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Subject: Dupilumab (Dupixent®) Injection

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DESCRIPTION:

Dupilumab (Dupixent) is a human monoclonal antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by binding to the IL-4R alpha subunit shared by IL-4 and IL-13 receptors. This reduces IL-4 and IL-13 cytokine-induced inflammatory response such as the release of proinflammatory cytokines, chemokines, and IgE, which play roles in the development of atopic dermatitis and asthma. Dupilumab was approved in March 2017 by the US Food and Drug Administration (FDA) for "the treatment of adult patients with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable". In September 2017 dupilumab was granted orphan drug designation by the FDA for the treatment of eosinophilic esophagitis. In October 2018, the indications for dupilumab were expanded when the FDA approved use "as an add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma." In March 2019, the moderate-to-severe atopic dermatitis indication was expanded to include adolescent patients 12 to 17 years of age. In June 2019, the indications for dupilumab were expanded again when the FDA approved use as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP). Dupilumab was the first systemic agent FDA-approved for the treatment of nasal polyps. In May 2020, the moderate-to-severe atopic dermatitis indication was expanded to include pediatric patients 6 to 11 years of age, making the current indication for patients aged 6 years and older. In October 2021, the moderate-to-severe asthma indication was also expanded to include pediatric patients 6 to 11 years of age, making the current indication for patients aged 6 years and older. In May 2022, the FDA approved a new indication of treatment of eosinophilic esophagitis (EoE) in adults and pediatric patients 12 years and older weighing at least 40 kilograms. Dupilumab was the first FDA-approved treatment for EoE. This indication was expanded in January 2024 to include pediatric patients down to the age of 1 year and weighing at least 15 kg. In June 2022, the moderate-to-severe atopic dermatitis indication was again expanded to include pediatric patients 6 months of age

and older. In September 2022, the FDA approved a new indication of treatment of adult patients with prurigo nodularis (PN). Dupilumab is the first FDA-approved treatment for PN. The National Comprehensive Cancer Network (NCCN) guidelines on the Management of Immunotherapy-Related-Toxicities include dupilumab as a consideration for the management of refractory cases of immunotherapy-related severe (Grade 3) pruritus.

Atopic Dermatitis

Atopic dermatitis (AD), also known as atopic eczema, is a chronic, pruritic inflammatory dermatosis affecting up to 25% of children and 1 to 5% of adults. AD follows a relapsing course and is associated with elevated serum immunoglobulin (IgE) levels and a personal or family history of type I allergies, allergic rhinitis, and/or asthma. Onset is most common between 3 and 6 months of age, with approximately 60% of patients developing the eruption in the first year of life and 90% by age 5. While the majority of affected individuals have resolution of disease by adulthood, 10 to 30% do not, and a smaller percentage first develop symptoms as adults. AD has a complex pathogenesis involving genetic, immunologic, and environmental factors, which lead to a dysfunctional skin barrier and dysregulation of the immune system. Clinical findings include erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and lichenification. These clinical findings vary by patient age and chronicity of lesions. Pruritus is a hallmark of the condition that is responsible for much of the disease burden borne by patients and their families. Typical patterns include facial, neck and extensor involvement in infants and children; flexure involvement in any age group, with sparing of groin and axillary regions.

Goals of treatment are to reduce symptoms (pruritus and dermatitis), prevent exacerbations, and minimize therapeutics risks. Despite its relapsing and remitting nature, the majority of patients with AD can achieve clinical improvement and disease control with nonpharmacological interventions (e.g., emollient use, wet wrap therapy), conventional topical therapies (including corticosteroids and calcineurin inhibitors) and environmental and occupational modifications, when necessary.

Topical therapies remain the mainstay of treatment due to their proven track record and generally favorable safety profile. They can be utilized individually or in combination with other topical, physical, and/or systemic treatments; as different classes of treatment have different mechanisms of action, combining therapies allows for the targeting of AD via multiple disease pathways. The American Academy of Dermatology (AAD) strongly recommends the following topical agents:

- Calcineurin inhibitors (TCIs) (e.g., tacrolimus, pimecrolimus)
- Topical corticosteroids (TCS)
- Topical PDE-4 inhibitors (e.g., crisaborole)
- Topical JAK inhibitors (e.g., ruxolitinib)

Targeting a variety of immune cells and suppressing the release of proinflammatory cytokines, TCS are the most commonly utilized FDA-approved therapies in AD and are commonly used as first-line treatment for mild-to severe dermatitis in all skin regions. When choosing a steroid potency, it is important to consider the anatomical site (i.e., using lower potency agents on the face, neck, genitals, and body folds). Most studies of TCS in AD management involve twice daily application, but some studies (particularly for potent TCS) suggest once daily use may be sufficient. Traditionally, TCS were

stopped once AD signs and symptoms of an AD flare were controlled. Maintenance in between AD flares with once to twice weekly use of TCS is another approach. TCIs are a safe anti-inflammatory option for AD, particularly when there is concern for adverse events secondary to corticosteroid use. Topical tacrolimus has shown flare prevention and disease control when used intermittently from 2 to 3 times per week in in patients with stable disease. Prescribing information for pimecrolimus cream and tacrolimus ointment indicate evaluation after 6 weeks if symptoms of AD do not improve for adults and pediatrics.

When AD is more severe or refractory to topical treatment, advanced treatment with phototherapy or systemic medications can be considered. Phototherapy is conditionally recommended by the AAD as a treatment for AD based on low certainty evidence. The AAD strongly recommends the following systemic therapies:

- Monoclonal antibodies (biologics) (e.g., dupilumab, tralokinumab)
- JAK inhibitors (e.g., upadacitinib, abrocitinib, baricitinib)

In a change from the 2014 AAD AD guidelines the use of systemic antimetabolites such as methotrexate, immunosuppressants such as systemic corticosteroids, mycophenolate mofetil, azathioprine, and cyclosporine are now conditionally recommended for AD only in a small number of select patients due to low or very low certainty of evidence and need for monitoring. The most favored first-line systemic is dupilumab.

There is no clear consensus on how to operationalize a definition of the FDA indication for treatment of patients with "moderate to severe" AD. The severity of AD can vary substantially over time and, from a patient's perspective, can include a complex combination of intensity of itch, location, body surface area (BSA) involvement, and degree of skin impairment. Given the variability of patient phenotype and lack of familiarity among clinicians with scoring systems used in clinical trials, it is advisable to create a broad clinically relevant definition inclusive of multiple specific measures of disease intensity for example:

- One of the following:
    - Affected BSA greater than or equal to 10%
    - Investigator Global Assessment (IGA) greater than or equal to 3
    - Eczema Area and Severity Index (EASI) greater than or equal to 16

    OR

- One of the following:
    - Affected BSA greater than or equal to 10%
    - Involvement of body sites that are difficult to treat with prolonged topical corticosteroid therapy (e.g., hands, feet, face, neck, scalp, genitals/groin, skin folds)
    - Severe itch that has been unresponsive to topical therapies

<u>Efficacy</u>

Dupilumab was FDA approved through two randomized, double-blind, placebo-controlled phase 3 trials (SOLO 1 and SOLO 2). All patients in both trials were at least 18 years old, had chronic AD (according to

American Academy of Dermatology Consensus Criteria Eichenfield 2014) that had been present for at least 3 years, and had ≥10% body surface area (BSA) involvement at the screening and baseline visits. Additionally, all patients had a documented recent history (within 6 months before the screening visit) of inadequate response to treatment with topical medications (defined as failure to achieve and maintain remission or a low disease activity state despite treatment with a daily regimen of topical corticosteroids of medium to higher potency applied for ≥28 days or for the maximum duration recommended by the product prescribing information [e.g., 14 days for super-potent topical corticosteroids], whichever is shorter), or whom topical treatments are otherwise medically inadvisable. The primary outcome measure in both trails was proportion of patients with both IGA (Investigator Global Assessment) 0 to 1 (on a 5-point scale) and a reduction from baseline of ≥2 points at week 16. There were several secondary endpoints included. Some examples include proportion of patients with Eczema Area and Severity Index (EASI) -75 (≥75% improvement from baseline) at week 16, percent change from baseline to week 16 in pruritus numerical rating scale (NRS), change from baseline to week 16 in % BSA, and changes in quality of life, anxiety, and depression.

The manufacturer reports the following results from SOLO 1 and SOLO 2. In SOLO 1, the primary outcome (an IGA of 0-1 and a reduction of ≥2 points from baseline at week 16) occurred in 85 patients (38%) who received dupilumab every other week and in 83 (37%) who received dupilumab weekly, as compared with 23 (10%) who received placebo (P<0.001 for both comparisons with placebo). The results were similar in SOLO 2, with the primary outcome occurring in 84 patients (36%) who received dupilumab every other week and in 87 (36%) who received dupilumab weekly, as compared with 20 (8%) who received placebo (P<0.001 for both comparisons). In addition, in the two trials, an improvement from baseline to week 16 of at least 75% on the Eczema Area and Severity Index was reported in significantly more patients who received each regimen of dupilumab than in patients who received placebo (P<0.001 for all comparisons). Dupilumab was also associated with improvement in other clinical end points, including reduction in pruritus and symptoms of anxiety or depression and improvement in quality of life.

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 AD and a minimum BSA involvement of ≥10%. Eligible subjects enrolled into this trial had previous inadequate response to topical medication. 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 Q2W for 16 weeks. Subjects with baseline weight of ≥60 kg received an initial dose of 600 mg at Week 0, followed by 300 mg Q2W for 16 weeks. Subjects were permitted to receive rescue treatment at the discretion of the investigator. Subjects who received rescue treatment were considered non-responders. 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. Other evaluated outcomes included the proportion of subjects with EASI-75 or EASI-90 (improvement of at least 75% or 90% in EASI from baseline, respectively), and reduction in itch as measured by the Peak Pruritus NRS (≥4-point improvement).

The efficacy results at Week 16 were as follows:

- IGA 0 or 1: 24% for Dupixent and 2% for placebo
- EASI-75: 42% for Dupixent and 8% for placebo

- EASI-90: 23% for Dupixent and 2% for placebo
- Peak Pruritus NRS (≥4-point improvement): 37% for Dupixent and 5% for placebo

Asthma

Asthma is a chronic inflammatory disorder of the airways. It is characterized by variable and recurring clinical symptoms, airflow obstruction, bronchial hyperresponsiveness, and underlying inflammation. Symptoms of asthma include wheezing, coughing, recurrent difficulty breathing, shortness of breath, and chest tightness. Generally, these symptoms will occur or worsen with exposure to allergens and irritants, infections, exercise, changes in weather, stress, or menstrual cycles. Guidelines recommend the use of detailed medical history, physical examination, and spirometry to make a diagnosis of asthma.

