dupilumab (Dupixent®)

Policy # 00567
Original Effective Date: 06/21/2017
Current Effective Date: 04/10/2023

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Atopic Dermatitis

Based on review of available data, the Company may consider dupilumab (Dupixent®)‡ for the treatment of atopic dermatitis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for dupilumab (Dupixent) for the treatment of atopic dermatitis will be considered when the patient selection criteria are met:

Initial

I. Patient has a diagnosis of moderate to severe atopic dermatitis; AND
II. Patient is 6 months of age or older; AND
III. Patient has had chronic atopic dermatitis for at least 6 months; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
IV. Patient has atopic dermatitis involvement estimated to be ≥ 10% of the body surface area (BSA) according to the prescribing physician; AND
*(Note: This specific patient selection criterion is an additional Company requirement, based on clinical trials, for coverage eligibility and will be denied as not medically necessary** if not met.)*
V. Patient has tried and failed (e.g., intolerance or inadequate response) at least ONE prescription GENERIC topical corticosteroid, unless there is clinical evidence or patient history that suggests the use of ONE prescription GENERIC topical corticosteroid will be ineffective or cause an adverse reaction to the patient; AND

VI. Patient has tried and failed (e.g., intolerance or inadequate response) GENERIC tacrolimus ointment OR GENERIC pimecrolimus cream, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND

VII. Requested drug is NOT being used in combination with other monoclonal antibodies (e.g., tralokinumab-ldrm [Adbry™]‡) or JAK (janus kinase) inhibitors (e.g., upadicitinib [Rinvoq®]‡, ruxolitinib [Opzelura™]‡, abrocitinib [Cibinqo™]‡) typically used to treat atopic dermatitis.

Continuation

I. Patient has received an initial authorization; AND

II. Patient has received at least 6 months of therapy with the requested drug; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

III. Patient has been adherent to the requested drug and other medications for the condition being treated; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

IV. Patient has had a clinically meaningful beneficial response to Dupixent therapy as compared to their baseline status (before Dupixent therapy) as evidenced by TWO or more of the following:
    a) Reduction in disease severity (e.g., erythema, dryness, edema/papulation, excoriations, lichenification, oozing/crusting)
    b) Reduction in the frequency or intensity of pruritus
    c) Reduction in the frequency of disease exacerbations/flares
    d) Reduction in the BSA with atopic dermatitis involvement (a 20% reduction in percent BSA involved over baseline)
    e) Improvement in overall patient quality of life (e.g., improved sleep, less depression or anxiety, etc.); AND

    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

V. Requested drug is NOT being used in combination with other monoclonal antibodies (e.g., tralokinumab-ldrm [Adbry]) or JAK inhibitors (e.g., upadicitinib [Rinvoq], ruxolitinib [Opzelura], abrocitinib [Cibinqo]) typically used to treat atopic dermatitis.

dupilumab (Dupixent®)

Policy # 00567
Original Effective Date: 06/21/2017
Current Effective Date: 04/10/2023

Asthma

Based on review of available data, the Company may consider dupilumab (Dupixent) for the treatment of moderate to severe asthma to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for dupilumab (Dupixent) for the treatment of moderate to severe asthma will be considered when the patient selection criteria are met:

Initial

I. Patient has a diagnosis of moderate to severe asthma; AND
II. Patient is 6 years of age or older; AND
III. Patient meets one of the following (a or b):
    a) Patient has a blood eosinophil level of greater than or equal to 150 cells per microliter within the previous 6 weeks or within 6 weeks prior to treatment with any interleukin therapy (e.g., mepolizumab [Nucala®]‡, reslizumab [Cinqair®]‡, benralizumab [Fasenra®]‡); OR
    b) Patient has oral (systemic) corticosteroid dependent asthma per the prescriber; AND
IV. The requested drug is NOT used in combination with other monoclonal antibodies typically used to treat asthma (e.g., mepolizumab [Nucala], reslizumab [Cinqair], benralizumab [Fasenra], omalizumab [Xolair®]‡, tezepelumab-ekko [Tezspire™]‡); AND
V. Patient has received at least 3 consecutive months of combination therapy with BOTH of the following (a and b):
    *(Note that the 3 month timeframe is an additional company requirement and will be denied as not medically necessary** if not met.)*
    a) Inhaled corticosteroid (ICS), (e.g., fluticasone products [Flovent® HFA, Flovent Diskus®, Arnuity™ Ellipta®, Armonair™ Respiclick®]‡, mometasone products [Asmanex® Twisthaler®, Asmanex HFA]‡, flunisolide products (Aersopan™)‡, ciclesonide products (Alvesco®)‡, budesonide products [Pulmicort Flexhaler®]‡, beclomethasone products [QVAR®]‡); AND
    b) At least ONE of the following (1, 2, 3, OR 4):
        1) Inhaled long-acting beta-agonist (LABA), (e.g., salmeterol products [Serevent® Diskus]‡, olodaterol products [Striverdi® Respimat®]‡, indacaterol products [Arcapta™ Neohaler™]‡); OR
        Note: Use of a combination inhaler containing both an ICS and a LABA would fulfill the requirement for both criteria a.) and b.) (e.g., fluticasone

propionate and salmeterol inhalation powder/aerosol [Advair® Diskus/HFA, fluticasone/salmeterol generics, Wixela™ Inhub, AirDuo™ Respiclick]‡, budesonide and formoterol fumarate inhalation aerosol [Symbicort®]‡, fluticasone furoate and vilanterol inhalation powder [Breo® Ellipta®]‡, mometasone furoate and formoterol fumarate inhalation aerosol [Dulera®]‡).

2) Inhaled long-acting muscarinic antagonist (LAMA), (e.g., tiotropium bromide inhalation spray [Spiriva® Respimat®, Spiriva Handihaler®, Stiolto® Respimat]‡, aclidinium products [Tudorza® Pressair®]‡, glycopyrrolate products [Seebri™ Neohaler, Bevespi™ Aerosphere, Utibron™ Neohaler]‡, umeclidinium products [Incruse® Ellipta, Anoro® Ellipta] ‡); OR
3) Leukotriene receptor antagonist (LTRA), (e.g., montelukast tablets/granules [Singulair®, generics], zafirlukast tablets [Accolate®])‡; OR
4) Theophylline (Theo-24, Uniphyl, TheoChron ER, generics); AND

VI. Patient's asthma continues to be uncontrolled as defined by ONE of the following (a, b, c, d, or e):
   a) Patient experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year; OR
   b) Patient experienced one or more asthma exacerbations 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) Patient's asthma worsens upon tapering of oral corticosteroid therapy.

