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Policy Number: 057.000

Title: Coverage Determination Policy for Dupilumab (Dupixent)

Regions: ☒ **Texas** ☐ **Florida** ☐ **Indiana** ☐ **New Jersey** ☒ **New Mexico**

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: A53127

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Doctors helping patients for more than 25 years

Title: Coverage Determination Policy for Dupilumab (Dupixent)

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Coverage Policy Number: 057.000

Line of Business: Medicare Part B

Policy Type: Prior Authorization

Coverage Determination

The following criteria are applicable to ALL indications in addition to indication specific criteria below:

All requests for subcutaneous dupilumab (Dupixent) must include documented medical justification as to why the patient is unable to self-administer subcutaneous doses. Requests for subcutaneous dupilumab should generally be covered under the member's pharmacy benefit

- Medicare rules expect that if a patient is clinically able to self-administer a drug and there is no clear medical justification to do otherwise. For example, an individual afflicted with paraplegia or advanced dementia would not have the capacity to self-administer any injectable drug. See the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals at http://www.cms.hhs.gov/manuals/Downloads/bp102c15.pdf
- The following factors are considered unrelated to medical decision making: 1. Patient convenience, 2. Patient co-pays and financial liability

Initial/New Requests

WellMed Medical Management will cover **dupilumab (Dupixent)** as medically necessary when **ALL** of the following are met:

1. **Asthma:**
   A. Diagnosis of moderate-to-severe asthma
   B. Classification of asthma as uncontrolled or inadequately controlled as defined by at least one of the following:
      I. Poor symptom control (frequent symptoms or reliever use, activity limited by asthma, night waking due to asthma)
      II. Two or more bursts of systemic corticosteroids for at least 3 days each in the previous 12 months
      III. Asthma-related emergency treatment (e.g., emergency room visit, hospital admission, or unscheduled physician's office visit for nebulizer or other urgent treatment)
      IV. Airflow limitation (e.g., after appropriate bronchodilator withhold forced expiratory volume in 1 second [FEV1] less than 80% predicted [in the face of reduced FEV1/forced vital capacity [FVC] defined as less than the lower limit of normal])
      V. Patient is currently dependent on oral corticosteroids for the treatment of asthma
   C. Documentation that asthma is an eosinophilic phenotype as defined by a baseline (pre-dupilumab treatment) peripheral blood eosinophil level ≥ 150 cells/µL OR currently dependent on oral corticosteroids for the treatment of asthma
   D. Dupixent will be used in combination with **ONE** of the following:
      I. One high dose (appropriately adjusted for age) combination inhaled corticosteroid (ICS)/long-acting beta2 agonist (LABA) [e.g., Advair/AirDuo Respiclick (fluticasone propionate/salmeterol), Symbicort (budesonide/formoterol), Breo Ellipta (fluticasone furoate/vilanterol)]
      II. Combination therapy including **BOTH** of the following:
         a. One high-dose (appropriately adjusted for age) ICS product [e.g., ciclesonide (Alvesco), mometasone furoate (Asmanex), beclomethasone dipropionate (QVAR)]
         b. One additional asthma controller medication [e.g., LABA - olodaterol (Striverdi) or indacaterol (Arcapta); leukotriene receptor antagonist – montelukast (Singulair); theophylline]
   E. Patient is **NOT** receiving Dupixent in combination with **ANY** of the following:
      I. Anti-interleukin-5 therapy [e.g., Nucala (mepolizumab), Cinqair (resilizumab), Fasenra (benralizumab)]
      II. Anti-IgE therapy [e.g., Xolair (omalizumab)]
      III. Thymic stromal lymphopoietin (TSLP) inhibitor [e.g., Tezspire (tezepelumab)]

2. **Atopic Dermatitis:**

A. Diagnosis of moderate-to-severe chronic atopic dermatitis
B. History of failure, contraindication, or intolerance to **TWO** of the following therapeutic classes of topical therapies:
    I. Medium to very-high potency topical corticosteroid [e.g., Elocon (mometasone furoate), Synalar (fluocinolone acetonide), Lidex (fluocinonide)]
    II. Topical calcineurin inhibitor [e.g., Elidel (pimecrolimus), Protopic (tacrolimus)].
    III. Eucrisa (crisaborole)
C. Patient is **NOT** receiving Dupixent in combination with another biologic medication (e.g. Adbry, Xolair)