The Global Initiative for Asthma (GINA) guidelines recommend a stepwise approach for managing asthma. Long-term goals for asthma management are to achieve good control of symptoms, maintain normal activity level, and to minimize the future risk of exacerbations, fixed airflow limitation, and side-effects. IgE is the antibody responsible for activation of allergic reactions and is important to the pathogenesis of allergic asthma and the development and persistence of inflammation. GINA guidelines define moderate asthma as that which is well controlled with Step 3 or Step 4 treatment (e.g., low- or medium-dose inhaled corticosteroids [ICS] in combination with a long-acting beta agonist [LABA] in either treatment track). Severe asthma is defined as asthma that remains uncontrolled despite optimized treatment with high-dose ICS-LABA, or that requires high-dose ICS-LABA to prevent it from becoming uncontrolled. Severe asthma must be distinguished from asthma that is difficult to treat due to inadequate or inappropriate treatment, or persistent problems with adherence or comorbidities such as chronic rhinosinusitis or obesity, as they need very different treatment compared with if asthma is relatively refractory to high-dose ICS-LABA or even oral corticosteroids (OCS). Early initiation of low dose ICS in patients with asthma has led to greater improvement in lung function than initiation of ICS after symptoms have been present for more than 2 to 4 years. The 2023 GINA guidelines recommend every adult and adolescent with asthma should receive ICS-containing controller medication to reduce the risk of serious exacerbation, even in patients with infrequent symptoms.

2023 GINA STEP recommendations for adults and adolescents (12 years of age and over) are intended to reduce the risk of serious exacerbations and are broken into two tracks based on reliever therapy.

Track 1 is the preferred approach recommended by GINA, because using low dose ICS-formoterol as reliever reduces the risk of exacerbations compared with regimens with short-acting β2-agonist (SABA) as reliever, and is a simpler regimen. Note ICS-formoterol should not be used as the reliever by patients taking any other (non-formoterol) ICS-LABA or ICS-LAMA:

- Step 1:
  - As-needed low dose ICS-formoterol
- Step 2:
  - As-needed low dose ICS-formoterol
- Step 3: address and treat modifiable risk factors (e.g., adherence, technique) before considering step up

    - Maintenance: low dose ICS-formoterol
    - Reliever: as-needed low dose ICS-formoterol
- Step 4:
    - Maintenance: medium dose ICS-formoterol
    - Reliever: as-needed low dose ICS-formoterol
- Step 5: patients with uncontrolled symptoms and/or exacerbations despite Step 4 treatment should be assessed for contributory factors, have their treatment optimized, and be referred for expert assessment including severe asthma phenotype, and potential add on treatment
    - Maintenance: consider high dose ICS-formoterol
    - Reliever: as-needed low dose ICS-formoterol
    - Add-on LAMA for patients greater than or equal to 18 years (greater than or equal to 6 years for tiotropium) in separate or combination inhalers
    - Refer for phenotypic assessment +/- biologic therapy
        - Add-on anti-IgE for severe allergic asthma
        - SC omalizumab in patients greater than or equal to 6 years
        - Add-on anti-interleukin (IL)5 or anti-IL5R or anti-IL4R for severe eosinophilic/Type 2 asthma
        - Anti-IL5: SC mepolizumab for patients greater than or equal to 6 years OR IV reslizumab for patients greater than or equal to 18 years of age
        - Anti-IL5R: SC benralizumab for patients greater than or equal to 12 years
        - Anti-IL4R: SC dupilumab for patients greater than or equal to 6 years
    - Add-on anti-thymic stromal lymphopoietin (TSLP) for severe asthma
        - SC tezepelumab for patients greater than or equal to 12 years
    - Add-on azithromycin three days/week reduces exacerbations, but increases antibiotic resistance
    - Maintenance oral corticosteroids (OCS) should be used only as last resort, because short-term and long-term systemic side-effects are common and serious

Track 2 is an alternative approach if Track 1 is not possible or is not preferred by a patient with no exacerbations on their current therapy. Before considering a regimen with SABA reliever, the clinician should consider whether the patient is likely to be adherent with their controller therapy; if not, they will be exposed to the higher risk of exacerbations with SABA-only treatment:

- Step 1:
    - Take ICS whenever SABA taken
    - Reliever: as-needed ICS-SABA or as needed SABA
- Step 2:
    - Preferred maintenance: low dose ICS

- Preferred reliever: as-needed ICS-SABA or as-needed SABA
- Alternative options with limited indications, or less evidence for efficacy and/or safety:
  - Low dose ICS whenever SABA taken
  - Daily LTRA. These are less effective than daily ICS, particularly for preventing exacerbations and there is a US FDA boxed warning about the risk of serious mental health effects with montelukast
- Daily low-dose ICS-LABA as initial therapy leads to faster improvement in symptoms and FEV1 than ICS alone but is costlier, and the reduction in exacerbations compared with SABA is similar to that with ICS
- For adults with rhinitis who are allergic to house dust mite and have FEV1 > 70% predicted, consider adding sublingual immunotherapy (SLIT)

- Step 3: address and treat modifiable risk factors (e.g., adherence, technique) before considering step up
  - Preferred maintenance: low dose ICS-LABA
  - Preferred reliever: as-needed ICS-SABA or as-needed SABA
  - Alternative options:
    - Medium dose ICS
    - Low-dose ICS plus LTRA but review US FDA boxed warning
  - For adults with rhinitis who are allergic to house dust mite and have FEV1 > 70% predicted, consider adding SLIT
- Step 4:
  - Preferred maintenance: medium/high dose ICS-LABA
  - Preferred reliever: as-needed ICS-SABA or as-needed SABA
  - Alternative options:
    - Add-on LAMA for patients greater than or equal to 18 years (greater than or equal to 6 years for tiotropium my mist inhaler)
    - Before considering add-on LAMA for patients with exacerbations, increase ICS dose to at least medium
    - For adults with rhinitis who are allergic to house dust mite and have FEV1 > 70% predicted, consider adding sublingual immunotherapy (SLIT)
- Step 5: patients with uncontrolled symptoms and/or exacerbations despite Step 4 treatment should be assessed for contributory factors, have their treatment optimized, and be referred for expert assessment including severe asthma phenotype, and potential add on treatment
  - Maintenance: medium/high dose ICS-LABA

- Reliever: as-needed ICS-SABA or as-needed SABA
- Add-on LAMA for patients greater than or equal to 18 years (greater than or equal to 6 years for tiotropium) in separate or combination inhalers
- Refer for phenotypic assessment +/- biologic therapy
- Add-on anti-IgE for severe allergic asthma
  - SC omalizumab in patients greater than or equal to 6 years
- Add-on anti-interleukin (IL)5 or anti-IL5R or anti-IL4R for severe eosinophilic/Type 2 asthma
  - Anti-IL5: SC mepolizumab for patients greater than or equal to 6 years OR IV reslizumab for patients greater than or equal to 18 years of age
  - Anti-IL5R: SC benralizumab for patients greater than or equal to 12 years
  - Anti-IL4R: SC dupilumab for patients greater than or equal to 6 years
- Add-on anti-thymic stromal lymphopoietin (TSLP) for severe asthma
  - SC tezepelumab for patients greater than or equal to 12 years
- Add-on azithromycin three days/week reduces exacerbations, but increases antibiotic resistance
- Maintenance OCS should only be used as last resort, because short-term and long-term systemic side-effects are common and serious

2023 GINA STEP recommendations for children (6 to 11 years of age) are intended to reduce the risk of serious exacerbations:

- Step 1:
  - Low dose ICS taken whenever SABA taken
  - Reliever: as needed SABA
- Step 2
  - Preferred: daily low dose ICS
  - Preferred reliever: as needed SABA
  - Alternative options:
    - Low-dose ICS whenever SABA is taken using separate inhalers
    - Daily LTRA are less effective for exacerbation reduction. Advise parents about US FDA warning on montelukast
- Step 3: after checking inhaler technique and adherence, and treating modifiable risk factors (any of the following):
  - Medium-dose ICS maintenance plus as-needed SABA
  - Low-dose ICS-LABA maintenance plus as-needed SABA
  - Maintenance and reliever therapy (MART) with a very low dose of budesonide-formoterol DPI

- Step 4: Individual children's responses vary, so each of the Step 3 options may be tried before considering a step-up to Step 4. Refer for expert advice
    - Preferred: medium dose ICS-LABA plus as-needed SABA
    - Preferred: low dose ICS-formoterol MART plus as-needed low-dose ICS-formoterol
    - Alternative options:
        - Add-on tiotropium
        - Add-on LTRA
- Step 5:
    - Refer for phenotypic assessment with or without higher dose ICS-LABA
    - Reliever: as needed SABA (or ICS-formoterol reliever for MART)
    - Add on therapy with anti-IgE or anti-IL4R, anti-IL5
    - As a last resort consider add on low dose OCS but consider side effects

Severe Asthma Phenotype and Eosinophilic Asthma Subphenotype

Roughly 3% to 10% of adults with asthma have severe asthma as defined by the GINA 2023 guidelines. The European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines (2014; updated 2020) and the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group mirror the GINA definition of severe asthma, and defined uncontrolled asthma for adult and pediatric patients 5 years of age and over:

- Frequent severe exacerbations (i.e., two or more bursts of systemic corticosteroids within the past 12 months)
- Serious exacerbations (i.e., at least one hospitalization, intensive care unit stay, or mechanical ventilation in the past 12 months)
- Airflow limitation (i.e., FEV1 less than 80% predicted)
- Asthma that worsens upon tapering of high-dose ICS or systemic corticosteroids

A specialist, preferably in a multidisciplinary severe asthma clinic (if available) performs further assessment, which includes the patient’s inflammatory phenotype (i.e., Type 2 or non-Type 2).

Type 2 inflammation is characterized by the presence of cytokines such as interleukin (IL)-4, IL-5, and IL-13, which are often produced by the adaptive immune system on recognition of allergens. It is also characterized by eosinophilia or increased fraction of exhaled nitric oxide (FeNO) and may be accompanied by atopy. In many patients with asthma, Type 2 inflammation rapidly improves when ICS are taken regularly and correctly; this is classified as mild or moderate asthma. In severe asthma, Type 2 inflammation may be relatively refractory to high dose ICS. Type 2 inflammation is considered refractory if any of the following are found while the patient is taking high dose ICS or daily OCS:

- Blood eosinophils greater than or equal to 150 cells/microliter

- FeNO greater than or equal to 20 ppb
- Sputum eosinophils greater than or equal to 2%
- Asthma is clinically allergen-driven

Biologic agents should be considered as add-on therapy for patients with refractory Type 2 inflammation with exacerbations or poor symptom control despite taking at least high dose ICS/LABA, and who have allergic or eosinophilic biomarkers or need maintenance OCS. 2023 GINA recommends the biologics below based on patient eligibility factors:

- Anti-IgE (omalizumab):
  - Sensitization on skin prick testing or specific IgE
  - Total serum IgE and weight within dosage range
  - Exacerbations in the last year
- Anti-IL5/Anti-IL5R (benralizumab, mepolizumab, reslizumab):
  - Exacerbations in the last year
  - Blood eosinophils greater than or equal to 150 cells/microliter (for benralizumab and mepolizumab) or greater than or equal to 300 cells/microliter (for reslizumab)
- Anti-IL4R (dupilumab):
  - Exacerbations in the last year
  - Blood eosinophil greater than or equal to 150 cells/microliter but less than or equal to 1500 cells/microliter, or FeNO greater than or equal to 25 ppb, or taking maintenance OCS
- Anti-TSLP (tezepelumab):
  - Exacerbations in the last year

Patient response should be evaluated 4 months after initiating therapy and follow up should occur every 3 to 6 months thereafter. 2023 GINA recommends the following step-down therapy process in patients responding well to targeted biologic therapy:

- Reevaluate the need for each asthma medication every 3 to 6 months, but inhaled therapy should not be completely stopped
- Oral treatments: gradually decreased starting with OCS due to significant adverse effects.
- Inhaled treatments: consider reducing ICS dose after 3 to 6 months, but do not completely stop inhaled therapy. Continue at least medium dose ICS and remind patients of the importance of continued inhaled controller therapy.

