellipta, Stiolto Respimat, Bevespi Aerosphere); **AND**
            1. ICS has been contraindicated or not tolerated (e.g., beclomethasone (Qvar), budesonide (Pulmicort), ciclesonide (Alvesco), fluticasone (Arnuity, Flovent), mometasone (Asmanex)); **AND**
   v. Background controller medications (e.g., Trelegy, Anoro, Stiolto, Bevespi) will be continued with the use of dupilumab (Dupixent), unless contraindicated.

II. Dupilumab (Dupixent) is considered <u>investigational</u> when used for all other conditions, including but <u>not limited to</u>:

A. Food and environmental allergies
B. Other forms of esophagitis
C. Gastrointestinal reflux disorder (GERD)
D. Non-EoE eosinophilic gastrointestinal disorders
E. Chronic spontaneous urticaria (CSU)
F. Bullous pemphigoid/prurigo and related conditions (e.g., pemphigoid nodularis, actinic purigo, lichen planus, multiple keratoacanthomas, epidermolysis bullosa pruriginosa, etc.)
G. Emergency treatment of allergic reactions, including anaphylaxis
H. Add on therapy for COPD when used in pediatric patients less than 18 years of age

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Must not be used in combination with another monoclonal antibody (e.g., benralizumab, mepolizumab, omalizumab, reslizumab, etc.); **AND**
IV. A diagnosis of one of the following:
    - **Atopic dermatitis (moderate to severe); AND**
        i. Member has exhibited improvement or stability of disease symptoms (e.g., improvement in IGA score from baseline, BSA involvement, pruritis symptoms); **OR**
    - **Asthma (moderate to severe); AND**
        i. Member has exhibited improvement or stability of disease symptoms (e.g., reduced asthma exacerbations, FEV1, reduced systemic corticosteroid requirements, reduced hospitalizations); **AND**
        ii. Background controller medications (e.g., ICS/LABA product listed above) will be continued with the use of dupilumab (Dupixent), unless contraindicated; **OR**
    - **Chronic rhinosinusitis with nasal polyposis (CRSwNP); AND**
        i. Member has exhibited improvement or stability of disease symptoms (e.g., improvement in nasal congestion/obstruction severity, reduction in nasal polyps); **AND**
        ii. Background intranasal corticosteroid (e.g., beclomethasone [Qnasl], budesonide [Rhinocort], ciclesonide [Omnaris; Zetonna], flunisolide, fluticasone [Flonase], mometasone [Nasonex], triamcinolone

[Nasacort]) will be continued with the use of dupilumab (Dupixent), unless contraindicated; **OR**

- **Eosinophilic esophagitis; AND**
  i. Member has exhibited improvement or stability of disease (e.g., improvement in dysphagia/vomiting/abdominal pain, reduction in eosinophils); **OR**
- **Prurigo nodularis; AND**
  i. Member has exhibited improvement or stability of disease symptoms (e.g., reduced itching/pruritis, improved skin appearance, reduction in number of nodules, etc.); **OR**
- **Chronic obstructive pulmonary disease; AND**
  i. Member has exhibited improvement or stability of disease symptoms (e.g., reduced COPD exacerbations, reduced hospitalizations, improved FEV1); **AND**
  ii. Background controller medications (e.g., LAMA/LABA/ICS products (e.g., Trelegy Ellipta, Breztri Aerosphere) or LABA/LAMA products (e.g., Anoro Ellipta, Stiolto Respimat, Bevespi Aerosphere) will be continued with the use of dupilumab (Dupixent), unless contraindicated

Supporting Evidence

I. Dupilumab (Dupixent) is FDA approved in the following settings:
- Moderate to severe asthma with eosinophilic phenotype in members 6 years of age or older
- Oral corticosteroid dependent asthma in members 6 years of age or older
- Moderate to severe atopic dermatitis for patients 6 months and older whose disease is not adequately controlled with topical prescription therapies
- Add-on maintenance treatment for patients 12 years of age or older with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP)
- Treatment of adult patients with prurigo nodularis (PN)
- Add-on maintenance treatment for adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) associated with a history of exacerbations and eosinophilic phenotype.

II. Dupilumab trials excluded concomitant biologic therapy; moreover, there is lack of evidence supporting treatment with dual use of biologic therapies and a potential for increased risk of side effects.

III. **Moderate to severe atopic dermatitis**
- For patients aged 12 years or older, dupilumab (Dupixent) was studied in four randomized, double-blind, placebo-controlled trials. In all four trials, investigators enrolled patients who

had previous inadequate responses to a topical medication with a PGA score of at least three (scale of zero to four) and a minimum BSA involvement of ≥10%. In all four trials, patients in the dupilumab (Dupixent) arm achieved statistically significant improvement when compared to the placebo arm. See table below for details.

	Trial 1		Trial 2		Trial 3		Trial 4	
	DUPIXENT 300 mg Q2W N=224	PBO N=224	DUPIXENT 300 mg Q2W N=233	PBO N=236	DUPIXENT 300 mg Q2W + TCS N=106	PBO + TCS N=315	DUPIXENT 200 mg (<60 kg) or 300 mg (>60 kg) Q2W N=82	PBO N=85
% of patients with IGA 0 or 1	38%	10%	36%	9%	39%	12%	24%	2%
% of patients with EASI-75	51%	15%	44%	12%	69%	23%	42%	8%

- For patients aged 6 to 11 years, dupilumab (Dupixent) approval was based on the results from a 16-week, phase III, double-blind, placebo-controlled trial. Investigators enrolled pediatric patients who have had a previous inadequate response to a topical medication with a PGA score of four (scale of zero to four) and a minimum BSA involvement of ≥15%. Patients in both dupilumab arms achieved statistically significant improvements when compared to the placebo arm, see table below for details.