3. **Chronic Rhinosinusitis with Nasal Polyposis:**
   A. Diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP) defined by **ALL** of the following:
      I. **TWO** or more of the following symptoms for longer than 12 weeks duration:
         a. Nasal mucopurulent discharge
         b. Nasal obstruction, blockage, or congestion
         c. Facial pain, pressure, and/or fullness
         d. Reduction or loss of sense of smell
      II. **ONE** of the following findings using nasal endoscopy and/or sinus computed tomography (CT):
         a. Purulent mucus or edema in the middle meatus or ethmoid regions
         b. Polyps in the nasal cavity or the middle meatus
         c. Radiographic imaging demonstrating mucosal thickening or partial or complete opacification of paranasal sinuses
      III. **ONE** of the following:
         a. Presence of bilateral nasal polyposis
         b. Patient has previously required surgical removal of bilateral nasal polyps
      IV. **ONE** of the following:
         a. Patient has required prior sinus surgery
         b. Patient has required systemic corticosteroids (e.g., prednisone, methylprednisolone) for CRSwNP in the previous 2 years
         c. Patient has been unable to obtain symptom relief after trial of two of the following classes of agents:
            i. Nasal saline irrigations
            ii. Intranasal corticosteroids (e.g., fluticasone, mometasone, triamcinolone)
            iii. Antileukotriene agents (e.g., montelukast, zafirlukast, zileuton)
   B. Patient will receive Dupixent as add-on maintenance therapy in combination with intranasal corticosteroids (e.g., fluticasone, mometasone, triamcinolone).
   C. Patient is **NOT** receiving Dupixent in combination with **ANY** of the following:
      I. Anti-interleukin-5 therapy [e.g., Cinqair (resilizumab), Fasenra (benralizumab), Nucala (mepolizumab)]
      II. Anti-IgE therapy [e.g., Xolair (omalizumab)]
      III. Thymic stromal lymphopoietin (TSLP) inhibitor [e.g., Tezspire (tezepelumab)]

4. **Eosinophilic Esophagitis:**
   A. Diagnosis of eosinophilic esophagitis
   B. Patient is experiencing symptoms related to esophageal dysfunction (e.g., dysphagia, food impaction, chest pain that is often centrally located and may not respond to antacids, gastroesophageal reflux disease-like symptoms/refractory heartburn, upper abdominal pain)
   C. Documentation of eosinophil-predominant inflammation on esophageal biopsy, consisting of a peak value of ≥15 intraepithelial eosinophils per high power field (HPF) (or 60 eosinophils per mm2)
   D. Secondary causes of esophageal eosinophilia have been ruled out
   E. Mucosal eosinophilia is isolated to the esophagus and symptoms have persisted after an 8-week trial of <u>at least one</u> of the following:
      I. Proton pump inhibitors (e.g., pantoprazole, omeprazole)
      II. Topical (esophageal) corticosteroids (e.g., budesonide, fluticasone)
   F. Patient weighs at least 40 kg
   G. Patient is **NOT** receiving Dupixent in combination with **ANY** of the following:
      I. Anti-interleukin-5 therapy [e.g., Cinqair (resilizumab), Fasenra (benralizumab), Nucala (mepolizumab)]
      II. Anti-IgE therapy [e.g., Xolair (omalizumab)]
      III. Thymic stromal lymphopoietin (TSLP) inhibitor [e.g., Tezspire (tezepelumab)]

5. **Prurigo Nodularis:**
   A. Diagnosis of prurigo nodularis
   B. Patient has greater than or equal to 20 nodular lesions
   C. History of failure, contraindication, or intolerance to previous prurigo nodularis treatment(s) (e.g., topical corticosteroids, topical calcineurin inhibitors, topical capsaicin)
   D. Patient is **NOT** receiving Dupixent in combination with another biologic medication [e.g., Adbry (tralokinumab), Xolair (omalizumab)]

Renewal/Continuation of Therapy Requests

1. **Asthma:** Documentation of positive clinical response to Dupixent therapy as demonstrated by at least one of the following:
    I. Reduction in the frequency of exacerbations
    II. Decreased utilization of rescue medications
    III. Increase in percent predicted FEV1 from pretreatment baseline
    IV. Reduction in severity or frequency of asthma-related symptoms (e.g., wheezing, shortness of breath, coughing, etc.)
    V. Reduction in oral corticosteroid requirements
    B. Dupixent is being used in combination with an ICS-containing controller medication
    C. Patient is not receiving Dupixent in combination with any of the following:
        I. Anti-interleukin-5 therapy [e.g., Nucala (mepolizumab), Cinqair (resilizumab), Fasenra (benralizumab)]
        II. Anti-IgE therapy [e.g., Xolair (omalizumab)]
        III. Thymic stromal lymphopoietin (TSLP) inhibitor [e.g., Tezspire (tezepelumab)]