Biologic treatments: trial withdrawal after 12 months of treatment and only if patient's asthma remains well controlled on medium dose ICS, and for allergic asthma, there is no further exposure to a previous allergic trigger.

<u>Efficacy</u>

The asthma development program included three randomized, double-blind, placebo controlled, parallel-group, multi-center trials (AS Trials 1, 2, and 3) of 24 to 52 weeks in treatment duration which enrolled a total of 2888 subjects (12 years of age and older). Subjects enrolled in AS Trials 1 and 2 were required to have a history of 1 or more asthma exacerbations that required treatment with systemic corticosteroids or emergency department visit or hospitalization for the treatment of asthma in the year prior to trial entry. Subjects enrolled in AS Trial 3 required dependence on daily oral corticosteroids in addition to regular use of high-dose inhaled corticosteroids plus an additional controller(s). In all 3 trials, subjects were enrolled without requiring a minimum baseline blood eosinophil count. In AS Trials 2 and 3 subjects with screening blood eosinophil level of >1500 cells/mcL (<1.3%) were excluded. Dupixent was administered as add-on to background asthma treatment. Subjects continued background asthma therapy throughout the duration of the studies, except in AS Trial 3 in which OCS dose was tapered as described below.

AS Trial 1 was a 24-week dose-ranging study which included 776 subjects (18 years of age and older). Dupixent compared with placebo was evaluated in adult subjects with moderate to severe asthma on a medium or high-dose inhaled corticosteroid and a long-acting beta agonist. Subjects were randomized to receive either 200 mg (N=150) or 300 mg (N=157) Dupixent every other week (Q2W) or 200 mg (N=154) or 300 mg (N=157) Dupixent every 4 weeks following an initial dose of 400 mg, 600 mg or placebo (N=158), respectively. The primary endpoint was mean change from baseline to Week 12 in FEV1 (L) in subjects with baseline blood eosinophils ≥300 cells/mcL. Other endpoints included percent change from baseline in FEV1 and annualized rate of severe asthma exacerbation events during the 24-week placebo-controlled treatment period. Results were evaluated in the overall population and subgroups based on baseline blood eosinophil count (≥300 cells/mcL and <300 cells/mcL. Additional secondary endpoints included responder rates in the patient reported Asthma Control Questionnaire (ACQ-5) and Asthma Quality of Life Questionnaire, Standardized Version (AQLQ(S)) scores.

AS Trial 2 was a 52-week study which included 1902 subjects (12 years of age and older). Dupixent compared with placebo was evaluated in 107 adolescents and 1795 adult subjects with moderate-to-severe asthma on a medium or high-dose inhaled corticosteroid (ICS) and a minimum of one and up to two additional controller medications. Subjects were randomized to receive either 200 mg (N=631) or 300 mg (N=633) Dupixent Q2W (or matching placebo for either 200 mg [N=317] or 300 mg [N=321] Q2W) following an initial dose of 400 mg, 600 mg or placebo respectively. The primary endpoints were the annualized rate of severe exacerbation events during the 52-week placebo-controlled period and change from baseline in pre-bronchodilator FEV1 at Week 12 in the overall population (unrestricted by minimum baseline blood eosinophils count). Additional secondary endpoints included annualized severe exacerbation rates and FEV1 in patients with different baseline levels of blood eosinophils as well as responder rates in the ACQ-5 and AQLQ(S) scores.

AS Trial 3 was a 24-week oral corticosteroid-reduction study in 210 subjects with asthma who required daily oral corticosteroids in addition to regular use of high dose inhaled corticosteroids plus an additional controller. After optimizing the OCS dose during the screening period, subjects received 300 mg Dupixent (N=103) or placebo (N=107) once Q2W for 24 weeks following an initial dose of 600 mg or placebo. Subjects continued to receive their existing asthma medicine during the study; however, their OCS dose was reduced every 4 weeks during the OCS reduction phase (Week 4-20), as long as asthma control was maintained. The primary endpoint was the percent reduction of oral corticosteroid dose at Weeks 20 to 24 compared with the baseline dose, while maintaining asthma control in the overall

population (unrestricted by minimum baseline blood eosinophils count). Additional secondary endpoints included the annualized rate of severe exacerbation events during treatment period and responder rate in the ACQ-5 and AQLQ(S) scores.

AS Trials 1 and 2 evaluated the frequency of severe asthma exacerbations defined as deterioration of asthma requiring the use of systemic corticosteroids for at least 3 days or hospitalization or emergency room visit due to asthma that required systemic corticosteroids. In the primary analysis population (subjects with baseline blood eosinophil count of ≥300 cells/mcL in AS Trial 1 and the overall population in AS Trial 2), subjects receiving either Dupixent 200 mg or 300 mg Q2W had significant reductions in the rate of asthma exacerbations compared to placebo. In the overall population in AS Trial 2, the rate of severe exacerbations was 0.46 and 0.52 for Dupixent 200 mg Q2W and 300 mg Q2W, respectively, compared to matched placebo rates of 0.87 and 0.97. The rate ratio of severe exacerbations compared to placebo was 0.52 (95% CI: 0.41, 0.66) and 0.54 (95% CI: 0.43, 0.68) for Dupixent 200 mg Q2W and 300 mg Q2W, respectively.

Prespecified subgroup analyses of AS Trials 1 and 2 demonstrated that there were greater reductions in severe exacerbations in subjects with higher baseline blood eosinophil levels. In AS Trial 2, reductions in exacerbations were significant in the subgroup of subjects with baseline blood eosinophils ≥ 150 cells/mcL. In subjects with baseline blood eosinophil count < 150 cells/mcL, similar severe exacerbation rates were observed between Dupixent and placebo.

Significant increases in pre-bronchodilator FEV1 were observed at Week 12 for AS Trials 1 and 2 in the primary analysis populations (subjects with baseline blood eosinophil count of ≥ 300 cells/mcL in AS Trial 1 and the overall population in AS Trial 2). In the overall population in AS Trial 2, the FEV1 LS mean change from baseline was 0.32 L (21%) and 0.34 L (23%) for Dupixent 200 mg Q2W and 300 mg Q2W, respectively, compared to matched placebo means of 0.18 L (12%) and 0.21 L (14%). The mean treatment difference versus placebo was 0.14 L (95% CI: 0.08, 0.19) and 0.13 L (95% CI: 0.08, 0.18) for Dupixent 200 mg Q2W and 300 mg Q2W, respectively. Subgroup analysis of AS Trials 1 and 2 demonstrated greater improvement in subjects with higher baseline blood eosinophils.

Chronic Rhinosinusitis with Nasal Polyposis

Chronic rhinosinusitis with nasal polyposis (CRSwNP) is an inflammatory condition affecting the paranasal sinuses. The International Consensus Statement on Allergy and Rhinology: Rhinosinusitis indicates that the diagnostic criteria for chronic rhinosinusitis (CRS) consist of ALL the following:

- Symptoms greater than or equal to 12 weeks
- Two of the following symptoms:
    - Nasal discharge (rhinorrhea or post-nasal drainage)
    - Nasal obstruction or congestion
    - Hyposmia (loss or decreased sense of smell)
    - Facial pressure or pain
- One or more of the following findings:
    - Evidence of inflammation on nasal endoscopy or computed tomography

- Evidence of purulence coming from paranasal sinuses or ostiomeatal complex

Sinus computed tomography (CT) and/or nasal endoscopy are needed to determine the presence of sinonasal inflammation and nasal polyps. The exact cause of CRSwNP is unknown, but biopsies of nasal polyps have shown elevated levels of eosinophils.

Intranasal corticosteroids (INCS) are recommended in the guidelines for CRSwNP. There are several formulations of INCS and it is recommended that clinicians must help each patient arrive at management decision consistent with that patient's values and preferences as no formulation is recommended over another. For patients using INCS for at least 4 weeks and who continue to have high disease burden, biologics are preferred over other medical treatment choices. Biologics vary in their magnitude of benefits and harms and certainty of evidence across outcomes. Dupilumab and omalizumab are the most beneficial for most patient important outcomes when comparing with other biologics, followed by mepolizumab. Other management options for CRSwNP that patients and their caregivers could consider include saline rinse, surgery, antibiotics, and for people with aspirin (non-steroidal anti-inflammatory)-exacerbated respiratory disease consider using aspirin therapy after desensitization.

Efficacy

Two randomized, double-blind, parallel-group, multicenter, placebo-controlled studies (CSNP Trial 1 and CSNP Trial 2) evaluated Dupixent in CRSwNP. There were 724 subjects aged 18 years and older on background intranasal corticosteroids (INCS) included in the trials. These studies included subjects with CRSwNP despite prior sinonasal 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. 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 sinonasal outcome test (SNOT-22). In the pooled efficacy results, the reduction in the proportion of subjects rescued with systemic corticosteroids and/or sinonasal surgery (up to Week 52) were evaluated.

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. In both studies, significant improvements in nasal congestion were observed as early as the first assessment at Week 4. A significant decrease in the LMK sinus CT scan score was observed. Dupilumab significantly improved the loss of smell compared to placebo. In both studies, significant improvements in daily loss of smell severity were observed as early as the first assessment at Week 4. Dupilumab significantly decreased sinonasal symptoms as measured by SNOT-22 compared to placebo.

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 sinonasal 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

Eosinophilic Esophagitis (EoE) is an allergen/immune-mediated disease characterized by symptoms of esophageal dysfunction and marked eosinophilic inflammation of the esophageal mucosa in the absence of secondary causes. EoE has dramatically increased in prevalence over the years. EoE is characterized by symptoms related to esophageal dysfunction and histologically with eosinophil-predominant inflammation (a peak count of greater than or equal to 15 eosinophils per high-power field on esophageal biopsy). Atopic and allergic inflammatory conditions commonly occur concomitantly with EoE.

The symptoms of EoE are age dependent. Young children may refuse to eat, have decreased appetite, recurring abdominal pain, trouble swallowing, and vomiting. Young adults and adults have the same symptoms, but often struggle to swallow dry or dense, solid foods due to inflammation. Food impaction is a common cause for emergency room visits in patients with EoE. Patients may also have concurrent gastroesophageal reflux disease (GERD). EoE is a progressive disease if left untreated. The chronic inflammation can lead to tissue fibrosis and strictures in the esophagus that require esophageal dilation.

The diagnosis of EoE is suspected on the basis of chronic symptoms such as dysphagia, food impaction, food refusal, failure to progress with food introduction, heartburn, regurgitation, vomiting, chest pain, odynophagia, abdominal pain, and malnutrition. Due to the wide range of chronic symptoms, the diagnosis should be highly considered in the presence of concomitant atopic conditions and if there are endoscopic findings. Endoscopic findings associated with EoE include esophageal rings, longitudinal furrows, exudates, edema, strictures, or narrow caliber esophagus. Assessment of non-EoE disorders and esophageal biopsy are required to confirm the diagnosis of EoE, with at least 15 eosinophils (eos)/ high-power field (hpf) present on esophageal biopsy.

The American Gastroenterology Association (AGA) and the Joint Task Force on Allergy-Immunology Practice Parameters (JTF) guideline for the management of EoE strongly recommend the use of topical corticosteroids for the treatment of EoE. Studies showed that topical budesonide or topical fluticasone induced histological remission significantly better than placebo and had similar adverse events to placebo. The AGA/JTF conditionally recommend continuing topical corticosteroids for maintenance therapy once remission is achieved. Dilation is only conditionally recommended for patients with dysphagia associated with strictures due to EoE, noting that the dilation does not address the underlying inflammation.