	<30 kg			≥30 kg		
	PBO + TCS n=61	Q4W + TCS n=61	Q2W + TCS n=63	PBO + TCS n=62	Q4W + TCS n=61	Q2W + TCS n=59
% of patients with IGA 0 or 1	13.1%	29.5% p<0.05	20.6%	9.7%	36.1% p<0.001	39% p<0.001
% of patients with EASI-75	27.9%	75.4% p<0.0001	60.3% p<0.001	25.8%	63.9% p<0.0001	74.6% p<0.0001

- For patients aged 6 months to 5 years, dupilumab (Dupixent) approval was based on the safety results from a 16-week trial consisting of 161 patients with a diagnosis of moderate-to-severe atopic dermatitis who were using dupilumab (Dupixent) in combination with a topical corticosteroid (AD-1539). Additionally, long-term safety of dupilumab (Dupixent) with or without a concomitant topical corticosteroid was evaluated in a 52-week open-label extension study consisting of 180 pediatric patients with atopic dermatitis (AD-1434); the majority of patients received dupilumab (Dupixent) dosed at 300mg every 4 weeks. The safety profile of dupilumab (Dupixent) with or without concurrent topical corticosteroid was similar between these two studies and consistent with the known safety profile of this medication in the adult and pediatric 6–17-years-old population. Notably, hand-foot-and-mouth disease and skin papilloma were reported in 9 (5%) and 4 (2%) of subjects, respectively. However, none of these cases led to study drug discontinuation during the trial.

- Treatments for mild-to-moderate atopic dermatitis include topical corticosteroids (TCS), topical calcineurin inhibitors (TCI), and/or crisaborole (Eucrisa) – a PDE4 inhibitor, and phototherapy. Symptomatic treatments include oral and topical antihistamines and sleep aids for nighttime pruritus. Treatment choice between these products is dependent on severity, location, and other patient specific factors (e.g., allergies, age). According to AAD guidelines, TCIs may be preferable to TCS in patients with recalcitrance to steroids, sensitive areas involved, steroid-induced atrophy, and long-term uninterrupted topical steroid use.
- Treatment for moderate to severe disease includes the same topical classes noted above and, for those not amenable to topical, systemic immunosuppressants (e.g., corticosteroids, cyclosporine, methotrexate, azathioprine, mycophenolate mofetil), JAK inhibitors (e.g., abrocitinib, upadacitinib), and dupilumab (Dupixent), a biologic IgG4 that is FDA-approved for pediatrics and adults as a biologic option for moderate-to-severe atopic dermatitis. Currently, there are no head to head trials evaluating safety and/or efficacy differences or superiority between biologic therapies in atopic dermatitis. Dupilumab (Dupixent) has an established safety and efficacy profile for the treatment of atopic dermatitis and is approved down to six years of age. Upadacitinib (Rinvoq) has been evaluated and is FDA approved in patients down to 12 years of age. Abrocitinib (Cibinqo) is FDA approved in adult patients only.
- There may be patient specific scenarios in which the use of additional topical agents following failure of one class of topical agents would be impractical. Insight from dermatology specialists indicate that patients who have at least 15% BSA involvement, or involvement in sensitive areas (e.g., eyelids, axilla, genitals, gluteal cleft), and have severe disease are potential candidates for systemic biologic therapy. Severe disease, as defined by NICE guidelines, includes widespread areas of dry skin, incessant itching, redness (with or without excoriation, extensive skin thickening, bleeding, oozing, cracking, and alteration of pigmentation), and severe limitation of everyday activities and psychosocial functioning, nightly loss of sleep; severe disease can also be classified as physician's global assessment (PGA) score of 4.0. Additionally, administration of topical agents may become impractical for patients with high disease burden (BSA ≥ 20%), considering twice daily administration is necessary for non-steroid topical agents for optimal efficacy.

IV. **Moderate to severe asthma**

- Dupilumab (Dupixent) was studied in three randomized, double-blind, placebo-controlled, multicenter trials. These trials did not require a minimum baseline blood eosinophilic count; mean baseline blood eosinophilic count for all trials were 353 cells/mcL. Trials 2 and 3 excluded patients with a screening blood eosinophil level of >1500 cells/mcL. Trials 1 and 2 required patients to have a history of at least one asthma exacerbation that required systemic corticosteroid treatment, or an emergency department visit or hospitalization for the treatment of asthma in the year prior to trial entry; patients continued background

asthma treatment throughout the study. Trial 3 required dependence on daily oral corticosteroids (OCS) in addition to regular use of high-dose ICS plus an additional controller(s).

i. Trial 1: Patients enrolled were at least 18 years of age with moderate to severe asthma on a medium or high-dose ICS and a LABA. Patients were randomized to receive either dupilumab (Dupixent) 200 mg or 300 mg every other week (Q2W) or every 4 weeks following an initial dose of 400 mg, 600 mg, or placebo. The primary endpoint was mean change from baseline to Week 12 in FEV1 in patients with baseline blood eosinophil ≥300 cells/mcL receiving 200 mg, 300mg, or placebo, which were 25.9%, 25.8%, and 10.2%, respectively. Mean difference compared to placebo for the 200 mg and 300 mg were 0.26 (95% CI 0.11, 0.4) and 0.21 (95% CI 0.06, 0.36), respectively.

ii. Trial 2: Patients enrolled were at least 12 years of age with moderate to severe asthma on a medium to high-dose ICS and a minimum of one and up to two additional controller medications. Patients were randomized to receive either dupilumab (Dupixent) 200 mg or 300 mg every 2 weeks following initial dose of 400 mg, 600 mg, or placebo. The primary endpoints were the annualized rate of severe exacerbation events during the 52-week placebo-controlled period receiving 200 mg vs placebo or 300 mg vs placebo, which were RR 0.52 (95% CI 0.41, 0.66) and RR 0.54 (95% CI 0.43, 0.68), respectively, and change from baseline in FEV1 at Week 12 receiving 200 mg vs placebo or 300mg vs placebo, which were 29% vs 15.9% and 32.5% vs 14.4%. Mean difference compared to placebo for the 200 mg and 300 mg were 0.21 (95% CI 0.13, 0.29) and 0.24 (95% CI 0.16, 0.32), respectively.