Continuation

I. Patient has received an initial authorization; AND
II. Requested drug is NOT being used in combination with other monoclonal antibodies typically used to treat asthma (e.g., mepolizumab [Nucala], reslizumab [Cinqair], benralizumab [Fasenra], omalizumab [Xolair], tezepelumab-ekko [Tezspire]); AND
III. Patient continues to receive the medications required in criterion V. in the "Initial Criteria"; AND
IV. Patient has responded to requested therapy as determined by the prescribing physician (e.g., decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, ED/urgent care, or physician visits due to asthma; decreased requirement for oral corticosteroid therapy).

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

Chronic Sinusitis with Nasal Polyposis

Based on review of available data, the Company may consider dupilumab (Dupixent) for the treatment of chronic sinusitis with nasal polyposis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for dupilumab (Dupixent) for the treatment of chronic sinusitis with nasal polyposis will be considered when the patient selection criteria are met:

Initial

I. Patient has inadequately controlled chronic rhinosinusitis with nasal polyposis; AND
II. Patient is 18 years of age or older; AND
III. Patient has recurrent polyposis after at least ONE surgical resection (unless resection is contraindicated); AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
IV. Patient's nasal polyposis has been confirmed as grade 3 or higher with nasal endoscopy; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
V. Patient's polyposis recurrence occurred within 6 months of at least one high dose oral steroid taper after the most recent resection unless there is clinical evidence or patient history that suggests the use of a high dose oral steroid taper will be ineffective or cause an adverse effect to the patient; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
VI. Patient has tried and failed (e.g., intolerance or inadequate response) BOTH fluticasone 50 mcg (generic OR over the counter) AND GENERIC mometasone after at least 30 days with EACH product unless there is clinical evidence or patient history that suggests the use of these nasal sprays will be ineffective or cause an adverse effect to the patient; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

VII. Patient has tried and failed (e.g., intolerance or inadequate response) Xhance®‡ (fluticasone 93 mcg) after at least 30 days of therapy unless there is clinical evidence or patient history that suggests the use of Xhance (fluticasone 93 mcg) will be ineffective or cause an adverse effect to the patient; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

VIII. Patient has tried and failed (e.g., intolerance or inadequate response) GENERIC montelukast after at least 30 days of therapy unless there is clinical evidence or patient history that suggests the use of GENERIC montelukast will be ineffective or cause an adverse effect to the patient; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

IX. Patient will continue to use an intra-nasal corticosteroid (e.g., fluticasone, mometasone, Xhance) in combination with Dupixent (if the intra-nasal corticosteroid was tolerated); AND

X. Requested drug is NOT being used in combination with other monoclonal antibodies typically used to treat nasal polyps (e.g., omalizumab [Xolair], mepolizumab [Nucala]).

Continuation

I. Patient has received an initial authorization; AND

II. Patient will continue to use an intra-nasal corticosteroid (e.g., fluticasone, mometasone, Xhance) in combination with Dupixent (if the intra-nasal corticosteroid was tolerated); AND

III. Requested drug is NOT being used in combination with other monoclonal antibodies typically used to treat nasal polyps (e.g., omalizumab [Xolair], mepolizumab [Nucala]); AND

IV. Patient has responded to requested therapy as determined by the prescribing physician (e.g., decrease in nasal polyps, decreased congestion/obstruction, etc).
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

<u>Eosinophilic Esophagitis</u>

Based on review of available data, the Company may consider dupilumab (Dupixent) for the treatment of eosinophilic esophagitis to be eligible for coverage.**

dupilumab (Dupixent®)

Policy # 00567
Original Effective Date: 06/21/2017
Current Effective Date: 04/10/2023

Patient Selection Criteria

Coverage eligibility for dupilumab (Dupixent) for the treatment of eosinophilic esophagitis will be considered when the patient selection criteria are met:

Initial

I. Patient has a diagnosis of eosinophilic esophagitis that has been confirmed by an endoscopic biopsy demonstrating greater than or equal to 15 intraepithelial eosinophils per high power field; AND
II. Patient is 12 years of age or older; AND
III. Patient weighs at least 40 kg; AND
IV. Eosinophilic esophagitis diagnosis is not due to a secondary cause (e.g., hypereosinophilic syndrome, eosinophilic granulomatosis with polyangiitis, or food allergy); AND
V. Patient has tried and failed (e.g., intolerance or inadequate response) at least eight weeks of therapy with a proton pump inhibitor (e.g., pantoprazole, omeprazole, esomeprazole, lansoprazole, etc.) unless there is clinical evidence or patient history that suggests the use of a proton pump inhibitor will be ineffective or cause an adverse effect to the patient; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
VI. Patient meets one of the following (a or b):
    a) Patient has tried and failed (e.g., intolerance or inadequate response) dietary modifications (e.g., elemental diet, elimination diet, etc.) to treat or manage eosinophilic esophagitis; OR
    b) Patient is not a candidate for dietary modifications (e.g., elemental diet, elimination diet, etc.)

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

Continuation

I. Patient has received an initial authorization; AND
II. Patient has received at least 6 months of therapy with the requested drug; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
III. Patient has had a clinically meaningful beneficial response to Dupixent therapy as compared to their baseline status (before Dupixent therapy) as evidenced by ONE or more of the following:

a) Reduction in intraepithelial eosinophil count
b) Decrease in dysphagia or pain upon swallowing
c) Reduction in frequency or severity of food impaction

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

Prurigo Nodularis

Based on review of available data, the Company may consider dupilumab (Dupixent) for the treatment of prurigo nodularis to be eligible for coverage.**

Patient Selection Criteria

Coverage eligibility for dupilumab (Dupixent) for the treatment of prurigo nodularis will be considered when the patient selection criteria are met:

Initial

I. Patient has a diagnosis of prurigo nodularis; AND
II. Patient has greater than or equal to 20 prurigo nodularis nodular lesions; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
III. Patient is 18 years of age or older; AND
IV. Patient has experienced pruritus for greater than or equal to 6 weeks; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
V. Patient's pruritus is categorized as severe according to prescriber; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
VI. Patient meets one of the following:
a) Patient's prurigo nodularis is NOT medication induced or secondary to a non-dermatologic condition such as neuropathy or a psychiatric disease; OR
b) Patient has a secondary cause of prurigo nodularis that has been identified and adequately managed, yet symptoms of prurigo nodularis still persist; AND