Efficacy

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 EoE (NCT03633617). In both parts, subjects were randomized to receive 300 mg Dupixent every week or placebo. Eligible subjects had greater than or equal to 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 less than or equal to 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 less than or equal to 6 eos/hpf) compared to placebo (Part A: 25% vs 2%; Part B: 47% vs 5%). Treatment with Dupixent also resulted in a significant improvement in LS mean change in DSQ score compared to placebo at week 24 (Part A: -21.9 vs -9.6; Part B -23.8 vs -13.9). 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

Prurigo nodularis (PN) is a skin disorder that is defined by the presence of chronic pruritus and multiple elevated, firm, and nodular lesions. PN is more common in older adults but can occur in children. The underlying cause of PN is unknown, but it appears neural and immunologic processes both play a role in its development. The nodules form in a subset of patients that have chronic pruritus, with the nodules forming in areas with continuous scratching over prolonged periods of time. There is significant disease burden associated with PN including sleep disruption, anxiety, and depression. The nodules are typically firm, dome-shaped, and itchy and range in size from millimeters to several centimeters. The nodules can range in color from flesh tones to brown/black and can range in number from a few to hundreds. The pruritis associated with PN can range from sporadic to continuous and generally the underlying cause is unknown. There are a number of conditions, both dermatologic and other diseases, that are associated with PN, such as atopic dermatitis, kidney disease, diabetes, and HIV.

The diagnosis of PN is generally one of exclusion. The American Academy of Dermatology (AAD) indicates that the diagnostic workup should include a clinical examination with a complete review of systems and assessment of PN severity, which should include both disease burden (e.g., quality of life, sleep disturbances) and pruritis intensity. The ADD notes three core features associated with PN:

- Presence of firm, nodular lesions
- Pruritus that lasts for at least 6 weeks
- History and/or signs of repeated scratching, picking, or rubbing

Management requires a multifaceted approach with a focus on controlling the underlying pruritis. Topical therapies are initial therapy for limited disease. Topical therapies include topical and intralesional corticosteroids. Topical calcineurin inhibitors and topical calcipotriol have been used but have not been adequately studied. Phototherapy is used in patients with more widespread and refractory PN. Systemic therapies include cyclosporine and methotrexate and are generally used in patients with widespread, refractory disease that does not respond to phototherapy.

Efficacy

The prurigo nodularis (PN) development program included two 24-week randomized, double-blind, placebo-controlled, multicenter, parallel-group trials (PRIME [NCT04183335] and PRIME 2 [NCT04202679]) in 311 adult subjects 18 years of age and older with pruritus (WINRS greater than or equal to 7 on a scale of 0 to 10) and greater than or equal to 20 nodular lesions. PRIME and PRIME 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.

At baseline, the mean Worst Itch-Numeric Rating Scale (WI-NRS) was 8.5, 66% had 20 to 100 nodules (moderate), and 34% had greater than 100 nodules (severe). Patients were required to have failed at least a 2-week trial of a medium to super potent topical corticosteroid or topical corticosteroids were not medically advised. 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 greater than or equal to 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. Overall, patients treated with Dupixent saw improvement in all endpoints over placebo.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore,

coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of dupilumab (Dupixent) **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "8"):

1. **ONE** of the following ("a", "b", or "c"):
    a. The member has been treated with dupilumab (starting on samples is not approvable) within the past 90 days
    b. The prescriber states the member has been treated with dupilumab (starting on samples is not approvable) within the past 90 days **AND** is at risk if therapy is changed
    c. Dupilumab will be used for the treatment of an indication listed in the Table, and **ALL** of the indication-specific criteria are met
2. **EITHER** of the following if the member has an FDA-approved indication ("a" or "b"):
    a. The member's age is within FDA labeling for the requested indication for dupilumab
    b. The prescriber has provided information in support of using dupilumab for the member's age for the requested indication
3. If the member has a diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP), **BOTH** of the following ("a" and "b'):
    a. The member is currently treated with standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids)
    b. The member will continue standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids) in combination with dupilumab
4. If the member has a diagnosis of moderate-to-severe asthma, **ALL** of the following ("a", "b", and "c"):
    a. **ONE** of the following ("i", "ii", "iii", or "iv"):
        i. The member is **NOT** currently being treated with the requested agent **AND** is currently treated with a maximally tolerated inhaled corticosteroid after at least a 3-month duration of therapy
        ii. The member is currently being treated with dupilumab, **AND ONE** of the following:
            - Is currently treated with an inhaled corticosteroid after at least a 3-month duration of therapy that is adequately dosed to control symptoms
            - Is currently treated with a maximally tolerated inhaled corticosteroid after at least a 3-month duration of therapy
        iii. The member has an intolerance or hypersensitivity to inhaled corticosteroid therapy
        iv. The member has an FDA labeled contraindication to ALL inhaled corticosteroids
    b. **ONE** of the following ("i", "ii", or "iii"):
        i. The member is currently being treated after at least a 3-month duration of therapy with **ONE** of the following:

- A long-acting beta-2 agonist (LABA)
- Long-acting muscarinic antagonist (LAMA)
- A leukotriene receptor antagonist (LTRA)
- Theophylline

ii. The member has an intolerance or hypersensitivity to therapy with long-acting beta-2 agonists (LABA), long-acting muscarinic antagonists (LAMA), leukotriene receptor antagonist (LTRA), or theophylline

iii. The member has an FDA labeled contraindication to **ALL** long-acting beta-2 agonists (LABA) AND long-acting muscarinic antagonists (LAMA)

c. The member will continue asthma control therapy (e.g., ICS, ICS/LABA, LTRA, LAMA, theophylline) in combination with the requested agent

5. The prescriber is a specialist in the area of the member's diagnosis (e.g., atopic dermatitis and prurigo nodularis - dermatologist, allergist, immunologist; asthma - allergist, immunologist, pulmonologist; CRSwNP -otolaryngologist, allergist, pulmonologist), **OR** the prescriber has consulted with a specialist in the area of the member's diagnosis
6. The member does **NOT** have any FDA labeled contraindications to Dupixent
7. The member will **NOT** be using dupilumab in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
8. **ONE** of the following ("a" or "b"):
   a. The requested quantity (dose) does **NOT** exceed the following based on indication and the member's age and weight:
      i. Atopic dermatitis
         - Adults (18 years of age and older)
            - Loading dose: 600 mg [two 300 mg injections] as a single dose (Week 0)
            - Subsequent doses: 300 mg every two weeks starting at Week 2
               - QL: 300 mg/2 mL pre-filled syringe - 2 syringes (4 mL) per 28 days
               - QL: 300 mg/2 mL pre-filled pen injector - 2 pens (4 mL) per 28 days
         - Pediatric members (6 months to 17 years of age)
            - Weight of 5 kg to less than 15 kg: 200 mg every four weeks (no loading dose)
               - QL: 200 mg/1.14 mL pre-filled syringe - 1 syringe (1.14 mL) per 28 days
               - QL: 200 mg/1.14 mL pre-filled pen injector - 1 pen (1.14 mL) per 28 days
            - Weight of 15 kg to less than 30 kg (6 months to 5 years of age): 300 mg every four weeks (no loading dose)
               - QL: 300 mg/2 mL pre-filled syringe - 1 syringe (2 mL) per 28 days

        - QL: 300 mg/2 mL pre-filled pen injector - 1 pen (2 mL) per 28 days
    - Weight of 15 kg to less than 30 kg (6 to 17 years of age)
        - Loading dose: 600 mg [two 300 mg injections] as a single dose (Week 0)
        - Subsequent doses: 300 mg every four weeks starting at Week 4
            - QL: 300 mg/2 mL pre-filled syringe - 1 syringe (2 mL) per 28 days
            - QL: 300 mg/2 mL pre-filled pen injector - 1 pen (2 mL) per 28 days
    - Weight of 30 kg to less than 60 kg
        - Loading dose: 400 mg [two 200 mg injections] as a single dose (Week 0)
        - Subsequent doses: 200 mg every two weeks starting at Week 2
            - QL: 200 mg/1.14 mL pre-filled syringe - 2 syringes (2.28 mL) per 28 days
            - QL: 200 mg/1.14 mL pre-filled pen injector - 2 pens (2.28 mL) per 28 days
    - Weight of 60 kg or more
        - Loading dose: 600 mg [two 300 mg injections] as a single dose (Week 0)
        - Subsequent doses: 300 mg every two weeks starting at Week 2
            - QL: 300 mg/2 mL pre-filled syringe - 2 syringes (4 mL) per 28 days
            - QL: 300 mg/2 mL pre-filled pen injector - 2 pens (4 mL) per 28 days

ii. Chronic rhinosinusitis with nasal polyposis - 300 mg every two weeks (no loading dose)
- QL: 300 mg/2 mL pre-filled syringe - 2 syringes (4 mL) per 28 days
- QL: 300 mg/2 mL pre-filled pen injector - 2 pens (4 mL) per 28 days

iii. Eosinophilic esophagitis
- Weight of 15 kg to less than 30 kg - 200 mg every two weeks (no loading dose)
    - QL: 200 mg/1.14 mL pre-filled syringe - 2 syringes (2.28 mL) per 28 days
    - QL: 200 mg/1.14 mL pre-filled pen injector - 2 pens (2.28 mL) per 28 days
- Weight of 30 kg to less than 40 kg - 300 mg every two weeks (no loading dose)
    - QL: 300 mg/2 mL pre-filled syringe - 2 syringes (4 mL) per 28 days
    - QL: 300 mg/2 mL pre-filled pen injector - 2 pens (4 mL) per 28 days
- Weight of 40 kg or more - 300 mg every week (no loading dose)
    - QL: 300 mg/2 mL pre-filled syringe - 4 syringes (8 mL) per 28 days
    - QL: 300 mg/2 mL pre-filled pen injector - 4 pens (8 mL) per 28 days

iv. Moderate-to-severe asthma
- 12 years of age and older:
    - Loading dose: 600 mg as a single dose (Week 0)
    - Subsequent doses: 300 mg every two weeks starting at Week 2

- QL: 300 mg/2 mL pre-filled syringe - 2 syringes (4 mL) per 28 days
- QL: 300 mg/2 mL pre-filled pen injector – 2 pens (4 mL) per 28 days

- 6 to 11 years of age (no loading dose):
  - Weight of 15 kg to less than 30 kg: 100 mg every other week, **OR** 300 mg every four weeks
    - QL: 100 mg/0.67 mL pre-filled syringe - 2 syringes (1.34 mL) per 28 days
    - QL: 300 mg/2 mL pre-filled syringe - 1 syringe (2 mL) per 28 days
    - QL: 300 mg/2 mL pre-filled pen injector – 1 pen (2 mL) per 28 days
  - Weight of 30 kg or greater: 200 mg every other week
    - QL: 200 mg/1.14 mL pre-filled syringe - 2 syringes (2.28 mL) per 28 days
    - QL: 200 mg/1.14 mL pre-filled pen injector - 2 pens (2.28 mL) per 28 days

v. Prurigo nodularis

- Loading dose: 600 mg [two 300 mg injections] as a single dose (Week 0)
- Subsequent doses: 300 mg every two weeks starting at Week 2
  - QL: 300 mg/2 mL pre-filled syringe - 2 syringes (4 mL) per 28 days
  - QL: 300 mg/2 mL pre-filled pen injector - 2 pens (4 mL) per 28 days