iii. Trial 3: Patients enrolled were at least 12 years of age with asthma who required daily OCS in addition to regular use of high-dose ICS plus an additional controller. Patients were randomized to receive either dupilumab (Dupixent) 300 mg or placebo every 2 weeks for 24 weeks following an initial dose of 600 mg or placebo. Patients continued existing asthma therapy during the trial; OCS dose was reduced every 4 weeks during the OCS reduction phase (Weeks 4 to 20) as long as asthma control was maintained. The primary endpoint was the percent of reduction from baseline of the final oral corticosteroid dose at week 24 while maintaining asthma control in those receiving either 300 mg or placebo, which was 90% (95% CI 60%, 80%) vs 42% (95% CI 33%, 51%), respectively.

- The Global Initiative for Asthma (GINA) 2020 update recommends the addition of respiratory biologics, with respect to their allergic biologics, after inadequate asthma control despite good adherence and inhaler technique on maximized Step 4 (medium dose

ICS-LABA) or Step 5 (high dose ICS-LABA) therapy. Other controller options for Step 4 include high dose ICS-LABA or add-on tiotropium, or add-on LTRA. Other controller options for Step 5 include add-on anti-IL5, or add-on low dose OCS, though guidelines note to consider side effects.

V. **Chronic rhinosinusitis with nasal polyposis (CRSwNP)**

- Dupilumab (Dupixent) approval was based on the results from two phase 3 pivotal trials SINUS-24 and SINUS-52. SINUS-24 was a 24-week study, while SINUS-52 was a 52-week study. Both trials evaluated dupilumab (Dupixent) 300mg administered every two weeks combined with standard-of-care mometasone furoate nasal spray (MFNS) and compared to placebo injection plus MFNS. In both trials, there were two co-primary endpoints, improvement in nasal congestion/obstruction severity and reduction in nasal polyps. At 24 weeks, patients in the dupilumab (Dupixent) arm achieved statistically significant improvements when compared to the placebo arm.
    i. Fifty-seven percent and 51% improvement in their nasal congestion/obstruction severity compared to a 19% and 15% improvement with placebo in SINUS-24 and SINUS-52, respectively.
    ii. Thirty-three percent and 27% reduction in their nasal polyps score compared to a 7% and 4% increase with placebo in SINUS-24 and SINUS-52, respectively.
- Dupilumab (Dupixent) is approved as an add-on maintenance treatment for patients aged 12 years of age or older with inadequately controlled CRSwNP. Use of dupilumab (Dupixent) is supported by data from the SINUS-24 and SINUS-52 trials in adults with CRSwNP, that showed dupilumab significantly improved nasal congestion/obstruction severity, nasal polyp size and sense of smell compared with placebo at 24 weeks, while also reducing the need for systemic corticosteroids and surgery. The expanded approval was also supported by current pharmacokinetic and safety data for adolescents using the drug for other approved indications.
- Guidelines and compendia recommend the use of topical saline irrigation and intranasal corticosteroids (INCS) as initial treatment options in CRSwNP. Intranasal corticosteroids (INCS) have a positive impact on the disease and improve symptoms, reduce nasal polyp size, reduce nasal poly recurrence, and improve sense of smell. The guidelines also recommend short-term treatment with oral steroids in patients with CRSwNP to reduce symptoms and decrease nasal poly size. Biologics are considered in patients where their disease remains uncontrolled despite appropriate medical treatment and endoscopic sinus surgery (ESS).
- There are no completed head-to-head studies comparing biologic agents for treatment of CRSwNP. However, dupilumab (Dupixent) has been consistently found to be the most effective in multiple systematic reviews and indirect comparisons. A head-to-head comparison of omalizumab (Xolair) versus dupilumab (Dupixent) for treatment of CRSwNP is underway (NCT04998604) with an estimated completion in early 2025.

VI. **Eosinophilic esophagitis (EoE)**

- Dupilumab (Dupixent) was approved for the treatment of eosinophilic esophagitis (EoE) in patients aged 12 years and older weighing at least 40kg based on data from a single Phase 3, randomized, double-blind, placebo-controlled (Liberty EoE TREET) trial consisting of three parts (A, B, and C).
- Results from Parts A and B 24-week treatment periods of the Liberty EoE TREET trial were evaluated for the FDA approval of the EoE indication, as Part C is still ongoing. In both parts, there were two co-primary endpoints: the proportion of subjects achieving histological remission defined as peak esophageal intraepithelial eosinophil count of ≤6 eos/hpf at Week 24 and the absolute change in the subject reported DSQ score from baseline to Week 24. Dupilumab (Dupixent) met the co-primary endpoint in both Parts A and B for the 300mg weekly dose only. The dupilumab (Dupixent) 300mg every two-week dosing failed to meet statistical significance for the absolute change in subject reported DSQ score. Notably, the FDA has chosen to only approve the 300mg weekly dose for treatment of EoE.

