Clinical Criteria

Subject:	Dupixent (dupilumab)		
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Overview

This document addresses the use of Dupixent (dupilumab). Dupixent, an interleukin-4 (IL-4)/interleukin 13 (IL-13) inhibitor, is approved in individuals 6 years and older for the treatment of moderate to severe atopic dermatitis (AD) when disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. It is also approved for treatment of moderate to severe asthma in individuals 12 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma. IL-4 and IL-13 are thought to be major drivers in atopic dermatitis and asthma. Additionally, Dupixent is approved for add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP). The dose of Dupixent for AD is an initial dose of 600 mg (two 300 mg injections) followed by 300 mg given every other week. The dose of Dupixent for asthma is an initial dose of 400 mg or 600 mg followed by 200 mg or 300 mg every other week. The recommended dose for CRSwNP is 300mg every other week.

Per the American Academy of Dermatology (AAD 2014) AD, the most common form of eczema, affects approximately 2% to 3% of adults and 25% of children. AD is frequently associated with a personal or family history of allergies, allergic rhinitis and asthma. AD typically follows a relapsing/chronic course but often resolves by adulthood. Symptoms can include erythema, edema, xerosis, excoriations, pruritus, oozing and crusting, or lichenification. While there is no accepted standardized method of classifying disease severity, categorization is usually based upon objective disease features, extent of skin involvement and possibly subjective disease features. Due to the impaired skin integrity, affected individuals are more susceptible to skin infections.

Guidelines from the AAD regarding the treatment of AD recommend non-pharmacologic therapy, pharmacologic therapy and phototherapy (AAD 2014). Non-pharmacologic therapy include use of moisturizers (I, A) and use of wet wrap therapy with or without a topical corticosteroid for those with moderate to severe AD during flares (II, B). First line topical pharmacologic therapy are topical corticosteroids (I, A). Labeled dosage guidance from high dose topical steroids recommend limiting consecutive use to 2 weeks (Ultravate 2020, Diprolene 2019). Topical calcineurin inhibitors are recommended for use on actively affected areas as a steroid sparing agent (I, A). Labeled dosage guidance for Elidel and Protopic recommend re-evaluation if signs and symptoms persist beyond 6 weeks of use (Elidel 2017, Protopic 2019). Phototherapy is recommended as a second line treatment, after failure of first-line treatment (topical therapy) (II, B). In addition, phototherapy can be used as maintenance therapy in those with chronic disease. Systemic immunomodulatory agents (such as cyclosporine, azathioprine, methotrexate) are indicted when individuals have disease symptoms not controlled by optimized topical regimens and/or phototherapy (I,II, B).

Dupixent is FDA approved to treat moderate-to-severe asthma in those 12 and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma. Dupixent was studied in individuals with moderate to severe asthma who were currently utilizing moderate to high dose inhaled corticosteroids (ICS) along with another controller medication and 2 or more exacerbations in the previous year (Castro 2018) or daily corticosteroids along with high dose ICS and another controller medication and 2 or more exacerbations in the previous year (Rabe 2018). In individuals using ICS plus another controller medication, Dupixent reduced exacerbations in individuals with baseline blood eosinophils ≥ 150 cells/µL (cells per microliter); however, exacerbation rates in individuals with eosinophil counts < 150 cells/µL were similar to placebo. In those using daily oral corticosteroids, Dupixent use achieved greater reductions in daily maintenance oral corticosteroid doses and had fewer exacerbations while maintaining asthma control compared to placebo. The 2019 Global Initiative for Asthma (GINA) issued guidelines for the diagnosis and treatment of difficult-to-treat and severe asthma noting in Step 6b that Dupixent may be an option in those with severe asthma despite high-dose inhaled corticosteroid, long-acting beta adrenergic (ICS-LABA) with or without daily oral corticosteroids.

Dupixent is approved as add-on maintenance treatment for CRSwNP in adults 18 years and older who were previously inadequately controlled. Studies included adults with nasal polyposis currently using intranasal corticorsteroids, and who were refractory to surgical

intervention or treatment with systemic corticosteroids in the past 2 years, or who were otherwise ineligible/intolerant to systemic corticorsteroids. Clinical diagnosis of CRSwNP should be confirmed with objective documentation on imaging or direct visualization, such as anterior rhinoscopy, nasal endoscopy, or computed tomography (CT) according to the American Academy of Otolaryngology – Head and Neck Surgery Foundation (AAO-HNSF 2015). Guidance from AAO-HNSF in the 2015 Adult Sinusitis update also recommends topical nasal steroids for long term treatment of nasal polyps, and if no response is seen, then a trial of oral corticosteroids is reasonable. Practice guidelines developed in 2014 by a joint task force representing 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) also strongly recommend use of intranasal corticosteroids and oral steroids in the treatment of CRSwNP as it an inflammatory disease. Other adjunctive therapy, such as nasal saline irrigation, may be beneficial for symptoms in some cases.

Comparative doses for Inhaled Corticosteroids (ICS) (Adults and Adolescents) (Wenzel 2019)

Drug	Low Daily Dose	Medium Daily Dose	High Daily Dose
Beclomethasone 40 or 80 mcg/actuation	80-160 mcg	>160-320 mcg	>320 mcg
Budesonide 90 or 180 mcg/actuation	180-360 mcg	>360–720 mcg	>720 mcg
Ciclesonide 80 or 160 mcg/actuation	80-160 mcg	>160-320 mcg	>320 mcg
Flunisolide 80 mcg/dose	320 mcg	>320-640 mcg	Insufficient data
Fluticasone propionate MDI: 44, 110 or 220 mcg/actuation DPI: 50, 100 or 250 mcg/dose	88–220 mcg 100-250 mcg	>220–440 mcg >250–500 mcg	>440 mcg >500 mcg
Fluticasone furoate 50, 100 or 200 mcg/dose	50 mcg	100 mcg	200 mcg
Mometasone MDI: 50, 100 or 200 mcg/actuation DPI: 110 or 220 mcg/actuation	100-200 mcg 110-220 mcg	>200-400 mcg >220-440 mcg	>400 mcg >440 mcg

DPI = dry powder inhaler; MDI = metered-dose inhaler

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Dupixent (Dupilumab)

Initial requests for Dupixent (dupilumab) for the treatment of asthma may be approved if the following criteria are met:

I. Individual is 12 years of age or older; **AND**
II. Individual has a diagnosis of moderate-to-severe asthma as demonstrated by the following (NHLBI 2007):
  A. A pretreatment forced expiratory volume in 1 second (FEV_1) less than or equal to (≤) 80% predicted; **AND**
  B. FEV_1 reversibility of at least 12% and 200 milliliters (ml) after albuterol (salbutamol) administration; **AND**
III. One of the following:
  A. Individual has a blood eosinophil count (in the absence of other potential causes of eosinophilia, including hypereosinophilic syndromes, neoplastic disease, and known or suspected parasitic infection) greater than or equal to 150 cells/microliter [1 microliter (µL) is equal to 1 cubic millimeter (mm^3)] at initiation of therapy; **AND**
  B. Individual has had a 3 month trial and inadequate response or intolerance to combination controller therapy (~~medium-to-~~high dose inhaled corticosteroids plus long acting $beta_2$ –agonists, leukotriene modifiers, theophylline or oral corticosteroids) (ERS/ATS 2013, GINA2019);

  OR
  C. Individual has oral corticosteroid dependent asthma; **AND**
  D. Individual has had a 3 month trial and inadequate response or intolerance to high dose inhaled corticosteroid with daily oral glucocorticoids given in combination with a controller medication (either a long-acting beta2-agonist, **or** leukotriene receptor antagonist, **or** theophylline) (ERS/ATS 2013, GINA2019); **AND**
IV. Individual has experienced two or more asthma exacerbations in the prior 12 months requiring use of a systemic corticosteroid **or** temporary increase in the individual's usual maintenance dosage of oral corticosteroids (Castro 2018, Rabe 2018).

Continuation of therapy with Dupixent (dupilumab) after 12 months may be approved if the following criteria are met:

I. Individual has experienced one or more of the following:
   A. Decreased utilization of rescue medications; **OR**
   B. Decreased frequency of exacerbations (defined as worsening of asthma that requires an increase in inhaled corticosteroid dose or treatment with systemic corticosteroids); **OR**
   C. Increase in predicted FEV_1 from pretreatment baseline; **OR**
   D. Reduction in reported asthma-related symptoms, such as, asthmatic symptoms upon awakening, coughing, fatigue, shortness of breath, sleep disturbance, or wheezing.

Requests for Dupixent (dupilumab) for the treatment of atopic dermatitis may be approved if the following criteria are met:

I. Individual is age ~~12~~6 years or older; **AND**
II. Individual has a diagnosis of moderate to severe atopic dermatitis; **AND**
III. Individual meets *one* of the following (A or B):
   A. Failure of topical pharmacological therapy as indicated by **both** (1 and 2) ~~**one or more**~~ of the following:
      ~~1.~~ 1. Daily treatment of topical corticosteroids of medium to higher potency for at least fourteen (14) days ~~the maximum treatment period indicated in the product prescribing information~~ has failed to achieve and maintain remission of low or mild disease activity state;
         OR
         a. Topical corticosteroids are not indicated due to severe hypersensitivity reactions or concomitant clinical situations, including but not limited to (AAD 2014):
            i. Individual has lesions located in sensitive areas (including, but not limited to, face, anogenital area or skin folds); **OR**
            ii. Individual has steroid-induced atrophy; **OR**
            iii. History of long-term or uninterrupted topical steroid use;

      AND
      2. Daily treatment of ~~T~~topical calcineurin inhibitors ~~if topical corticosteroids are not indicated*, for the maximum treatment period indicated in the product prescribing information~~for six (6) weeks has failed to achieve and maintain remission of low or mild disease activity state; **OR**
         a. Topical calcineurin inhibitors (TCI) are not indicated due to severe hypersensitivity reactions or concomitant clinical situations, including but not limited to (Elidel 2017, Protopic 2019):
            i. History of or active malignant or pre-malignant skin conditions; **OR**
            ii. Individual has Netherton's Syndrome or other skin diseases that can increase the risk of systemic absorption of TCI; **OR**
            iii. Individual is considered to be immunocompromised, including those on systemic immunosuppressive medications on an ongoing basis;

~~A. Topical treatment is medically inadvisable as defined by treatments which have side effects or safety concerns which outweigh potential treatment benefits as evidenced by **any** of the following:~~
~~1. Intolerance to treatment~~
~~2. Hypersensitivity reactions~~
~~3. Significant skin atrophy~~
~~4. Systemic effects;~~

~~**AND**~~**OR**
   B. One of the following:
      1. Phototherapy (UVB or PUVA) has failed to achieve and maintain remission of low or mild disease activity state or is contraindicated; **OR**
      2. Systemic treatment (for example, immunosuppressants) has failed to achieve and maintain remission of low or mild disease activity state or is contraindicated.

~~* Topical corticosteroids may not be indicated in the following concomitant clinical situations:~~
~~A. Individual has lesions located in sensitive areas (such as face, anogenital area or skin folds); **OR**~~
~~B. Individual has steroid-induced atrophy; **OR**~~
~~C. History of long-term or uninterrupted topical steroid use.~~

Requests for Dupixent (dupilumab) for the treatment of chronic rhinosinusitis with nasal polyposis (CRSwNP) may be approved if the following criteria are met:

I. Individual is age 18 years and older; **AND**
II. Individual has a diagnosis of CRSwNP confirmed by one of the following (AAO-HNSF 2015):
   A. Anterior rhinoscopy; **OR**
   B. Nasal endoscopy; **OR**
   C. Computed tomography (CT);

AND

III. Individual has had recent trial and inadequate response to maintenance intranasal corticosteroids (AAO-HNSF 2015);
AND
IV. Individual is refractory to, or is ineligible or intolerant to the following:
A. Systemic corticosteroids; **OR**
B. Sino-nasal surgery;
AND
V. Individual is requesting Dupixent (dupilumab) as add-on therapy to maintenance intranasal corticosteroids.

Requests for Dupixent (dupilumab) may not be approved when the above criteria are not met and for all other indications.

Quantity Limits

Dupixent (dupilumab) Quantity Limits

Drug	Limit
Dupixent (dupilumab) 200 mg/1.14 mL pre-filled syringe, 300 mg/2 mL pre-filled syringe*, 300 mg/2 mL pre-filled pen*	2 syringes or pens per 28 days
Override Criteria	
*Initiation of therapy: May approve two additional 200 mg/1.14 mL prefilled syringe OR 300 mg/2 mL pre-filled syringes in the first month of therapy for initiation dose for the indication of atopic dermatitis or asthma.	

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J3490	Unclassified drugs [when specified as dupilumab (Dupixent)]
J3590	Unclassified biologics [when specified as dupilumab (Dupixent)]

ICD-10 Diagnosis

L20.0-L20.9	Atopic dermatitis
J44.0-J44.9	Other chronic obstructive pulmonary disease
J45.40-J45.52	Moderate/severe persistent asthma
J45.901-J45.998	Other and unspecified asthma
J82	Pulmonary eosinophilia, not elsewhere classified
J32.9	Chronic sinusitis, unspecified
J33.0-J33.9	Nasal Polyp

Document History

Revised: 08/21/2020
Document History:

- 08/21/2020 – Annual Review: Update asthma criteria to remove medium dose inhaled corticosteroids from requirements per GINA guidance. Update atopic dermatitis criteria to require use of both topical steroids and topical calcineurin inhibitors, OR use of phototherapy or systemic treatment. Wording, formatting, and reference updates. Administrative update to add drug specific quantity limit. Coding reviewed: No changes.
- 06/08/2020 – Select Review: Update criteria for atopic dermatitis to expand pediatric use per FDA label. Coding Reviewed: No changes
- 08/16/2019 – Annual Review: Add new FDA indication for chronic rhinosinusitis with nasal polyposis. Update QL override criteria. Update atopic dermatitis criteria to remove requirement for diagnosis present for 3 years. Coding Reviewed: Added ICD-10 codes J32.9, J33.0-J33.9
- 05/17/2019 – Selected Review: Update Dupixent PA to allow for age 12 and older for the diagnosis of atopic dermatitis. Coding Reviewed: No changes

- 10/23/2018 – Selected Review: Updated to add criteria for new asthma indication; added ICD-10 codes for moderate persistent and severe persistent asthma. Updated diagnosis codes: J44.0-J44.9, J45.40-J45.52, J82 due to FDA approved indication for Asthma.
- 08/17/2018 – Annual Review: First review of Dupixent; Annual review. No changes. Review preliminary criteria for Asthma indication. Added diagnoses codes J45.901-J45.998 for other and unspecified asthma.

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Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.