OR

b. The requested quantity (dose) exceeds the program quantity limit but does **NOT** exceed the maximum FDA labeled dose **OR** the maximum compendia-supported dose (i.e., DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a) for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit

Table

Indications and Specific Criteria	
Indication	**Specific Criteria**
Moderate-to-severe atopic dermatitis (AD)	When **ALL** of the following are met ("1" to "4"): 1. **ONE** of the following ("a", "b", "c", or "d"): a. The member has at least 10% body surface area involvement **OR** b. The member has involvement of body sites that are difficult to treat with prolonged topical corticosteroid therapy (e.g., hands, feet, face, neck, scalp, genitals/groin, skin folds)

	OR c. The member has an Eczema Area and Severity Index (EASI) score of greater than or equal to 16 **OR** d. The member has an Investigator Global Assessment (IGA) score of greater than or equal to 3 **AND** 2. **EITHER** of the following ("a" or "b"): a. **BOTH** of the following ("i" and "ii"): i. **ONE** of the following: • The member has tried and had an inadequate response to at least a mid-potency topical steroid used after at least a 4-week duration of therapy **OR** • The member has an intolerance or hypersensitivity to at least a mid-potency topical steroid **AND** ii. **ONE** of the following: • The member has tried and had an inadequate response to a topical calcineurin inhibitor (e.g., Elidel/pimecrolimus, Protopic/tacrolimus) used after at least a 6-week duration of therapy **OR** • The member has an intolerance or hypersensitivity to a topical calcineurin inhibitor **OR** b. The member has an FDA labeled contraindication to **ALL** mid-, high-, and super-potency topical steroids, **AND** topical calcineurin inhibitors **AND** 3. The prescriber has documented the member's baseline (prior to therapy with dupilumab) pruritus and other symptom severity (e.g., erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and/or lichenification) **AND** 4. **BOTH** of the following:

	a. The member is currently treated with topical emollients and practicing good skin care **AND** b. The member will continue the use of topical emollients and good skin care practices in combination with the requested agent
Moderate-to-severe asthma	When **BOTH** of the following are met ("1" and "2"): 1. **ONE** of the following ("a" or "b"): a. The member has eosinophilic type asthma, **AND ONE** of the following: i. The member has a baseline (prior to therapy with dupilumab) blood eosinophilic count of 150 cells/microliter or higher while on high-dose inhaled corticosteroids or daily oral corticosteroids **OR** ii. The member has a fraction of exhaled nitric oxide (FeNO) of 20 parts per billion or higher while on high-dose inhaled corticosteroids or daily oral corticosteroids **OR** iii. The member has sputum eosinophils 2% or higher while on high-dose inhaled corticosteroids or daily oral corticosteroids **OR** b. The member has oral corticosteroid dependent type asthma **AND** 2. The member has a history of uncontrolled asthma while on asthma control therapy as demonstrated by **ONE** of the following: a. Frequent severe asthma exacerbations requiring two or more courses of systemic corticosteroids (steroid burst) within the past 12 months **OR** b. Serious asthma exacerbations requiring hospitalization, mechanical ventilation, or visit to the emergency room or urgent care within the past 12 months **OR** c. Controlled asthma that worsens when the doses of inhaled and/or systemic corticosteroids are tapered **OR**

	d. The member has baseline (prior to therapy with dupilumab) Forced Expiratory Volume (FEV1) that is less than 80% of predicted
Chronic rhinosinusitis with nasal polyposis (CRSwNP)	When **ALL** of the following are met ("1" to "5"): 1. The member has at least **TWO** of the following symptoms consistent with chronic rhinosinusitis (CRS): a. Nasal discharge (rhinorrhea or post-nasal drainage) b. Nasal obstruction or congestion c. Loss or decreased sense of smell (hyposmia) d. Facial pressure or pain **AND** 2. The member has had symptoms consistent with CRS for at least 12 consecutive weeks **AND** 3. The member's diagnosis was confirmed by **ONE** of the following ("a" or "b"): a. Anterior rhinoscopy or endoscopy **OR** b. Computed tomography (CT) of the sinuses **AND** 4. **ONE** of the following ("a" or "b"): a. **ONE** of the following: i. The member had an inadequate response to sinonasal surgery **OR** ii. The member is **NOT** a candidate for sinonasal surgery **OR** b. **ONE** of the following: i. The member has tried and had an inadequate response to oral systemic corticosteroids **OR** ii. The member has an intolerance or hypersensitivity to therapy with oral systemic corticosteroids **OR**

	iii. The member has an FDA labeled contraindication to **ALL** oral systemic corticosteroids **AND** 5. **ONE** of the following: a. The member has tried and had an inadequate response to intranasal corticosteroids (e.g., fluticasone, Sinuva) used after at least a 4-week duration of therapy **OR** b. The member has an intolerance or hypersensitivity to therapy with intranasal corticosteroids (e.g., fluticasone, Sinuva) **OR** c. The member has an FDA labeled contraindication to **ALL** intranasal corticosteroids
Eosinophilic esophagitis (EoE)	When **BOTH** of the following are met ("1" and "2"): 1. The member's diagnosis was confirmed by **ALL** of the following: a. Chronic symptoms of esophageal dysfunction **AND** b. Greater than or equal to 15 eosinophils per high-power field on esophageal biopsy **AND** c. Other causes that may be responsible for or contributing to symptoms and esophageal eosinophilia have been ruled out **AND** 2. **ONE** of the following: a. The member has tried and had an inadequate response to **ONE** standard corticosteroid therapy for EoE (i.e., budesonide suspension, budesonide nebulizer solution, fluticasone MDI swallowed) **OR** b. The member has an intolerance or hypersensitivity to standard corticosteroid therapy for EoE **OR** c. The member has an FDA-labeled contraindication to standard corticosteroid therapy for EoE **OR**

	d. The member has tried and had an inadequate response to **ONE** proton pump inhibitor (PPI) used in the treatment of EoE **OR** e. The member has an intolerance or hypersensitivity to PPI therapy used in the treatment of EoE **OR** f. The member has an FDA labeled contraindication to **ALL** PPI therapy used in the treatment of EoE
Prurigo nodularis (PN)	When **BOTH** of the following are met ("1" and "2"): 1. The member has **ALL** of the following features associated with PN: a. Presence of firm, nodular lesions **AND** b. Pruritus that has lasted for at least 6 weeks **AND** c. History and/or signs of repeated scratching, picking, or rubbing **AND** 2. **ONE** of the following: a. The member has tried and had an inadequate response to at least a mid-potency topical steroid after at least a 2-week duration of therapy **OR** b. The member has an intolerance or hypersensitivity to therapy with at least a mid-potency topical steroid **OR** c. The member has an FDA-labeled contraindication to **ALL** mid-, high-, and super-potency topical steroids
Other indications	The member has another FDA-approved indication for subcutaneous dupilumab **OR** an indication supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium 1 or 2a recommended use for subcutaneous dupilumab
Approval duration: 6 months* *Please approve initial loading dose for asthma (age 12 years and older), atopic dermatitis, and prurigo nodularis ONLY	

- 300 mg strength requested: 600 mg (two 300 mg injections) followed by maintenance dose
- 200 mg strength requested: 400 mg (two 200 mg injections) followed by maintenance dose

Continuation of dupilumab (Dupixent) **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "6"):

1. An authorization or reauthorization for dupilumab has been previously approved by Florida Blue [Note: members not previously approved for the requested agent will require initial evaluation review]
2. **ONE** of the following:
    a. The member has a diagnosis of moderate-to-severe atopic dermatitis, **AND BOTH** of the following:
        i. The member has had a reduction or stabilization from baseline (prior to therapy with dupilumab) of **ONE** of the following:
            - Affected body surface area
            - Flares
            - Pruritus, erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and/or lichenification
            - A decrease in the Eczema Area and Severity Index (EASI) score
            - A decrease in the Investigator Global Assessment (IGA) score

        AND

        ii. The member will continue standard maintenance therapies (e.g., topical emollients, good skin care practices) in combination with dupilumab

    OR

    b. The member has a diagnosis of moderate to severe asthma, **AND BOTH** of the following:
        i. The patient has had improvements or stabilization with dupilumab from baseline (prior to therapy with dupilumab) as indicated by **ONE** of the following:
            - The member has had an increase in percent predicted Forced Expiratory Volume (FEV1)
            - The member has had a decrease in the dose of inhaled corticosteroids required to control the patient's asthma
            - The member has had a decrease in need for treatment with systemic corticosteroids due to exacerbations of asthma
            - The member has had a decrease in number of hospitalizations, need for mechanical ventilation, or visits to urgent care or emergency room due to exacerbations of asthma

        AND

        ii. The member is currently treated and is compliant with asthma control therapy [e.g., inhaled corticosteroids, ICS/long-acting beta-2 agonist (LABA), leukotriene receptor antagonist (LTRA), long-acting muscarinic antagonist (LAMA), theophylline]

OR

c. The member has a diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP), **AND BOTH** of the following:

   i. The member has had clinical benefit with dupilumab

   ii. The member will continue standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids) in combination with dupilumab

   OR

d. The member has another FDA approved indication for subcutaneous dupilumab **AND** has had clinical benefit with dupilumab

   OR

e. The member has another indication that is supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium 1 or 2a recommended use for subcutaneous dupilumab **AND** has had clinical benefit with dupilumab

3. The prescriber is a specialist in the area of the member's diagnosis (e.g., atopic dermatitis and prurigo nodularis - dermatologist, allergist, immunologist; asthma - allergist, immunologist, pulmonologist; CRSwNP - otolaryngologist, allergist, pulmonologist), **OR** the prescriber has consulted with a specialist in the area of the member's diagnosis
4. The member does **NOT** have any FDA-labeled contraindications to Dupixent
5. The member will **NOT** be using dupilumab in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
6. **ONE** of the following ("a" or "b"):

   a. The requested quantity (dose) does **NOT** exceed the following based on indication and the member's age and weight:

      i. Atopic dermatitis

         - Adults (18 years of age and older): 300 mg every two weeks starting at Week 2
         - QL: 300 mg/2 mL pre-filled syringe - 2 syringes (4 mL) per 28 days
         - QL: 300 mg/2 mL pre-filled pen injector - 2 pens (4 mL) per 28 days
         - Pediatric members (6 months to 17 years of age)
            - Weight of 5 kg to less than 15 kg: 200 mg every four weeks (no loading dose)
               - QL: 200 mg/1.14 mL pre-filled syringe - 1 syringe (1.14 mL) per 28 days
               - QL: 200 mg/1.14 mL pre-filled pen injector - 1 pen (1.14 mL) per 28 days
            - Weight of 15 kg to less than 30 kg (6 months to 5 years of age): 300 mg every four weeks (no loading dose)