	Part A		Part B		
	Dupixent 300mg QW N = 42	Placebo N = 39	Dupixent 300mg QW N = 80	Dupixent 300mg Q2W N = 81	Placebo N = 79
Co-primary Endpoints					
Proportion of subjects achieving histological remission (peak esophageal intraepithelial eosinophil count ≤6 eos/hpf), n (%)	25* (59.5)	2 (5.1)	47* (58.5)	49* (60.5)	5 (6.3)
Absolute change from baseline in DSQ score, LS mean (SE)	-21.9* (2.5)	-9.6 (2.8)	-23.8* (1.9)	-14.4 (1.86)	-13.9 (1.9)
*denotes statistically significant difference compared to placebo					

- No new safety concerns emerged during the Liberty EoE TREET trials. Overall, approximately 85% of patients treated with dupilumab (Dupixent) during the clinical trial experienced an adverse event, although most of the treatment emergent adverse events were considered to be mild or moderate. The most common adverse events experienced by patients included injection-site reaction, including erythema, pain and swelling, headache and diarrhea.
- EoE is a chronic, immune/antigen-mediated esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation. Diagnosis of EoE is made when all of the following are present: symptoms related to esophageal dysfunction (e.g., dysphagia, food impaction, abdominal pain), eosinophil-predominant inflammation on esophageal biopsy, characteristically consisting of a peak value of ≥15 eosinophils per high power field (HPF) (or 60 eosinophils per mm2), and exclusion of other

conditions that may be responsible for or contributing to symptoms of esophageal eosinophilia (e.g., eosinophilic gastritis, GERD, hyper-eosinophilic syndrome, Crohn's disease, etc.). Because EoE has a strong association with allergies, patients are recommended to undergo an evaluation by an allergist to rule out allergy-related conditions. Additionally, due to overlap of symptoms with GERD and alimentary tract involvement, evaluation by a gastroenterologist may also be appropriate.

- Dietary restriction is used as a first-line strategy to combat EoE symptoms, including dysphagia and abdominal pain. The most commonly used dietary therapy is an empiric elimination diet based on the concept of avoiding the six foods/food groups that most commonly cause the majority of IgE-mediated food reactions (e..g, milk, egg, soy, wheat, peanuts/tree nuts, fish/shellfish). Other dietary therapies including testing-directed elimination diets, which utilize antigen or allergy testing to eliminate foods that trigger a positive test result, and elemental diet, which utilizes amino acid based (elemental) formula. However, these other methods are less commonly used to due to expense and difficulty to follow.
- Dupilumab (Dupixent) is the first medication to gain FDA approval for the EoE indication, and there are limited pharmacological treatment options used off-label for this indication. AGA guidelines strongly recommend treatment with swallowed topical steroids. Supported therapies in this class include fluticasone and budesonide. Fluticasone is administered as a metered-dose inhaler that is sprayed into the mouth and swallowed, while budesonide is administered as a slurry (nebulizer ampules mixed with sucralose) over the course of five to ten minutes. Guidelines also conditionally recommend the use of proton pump inhibitors (PPIs); however, PPIs have been considered standard of care for EoE and subjects in the LIBERTY EoE TREET trial were required to have failed an 8-week treatment with a high-dose PPI (i.e., twice daily dosing) prior to inclusion in the study population. Therefore, although there is limited guideline support for use of PPIs in EoE, requiring prior treatment with PPIs is appropriate as efficacy and safety of dupilumab (Dupixent) in patients with EoE and no prior use of PPIs remains unknown.

VII. **Prurigo nodularis (PN)**

- Prurigo nodularis (PN) is distinct from other pruritic disorders as its core symptoms include presence of multiple firm, nodular lesions distributed symmetrically on the trunk, arms, and/or legs with chronic pruritis lasting greater than 6 weeks in duration. A history of a persistent scratch-itch cycle is accompanied by burning, stinging, pain, and scarring, significantly impacting quality of life. Complete resolution of lesions may not occur even if there is remission in pruritic symptoms.
- Literature suggests up to 60% of patients with PN have a history of atopic conditions (atopic dermatitis, allergic rhinitis, asthma, etc.), but drug induced PN (e.g., opioids,

ACE inhibitors, etc.) or PN due to other medical conditions such as neuropathy or psychiatric disease (i.e. dermatillomania, obsessive compulsive disorder, etc.) should be considered and ruled out.

- Treatment approaches: Dupilumab (Dupixent) is the first FDA-approved treatment for adults with PN. Efficacy for PN therapies are based on case reports or small observation studies, and all treatments are currently used off-label. Clinical experience and expert consensus guidelines recommend the use of the following treatment modalities with goals to reduce pruritis and reduce/heal PN nodules, often used in combination:
    i. Similar to atopic dermatitis management, moderate to very high potency topical corticosteroids (TCS) are often used as first line therapy based on clinical experience and expert consensus guideline recommendations for PN. Treatment with intralesional corticosteroids injection(s) (e.g., triamcinolone 5 – 20mg/mL) may also be an option for thick PN nodules to reduce pruritis and flatten large PN lesions. Trials of calcineurin inhibitors, capsaicin, may be used in recalcitrant disease or when TCS are not appropriate, although their use is based on small observational studies. The efficacy of topical therapies for PN has not been adequately evaluated in randomized trials.
    ii. Narrowband ultraviolet B (UVB) phototherapy is occasionally used as an adjunct therapy for patients who have not responded to topical pharmacotherapy, based on evidence from small observational studies and one randomized study. In one study, ten patients treated with UVB therapy 2-3 times weekly in combination with TSC reported significant improvement in skin lesions after 16 weekly treatments; however, accessing therapy may prove to be a barrier for many patients.
    iii. Systemic therapies: oral immunosuppressants, such as low dose methotrexate and cyclosporine, have been used off-label with success in reducing the number and severity of skin lesions. Although safety and efficacy of oral systemic therapies for PN have not been evaluated in randomized trials, expert consensus guidelines conditionally recommend systemic immunologic treatments as reasonable therapy options. Use of systemic therapies with antipruritic activity, including, but not limited to gabapentin, pregabalin, amitriptyline, thalidomide, or naltrexone, have been used in clinical practice; however, data in PN is limited and efficacy cannot be determined.
- Prurigo nodularis rarely occurs in pediatric patients and the safety and efficacy of dupilumab (Dupixent) for the treatment of PN in patients younger than 18 years of age has not been established.