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

VII. Patient has tried and failed (e.g., intolerance or inadequate response) a generic medium to very high potency topical corticosteroid product (e.g., betamethasone valerate,

desoximetasone, fluocinolone acetonide, fluticasone propionate, hydrocortisone butyrate, mometasone furoate, prednicarbate, triamcinolone acetonide, trianex, triderm, amcinonide, augmented betamethasone dipropionate, apexicon E, betamethasone dipropionate, diflorasone diacetate, fluocinonide, fluocinonide E, clobetasol emollient, clobetasol propionate, clodan, cormax, diflorasone diacetate, and halobetasol propionate) for at least TWO consecutive weeks unless there is clinical evidence or patient history that suggest the use of these products will be ineffective or cause an adverse reaction to the patient.
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

Continuation

IV. Patient has received an initial authorization; AND

V. Patient has received at least 6 months of therapy with the requested drug; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

VI. Patient has had a clinically meaningful beneficial response to Dupixent therapy as compared to their baseline status (before Dupixent therapy) as evidenced by ONE or more of the following:
   a) Reduction in pruritus severity
   b) Decrease in number of prurigo nodularis nodules
   c) Reduced nodular lesion size

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of dupilumab (Dupixent) when ANY of the following criteria for the requested diagnosis are NOT met to be **not medically necessary**:**

- Atopic Dermatitis:
  - Patient has had chronic atopic dermatitis for at least 6 months
  - Patient has atopic dermatitis involvement estimated to be ≥ 10% of the BSA according to the prescribing physician

  - For continuation requests: Patient has received at least 6 months of therapy with the requested drug
  - For continuation requests: Patient has been adherent to the requested drug and other medications for the condition being treated
  - For continuation requests: Patient has had a clinically meaningful beneficial response to Dupixent therapy as compared to their baseline status (before Dupixent therapy) as evidenced by TWO or more of the following:
    - Reduction in disease severity (e.g., erythema, dryness, edema/papulation, excoriations, lichenification, oozing/crusting)
    - Reduction in the frequency or intensity of pruritus
    - Reduction in the frequency of disease exacerbations/flares
    - Reduction in the BSA with AD involvement (a 20% reduction in percent BSA involved over baseline)
    - Improvement in overall patient quality of life (e.g., improved sleep, less depression or anxiety, etc.)
- Moderate to Severe Asthma:
  - Patient has been on the listed pre-requisite asthma medications (criteria V.) for at least 3 months
  - For continuation requests: Patient has responded to requested therapy as determined by the prescribing physician (e.g., decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, ED/urgent care, or physician visits due to asthma; decreased requirement for oral corticosteroid therapy).
- Chronic Rhinosinusitis with Nasal Polyposis:
  - Patient has recurrent polyposis after at least ONE surgical resection (unless resection is contraindicated)
  - Patient's nasal polyposis has been confirmed as grade 3 or higher with nasal endoscopy
  - Patient's polyposis recurrence occurred within 6 months of at least one high dose oral steroid taper after the most recent resection
  - Patient has tried and failed BOTH fluticasone 50 mcg (generic OR over the counter) AND GENERIC mometasone after at least 30 days with EACH product
  - Patient has tried and failed Xhance (fluticasone 93 mcg) after at least 30 days of therapy
  - Patient has tried and failed GENERIC montelukast after at least 30 days of therapy

  - For continuation requests: Patient has responded to requested therapy as determined by the prescribing physician (e.g., decrease in nasal polyps, decreased congestion/obstruction, etc.).
- Eosinophilic esophagitis
  - Patient has tried and failed at least eight weeks of therapy with a proton pump inhibitor (e.g., pantoprazole, omeprazole, esomeprazole, lansoprazole, etc.)
  - Patient has tried and failed dietary modifications (e.g., elemental diet, elimination diet, etc.) to treat or manage eosinophilic esophagitis OR patient is not a candidate for dietary modifications (e.g., elemental diet, elimination diet, etc.)
  - For continuation requests: Patient has received at least 6 months of therapy with the requested drug
  - For continuation requests: Patient has had a clinically meaningful beneficial response to Dupixent therapy as compared to their baseline status (before Dupixent therapy) as evidenced by ONE or more of the following:
    - Reduction in intraepithelial eosinophil count
    - Decrease in dysphagia or pain upon swallowing
    - Reduction in frequency or severity of food impaction
- Prurigo Nodularis
  - Patient has greater than or equal to 20 prurigo nodularis nodular lesions
  - Patient has experienced pruritus for greater than or equal to 6 weeks
  - Patient's pruritus is categorized as severe
  - Patient's prurigo nodularis is NOT medication induced or secondary to a non-dermatologic condition such as neuropathy or a psychiatric disease OR Patient has a secondary cause of prurigo nodularis that has been identified and adequately managed, yet symptoms of prurigo nodularis still persist; AND
  - Patient has tried and failed a generic medium to very high potency topical corticosteroid product (e.g., betamethasone valerate, desoximetasone, fluocinolone acetonide, fluticasone propionate, hydrocortisone butyrate, mometasone furoate, prednicarbate, triamcinolone acetonide, trianex, triderm, amcinonide, augmented betamethasone dipropionate, apexicon E, betamethasone dipropionate, diflorasone diacetate, fluocinonide, fluocinonide E, clobetasol emollient, clobetasol propionate, clodan, cormax, diflorasone diacetate, and halobetasol propionate) for at least TWO consecutive weeks

dupilumab (Dupixent®)

Policy # 00567
Original Effective Date: 06/21/2017
Current Effective Date: 04/10/2023

- For continuation requests: Patient has received at least 6 months of therapy with the requested drug
- For continuation requests: Patient has had a clinically meaningful beneficial response to Dupixent therapy as compared to their baseline status (before Dupixent therapy) as evidenced by ONE or more of the following:
  - Reduction in pruritus severity
  - Decrease in number of prurigo nodularis nodules
  - Reduced nodular lesion size

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of dupilumab (Dupixent) when the patient selection criteria are not met (EXCEPT those denoted as **not medically necessary****) to be **investigational.***

Based on review of available data, the Company considers the use of dupilumab (Dupixent) for any non-FDA approved indication to be **investigational.***

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Dupixent Quantity Coverage

Based on review of available data, the Company may consider a quantity override for dupilumab (Dupixent) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for a 300 mg per week quantity override for dupilumab (Dupixent) will be considered when the patient selection criterion is met:

- Patient has a diagnosis of eosinophilic esophagitis.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers requests for a dosing override of dupilumab (Dupixent) when the patient selection criterion is not met to be **investigational.***

Background/Overview

Dupixent is an interleukin-4 receptor alpha antagonist indicated for the treatment of patients aged 6 months and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent is also approved as add-on maintenance treatment in patients with moderate to severe asthma aged 6 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma. Dupixent later gained an indication as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis and an indication for the treatment of eosinophilic esophagitis in adults and pediatric patients aged 12 years and older, weighing at least 40 kg. Dupixent most recently gained an indication for the treatment of prurigo nodularis. Please see the package insert for details on dosing.