        - QL: 300 mg/2 mL pre-filled syringe - 1 syringe (2 mL) per 28 days
        - QL: 300 mg/2 mL pre-filled pen injector - 1 pen (2 mL) per 28 days
    - Weight of 15 kg to less than 30 kg (6 to 17 years of age): 300 mg every four weeks starting at Week 4
        - QL: 300 mg/2 mL pre-filled syringe - 1 syringe (2mL) per 28 days
        - QL: 300 mg/2 mL pre-filled pen injector - 1 pen (2 mL) per 28 days
    - Weight of 30 kg to less than 60 kg: 200 mg every two weeks starting at Week 2
        - QL: 200 mg/1.14 mL pre-filled syringe - 2 syringes (2.28 mL) per 28 days
        - QL: 200 mg/1.14 mL pre-filled pen injector - 2 pens (2.28 mL) per 28 days
    - Weight of 60 kg or more: 300 mg every two weeks starting at Week 2
        - QL: 300 mg/2 mL pre-filled syringe - 2 syringes (4 mL) per 28 days
        - QL: 300 mg/2 mL pre-filled pen injector - 2 pens (4 mL) per 28 days

ii. Chronic rhinosinusitis with nasal polyposis - 300 mg every two weeks
    - QL: 300 mg/2 mL pre-filled syringe - 2 syringes (4 mL) per 28 days
    - QL: 300 mg/2 mL pre-filled pen injector - 2 pens (4 mL) per 28 days

iii. Eosinophilic esophagitis
    - Weight of 15 kg to less than 30 kg - 200 mg every two weeks (no loading dose)
        - QL: 200 mg/1.14 mL pre-filled syringe - 2 syringes (2.28 mL) per 28 days
        - QL: 200 mg/1.14 mL pre-filled pen injector - 2 pens (2.28 mL) per 28 days
    - Weight of 30 kg to less than 40 kg - 300 mg every two weeks (no loading dose)
        - QL: 300 mg/2 mL pre-filled syringe - 2 syringes (4 mL) per 28 days
        - QL: 300 mg/2 mL pre-filled pen injector - 2 pens (4 mL) per 28 days
    - Weight of 40 kg or more - 300 mg every week (no loading dose)
        - QL: 300 mg/2 mL pre-filled syringe - 4 syringes (8 mL) per 28 days
        - QL: 300 mg/2 mL pre-filled pen injector - 4 pens (8 mL) per 28 days

iv. Moderate-to-severe asthma
    - 12 years of age and older: 300 mg every two weeks starting at Week 2
        - QL: 300 mg/2 mL pre-filled syringe - 2 syringes (4 mL) per 28 days
        - QL: 300 mg/2 mL pre-filled pen injector – 2 pens (4 mL) per 28 days
    - 6 to 11 years of age
    - Weight of 15 kg to less than 30 kg: 100 mg every other week, **OR** 300 mg every four weeks
        - QL: 100 mg/0.67 mL pre-filled syringe - 2 syringes (1.34 mL) per 28 days
        - QL: 300 mg/2 mL pre-filled syringe - 1 syringe (2 mL) per 28 days

- QL: 300 mg/2 mL pre-filled pen injector – 1 pen (2 mL) per 28 days
- Weight of 30 kg or greater: 200 mg every other week
  - QL: 200 mg/1.14 mL pre-filled syringe - 2 syringes (2.28 mL) per 28 days
  - QL: 200 mg/1.14 mL pre-filled pen injector - 2 pens (2.28 mL) per 28 days

v. Prurigo nodularis

- Loading dose: 600 mg [two 300 mg injections] as a single dose (Week 0)
- Subsequent doses: 300 mg every two weeks starting at Week 2
  - QL: 300 mg/2 mL pre-filled syringe - 2 syringes (4 mL) per 28 days
  - QL: 300 mg/2 mL pre-filled pen injector - 2 pens (4 mL) per 28 days

OR

b. The requested quantity (dose) exceeds the program quantity limit but does **NOT** exceed the maximum FDA labeled dose **OR** the maximum compendia-supported dose (i.e., DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a) for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit

Approval duration: 12 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

Atopic dermatitis

- For the treatment of adult and pediatric 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. Dupilumab can be used with or without topical corticosteroids. Dupilumab is administered by subcutaneous injection. A member may self-inject after training in subcutaneous injection technique using the pre-filled syringe or pre-filled pen. The pre-filled pen is only for use in adults and adolescents aged 12 years and older. In adolescents 12 years of age and older, it is recommended that dupilumab be given by or under the supervision of an adult. Dupixent pre-filled syringe should be given by a caregiver in pediatric patients 6 months to 11 years of age. Before injection, the pre-filled syringe or pen should be removed from the refrigerator and allowed to reach room temperature (45 minutes for 300 mg and 30 min for 200 mg).
- The recommended dose in adults (18 years of age and older) is an initial dose of 600 mg (two 300 mg injections), followed by 300 mg given every other week (every 2 weeks). The recommended dose in pediatric and adolescent patients (6 to 17 years of age) is based on weight. For weight of 15 kg to less than 30 kg, the recommended dose is an initial dose of 600 mg (two 300 mg injections), followed by 300 mg given every four weeks. For weight of 30 kg to less than 60 kg, the recommended dose is an initial dose of 400 mg (two 200 mg injections), followed by 200 mg given every other week (every

2 weeks). For weight of 60 kg or more, the recommended dose is an initial dose of 600 mg (two 300 mg injections), followed by 300 mg given every other week (every 2 weeks). The recommended dose in patients 6 months to 5 years of age is also based on weight. For weight of 5 kg to less than 15 kg, the recommended dose is 200 mg given every four weeks. For weight of 15 kg to less than 30 kg, the recommended dose is 300 mg given every four weeks. Dupilumab can be used with or without topical corticosteroids. Topical calcineurin inhibitors may be used, but should be reserved for problem areas only, such as the face, neck, intertriginous and genital areas.

Asthma

- Indicated as an add-on maintenance treatment in patients aged 6 years and older with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma. The package label includes the following "Limitation of Use" statement - "Dupixent is not indicated for the relief of acute bronchospasm or status asthmaticus". Dupilumab is administered by subcutaneous injection. A member may self-inject after training in subcutaneous injection technique using the pre-filled syringe or pre-filled pen. The pre-filled pen is only for use in adults and adolescents aged 12 years and older. In adolescents 12 years of age and older, it is recommended that dupilumab be given by or under the supervision of an adult. Dupixent pre-filled syringe should be given by a caregiver in children 6 to 11 years of age. Before injection, the pre-filled syringe or pen should be removed from the refrigerator and allowed to reach room temperature (45 minutes for 300 mg and 30 min for 100 and 200 mg).
- The recommended dose for adults and adolescents (12 years of age and older) is:
    - An initial dose of 400 mg (two 200 mg injections) followed by 200 mg given every other week (every 2 weeks), **OR**
    - An initial dose of 600 mg (two 300 mg injections) followed by 300 mg given every other week (every 2 weeks).
    - For patients with oral corticosteroids-dependent asthma, or with co-morbid moderate-to-severe atopic dermatitis, start with an initial dose of 600 mg followed by 300 mg given every other week (every 2 weeks).
- The recommended dose for pediatric patients (6 to 11 years of age) is:
    - 15 to less than 30 kg - 100 mg every other week (every 2 weeks), **OR** 300 mg every four weeks
    - 30 kg or greater - 200 mg every other week (every 2 weeks).
    - No initial loading dose is recommended
    - For pediatric patients with asthma **AND** co-morbid moderate-to-severe atopic dermatitis, follow the recommended dosage for atopic dermatitis which includes an initial loading dose

Chronic Rhinosinusitis with Nasal Polyposis (CRSwNP)

- Indicated as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis.
- The recommended dose for adult patients is 300 mg given every other week (every 2 weeks).

Eosinophilic esophagitis (EoE)

- Indicated for the treatment of adult and pediatric patients aged 1 year and older, weighing at least 15 kg, with eosinophilic esophagitis.
- The recommended dosage is:
    - 15 to less than 30 kg - 200 mg every other week (every 2 weeks)

- 30 to less than 40 kg - 300 mg every other week (every 2 weeks)
- 40 kg or greater - 300 mg every week
- No initial loading dose is recommended

Prurigo Nodularis (PN)

- Indicated for the treatment of adult patients with prurigo nodularis.
- The recommended dose for adult patients is an initial dose of 600 mg (two 300 mg injections) followed by 300 mg given every other week (every 2 weeks)

Dose Adjustments

- No formal trial of the effect of hepatic or renal impairment on the pharmacokinetics of dupilumab was conducted

Drug Availability

- Carton containing two single-dose, pre-filled pens (300 mg/2 mL)
- Carton containing two single-dose, pre-filled syringes (300 mg/2 mL) with needle shield
- Carton containing two single-dose, pre-filled pens (200 mg/1.14 mL)
- Carton containing two single-dose, pre-filled syringes (200 mg/1.14 mL) with needle shield
- Carton containing two single-dose, pre-filled syringes (100 mg/0.67 mL) with needle shield
- Store refrigerated at 36°F to 46°F (2°C to 8°C) in the original carton to protect from light. If necessary, dupilumab may be kept at room temperature up to 77°F (25°C) for a maximum of 14 days.

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Known hypersensitivity to dupilumab or any of its excipients

Precautions/Warnings

- **Hypersensitivity** - Hypersensitivity reactions, including anaphylaxis, serum sickness or serum sickness-like reactions, angioedema, generalized urticaria, rash, erythema nodosum, and erythema multiforme have been reported. If a clinically significant hypersensitivity reaction occurs, discontinue dupilumab immediately and initiate appropriate therapy.
- **Conjunctivitis and Keratitis** - Conjunctivitis and keratitis adverse reactions have been reported in clinical trials. Conjunctivitis and keratitis occurred more frequently in atopic dermatitis subjects who received dupilumab. Among asthma subjects the frequency of conjunctivitis was similar to placebo. In subjects with CRSwNP, the frequency of conjunctivitis was 2% in the dupilumab group vs. 1% in the

placebo group in the 24-week safety pool; these subjects recovered. There were no cases of keratitis reported in the CRSwNP development program. Among subjects with EoE, there were no reports of conjunctivitis and keratitis in the dupilumab group in placebo-controlled trials. In subjects with PN, the frequency of conjunctivitis was 4% in the dupilumab group compared to 1% in the placebo group; these subjects recovered or were recovering during the treatment period. There were no cases of keratitis reported in the PN development program. Members should report new onset or worsening eye symptoms to their healthcare provider. Consider ophthalmological examination for patients who develop conjunctivitis that does not resolve following standard treatment or signs and symptoms suggestive of keratitis, as appropriate.