- The duration of initial approval at six months is derived from the evidence reported in the dupilumab (Dupixent) trials for PN, whose results were reported at 12 and 24 weeks.
- Safety and efficacy of dupilumab (Dupixent) for adults with PN was evaluated in two Phase III, randomized, double blind, placebo-controlled trials (LIBERTY-PN-PRIME and PRIME2). The trials evaluated a total of 311 participants ages 18 to 80 years of age with a clinical diagnosis of uncontrolled PN for at least 3 months in duration, average worst itch score (WI-NRS) of ≥7, minimum of 20 PN lesions, and a history of failing a 2-week course of medium to very high potency TCS or ineligible for TCS therapy. Background therapy including low to medium potency TCS or topical calcineurin inhibitors were allowed to be used throughout the trial. The trials excluded patients with PN secondary to medications, other medical conditions, or uncontrolled thyroid disease. At baseline, the mean WI-NRS was 8.5 (severe pruritis), 66% of participants had 20 - 100 nodules (moderate), and 34% had greater than 100 nodules (severe). Less than half of the participants (43%) had a history of atopy (medical history of AD, allergic rhinitis, asthma, or food allergy). The primary endpoint assessed improvement in WI-NRS score ≥4 from baseline at 12-weeks (PRIME2) and 24-weeks (PRIME2). Key secondary outcomes assessed pruritic improvement and reduction in PN lesions (clear skin) as measured by the Investigator's Global Assessment PN-Stage [IGA PN-S] 0-4 scale. Both primary and key secondary endpoints were met as patients on dupilumab (Dupixent) experienced an improvement in itch reduction and skin clearing compared to placebo. No new safety signals were discovered, and adverse effects were consistent with the established safety profile of dupilumab (Dupixent).

	PRIME		PRIME2	
	Dupilumab (n=75)	Placebo (n=76)	Dupilumab (n=78)	Placebo (n=82)
% patients with improvement (reduction) in WI-NRS* by ≥4 points from baseline at week 12	44%	16%	37%	22%
% patients with improvement (reduction) in WI-NRS* by ≥4 points from baseline at week 24	60%	18%	58%	20%
% patients with IGA PN-S† 0 or 1 at week 24	48%	18%	45%	16%
**Worst itch score (WI-NRS) is a patient-reported outcome comprised of a single item rated on a scale from 0 ("No itch") to 10 ("Worst imaginable itch")*				
†The Investigator's Global Assessment PN-Stage (IGA PN) is a clinician-reported outcome assess the activity of PN (IGA PN-A) using a 5-point scale from 0 (clear) to 4 (severe)				

VIII. **Chronic obstructive pulmonary disease (COPD)**

- Dupilumab (Dupixent) was studied in a Phase 3 multicenter, international, double-blind, randomized, placebo-controlled, parallel groups (2 groups), 52-week trial, known as the BOREAS trial, as add-on maintenance treatment for adults with

chronic obstructive pulmonary disease (COPD) associated with history of exacerbations and eosinophilic phenotype.

- The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2024 report mentioned the trial and stated the findings are potentially important and clinical practice changing but require confirmation in further studies.
- BOREAS trial
  i. Patients enrolled were between ages 40-80 with moderate to severe COPD, blood eosinophils ≥300 cells/µL, smoking history of ≥10 pack-years (current smokers capped at 30%), MRC Dyspnea Scale grade ≥2, documented history of high exacerbation risk, background triple therapy (ICS+LAMA+LABA) [unless ICS was contraindicated] for 3 months, and signs and symptoms of chronic bronchitis for 3 months. Patients were randomized 1:1 to receive either dupilumab (Dupixent) 300 mg every other week (Q2W) or placebo. The primary endpoint was annualized rate of moderate or severe exacerbations of COPD in patients receiving dupilumab or placebo, which was 0.78 (95% CI, 0.64 to 0.93) and 1.10 (95% CI, 0.93 to 1.30), respectively. Rate ratio compared to placebo was 0.70 (95% CI 0.58 to 0.86, p <0.001).
- The BOREAS trial included patients who were 40-80 years of age. The safety and efficacy of dupilumab (Dupixent) has not been studied in pediatric patients less than 18 years of age. There is currently insufficient evidence to support the use of dupilumab (Dupixent) in patients who are less than 18 years of age.
- The BOREAS trial studied dupilumab (Dupixent) in patients with moderate to severe COPD with eosinophilic phenotype, as defined by GOLD guidelines (GOLD 2 or 3). There is currently insufficient evidence to support the use of dupilumab (Dupixent) for mild or very severe COPD (GOLD 1 or 4) and COPD without eosinophilic phenotype.
  i. According to the GOLD 2024 report, the standard grading of severity of COPD is as follows:

Grade	Severity	FEV1 % predicted
GOLD 1	Mild	≥80
GOLD 2	Moderate	50-79
GOLD 3	Severe	30-54
GOLD 4	Very Severe	<30

- Patients in the BOREAS trial were required to have had ≥2 moderate or ≥1 severe exacerbation within the last 12 months. This criterion would place patients in COPD treatment Group E per GOLD 2024 guidelines. These is currently insufficient evidence to support the use of dupilumab (Dupixent) in patients in COPD treatment group A or B, defined by 0 or 1 moderate exacerbations.

- The BOREAS trial studied dupilumab (Dupixent) as add-on treatment for patients already established on background triple inhaler therapy (LAMA+LABA+ICS), unless ICS was contraindicated. Background triple inhaler therapy (LAMA+LABA+ICS) is first-line recommended treatment for Group E COPD patients.
- Per the GOLD 2024 report, background triple inhaler therapy (LAMA+LABA+ICS) has been shown to improve lung function, patient reported outcomes, reduce exacerbations, and improve mortality in patients with COPD. There is currently insufficient evidence to support the use of dupilumab (Dupixent) as monotherapy or with single inhaler therapy.

Investigational or Not Medically Necessary Uses

I. Dupilumab (Dupixent) is and has been studied in a variety of other conditions, there is currently insufficient evidence to support the use of dupilumab (Dupixent) outside of the FDA approved indications.

Appendix

I. Table 1: Topical Corticosteroid Potency Chart[12]

Potency Group	Corticosteroid	Vehicle type/form	Brand names	Available strength(s), percent (except as noted)
Super-high potency (Group 1)	Betamethasone dipropionate, augmented	Gel, lotion, ointment (optimized)	Diprolene	0.05
	Clobetasol propionate	Cream, gel, ointment, solution (scalp)	Temovate	0.05
		Cream, emollient base	Temovate E	0.05
		Lotion, shampoo, spray aerosol	Clobex	0.05
		Foam aerosol	Olux-E, Tovet	0.05
		Solution (scalp)	Cormax	0.05
	Fluocinonide	Cream	Vanos	0.1
	Flurandrenolide	Tape (roll)	Cordran	4 mcg/cm2
	Halobetasol propionate	Cream, lotion, ointment	Ultravate	0.05
High potency (Group 2)	Amcinonide	Ointment	Cyclocort¶, Amcort¶	0.1
	Betamethasone dipropionate	Ointment	Diprosone¶	0.05
		Cream, augmented formulation (AF)	Diprolene AF	0.05
	Clobetasol propionate	Cream	Impoyz	0.025
	Desoximetasone	Cream, ointment, spray	Topicort	0.25
		Gel	Topicort	0.05

	Diflorasone diacetate	Ointment	ApexiCon¶, Florone¶	0.05
		Cream, emollient	ApexiCon E	0.05
	Fluocinonide	Cream, gel, ointment, solution	Lidex¶	0.05
	Halcinonide	Cream, ointment, solution	Halog	0.1
	Halobetasol propionate	Lotion	Bryhali	0.01
High potency (Group 3)	Amcinonide	Cream	Cyclocort¶, Amcort¶	0.1
		Lotion	Amcort¶	0.1
	Betamethasone dipropionate	Cream, hydrophilic emollient	Diprosone¶	0.05
	Betamethasone valerate	Ointment	Valisone¶	0.1
		Foam	Luxiq	0.12
	Desoximetasone	Cream	Topicort LP¶	0.05
	Diflorasone diacetate	Cream	Florone¶	0.05
	Diflucortolone valerate (not available in United States)	Cream, oily cream, ointment	Nerisone (Canada, United Kingdom, others)	0.1
	Fluocinonide	Cream aqueous emollient	Lidex-E¶	0.05
	Fluticasone propionate	Ointment	Cutivate	0.005
	Mometasone furoate	Ointment	Elocon	0.1
	Triamcinolone acetonide	Cream, ointment	Aristocort HP¶, Kenalog¶, Triderm	0.5
Medium potency (Group 4)	Betamethasone dipropionate	Spray	Sernivo	0.05
	Clocortolone pivalate	Cream	Cloderm	0.1
	Fluocinolone acetonide	Ointment	Synalar¶	0.025
	Flurandrenolide	Ointment	Cordran	0.05
	Hydrocortisone valerate	Ointment	Westcort	0.2
	Mometasone furoate	Cream, lotion, ointment, solution	Elocon¶	0.1
	Triamcinolone acetonide	Cream	Kenalog¶, Triderm	0.1
		Ointment	Kenalog¶	0.1
		Ointment	Trianex	0.05

		Aerosol spray	Kenalog	0.2 mg per 2 second spray
		Dental paste	Oralone	0.1
Lower-mid potency (Group 5)	Betamethasone dipropionate	Lotion	Diprosone¶	0.05
	Betamethasone valerate	Cream	Beta-Val, Valisone¶	0.1
	Desonide	Ointment	DesOwen, Tridesilon¶	0.05
		Gel	Desonate	0.05
	Fluocinolone acetonide	Cream	Synalar¶	0.025
	Flurandrenolide	Cream, lotion	Cordran	0.05
	Fluticasone propionate	Cream, lotion	Cutivate	0.05
	Hydrocortisone butyrate	Cream, lotion, ointment, solution	Locoid, Locoid Lipocream	0.1
	Hydrocortisone probutate	Cream	Pandel	0.1
	Hydrocortisone valerate	Cream	Westcort¶	0.2
	Prednicarbate	Cream (emollient), ointment	Dermatop	0.1
	Triamcinolone acetonide	Lotion	Kenalog¶	0.1
		Ointment	Kenalog¶	0.025
Low potency (Group 6)	Alclometasone dipropionate	Cream, ointment	Aclovate	0.05
	Betamethasone valerate	Lotion	Beta-Val¶, Valisone¶	0.1
	Desonide	Cream	DesOwen, Tridesilon¶	0.05
		Lotion	DesOwen, LoKara	0.05
		Foam	Verdeso	0.05
	Fluocinolone acetonide	Cream, solution	Synalar¶	0.01
		Shampoo	Capex	0.01
		Oil (48% refined peanut oil)	Derma-Smoothe/FS Body, Derma-Smoothe/FS Scalp	0.01
	Triamcinolone acetonide	Cream, lotion	Kenalog¶, Aristocort¶	0.025
Least potent (Group 7)	Hydrocortisone (base, ≥2%)	Cream, ointment	Hytone, Nutracort¶	2.5
		Lotion	Hytone, Ala Scalp, Scalacort	2
		Solution	Texacort	2.5

	Hydrocortisone (base, <2%)	Ointment	Cortaid, Cortizone 10, Hytone, Nutracort	1
		Cream	Cortaid¶, Cortizone 10, Hytone, Synacort	1
		Gel	Cortizone 10	1
		Lotion	Aquanil HC, Sarnol-HC, Cortizone 10	1
		Spray	Cortaid	1
		Solution	Cortaid, Noble, Scalp Relief	1
		Cream, ointment	Cortaid	0.5
	Hydrocortisone acetate	Cream	MiCort-HC	2.5
		Lotion	Nucort	2