Atopic Dermatitis

There are various treatment options for atopic dermatitis, including first line agents such as topical corticosteroids (many of which are in generic form) and topical immunomodulatory agents such as generic tacrolimus and generic pimecrolimus. For those that are refractory to topical therapies, systemic immunomodulatory agents are an option for therapy. Dupixent has not yet been integrated into the American Academy of Dermatology guidelines at the time of this publication.

Asthma

Asthma is a respiratory disorder characterized by increased responsiveness of the trachea and bronchi to various stimuli resulting in the narrowing of the airways, along with mucous secretion. Symptoms vary in severity and intensity and include wheezing, cough and dyspnea. Attacks can be

triggered by exercise, allergens, irritants, and viral infections. Based on symptoms, the four levels of asthma severity are:

- Mild intermittent (comes and goes)—you have episodes of asthma symptoms twice a week or less, and you are bothered by symptoms at night twice a month or less; between episodes, however, you have no symptoms and your lung function is normal.
- Mild persistent asthma—you have asthma symptoms more than twice a week, but no more than once in a single day. You are bothered by symptoms at night more than twice a month. You may have asthma attacks that affect your activity.
- Moderate persistent asthma—you have asthma symptoms every day, and you are bothered by nighttime symptoms more than once a week. Asthma attacks may affect your activity.
- Severe persistent asthma—you have symptoms throughout the day on most days, and you are bothered by nighttime symptoms often. In severe asthma, your physical activity is likely to be limited.

Treatment of asthma is based on a step up and step down approach based on the asthma severity and symptoms. Medications include short acting beta agonists for fast relief. Long term treatment centers around the use of ICSs and possible addition of medications such as long acting beta agonists, LTRAs, inhaled long acting muscarinic antagonists, or theophylline. In the past few years, biologic products have been approved for the treatment of asthma, including Xolair, Nucala, Fasenra, and Cinqair for those that are not controlled on traditional agents. Guidelines have not been updated to include Dupixent.

Chronic Rhinosinusitis with Nasal Polyposis

Chronic rhinosinusitis is an inflammatory condition involving the nasal sinuses and the lining of the nasal passages. Chronic rhinosinusitis often involves nasal drainage, nasal obstruction, facial pain and/or pressure and decreased sense of smell. Chronic rhinosinusitis with nasal polyposis is characterized by the presence of bilateral nasal polyps in the middle meatus. As imagined, these polyps lead to worsening nasal congestion, pressure, drainage, etc. Treatments for chronic rhinosinusitis with nasal polyposis includes various treatment modalities including, but not limited to, intranasal saline, intranasal steroids, oral steroids, surgery, non-sedating antihistamines, anti-leukotriene agents, and for those who have failed these more traditional therapies, Dupixent (which is the first monoclonal antibody approved for this condition).

dupilumab (Dupixent®)

Policy # 00567
Original Effective Date: 06/21/2017
Current Effective Date: 04/10/2023

Eosinophilic esophagitis
Eosinophilic esophagitis is a chronic allergic/immune condition of the esophagus. It is characterized by an increased number of eosinophils in the esophagus, which are normally not present at all. It often presents as dysphagia, food impaction, chest pain that may not respond to antacids, gastroesophageal reflux disease-like symptoms, or upper abdominal pain in adults and feeding dysfunction, vomiting, abdominal pain, dysphagia, or food impaction in children. Effective non-pharmacologic therapy for the treatment of this condition consists of dietary modifications. Elimination and elemental diets are the two recommended dietary modifications in which known or suspected allergens be removed from the diet in elimination or an individual is limited to an amino acid formula as the main source of nutrition in elemental. Dupixent is the first and only medication currently approved for the treatment of eosinophilic esophagitis, however, proton pump inhibitors have remained as first line treatment options.

Prurigo Nodularis
Prurigo nodularis (PN) is an uncommon skin disorder that is characterized by symmetrically distributed multiple, firm, pruritic nodules. The exact pathogenesis of the disorder is unclear. PN typically presents with firm, dome-shaped nodules that range in size and can be flesh-colored, erythematous, brown, or black. They often range in number from just a few to hundreds of lesions. Another core symptom of PN is pruritus lasting greater than or equal to 6 weeks that has led to signs of repeated scratching, picking, or rubbing. PN can occur all over the body, but the face, palms of the hand, soles of the feet, and genitalia are rarely affected. PN has a profound impact on a patient's quality of life, often due to sleep deprivation, depression, and anxiety. Several medical conditions are associated with PN such as atopic dermatitis, chronic kidney disease, diabetes, heart failure, hepatitis B or C virus, HIV, and non-Hodgkin lymphoma. When diagnosing PN, it is recommended for clinicians to do a full review of systems, especially in patients who do not have a history of a pruritic skin condition, to assess if there is a systemic disease or malignancy possibly causing PN. Treatment goals for PN include reducing pruritus, interrupting the itch-scratch cycle, and completely healing PN lesions. Several recommended therapies are off-label treatments that include gentle skin care, antipruritic emollients, topical corticosteroids, topical calcineurin inhibitors, topical capsaicin, neuromodulators, antidepressants, phototherapy, and immunosuppressants. Dupixent is the first therapeutic agent to be FDA approved for PN.

dupilumab (Dupixent®)

Policy # 00567
Original Effective Date: 06/21/2017
Current Effective Date: 04/10/2023

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Dupixent is indicated for the treatment of patients aged 6 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent can be used with or without topical corticosteroids. Dupixent is also indicated for add-on maintenance treatment in patients with moderate to severe asthma aged 6 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma. Dupixent is also approved as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis and for the treatment of adult and pediatric patients aged 12 years and older, weighing at least 40 kg, with eosinophilic esophagitis. Dupixent's latest FDA approved indication is for the treatment of adult patients with prurigo nodularis.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Atopic Dermatitis