- **Eosinophilic Conditions** – Patients being treated for asthma may present with serious systemic eosinophilia sometimes presenting with clinical features of eosinophilic pneumonia or vasculitis consistent with eosinophilic granulomatosis with polyangiitis, conditions which are often treated with systemic corticosteroid therapy. These events may be associated with the reduction of oral corticosteroid therapy. Physicians should be alert to vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients with eosinophilia. Cases of eosinophilic pneumonia and cases of vasculitis consistent with eosinophilic granulomatosis with polyangiitis have been reported with dupilumab in adult patients who participated in the asthma development program. A causal association between dupilumab and these conditions has not been established.
- **Acute Asthma Symptoms or Deteriorating Disease** - Dupilumab should not be used to treat acute asthma symptoms or acute exacerbations. Do not use to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment.
- **Reduction of Corticosteroid Dosage** - do not discontinue systemic, topical, or inhaled corticosteroids abruptly upon initiation of therapy with dupilumab. Reductions in corticosteroid dose, if appropriate, should be gradual and performed under the direct supervision of a physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.
- **Patients with Comorbid Asthma** - advise atopic dermatitis or CRSwNP patients with comorbid asthma not to adjust or stop their asthma treatments without consultation with their physicians.
- **Arthralgia** - arthralgia has been reported with some patients reporting gait disturbances or decreased mobility associated with joint symptoms; some cases resulted in hospitalization. Advise patients to report new onset or worsening joint symptoms to their healthcare provider. If symptoms persist or worsen, consider rheumatological evaluation and/or discontinuation.
- **Parasitic (Helminth) Infections** – Patients with known helminth infections were excluded from participation in clinical studies. It is unknown if dupilumab will influence the immune response against helminth infections. Treat patients with pre-existing helminth infections before initiating therapy with dupilumab. If patients become infected while receiving treatment with dupilumab and do not respond to anti-helminth treatment, discontinue treatment with dupilumab until the infection resolves.
- **Vaccinations** - Consider completing all age-appropriate vaccinations as recommended by current immunization guidelines prior to initiating treatment with dupilumab. Avoid use of live vaccines in patients treated with dupilumab.
- **Interactions with CYP450 Substrates** - The formation of CYP450 enzymes can be altered by increased levels of certain cytokines; therefore, dupilumab could modulate the formation of CYP450

enzymes. Upon initiation or discontinuation of dupilumab in members receiving concomitant drugs which are CYP450 substrates, particularly those with a narrow therapeutic index, consider monitoring for effect (e.g., for warfarin) or drug concentration (e.g., for cyclosporine) and consider dosage modification of the CYP450 substrate.

- **Immunogenicity** - Approximately 6% of subjects with atopic dermatitis or asthma who received dupilumab for 52 weeks developed antibodies to dupilumab; approximately 2% exhibited persistent responses, and approximately 2% had neutralizing antibodies. Approximately 9% of subjects with asthma who received dupilumab for 52 weeks developed antibodies to dupilumab; approximately 4% exhibited persistent responses, and approximately 4% had neutralizing antibodies.
- **Pregnancy -** There are no available data on dupilumab use in pregnant women to inform any drug associated risk. Refer to the product label for more information.
- **Lactation** – There are no data on the presence of dupilumab in human milk, the effects on the breastfed infant, or the effects on milk production. Refer to the product label for more information.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J33.0 – J33.9	Nasal polyp
J45.40 – J45.42	Moderate persistent asthma
J45.50 – J45.52	Severe persistent asthma
J82.83	Eosinophilic asthma
K20.0	Eosinophilic esophagitis
L20.0	Besnier's prurigo
L20.81	Atopic neurodermatitis
L20.82	Flexural eczema
L20.84	Intrinsic (allergic) eczema
L20.89	Other atopic dermatitis
L20.9	Atopic dermatitis, unspecified
L28.1	Prurigo nodularis
L29.8	Other pruritus [for immunotherapy-related pruritus ONLY]
L29.9	Pruritus, unspecified [for immunotherapy-related pruritus ONLY]

ICD-10 Diagnosis Codes That Support Medical Necessity

J3590	Unclassified biologics

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

Eczema Area Severity Index score (EASI) - assesses severity (severity score) and body surface area affected by erythema, induration/papulation/edema, excoriations, and lichenification (area score), which are graded systematically for each of 4 anatomical regions (head and neck, trunk, upper limbs, lower limbs) and assembled in a composite score, with a score range of 0 to 72.

- EASI 50 - a percentage improvement of EASI score from baseline that is ≥50%
- EASI 75 - a percentage improvement of EASI score from baseline that is ≥75%
- EASI 90 - a percentage improvement of EASI score from baseline that is ≥90%

Eosinophilic esophagitis – a chronic, immune-mediated disease of the esophagus in which white blood cells called eosinophils build up in the esophagus. This causes damage and inflammation, which can cause pain and may lead to trouble swallowing.

FEV1 – forced expiratory volume in 1 second

FVC – forced vital capacity

Helper T cells (a.k.a., CD4+ T cells) – a type of lymphocyte or white blood cell (WBC) that matures in the thymus and play an important role in cell-mediated immunity. T helper cells assist other WBCs in immunologic processes by releasing T cell cytokines. Different types of T helper cells secrete different cytokines (e.g., type 2 release IL-4, IL-5, IL-9, IL-10 and IL-13)

Intertriginous area – an area where two skin areas may touch or rub together (e.g., axilla of the arm, the anogenital region, skin folds of the breasts, between digits)

Lichenified - skin that has become thickened and leathery. This often results from continuously rubbing or scratching the skin.

Patient-Oriented Eczema Measure (POEM) – a validated questionnaire, examining seven items (scored 0 to 4 based on frequency of event), used in clinical settings to assess time spent with symptoms and the impact of symptoms on sleep, with a score range of 0 to 28.

PEF – peak expiratory flow

Pruritus – itching

Scoring Atopic Dermatitis (SCORAD) - the extent and severity of AD over the body area and the severity of 6 specific symptoms (erythema, edema/papulation, excoriations, lichenification, oozing/crusts, and dryness) are assessed and scored by the investigator. Subjective assessment of itch and sleeplessness is

scored by the patient. The SCORAD score is a combined score of body area affected, and investigator and patient symptom scoring, with a score range of 0 to103.

RELATED GUIDELINES:

Abrocitinib (Cibinqo), 09-J4000-27
Benralizumab (Fasenra), 09-J2000-92
Mepolizumab (Nucala), 09-J2000-54
Omalizumab (Xolair), 09-J0000-44
Psoralens with Ultraviolet A (PUVA), 02-10000-16
Reslizumab (Cinqair) IV infusion, 09-J2000-63
Tezepelumab-ekko (Tezspire), 9-J4000-13
Tralokinumab-ldrm (Adbry), 09-J4000-20
Upadacitinib (Rinvoq), 09-J3000-51

OTHER:

Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy

Abrilada (adalimumab-afzb)
Actemra (tocilizumab)
Adalimumab
Adbry (tralokinumab-ldrm)
Amjevita (adalimumab-atto)
Arcalyst (rilonacept)
Avsola (infliximab-axxq)
Benlysta (belimumab)
Bimzelx (bimekizumab-bkzx)
Cimzia (certolizumab)
Cinqair (reslizumab)
Cosentyx (secukinumab)
Cyltezo (adalimumab-adbm)
Dupixent (dupilumab)
Enbrel (etanercept)
Entyvio (vedolizumab)
Fasenra (benralizumab)
Hadlima (adalimumab-bwwd)
Hulio (adalimumab-fkjp)
Humira (adalimumab)
Hyrimoz (adalimumab-adaz)
Idacio (adalimumab-aacf)
Ilaris (canakinumab)
Ilumya (tildrakizumab-asmn)
Inflectra (infliximab-dyyb)
Infliximab
Kevzara (sarilumab)

Kineret (anakinra)
Nucala (mepolizumab)
Omvoh (mirikizumab-mrkz)
Orencia (abatacept)
Remicade (infliximab)
Renflexis (infliximab-abda)
Riabni (rituximab-arrx)
Rituxan (rituximab)
Rituxan Hycela (rituximab/hyaluronidase human)
Ruxience (rituximab-pvvr)
Selarsdi (ustekinumab-aekn)
Siliq (brodalumab)
Simlandi (adalimumab-ryvk)
Simponi (golimumab)
Simponi Aria (golimumab)
Skyrizi (risankizumab-rzaa)
Spevigo (spesolimab-sbzo)
Stelara (ustekinumab)
Taltz (ixekizumab)
Tezspire (tezepelumab-ekko)
Tofidence ((tocilizumab-bavi)
Tremfya (guselkumab)
Truxima (rituximab-abbs)
Tyenne (tocilizumab-aazg)
Tyruko (natalizumab-sztn)
Tysabri (natalizumab)
Wezlana (ustekinumab-auub)
Xolair (omalizumab)
Yuflyma (adalimumab-aaty)
Yusimry (adalimumab-aqvh)
Zymfentra (infliximab-dyyb)

Mild Intermittent Asthma

- < or = to 2 times a week
- and normal PEF between exacerbations
- brief (from a few hours to a few days); intensity may vary
- symptoms < or = to 2 times a month
- or PEF > or = to 80% predicted
- variability < 20%

Mild Persistent Asthma

- > 2 times a week but < 1 time a day

- may affect activity
- symptoms > 2 times a month
- or PEF > or = to 80% predicted
- variability 20 to 30 %

Moderate Persistent Asthma

- symptoms
- symptoms > one time a week
- use of inhaled short-acting beta2-agonist
- may affect activity
- > or = to 2 times a week; may last days
- or PEF > 60% but less than 80% predicted
- variability > 30%

Severe Persistent Asthma

- symptoms (i.e., coughing, dyspnea, wheezing)
- physical activity
- exacerbations
- nighttime symptoms
- or PEF < or = 60% predicted
- variability > 30

Table 5: Definitions of Low, Medium, and High Daily Dose of Various Inhaled Corticosteroids in Adults and Adolescents (12 years of age and older)

Drug	Daily Dose (mcg)		
	Low	Medium	High
Beclomethasone dipropionate (CFC)	200 - 500	>500 – 1,000	>1,000
Beclomethasone dipropionate (HFA)	100 - 200	>200 - 400	>400
Budesonide DPI	200 - 400	>400 - 800	>800
Ciclesonide (HFA)	80 - 160	>160 - 320	>320
Fluticasone furoate (DPI)	100	N/A	200
Fluticasone propionate (DPI)	100 - 250	>250 - 500	>500
Fluticasone propionate (HFA)	100 - 250	>250 - 500	>500
Mometasone furoate	110 - 220	>220 - 440	>440
Triamcinolone acetonide	400 – 1,000	>1,000 – 2,000	>2,000

Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2019. Available from: www.ginaasthma.org.

REFERENCES:

1. Anderson K, Putterman E, Rogers RS, et al. Treatment of severe pediatric atopic dermatitis with methotrexate: A retrospective review. Pediatr Dermatol. 2019 Feb 27. [Epub ahead of print].
2. Ashcroft DM, Dimmock P, Garside R, et al. Efficacy and tolerability of topical pimecrolimus and tacrolimus in the treatment of atopic dermatitis: meta-analysis of randomised controlled trials. BMJ. 2005;330(7490):516.
3. Bachert C, Hellings PW, Mullol J, et al. Dupilumab improves health-related quality of life in patients with chronic rhinosinusitis with nasal polyposis. Allergy. 2019 Jul 15. [Epub ahead of print]
4. Bachert C, Mannent L, Naclerio RM, et al. Effect of Subcutaneous Dupilumab on Nasal Polyp Burden in Patients with Chronic Sinusitis and Nasal Polyposis: A Randomized Clinical Trial. JAMA. 2016 Feb 2;315(5):469-79.
5. Bieber T. Atopic dermatitis. Engl J Med. 2008 Apr 3;358(14):1483-94.
6. Blauvelt A, de Bruin-Weller M, Gooderham M, et al. Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial. Lancet. 2017 Jun 10;389(10086):2287-2303.
7. Castro M, Corren J, Pavord ID, et al. Dupilumab Efficacy and Safety in Moderate-to-Severe Uncontrolled Asthma. N Engl J Med. 2018 Jun 28;378(26):2486-2496.
8. 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.
9. Clinical Pharmacology powered by ClinicalKey [Internet]. Tampa, FL: Elsevier.; 2023. Available at: https://www.clinicalkey.com/pharmacology/. Accessed 10/24/23.
10. Cury Martins J, Martins C, Aoki V, et al. Topical tacrolimus for atopic dermatitis. Cochrane Database Syst Rev. 2015 Jul 1;(7):CD009864.
11. Davis DMR, Drucker AM, Alikhan A, et al. American Academy of Dermatology Guidelines: Awareness of comorbidities associated with atopic dermatitis in adults. J Am Acad Dermatol. 2022;86(6):1335-1336.e18.
12. Davis DMR, Drucker AM, Alikhan A, et al. Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies. J Am Acad Dermatol 2023;e1-e14.
13. Dellon ES, Liacouras CA, Molina-Infante J, et al. Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference. Gastroenterology 2018; 155:1022.
14. Drake LA, Dinehart SM, Farmer ER, et al: Guidelines of care for the use of topical glucocorticosteroids. J Am Acad Dermatol 1996; 35:615-619.
15. Dupixent (dupilumab injection) [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; January 2024.
16. Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis. Section 1. Diagnosis and assessment of atopic dermatitis. J Am Acad Dermatol. 2014 Feb;70(2):338-51.
17. 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; 84:747.
18. Fokkens WJ, Lund VJ, Mullol J, et al. European position paper on rhinosinusitis and nasal polyps 2012. Rhinol Suppl 2012;23: 1-298.
19. Galli E, Neri I, Ricci G, et al. Consensus Conference on Clinical Management of pediatric Atopic Dermatitis. Ital J Pediatr. 2016 Mar 2; 42:26.

20. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2023. Access 11/15/23 at www.ginasthma.org.
21. Hirano I, Chan ES, Rank MA, et al.; AGA Institute Clinical Guidelines Committee; Joint Task Force on Allergy-Immunology Practice Parameters. AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis. Gastroenterology. 2020 May;158(6):1776-1786.
22. Hirano I, Dellon ES, Hamilton JD, et al. Efficacy of Dupilumab in a Phase 2 Randomized Trial of Adults with Active Eosinophilic Esophagitis. Gastroenterology. 2020 Jan;158(1):111-122.e10. Epub 2019 Oct 5.
23. Institute For Clinical and Economic Review (ICER). JAK Inhibitors and Monoclonal Antibodies for the Treatment of Atopic Dermatitis: Effectiveness and Value. Final Evidence Report. August 2021. Updated February 2023.
24. International European Respiratory Society (ERS)/American Thoracic Society (ATS) Guidelines on Management of Severe Asthma. Eur Resp J. 2020; 55:1900588.
25. Jonstam K, Swanson BN, Mannent LP, et al. Dupilumab reduces local type 2 pro-inflammatory biomarkers in chronic rhinosinusitis with nasal polyposis. Allergy. 2019 Apr;74(4):743-752. Epub 2019 Jan 21.
26. Micromedex Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 10/24/23.
27. Mortz CG, Andersen KE, Dellgren C, et al. Atopic dermatitis from adolescence to adulthood in the TOACS cohort: prevalence, persistence and comorbidities. Allergy. 2015 Jul;70(7):836-45.
28. National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group. 2020 Focused updates to the asthma management guidelines. National Heart, Lung, and Blood Institute, 2007. Available at: https://www.nhlbi.nih.gov/health-topics/all-publications-and-resources/2020-focused-updates-asthma-management-guidelines
29. National Comprehensive Cancer Network. Cancer Guidelines. Cancer Guidelines and Drugs and Biologics Compendium. Accessed 10/24/23.
30. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Management of Immunotherapy-Related-Toxicities. Version 3.2023 - October 11, 2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf. Accessed 10/26/23.
31. Orlandi RR, Kingdom TT, Smith TL, et al. International consensus statement on rhinology and allergy: rhinosinusitis. Int Forum Allergy Rhinol. 2021; 11: 213-739.
32. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2023 [2023 Oct 24]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
33. O'Shea KM, Aceves SS, Dellon ES, Gupta SK, Spergel JM, Furuta GT, Rothenberg ME. Pathophysiology of Eosinophilic Esophagitis. Gastroenterology. 2018 Jan;154(2):333-345. Epub 2017 Jul 27.
34. Peters AT, Spector S, Hsu J, et al. Diagnosis and management of rhinosinusitis: a practice parameter update. Ann Allergy Asthma Immunol 2014; 113:347-85.
35. Rabe KF, Nair P, Brusselle G, et al. Efficacy and Safety of Dupilumab in Glucocorticoid-Dependent Severe Asthma. N Engl J Med. 2018 Jun 28;378(26):2475-2485.
36. Rank MA, Chu DK, Bognanni A, et al. The Joint Task Force on Practice Parameters GRADE guidelines for the medical management of chronic rhinosinusitis with nasal polyposis. J Allergy Clin Immunol. 2023 Feb;151(2):386-398. Epub 2022 Nov 9.

37. Ring J, Alomar A, Bieber T, et al; European Dermatology Forum (EDF), European Academy of Dermatology and Venereology (EADV), European Federation of Allergy (EFA), European Task Force on Atopic Dermatitis (ETFAD), European Society of Pediatric Dermatology (ESPD), Global Allergy and Asthma European Network (GA2LEN). Guidelines for treatment of atopic eczema (atopic dermatitis) part I. J Eur Acad Dermatol Venereol. 2012 Aug;26(8):1045-60.
38. Roekevisch E, Spuls PI, Kuester D, et al. Efficacy and safety of systemic treatments for moderate-to-severe atopic dermatitis: a systematic review. The Journal of allergy and clinical immunology. 2014;133(2):429-438.
39. Schmitt J, von Kobyletzki L, Svensson A, et al. Efficacy and tolerability of proactive treatment with topical corticosteroids and calcineurin inhibitors for atopic eczema: systematic review and meta-analysis of randomized controlled trials. Br J Dermatol. 2011;164(2):415.
40. Shaw TE, Currie GP, Koudelka CW, et al. Eczema prevalence in the United States: data from the 2003 National Survey of Children's Health. J Invest Dermatol. 2011;131(1):67.
41. Sidbury R, Alikhan A, Bercovitch L, et al. Guidelines of care for the management of atopic dermatitis in adults with topical therapies. J Am Acad Dermatol. 2023;89(1):e1-e20.
42. Sidbury R, Tom WL, Bergman JN, et al. Guidelines of care for the management of atopic dermatitis: Section 4. Prevention of disease flares and use of adjunctive therapies and approaches. J Am Acad Dermatol. 2014 Dec;71(6):1218-33.
43. Siegfried EC, Jaworski JC, Kaiser JD, et al. Systematic review of published trials: long-term safety of topical corticosteroids and topical calcineurin inhibitors in pediatric patients with atopic dermatitis. BMC Pediatr. 2016 Jun 7; 16:75.
44. Simpson EL, Bieber T, Guttman-Yassky E, et al. Two Phase 3 Trials of Dupilumab versus Placebo in Atopic Dermatitis. NEJM. 2016;375 (24):2335-2348.
45. Slater NA and Morrell DS. Systemic therapy of childhood atopic dermatitis. Clin Dermatol. 2015 May-Jun;33(3):289-99. Epub 2014 Dec 8.
46. Tsakok T and Flohr C. Methotrexate vs. ciclosporin in the treatment of severe atopic dermatitis in children: a critical appraisal. Br J Dermatol. 2014 Mar;170(3):496-8; discussion 498-9.
47. Totri CR, Eichenfield LF, Logan K, et al. Prescribing practices for systemic agents in the treatment of severe pediatric atopic dermatitis in the US and Canada: The PeDRA TREAT survey. J Am Acad Dermatol. 2017 Feb;76(2):281-285. Epub 2016 Nov 14.
48. 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 Jul 2;388(10039):31-44.
49. Wenzel S, Ford L, Pearlman D, et al. Dupilumab in persistent asthma with elevated eosinophil levels. N Engl J Med. 2013 Jun 27;368(26):2455-66.
50. Yang EJ, Sekhon S, Sanchez IM, et al. Recent Developments in Atopic Dermatitis. Pediatrics. 2018 Oct;142(4). pii: e20181102.
51. Zayed Y, Kheiri B, Banifadel M, et al. Dupilumab safety and efficacy in uncontrolled asthma: a systematic review and meta-analysis of randomized clinical trials. J Asthma. 2018 Oct 1:1-10.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 12/13/23.

GUIDELINE UPDATE INFORMATION:

06/15/17	New Medical Coverage Guideline.
01/15/18	Revision to the guideline consisting of updating the position statement in regard to the prerequisite requirements for members receiving systemic immunosuppressant therapy or phototherapy.
10/15/18	Review and revision to guideline consisting of updating the position statement, definitions, and references.
12/15/18	Revision to guideline consisting of updating the description, position statement, dosage/administration, precautions, coding/billing, related guidelines, and references based on the new FDA-approved indication for moderate to-severe asthma.
04/15/19	Revision to the guideline consisting of updating the description section, position statement, dosage/administration, and references based on the new FDA-approved indication for atopic dermatitis in adolescents.
05/15/19	Revision to guideline consisting of updating the description section, position statement, and references.
09/15/19	Review and revision to guideline consisting of updating the description section, position statement, dosage/administration, precautions, coding/billing, and references.
02/15/20	Revision to guideline consisting of updating the position statement.
07/15/20	Revision to guideline consisting of updating the description section, position statement, dosage/administration, and references based on a new FDA-approved expanded age for atopic dermatitis (ages 6 to 11 years).
10/01/20	Revision to guideline consisting of updating the position statement and billing/coding.
01/01/21	Review and revision to guideline consisting of updating the references.
02/15/21	Revision to guideline consisting of updating the position statement.
01/01/22	Review and revision to guideline consisting of updating the description, position statement, dosage/administration, billing/coding, and references.
02/15/22	Revision to guideline consisting of updating the description, position statement, other section, and references.
09/15/22	Revision to guideline consisting of updating the description, position statement, dosage/administration, precautions, related guidelines, and references based on a new FDA-approved indication for EoE and expanded age for atopic dermatitis (ages 6 months to 5 years).
10/15/22	Revision to guideline consisting of updating the position statement to include PPI therapy as a qualifying prerequisite treatment for EoE.
01/01/23	Review and revision to guideline consisting of updating the description, position statement, dosage/administration, billing/codling, and references based on the new FDA-approved indication of prurigo nodularis (PN). New drugs were added to the list of drugs that are not permitted for use in combination.
04/15/23	New drugs were added to the list of drugs that are not permitted for use in combination.
07/01/23	Revision to guideline consisting of updating the other section. Humira biosimilar products added to list of Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy.

01/01/24	Review and revision to guideline consisting of updating the description (asthma, atopic dermatitis, and NCCN info), position statement, billing/coding, other section, and references. Added additional parameters for diagnosis of “moderate-to-severe” atopic dermatitis and new parameter for diagnosis of CRSwNP. Clarified that standard of care requirements for asthma and CRSwNP apply to all members continuing treatment. Update to Table 1 in Position Statement. New drugs were added to the list of drugs that are not permitted for use in combination.
04/01/24	Revision to guideline consisting of updating the description section, position statement, dosage/administration, precautions, and references. Updated with expanded FDA-approved age for the treatment of eosinophilic esophagitis (EoE) and removal of the step requirement of a systemic immunosuppressant for AD (based on new AD guidelines).
04/25/24	Update to Position Statement.
07/01/24	Revision to guideline consisting of updating the position statement and other section. Drugs added to the list of Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy.