dupilumab (Dupixent®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO019

Description

Dupilumab (Dupixent) is an injectable human monoclonal IgG4 antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling, which inhibits the release of proinflammatory cytokines, chemokines and IgE.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
dupilimab (Dupixent)	200 mg/1.14mL prefilled syringe	Asthma (moderate to severe)	**First Month:** 4 (200mg OR 300mg) syringes/pens (8 mL)/42 days **Maintenance:** 2 (200mg OR 300mg) syringes/pens (4 mL)/28 days
	300 mg/2mL pen injector or prefilled syringe	Atopic Dermatitis (moderate to severe)	**First Month:** 4 (300mg) syringes/pens (8 mL)/42 days **Maintenance:** 2 (300mg) syringes/pens (4 mL)/28 days
		Chronic rhinosinusitis with nasal polyposis	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. Must not be used in combination with another monoclonal antibody (e.g., benralizumab, mepolizumab, omalizumab, reslizumab, etc.); **AND**
   B. Medication is prescribed by, or in consultation with, a dermatologist or a physician specializing in allergy, pulmonology, immunology, or ENT (ear, nose, throat); **AND**
   C. A diagnosis of one of the following:
      1. **Atopic dermatitis (moderate to severe)**; **AND**
         i. Member is 12 years of age or older; **AND**
            a. Minimum body surface area (BSA) involvement of at least 10%; **OR**
         ii. Member is six to 11 years of age; **AND**

a. Mininum body surface area (BSA) involvement of at least 15%; **AND**

iii. Prior treatment with at least <u>two</u> of the following groups has been ineffective or not tolerated, unless ALL are contraindicated.
   a. Group 1: Topical corticosteroids; **OR**
   b. Group 2: Topical calcineurin inhibitors (e.g. pimecrolimus cream, tacrolimus ointment); **OR**
   c. Group 3: Topical PDE-4 inhibitors (e.g. Eucrisa); **OR**

2. **Asthma (moderate to severe)**; **AND**
   i. Member is 12 years of age or older; **AND**
   ii. Member has <u>one</u> of the following:
      a. Moderate-to-severe persistent asthma of an eosinophilic phenotype; **OR**
      b. Moderate-to-severe persistent asthma that is dependent on oral corticosteroids; **AND**
   iii. Environmental triggers of asthma have been addressed, including, but not limited to smoking cessation or allergen limitations; **AND**
   iv. Member is currently being treated with:
      a. A medium- to high-dose inhaled corticosteroid; **AND**
      b. Two additional controller medications (e.g., long-acting beta-2 agonist, leukotriene receptor antagonist); **AND**
   v. Background controller medications will be continued with the use of Dupixent, unless contraindicated; **OR**

3. Chronic rhinosinusitis with nasal polyposis; AND
   i. Member is 18 years of age or older; **AND**
   ii. Member has a diagnosis of bilateral sinonasal polyposis as evidenced by an endoscopy or computed tomography (CT); **AND**
   iii. Member has ongoing nasal congestion/blockage/obstruction with moderate to severe symptom severity; **AND**
   iv. Member has nasal discharge; **OR**
      a. Member has facial pain or pressure**; OR**
      b. Member has reduction or loss of smell; **AND**
   v. Prior treatment with two intranasal corticosteroids has been ineffective or not tolerated, unless contraindicated; **AND**
   vi. Background intranasal corticosteroid will be continued with the use of Dupixent, unless contraindicated.

II. Dupilumab (Dupixent) is considered investigational when used for all other conditions, including but not limited to:
   A. Pediatric (six to 11 years of age) asthma
   B. Pediatric (six to 11 years of age) moderate atopic dermatitis
   C. Pediatric (six months to five years of age) atopic dermatitis
   D. Eosinophilic esophagitis
   E. Chronic obstructive pulmonary disease (COPD)
   F. Food and environmental allergies

Renewal Evaluation

I. The member has an absence of unacceptable toxicity from the medication; **AND**
II. A diagnosis of one of the following:
   A. **Atopic dermatitis (moderate to severe); AND**
      1. Member has exhibited improvement or stability of disease symptoms (e.g., improved PGA score from baseline, reduced BSA involvement); **OR**
   B. **Pediatric atopic dermatitis (severe); AND**
      1. Member has exhibited improvement or stability of disease symptoms (e.g., improved PGA score from baseline, reduced BSA involvement); **OR**
   C. **Asthma (moderate to severe)**; **AND**
      1. Member has exhibited improvement or stability of disease symptoms (e.g., reduced asthma exacerbations); **AND**
      2. Environmental triggers of asthma have been addressed, including, but not limited to smoking cessation or allergen limitations; **AND**
      3. Background controller medications will be continued with the use of Dupixent, unless contraindicated; **OR**
   D. **Chronic rhinosinusitis with nasal polyposis**; **AND**
      1. Member has exhibited improvement or stability of disease symptoms (e.g., improvement in nasal congestion/obstruction severity, reduction in nasal polyps); **AND**
      2. Background intranasal corticosteroid will be continued with the use of Dupixent, unless contraindicated.

Supporting Evidence

I. The duration of initial approval at six months is derived from the evidence reported in the ICER reports for atopic dermatitis and asthma; additionally, in the dupilumab (Dupixent) trials for chronic rhinosinusitis with nasal polyposis, the results were reported at 24 weeks (six months).

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. The FDA approval of dupilumab (Dupixent) in the setting of moderate to severe atopic dermatitis for patients aged 12 years or older was based on the results from 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%

IV. The FDA approval of dupilumab (Dupixent) for use in children with severe atopic dermatitis aged six to 11 years 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 improvement 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

V. The FDA approval of dupilumab (Dupixent) in the setting of moderate to severe asthma was based on the results of three randomized, placebo-controlled, multicenter trials.

- In both Trials 1 and 2, patients receiving either dupilumab (Dupixent) 200 mg or 300 mg every two weeks experienced a significant reduction in the rate of asthma exacerbations when compared with placebo.
- In Trial 3, the primary endpoint was the percent of reduction from baseline of the final oral corticosteroid dose at week 24 while maintaining asthma control. Patients in the dupilumab (Dupixent) arm (70%) achieved greater mean percent reductions in daily maintenance oral corticosteroid dose, while maintaining asthma control when compared to placebo arm (42%).

VI. The FDA approval of dupilumab (Dupixent) in the setting of chronic rhinosinusitis with nasal polyposis 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 fuorate 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 dupilmab (Dupixent) arm achieved statistically significant improvements when compared to the placebo arm.

- 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
- 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

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 FDA approved indications.

References

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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/

Policy Implementation/Update:

Action and Summary of Changes	Date
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