¶ Inactive United States brand name for specific product; brand may be available outside United States

References

1. Dupixent [Prescribing Information]. Tarrytown, NY and Bridgewater, NJ: Regeneron Pharmaceuticals, Inc and Sanofi Genzyme. September 2024.
2. Sidbury R, et al. Guidelines of care for the management of atopic dermatitis: section 4. Prevention of disease flares and use of adjunctive therapies and approaches. J Am Acad Dermatol 2014;71:1218-1233.
3. Wollenberg A, et al. ETFAD/EADV Eczema task force 2015 position paper on diagnosis and treatment of atopic dermatitis in adult and paediatric patients. JEADV 2016;30:729-747.
4. UpToDate, Inc. Management of severe refractory atopic dermatitis (eczema). UpToDate [database online]. Waltham, MA. Updated Dec 2016. Accessed January 18, 2017.
5. Totri CR, et al. Prescribing practices for systemic agents in the treatment of severe pediatric atopic dermatitis in the US and Canada: the PeDRA TREAT survey. J Am Acad Dermatol. 2017 Feb;76(2):281-285.
6. Solomon, CG and Hopkins C. Chronic Rhinosinusitis with Nasal Polyps. N Engl J Med 2019;381:55-63
7. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical Practice Guideline (Update): Adult Sinusitis. American Academy of Otolaryngology – Head and Neck Surgery 2015, Vol.I52(2S) SI-S39.
8. Institute for Clinical and Economic Review (ICER): Biologic Therapies for Treatment of Asthma Associated with Type 2 Inflammation: Effectiveness, Value, and Value-Based Price Benchmarks. December 2018. Available at: https://icer-review.org/wp-content/uploads/2018/04/ICER_Asthma_Final_Report_122018-1.pdf
9. Institute for Clinical and Economic Review (ICER): Dupilumab and Crisaborole for Atopic Dermatitis: Effectiveness and Value. June 2017. Available at: https://icer-review.org/wp-content/uploads/2016/10/MWCEPAC_ATOPIC_FINAL_EVIDENCE_REPORT_060717.pdf
10. Simpson EL, Paller AS, Siegfried EC et al. Efficacy and safety of dupilumab in adolescents with uncontrolled moderate to severe atopic dermatitis a phase 3 randomized clinical trial. JAMA Dermatol 2020;156(1):44-56. Available from: https://pubmed.ncbi.nlm.nih.gov/31693077/
11. Paller AS, Siegfried EC, Thaci D et al. Efficacy and safety of dupilumab with concomitant topical corticosteroids in children 6 to 11 years old with severe atopic dermatitis: a randomized, double blinded, placebo-controlled phase 3 trial. J Am Acad Dermatol 2020; S0190-9622(20)31152-X. Available from: https://pubmed.ncbi.nlm.nih.gov/32574587/
12. UpToDate, Inc. Topical corticosteroids: Use and adverse effects. UpToDate [database online]. Waltham, MA. Updated Feb 2020. Accessed March 12, 2021.

13. National Insititute for Health and Care Excellence (NICE). Dupilumab for treating moderate to severe atopic dermatitis. NICE. Published August 1, 2018.
14. UpToDate, Inc. Clinical manifestations and diagnosis of eosinophilic esophagitis (EoE). UpToDate [database online]. Waltham, MA. Updated Jun 2022. Accessed July 11, 2022.
15. UpToDate, Inc. Dietary management of eosinophilic esophagitis. UpToDate [database online]. Waltham, MA. Updated Aug 2020. Accessed July 11, 2022.
16. UpToDate, Inc. Treatment of eosinophilic esophagitis. UpToDate [database online]. Waltham, MA. Updated Jun 2022. Accessed July 11, 2022.
17. Hirano I, Chan ES, Rank MA, et al. AGA Institute and the Joing Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis. *Gastroenterology*. 2020;158:1776-1786.
18. Dellon et al. Updated international consensus diagnostic criteria for eosinophilic esophagitis: Proceedings of the AGREE conference. *Gastroenterology*. 2018 October; 155(4):1022-1033.
19. Dellon et al. Dupilumab Improves Clinical and Histologic Aspects of Disease in Adult and Adolescent Patients with Eosinophilic Esophagitis at Week 24: Weekly and Every 2 Weeks' Results from Part B of the 3-Part Liberty EoE TREET Study. Poster. 2021.
20. Dellon et al. The Efficacy and Safety of Dupilumab in Adult and Adolescent Patients with Eosinophilic Esophagitis: Results from Part A of a Randomized, Placebo-Controlled Three-Part, Phase 3 Study. Poster presented at the 34th Annual Eastern Allergy Conference; Palm Beach, FL; June 2021.
21. Study of dupilumab for the treatment of patients with prurigo nodularis, inadequately controlled on topical prescription therapies or when those therapies are not advisable (LIBERTY-PN PRIME). ClinicalTrials.gov identifier: NCT04183335. February 17, 2022. Accessed October 10, 2022. https://clinicaltrials.gov/ct2/show/NCT04183335.
22. Study of dupilumab for the treatment of patients with prurigo nodularis, inadequately controlled on topical prescription therapies or when those therapies are not advisable (PRIME2). ClinicalTrials.gov identifier: NCT04202679. September 28, 2022. Accessed October 10, 2022. https://clinicaltrials.gov/ct2/show/NCT04202679
23. Elmariah S, Kim B, Berger T, et al. Practical approaches for diagnosis and management of prurigo nodularis: United States expert panel consensus. *J Am Acad Dermatol*. 2021;84(3):747-760. doi:10.1016/j.jaad.2020.07.025
24. Ständer HF, Elmariah S, Zeidler C, et al. Diagnostic and treatment algorithm for chronic nodular prurigo. *J Am Acad Dermatol*. 2020;82(2):460-468. doi:10.1016/j.jaad.2019.07.022
25. Ständer S, Pereira MP, Berger T, et al. IFSI-guideline on chronic prurigo including prurigo nodularis. *Itch*. 2020;5(4):e42-e42.
26. Pereira MP, Steinke S, Zeidler C, et al. European academy of dermatology and venereology European prurigo project: expert consensus on the definition, classification and terminology of chronic prurigo. *J Eur Acad Dermatol Venereol*. 2018;32(7):1059-1065.
27. UpToDate, Inc. Prurigo nodularis. UpToDate [database online]. Waltham, MA. Updated May 2022. Accessed October 10, 2022.
28. Bhatt SP, Rabe KF, Hanania NA, et al. Dupilumab for COPD with Type 2 Inflammation Indicated by Eosinophil Counts. N Engl J Med. 2023;389(3):205-214. doi:10.1056/NEJMoa2303951
29. Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, et al. Global Initiative for Chronic Obstructive Lung Disease 2024 Report. Global Initiative for Chronic Obstructive Lung Disease; 2024.
30. Rank MA, Chu DK, Bognanni A, et al. The Joint Task Force on Practice Parameters GRADE guidelines for the medical management of chronic rhinosinusitis with nasal polyposis. *Journal of Allergy and Clinical Immunology*. 2023;151(2):386-398.
31. Orlandi RR, Kingdom TT, Smith TL, et al. International consensus statement on allergy and rhinology: rhinosinusitis 2021. International Forum of Allergy & Rhinology. 2021;11(3):213-739.
32. UpToDate, Inc. Chronic rhinosinusitis with nasal polyposis: Management and prognosis. UpToDate [database online]. Waltham, MA. Updated August 2023. Accessed October 1, 2024.