The safety and efficacy of Dupixent was established in three randomized, double-blind, placebo controlled pivotal studies. The populations in these trials included adults that had atopic dermatitis for at least 3 years and had involvement ≥ 10% of the BSA. The study entrants were also previously uncontrolled by topical therapies. SOLO-1 (n=671) and SOLO-2 (n=708) evaluated Dupixent as monotherapy, while CHRONOS (n=740) evaluated Dupixent as combination therapy. In all studies, the primary 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. In SOLO-1, the primary endpoint was met in 38% of subjects in the Dupixent group versus 10% of subjects in the placebo group (P<0.001). In SOLO-2, the primary endpoint was achieved in 36% of subjects in the Dupixent group versus 18% in the placebo group (P<0.001). In week 16 of the CHRONOS trial, 38.7% of Dupixent subjects met the primary endpoint versus 10% of those treated with placebo (P<0.001). At week 52, similar results were reported for the CHRONOS trial.

The efficacy and safety of Dupixent monotherapy in adolescent subjects was evaluated in a multicenter, randomized, double-blind, placebo-controlled trial in 251 adolescent subjects 12 to 17 years of age, with moderate-to-severe atopic dermatitis. Subjects in the Dupixent group with baseline weight of <60 kg received an initial dose of 400 mg at week 0, followed by 200 mg every two weeks for 16 weeks. Subjects with baseline weight of ≥60 kg received an initial dose of 600 mg at week 0, followed by 300 mg every two weeks for 16 weeks. The primary endpoint was the proportion of subjects with an IGA 0 (clear) or 1 (almost clear) and at least a 2-point improvement from baseline to week 16. In the Dupixent group, 24% of subjects achieved an IGA score of 0 or 1 vs. 2% in the placebo group.

The efficacy and safety of Dupixent in pediatric subjects was evaluated in a multicenter, randomized, double-blind, placebo-controlled trial in 367 subjects 6 to 11 years of age, with atopic dermatitis defined by an IGA score of 4 (scale of 0 to 4), an Eczema Area and Severity Index (EASI) score ≥21 (scale of 0 to 72), and a minimum BSA involvement of ≥15%. Subjects were given various doses of Dupixent depending on weight. Subjects were permitted to receive rescue treatment at the discretion of the investigator. The primary endpoint was the proportion of subjects with an IGA 0 (clear) or 1 (almost clear) at week 16. The proportion of subjects with an IGA of 0 or 1 ranged from 36-39% in the Dupixent group versus 9-12% in the placebo group.

Asthma

The efficacy of Dupixent for the treatment of asthma was established in three randomized, placebo-controlled studies in patients with persistent asthma. Study 1 (n = 776) was a Phase IIb, 24-week study that included adult patients with uncontrolled asthma despite therapy with a medium-to-high dose inhaled corticosteroid and up to two additional controller medications. The annualized exacerbation rate was reduced by 70% with Dupixent 200 mg once every 2 weeks and reduced by 70.5% with Dupixent 300 mg every 2 weeks compared with placebo ($P < 0.05$ for each comparison). The relative risk reduction was greater in the subgroup of patients with a baseline blood eosinophil count ≥ 300 cells/microliter (80.7% reduction with Dupixent 300 mg every 2 weeks vs. placebo). Significant improvements in the FEV_1 were also observed with both doses of Dupixent vs. placebo. The second study, LIBERTY ASTHMA QUEST (n = 1,902), was a Phase III study that included patients ≥ 12 years of age who had uncontrolled moderate-to-severe asthma despite treatment with a medium- to high-dose inhaled corticosteroid and up to two additional controller medications. Over the 52-week treatment period, Dupixent 200 mg every 2 weeks and 300 mg every 2 weeks reduced the adjusted annualized rate of severe asthma exacerbations vs. placebo by 47.7% and 46.0%,

respectively (P < 0.001 for both comparisons). At week 12, FEV_1 was increased by 0.14 L with Dupixent 200 mg vs. placebo and 0.13 L with Dupixent 300 mg vs. placebo. Larger improvements in both asthma exacerbations and FEV_1 values were observed in patients with a baseline blood eosinophil count ≥ 300 cells/microliter as well as in patients with an elevated baseline fraction of exhaled nitric oxide (FENO) ≥ 25 parts per billion. A second Phase III study, LIBERTY ASTHMA VENTURE (n = 210), included patients ≥ 12 years of age who had severe asthma that required regular treatment with systemic corticosteroids despite treatment with a high-dose ICS and up to two additional controller medications. From baseline to week 24, the oral corticosteroid dose was reduced by 70.1% with Dupixent 300 mg every two weeks compared with 41.9% with placebo (P < 0.001), while maintaining asthma control. In total, 80% of patients receiving Dupixent achieved at least a 50% corticosteroid dose reduction vs. 50% of patients assigned to placebo (P < 0.001). Dupixent was associated with a greater oral corticosteroid dose reduction regardless of baseline blood eosinophil count; however, the magnitude of the dose reduction was larger in patients with blood eosinophils > 300 cells/microliter. In addition to reducing oral corticosteroid use, Dupixent reduced the rate of severe asthma exacerbations by 59% compared with placebo.

It should be noted that higher baseline eosinophil levels were correlated with larger asthma exacerbation reductions and greater increases in lung function parameters than were observed in the overall patient population. In patients with baseline blood eosinophil levels < 150 cells/microliter, the magnitude of the reductions in asthma exacerbations observed with Dupixent vs. placebo were non-significant.

The efficacy and safety of Dupixent in pediatric subjects was evaluated in a 52-week multicenter, randomized, double-blind, placebo-controlled study (AS Trial 4) in 408 subjects 6 to 11 years of age, with moderate to severe asthma on current therapy. Subjects were randomized to Dupixent (n=273) or matching placebo (n=135) every other week based on body weight < 30 kg (100 mg every 2 weeks) or ≥30 kg (200 mg every 2 weeks). The effectiveness of Dupixent 300 mg every 4 weeks was extrapolated from efficacy of 100 mg every 2 weeks in AS Trial 4 with support from population pharmacokinetic analyses showing higher drug exposure levels with 300 mg every 4 weeks. The primary endpoint was the annualized rate of severe asthma exacerbation events during the 52-week placebo-controlled period. Dupixent significantly reduced the annualized rate of severe asthma exacerbation events during the 52 week treatment period compared to placebo in populations with an eosinophilic phenotype as indicated by elevated blood eosinophils and/or the population with elevated fraction of exhaled nitric oxide (FeNO).

dupilumab (Dupixent®)

Policy # 00567
Original Effective Date: 06/21/2017
Current Effective Date: 04/10/2023

Nasal Polyposis
The chronic rhinosinusitis with nasal polyposis (CRSwNP) development program included two randomized, double-blind, parallel-group, multicenter, placebo-controlled studies (CSNP Trial 1 and CSNP Trial 2) in 724 subjects aged 18 years and older on background intranasal corticosteroids. These studies included subjects with CRSwNP despite prior sino-nasal surgery or treatment with, or who were ineligible to receive or were intolerant to, systemic corticosteroids in the past 2 years. Patients with chronic rhinosinusitis without nasal polyposis were not included in these trials. Rescue with systemic corticosteroids or surgery was allowed during the studies at the investigator's discretion.

In CSNP Trial 1, a total of 276 subjects were randomized to receive either 300 mg Dupixent (n=143) or placebo (n=133) every other week for 24 weeks. In CSNP Trial 2, 448 subjects were randomized to receive either 300 mg Dupixent (n=150) every other week for 52 weeks, 300 mg Dupixent (n=145) every other week until week 24 followed by 300 mg Dupixent every 4 weeks until week 52, or placebo (n=153). All subjects had evidence of sinus opacification on the Lund Mackay (LMK) sinus CT scan and 73% to 90% of subjects had opacification of all sinuses. Subjects were stratified based on their histories of prior surgery and co-morbid asthma/nonsteroidal anti-inflammatory drug exacerbated respiratory disease (NSAID-ERD). A total of 63% of subjects reported previous sinus surgery, with a mean number of 2.0 prior surgeries, 74% used systemic corticosteroids in the previous 2 years with a mean number of 1.6 systemic corticosteroid courses in the previous 2 years, 59% had co-morbid asthma, and 28% had NSAID-ERD. The co-primary efficacy endpoints were change from baseline to week 24 in bilateral endoscopic nasal polyps score (NPS; 0-8 scale) as graded by central blinded readers and change from baseline to week 24 in nasal congestion/obstruction score averaged over 28 days (NC; 0-3 scale), as determined by subjects using a daily diary. For NPS, polyps on each side of the nose were graded on a categorical scale (0=no polyps; 1=small polyps in the middle meatus not reaching below the inferior border of the middle turbinate; 2=polyps reaching below the lower border of the middle turbinate; 3=large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle turbinate; 4=large polyps causing complete obstruction of the inferior nasal cavity). The total score was the sum of the right and left scores. Nasal congestion was rated daily by the subjects on a 0 to 3 categorical severity scale (0=no symptoms; 1=mild symptoms; 2=moderate symptoms; 3=severe symptoms). In both studies, key secondary end-points at week 24 included change from baseline in: LMK sinus CT scan score, daily loss of smell, and 22-item sino-nasal outcome test (SNOT-22). The LMK sinus CT scan score evaluated the opacification of each sinus using a 0 to 2 scale (0=normal; 1=partial

opacification; 2=total opacification) deriving a maximum score of 12 per side and a total maximum score of 24 (higher scores indicate more opacification). Loss of smell was scored reflectively by the patient every morning on a 0-3 scale (0=no symptoms, 1=mild symptoms, 2=moderate symptoms, 3=severe symptoms). SNOT-22 includes 22 items assessing symptoms and symptom impact associated with CRSwNP with each item scored from 0 (no problem) to 5 (problem as bad as it can be) with a global score ranging from 0 to 110. SNOT-22 had a 2 week recall period. In the pooled efficacy results, the reduction in the proportion of subjects rescued with systemic corticosteroids and/or sino-nasal surgery (up to week 52) were evaluated.

In CSNP Trial 1, the LS mean difference vs. placebo was -2.06 for the NPS and -0.89 for the NC scores. In CNSP Trial 2, the LS mean difference vs. placebo was -1.80 for the NPS and -0.87 for the NC scores. Statistically significant efficacy was observed in CSNP Trial 2 with regard to improvement in bilateral endoscopic NPS score at week 24 and week 52. Similar results were seen in CSNP Trial 1 at week 24. In the post-treatment period when subjects were off Dupixent, the treatment effect diminished over time.

At week 52, the LS mean difference for nasal congestion in the Dupixent group versus placebo was -0.98 (95% CI -1.17, -0.79). In both studies, significant improvements in nasal congestion were observed as early as the first assessment at week 4. The LS mean difference for nasal congestion at week 4 in the Dupixent group versus placebo was -0.41 (95% CI: -0.52, -0.30) in CSNP Trial 1 and -0.37 (95% CI: -0.46, -0.27) in CSNP Trial 2.

A significant decrease in the LMK sinus CT scan score was observed. The LS mean difference for LMK sinus CT scan score at week 24 in the Dupixent group versus placebo was -7.44 (95% CI: -8.35, -6.53) in CSNP Trial 1 and -5.13 (95% CI: -5.80, -4.46) in CSNP Trial 2. At week 52, in CSNP Trial 2 the LS mean difference for LMK sinus CT scan score in the Dupixent group versus placebo was -6.94 (95% CI: -7.87, -6.01). Dupixent significantly improved the loss of smell compared to placebo. The LS mean difference for loss of smell at week 24 in the Dupixent group versus placebo was -1.12 (95% CI: -1.31, -0.93) in CSNP Trial 1 and -0.98 (95% CI: -1.15, -0.81) in CSNP Trial 2. At week 52, the LS mean difference for loss of smell in the Dupixent group versus placebo was -1.10 (95% CI -1.31, -0.89). In both studies, significant improvements in daily loss of smell severity were observed as early as the first assessment at week 4.

Dupixent significantly decreased sino-nasal symptoms as measured by SNOT-22 compared to placebo. The LS mean difference for SNOT-22 at week 24 in the Dupixent group versus placebo was -21.12 (95% CI: -25.17, -17.06) in CSNP Trial 1 and -17.36 (95% CI: -20.87, -13.85) in CSNP Trial 2. At week 52, the LS mean difference in the Dupixent group versus placebo was -20.96 (95% CI -25.03, -16.89). In the pre-specified multiplicity-adjusted pooled analysis of two studies, treatment with Dupixent resulted in significant reduction of systemic corticosteroid use and need for sino-nasal surgery versus placebo (HR of 0.24; 95% CI: 0.17, 0.35). The proportion of subjects who required systemic corticosteroids was reduced by 74% (HR of 0.26; 95% CI: 0.18, 0.38). The total number of systemic corticosteroid courses per year was reduced by 75% (RR of 0.25; 95% CI: 0.17, 0.37). The proportion of subjects who required surgery was reduced by 83% (HR of 0.17; 95% CI: 0.07, 0.46).

The effects of Dupixent on the primary endpoints of NPS and nasal congestion and the key secondary endpoint of LMK sinus CT scan score were consistent in patients with prior surgery and without prior surgery.

Eosinophilic Esophagitis
A single randomized, double-blind, parallel-group, multicenter, placebo-controlled trial, including two 24-week treatment periods (Parts A and B), was conducted in adult and pediatric subjects 12 to 17 years of age, weighing at least 40 kg, with eosinophilic esophagitis (EoE). In both parts, subjects were randomized to receive 300 mg Dupixent every week or placebo. Eligible subjects had ≥15 intraepithelial eosinophils per high-power field (eos/hpf) following a treatment course of a proton pump inhibitor (PPI) either prior to or during the screening period and symptoms of dysphagia as measured by the Dysphagia Symptom Questionnaire (DSQ). At baseline, 43% of subjects in Part A and 37% of subjects in Part B had a history of prior esophageal dilations.

The coprimary efficacy endpoints in Parts A and B were the (1) proportion of subjects achieving histological remission defined as peak esophageal intraepithelial eosinophil count of ≤6 eos/hpf at week 24; and (2) the absolute change in the subject-reported DSQ score from baseline to week 24.

In Parts A and B, a greater proportion of subjects randomized to Dupixent achieved histological remission (peak esophageal intraepithelial eosinophil count ≤6 eos/hpf) compared to placebo (A: 59.5% vs. 5.1% and B: 58.5% vs. 6.3%). Treatment with Dupixent also resulted in a significant improvement in LS mean change in DSQ score compared to placebo (A: -21.9 vs. -9.6 and B: -23.8

vs. -13.9) at week 24. The results of the anchor-based analyses that incorporated the subjects' perspectives indicated that the observed improvement in dysphagia from Parts A and B is representative of a clinically meaningful within-subject improvement.

Prurigo Nodularis
The prurigo nodularis (PN) development program included two 24-week randomized, double blind, placebo-controlled, multicenter, parallel-group trials, Trial 1 and Trial 2, in 311 adult subjects 18 years of age and older with severe pruritus, defined by the Worst Itch-Numeric Rating Scale (WI-NRS) as a score of 7 or greater, and greater than or equal to 20 nodular lesions. Trial 1 and Trial 2 assessed the effect of Dupixent on pruritus improvement as well as its effect on PN lesions. In these two trials, subjects received either subcutaneous Dupixent 600 mg (two 300 mg injections) on day 1, followed by 300 mg once every other week (Q2W) for 24 weeks, or matching placebo.

The WI-NRS is comprised of a single item, rated on a scale from 0 ("no itch") to 10 ("worst imaginable itch"). Subjects were asked to rate the intensity of their worst pruritus (itch) over the past 24 hours using this scale. The Investigator's Global Assessment for Prurigo Nodularis-Stage (IGA PN-S) is a scale that measures the approximate number of nodules using a 5-point scale from 0 (clear) to 4 (severe).

Efficacy was assessed with the proportion of subjects with improvement (reduction) in WI-NRS by ≥4 points, the proportion of subjects with IGA PN-S 0 or 1 (the equivalent of 0-5 nodules), and the proportion of subjects who achieved a response in both WI-NRS and IGA PN-S per the criteria described above.

In Trial 1, the proportion of subjects with both an improvement (reduction) in WI-NRS by ≥4 points from baseline and an IGA PN-S 0 or 1 at week 24 was 38.7 % and 9.2% in the treatment group and placebo group, respectively. 60% of patients in the treatment group and 18.4% of patients in the placebo group had improvement in WI-NRS by ≥4 points from baseline at week 24, while 48% of patients in the treatment group and 18.4% of patients in the placebo group had an IGA PN-S 0 or 1 at week 24. Additionally, the proportion of patients who achieved a ≥4-point reduction in the WI-NRS at week 12 was 44.0% in the treatment group compared to 15.8% in the placebo group.

In Trial 2, the proportion of subjects with both an improvement (reduction) in WI-NRS by ≥4 points from baseline and an IGA PN-S 0 or 1 at week 24 was 32.1% in the treatment group compared to

8.5% in the placebo group. 57.7% of patients in the treatment group and 19.5% of patients in the placebo group had improvement in WI-NRS by ≥4 points from baseline at week 24, while 44.9% of patients in the treatment group and 15.9% of patients in the placebo group had an IGA PN-S 0 or 1 at week 24. The proportion of patients who achieved a ≥4-point reduction in the WI-NRS at week 12 was 37.2% in the treatment group compared to 22.0% in the placebo group.

References

1. Dupixent [package insert]. Regeneron Pharmaceuticals, Inc. Tarrytown, New York. Updated October 2022.
2. Dupixent Drug Evaluation. Express Scripts. Updated October 2018.
3. Dupixent Prior Authorization Policy. Express Scripts. Updated October 2022.
4. Sidbury R, et al. Guidelines of care for the management of atopic dermatitis Section 3. Management and treatment with phototherapy and systemic agents. J Am Acad Dermatol. 2014;71(2): 327-349.
5. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis. Section 2: management and treatment of atopic dermatitis with topical therapies. J Am Acad Dermatol. 2014;71(1):116-132.
6. Initiative for Asthma. Global strategy for asthma management and prevention. Updated February 2018. Available at: http://www.ginasthma.org. Accessed on: October 22, 2018.
7. Castro M, Corren J, Pavord ID, et al. Dupilumab efficacy and safety in moderate-to-severe uncontrolled asthma. N Engl J Med. 2018;378(26);2486-2496.
8. Rabe KF, Nair P, Brusselle G, et al. Efficacy and safety of dupilumab in glucocorticoid-dependent severe asthma. N Engl J Med. 2018;378(26):2475-2485.
9. Wenzel S, Castro M, Corren J, et al. Dupilumab efficacy and safety in adults with uncontrolled persistent asthma despite use of medium-to-high-dose inhaled corticosteroids plus a long-acting β2 agonist: a randomised double-blind placebo-controlled pivotal phase 2b dose-ranging trial. Lancet. 2016;388(10039):31-44.
10. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. Eur Respir J. 2014;43:343-373.
11. Chronic rhinosinusitis: Management. UpToDate. Accessed October 2019.
12. Chronic rhinosinusitis: Clinical manifestations, pathophysiology, and diagnosis. UpToDate. Accessed October 2019.