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
omalizumab (Xolair)	Allergic asthma
	Chronic rhinosinusitis with nasal polyposis (CRSwNP)
Systemic Janus Associated Kinase (JAK) Inhibitors in Chronic Inflammatory Disease	Atopic dermatitis
ruxolitinib (Jakafi, Opzelura)	Atopic dermatitis
tralokinumab (Adbry)	Atopic dermatitis
ensifentrine (Ohtuvayre)	Chronic Obstructive Pulmonary Disease
benralizumab (Fasenra Pen)	Asthma (severe)
tezepelumab (Tezspire)	Asthma (severe)
mepolizumab (Nucala)	Asthma (severe)
	Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)
reslizumab (Cinqair)	Asthma (severe)

Policy Implementation/Update

Action and Summary of Changes	Date
Removed oral steroid trial from CRSwNP indication. Updated patient weight for EoE.	03/2025
Updated age criteria in CRSwNP to reflect age expansion to patients 12 years of age or older. Updated supporting evidence, references, related policies. Updated definition/examples of moderate to severe disease in prurigo nodularis. Updated initial criteria to 12 months for all policy listed indications.	10/2024
Added new indication and supporting evidence for Dupixent in the setting of **COPD** (live 10/24/24).. Updated references and listed E/I for use in COPD for pediatric patients <18 years of age.	07/2024
Updated age criteria in eosinophilic esophagitis for the newly FDA approved indication in those one year and older. Updated supporting evidence and references.	02/2024
Review conducted. Update to supporting evidence.	02/2023
Added new indication and supporting evidence for Dupixent in the setting of prurigo nodularis. Added related pruritic conditions (urticaria, bullous pemphigoid/prurigo, etc.) to E/I. Updated references. Added related policies section.	10/2022
Added criteria and supporting evidence for new FDA-approved indication for eosinophilic esophagitis; Updated age criteria in atopic dermatitis to reflect FDA-approved age expansion from age 6 years to age 6 months and older	08/2022
Updated age criteria in asthma to reflect FDA extended indication from age 12 now to age 6 and older; updated QL table to include dosing for Atopic Dermatitis and comorbid Atopic Dermatitis and Severe to Moderate Asthma	11/2021
Added 200 mg/1.14mL pen injector; Updated to allow 12-month approval for initial therapy	07/2021
Updated Policy. Atopic dermatitis: combined pediatric and adolescent/adult criteria; updated BSA criterion and Group 1 corticosteroids. Asthma: updated criteria defining moderate or severe asthma; updated eosinophilic phenotype criterion; defined exacerbation criterion; revised maintenance treatment requirements; removed environmental trigger criterion. CRSwNP: revised diagnosis criteria to include provider attestation; updated treatment history to one intranasal corticosteroid and one OCS therapy. Renewal criteria: added standard renewal criteria documenting patient establishing treatment; added criterion excluding concomitant MCA use.	04/2021
Updated QL table to include pediatric dosing in AD	01/2021

Criteria update: updated age criteria to reflect newly FDA approved extended indication for atopic dermatitis use from 12 years of age to expanded use in pediatrics aged six to 11 years of age. Removal of PGA score as a requirement option with BSA in atopic dermatitis.	10/2020
Criteria was transitioned to policy format with the addition of supporting evidence and a section for investigation/not medically necessary usage. Addition of newly FDA approved age expansion for atopic dermatitis from 18 years of age to 12 years of age. Also, addition of newly FDA approved indication for chronic rhinosinusitis with nasal polyposis along with criteria for approval based on guidelines and clinical trials review. Lastly, the duration of initial approval has been increased form 3 months to 6 months based on evidence from ICER reports and the study design of the most recent FDA approved indication for chronic rhinosinusitis with nasal polyposis.	08/2019
Criteria update: Incorporated new diagnosis of moderate to severe asthma and appropriate criteria	12/2018
Updated format and added the renewal approval duration	01/2018
Criteria update: excluded samples and updated renewal language to general improvement	04/2017