13. Garrido Colmenero C, Blasco Morente G, Tercedor Sánchez J. Oral Cyclosporine Weekend Therapy: A New Maintenance Therapeutic Option in Patients with Severe Atopic Dermatitis. Pediatr Dermatol 2015; 32:551.
14. Schmitt J, Schmitt N, Meurer M. Cyclosporin in the treatment of patients with atopic eczema - a systematic review and meta-analysis. J Eur Acad Dermatol Venereol 2007; 21:606.
15. Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis: section 3. Management and treatment with phototherapy and systemic agents. J Am Acad Dermatol 2014; 71:327.
16. Shea B, Swinden MV, Ghogomu ET, et al. Folic acid and folinic acid for reducing side effects in patients receiving methotrexate for rheumatoid arthritis. J Rheumatol 2014; 41:1049.
17. Dvorakova V, O'Regan GM, Irvine AD. Methotrexate for Severe Childhood Atopic Dermatitis: Clinical Experience in a Tertiary Center. Pediatr Dermatol 2017; 34:528.
18. Deo M, Yung A, Hill S, Rademaker M. Methotrexate for treatment of atopic dermatitis in children and adolescents. Int J Dermatol 2014; 53:1037.
19. Rahman SI, Siegfried E, Flanagan KH, Armbrecht ES. The methotrexate polyglutamate assay supports the efficacy of methotrexate for severe inflammatory skin disease in children. J Am Acad Dermatol 2014; 70:252.
20. Roberts H, Orchard D. Methotrexate is a safe and effective treatment for paediatric discoid (nummular) eczema: a case series of 25 children. Australas J Dermatol 2010; 51:128.
21. Anderson K, Putterman E, Rogers RS, et al. Treatment of severe pediatric atopic dermatitis with methotrexate: A retrospective review. Pediatr Dermatol 2019; 36:298.
22. Purvis D, Lee M, Agnew K, et al. Long-term effect of methotrexate for childhood atopic dermatitis. J Paediatr Child Health 2019; 55:1487.
23. El-Khalawany MA, Hassan H, Shaaban D, et al. Methotrexate versus cyclosporine in the treatment of severe atopic dermatitis in children: a multicenter experience from Egypt. Eur J Pediatr 2013; 172:351.
24. Tsakok T, Flohr C. Methotrexate vs. ciclosporin in the treatment of severe atopic dermatitis in children: a critical appraisal. Br J Dermatol 2014; 170:496.
25. Taylor K, Swan DJ, Affleck A, et al. Treatment of moderate-to-severe atopic eczema in adults within the U.K.: results of a national survey of dermatologists. Br J Dermatol 2017; 176:1617.
26. Clinical manifestations and diagnosis of eosinophilic esophagitis (EoE). UpToDate. Accessed July 2022.

27. Eosinophilic Esophagitis. American Academy of Allergy Asthma and Immunology. Updated May 2022. Available at: https://www.aaaai.org/Conditions-Treatments/related-conditions/eosinophilic-esophagitis. Accessed on: July 25, 2022.
28. Prurigo nodularis. UpToDate. Accessed February 2023.
29. 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.

Policy History

Original Effective Date: 06/21/2017
Current Effective Date: 04/10/2023

06/01/2017	Medical Policy Committee review
06/21/2017	Medical Policy Implementation Committee approval. New policy.
06/07/2018	Medical Policy Committee review
06/20/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/10/2019	Medical Policy Committee review
01/23/2019	Medical Policy Implementation Committee approval. Added coverage for asthma as per the new FDA approved indication. Removed systemic steroids as a pre-requisite option prior to use of Dupixent for atopic dermatitis.
05/02/2019	Medical Policy Committee review
05/15/2019	Medical Policy Implementation Committee approval. Changed age from 18 years to 12 years per the FDA package insert indication change. Updated relevant background and rationale information.
11/07/2019	Medical Policy Committee review
11/13/2019	Medical Policy Implementation Committee approval. Updated with newest FDA indication for the treatment of chronic rhinosinusitis with nasal polyposis.
09/03/2020	Medical Policy Committee review
09/09/2020	Medical Policy Implementation Committee approval. Updated the age for use in atopic dermatitis (from 12 years down to 6 years of age) to align with the FDA approval update. Updated background and rationale/source sections.
04/01/2021	Medical Policy Committee review

dupilumab (Dupixent®)

Policy # 00567
Original Effective Date: 06/21/2017
Current Effective Date: 04/10/2023

04/14/2021	Medical Policy Implementation Committee approval. Changed the requirement for the chronicity of atopic dermatitis from 3 years to 6 months. Removed the requirement for the use of systemic immunosuppressants for atopic dermatitis. Updated the continuation criteria for atopic dermatitis to require documentation for improvement of atopic dermatitis symptoms.
10/07/2021	Medical Policy Committee review
10/13/2021	Medical Policy Implementation Committee approval. Removed the requirement for medical record documentation submission for atopic dermatitis continuation requests.
12/02/2021	Medical Policy Committee review
12/08/2021	Medical Policy Implementation Committee approval. Updated the asthma age to 6 years and older (previously 12 years and older) per the new FDA package insert update. Changed the nasal polyps surgery resection count requirement from two prior surgical resections to one prior surgical resection.
03/03/2022	Medical Policy Committee review
03/09/2022	Medical Policy Implementation Committee approval. Added pimecrolimus cream as an option for trial and failure in atopic dermatitis. Added to the list of newly approved products that Dupixent cannot be used in combination with.
08/04/2022	Medical Policy Committee review
08/10/2022	Medical Policy Implementation Committee approval. Updated age requirement for atopic dermatitis from 6 years to 6 months of age and older. Added new indication, eosinophilic esophagitis, to the policy. Added quantity override criteria for eosinophilic esophagitis.
03/02/2023	Medical Policy Committee review
03/08/2023	Medical Policy Implementation Committee approval. Added coverage for prurigo nodularis as per the new FDA approved indication.

Next Scheduled Review Date: 03/2024

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and

whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

dupilumab (Dupixent®)

Policy # 00567
Original Effective Date: 06/21/2017
Current Effective Date: 04/10/2023

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.