2. **Atopic Dermatitis:**
    A. Documentation of positive clinical response to Dupixent therapy
    B. Patient is **NOT** receiving Dupixent in combination with another biologic medication [e.g., Adbry (tralokinumab), Xolair (omalizumab)]

3. **Chronic Rhinosinusitis with Nasal Polyposis:**
   A. Documentation of positive clinical response to Dupixent therapy
   B. Patient will continue to receive Dupixent as add-on maintenance therapy in combination with intranasal corticosteroids (e.g., fluticasone, mometasone, triamcinolone).
   C. Patient is **NOT** receiving Dupixent in combination with **ANY** of the following:
      I. Anti-interleukin-5 therapy [e.g., Cinqair (resilizumab), Fasenra (benralizumab), Nucala (mepolizumab)]
      II. Anti-IgE therapy [e.g., Xolair (omalizumab)]
      III. Thymic stromal lymphopoietin (TSLP) inhibitor [e.g., Tezspire (tezepelumab)]

4. **Eosinophilic Esophagitis:**
   A. Documentation of positive clinical response to Dupixent therapy as evidenced by improvement of <u>at least one</u> of the following from baseline:
      I. Symptoms (e.g., dysphagia, chest pain, heartburn)
      II. Histologic measures (e.g., esophageal intraepithelial eosinophil count)
      III. Endoscopic measures (e.g., edema, furrows, exudates, rings, strictures)
   B. Patient is **NOT** receiving Dupixent in combination with **ANY** of the following:
      I. Anti-interleukin-5 therapy [e.g., Cinqair (resilizumab), Fasenra (benralizumab), Nucala (mepolizumab)]
      II. Anti-IgE therapy [e.g., Xolair (omalizumab)]
      III. Thymic stromal lymphopoietin (TSLP) inhibitor [e.g., Tezspire (tezepelumab)]

5. **Prurigo Nodularis:**
   A. Documentation of positive clinical response to Dupixent therapy
   B. Patient is **NOT** receiving Dupixent in combination with another biologic medication [e.g., Adbry (tralokinumab), Xolair (omalizumab)]

FDA Approved Dose and Indication

Indication	Approved Dosing
Asthma	**Initial LD:** 400mg or 600mg **Maintenance:** 200mg (following 400mg LD) or 300mg (following 600mg LD) every 2 weeks
Corticosteroid-Dependent Asthma	**Initial LD:** 600mg **Maintenance:** 300mg every 2 weeks
Atopic Dermatitis	**Initial LD:** 600mg **Maintenance:** 300mg every 2 weeks
Chronic Rhinosinusitis with Nasal Polyposis	300mg every other week
Eosinophilic Esophagitis	300mg every week (patients >40kg)
Prurigo Nodularis	**Initial LD:** 600mg **Maintenance:** 300mg every 2 weeks

General Background

Dupixent (dupilumab) is an interleukin-4 receptor alpha antagonist indicated for treatment of patients aged 6 months and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent can be used with or without topical corticosteroids. Dupixent is also indicated as an add-on maintenance treatment in patients with moderate-to-severe asthma aged 6 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma, as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP), for the treatment of adult and pediatric patients aged 12 years and older, weighing at least 40 kg, with eosinophilic esophagitis (EoE), and for adult patients with prurigo nodularis (PN).

Clinical Evidence

Asthma

The asthma development program for patients aged 12 years and older included three randomized, double-blind, placebo-controlled, parallel-group, multicenter trials (DRI12544 (NCT01854047), QUEST (NCT02414854), and VENTURE (NCT02528214)) of 24 to 52 weeks in treatment duration which enrolled a total of 2888 subjects. Subjects enrolled in DRI12544 and QUEST 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 VENTURE 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 QUEST and VENTURE, 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 VENTURE in which OCS dose was tapered as described below.

DRI12544 was a 24-week dose-ranging study which included 776 adult 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.

QUEST was a 52-week study which included 1902 adult and pediatric subjects (12 years of age and older). DUPIXENT compared with placebo was evaluated in 107 pediatric subjects 12 to 17 years of age 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 subjects with different baseline levels of blood eosinophils as well as responder rates in the ACQ-5 and AQLQ(S) scores.

VENTURE was a 24-week oral corticosteroid-reduction study in 210 adult and pediatric subjects 15 years of age and older 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.

In the primary analysis population (subjects with baseline blood eosinophil count of ≥300 cells/mcL in DRI12544 and the overall population in QUEST), subjects receiving either DUPIXENT 200 mg or 300 mg Q2W had significant reductions in the rate of asthma exacerbations compared to placebo. Significant increases in pre-bronchodilator FEV1 were observed at Week 12 for DRI12544 and QUEST in the primary analysis populations. Compared with placebo, subjects receiving DUPIXENT achieved greater reductions in daily maintenance oral corticosteroid dose, while maintaining asthma control.

Atopic Dermatitis
Three randomized, double-blind, placebo-controlled trials (SOLO 1 (NCT02277743), SOLO 2 (NCT02277769), and CHRONOS (NCT02260986)) enrolled a total of 2119 adult subjects 18 years of age and older with moderate-to-severe AD not adequately controlled by topical medication(s). Disease severity was defined by an Investigator's Global Assessment (IGA) score ≥3 in the overall assessment of AD lesions on a severity scale of 0 to 4, an Eczema Area and Severity Index (EASI) score ≥16 on a scale of 0 to 72, and a minimum body surface area involvement of ≥10%. At baseline, 59% of subjects were male, 67% were White, 52% of subjects had a baseline IGA score of 3 (moderate AD), and 48% of subjects had a baseline IGA of 4 (severe AD). The baseline mean EASI score was 33 and the baseline weekly averaged Peak Pruritus Numeric Rating Scale (NRS) was 7 on a scale of 0-10.

In all three trials, subjects in the DUPIXENT group received subcutaneous injections of DUPIXENT 600 mg at Week 0, followed by 300 mg every other week (Q2W). In the monotherapy trials (SOLO 1 and SOLO 2), subjects received DUPIXENT or placebo for 16 weeks.

In the concomitant therapy trial (CHRONOS), subjects received DUPIXENT or placebo with concomitant topical corticosteroids (TCS) and as needed topical calcineurin inhibitors for problem areas only, such as the face, neck, intertriginous and genital areas for 52 weeks.

All three trials assessed the primary endpoint, the change from baseline to Week 16 in the proportion of subjects with an IGA 0 (clear) or 1 (almost clear) and at least a 2-point improvement. Other endpoints included the proportion of subjects with EASI-75 (improvement

of at least 75% in EASI score from baseline), and reduction in itch as defined by at least a 4-point improvement in the Peak Pruritus NRS from baseline to Week 16.

In CHRONOS, of the 421 subjects, 353 had been on study for 52 weeks at the time of data analysis. Of these 353 subjects, responders at Week 52 represent a mixture of subjects who maintained their efficacy from Week 16 (e.g., 53% of DUPIXENT IGA 0 or 1 responders at Week 16 remained responders at Week 52) and subjects who were non-responders at Week 16 who later responded to treatment (e.g., 24% of DUPIXENT IGA 0 or 1 non-responders at Week 16 became responders at Week 52).
Treatment effects in subgroups (weight, age, gender, race, and prior treatment, including immunosuppressants) in SOLO 1, SOLO 2, and CHRONOS were generally consistent with the results in the overall study population.

In SOLO 1, SOLO 2, and CHRONOS, a third randomized treatment arm of DUPIXENT 300 mg QW did not demonstrate additional treatment benefit over DUPIXENT 300 mg Q2W.

Subjects in SOLO 1 and SOLO 2 who had an IGA 0 or 1 with a reduction of ≥2 points were re-randomized into SOLO CONTINUE (NCT02395133). SOLO CONTINUE evaluated multiple DUPIXENT monotherapy dose regimens for maintaining treatment response. The study included subjects randomized to continue with DUPIXENT 300 mg Q2W (62 subjects) or switch to placebo (31 subjects) for 36 weeks. IGA 0 or 1 responses at Week 36 were as follows: 33 (53%) in the Q2W group and 3 (10%) in the placebo group.

Chronic Rhinosinusitis with Nasal Polyposis
The chronic rhinosinusitis with nasal polyposis (CRSwNP) development program included two randomized, double-blind, parallel-group, multicenter, placebo-controlled studies (SINUS-24 (NCT02912468) and SINUS-52 (NCT02898454)) in 724 adult subjects 18 years of age and older on background intranasal corticosteroids (INCS). These studies included subjects with CRSwNP despite prior sino-nasal surgery or treatment with, or who were ineligible to receive or were intolerant to, systemic corticosteroids in the past 2 years. Subjects 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 SINUS-24, 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 SINUS-52, 448 subjects were randomized to receive either 300 mg DUPIXENT (N=150) every other week for 52 weeks, 300 mg DUPIXENT (N=145) every other week until Week 24 followed by 300 mg DUPIXENT every 4 weeks until Week 52, or placebo (N=153). All subjects had evidence of sinus opacification on the Lund Mackay (LMK) sinus CT scan and 73% to 90% of subjects had opacification of all sinuses. Subjects were stratified based on their histories of prior surgery and co-morbid asthma/nonsteroidal anti-inflammatory drug exacerbated respiratory disease (NSAID-ERD). A total of 63% of subjects reported previous sinus surgery, with a mean number of 2.0 prior surgeries, 74% used systemic corticosteroids in the previous 2 years with a mean number of 1.6 systemic corticosteroid courses in the previous 2 years, 59% had co-morbid asthma, and 28% had NSAID-ERD. The co-primary efficacy endpoints were change from baseline to Week 24 in bilateral endoscopic nasal polyps score (NPS; 0-8 scale) as graded by central blinded readers, and change from baseline to Week 24 in nasal congestion/obstruction score averaged over 28 days (NC; 0-3 scale), as determined by subjects

using a daily diary. For NPS, polyps on each side of the nose were graded on a categorical scale (0=no polyps; 1=small polyps in the middle meatus not reaching below the inferior border of the middle turbinate; 2=polyps reaching below the lower border of the middle turbinate; 3=large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle turbinate; 4=large polyps causing complete obstruction of the inferior nasal cavity). The total score was the sum of the right and left scores. Nasal congestion was rated daily by the subjects on a 0 to 3 categorical severity scale (0=no symptoms; 1=mild symptoms; 2=moderate symptoms; 3=severe symptoms). In both studies, key secondary end-points at Week 24 included change from baseline in: LMK sinus CT scan score, daily loss of smell, and 22-item sino-nasal outcome test (SNOT-22). The LMK sinus CT scan score evaluated the opacification of each sinus using a 0 to 2 scale (0=normal; 1=partial opacification; 2=total opacification) deriving a maximum score of 12 per side and a total maximum score of 24 (higher scores indicate more opacification). Loss of smell was scored reflectively by the subject every morning on a 0-3 scale (0=no symptoms, 1=mild symptoms, 2=moderate symptoms, 3=severe symptoms). SNOT-22 includes 22 items assessing symptoms and symptom impact associated with CRSwNP with each item scored from 0 (no problem) to 5 (problem as bad as it can be) with a global score ranging from 0 to 110. SNOT-22 had a 2 week recall period. In the pooled efficacy results, the reduction in the proportion of subjects rescued with systemic corticosteroids and/or sino-nasal surgery (up to Week 52) were evaluated.

In 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. Dupilumab significantly decreased sino-nasal 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 sino-nasal surgery versus placebo.

Eosinophilic Esophagitis

A single randomized, double-blind, parallel-group, multicenter, placebo-controlled trial, including two 24-week treatment periods (Parts A and B), was conducted in adult and pediatric subjects 12 to 17 years of age, weighing at least 40 kg, with EoE (NCT03633617). In both parts, subjects were randomized to receive 300 mg DUPIXENT every week or placebo. Eligible subjects had ≥15 intraepithelial eosinophils per high-power field (eos/hpf) following a treatment course of a proton pump inhibitor (PPI) either prior to or during the screening period and symptoms of dysphagia as measured by the Dysphagia Symptom Questionnaire (DSQ). At baseline, 43% of subjects in Part A and 37% of subjects in Part B had a history of prior esophageal dilations. Demographics and baseline characteristics were similar in Parts A and B. A total of 81 subjects (61 adults and 20 pediatric subjects) were enrolled in Part A and 159 subjects (107 adults and 52 pediatric subjects) were enrolled in Part B. The mean age in years was 32 years (range 13 to 62 years) in Part A and 28 years (range 12 to 66 years) in Part B. The majority of subjects were male (60% in Part A and 68% in Part B) and White (96% in Part A and 90% in Part B). The mean baseline DSQ score (SD) was 33.6 (12.4) in Part A and 37.2 (10.7) in Part B. The coprimary efficacy endpoints in Parts A and B were the (1) proportion of subjects achieving histological remission defined as peak esophageal intraepithelial eosinophil count of ≤6 eos/hpf at Week 24; and (2) the absolute change in the subject-reported DSQ score from baseline to Week 24.

In Parts A and B, a greater proportion of subjects randomized to DUPIXENT achieved histological remission (peak esophageal intraepithelial eosinophil count ≤6 eos/hpf) compared to placebo. Treatment with DUPIXENT also resulted in a significant improvement in LS mean change in DSQ score compared to placebo at Week 24. The results of the anchor-based analyses that incorporated the subjects' perspectives indicated that the observed improvement in dysphagia from Parts A and B is representative of a clinically meaningful within-subject improvement.

Prurigo Nodularis

The prurigo nodularis (PN) development program included two 24-week randomized, double-blind, placebo-controlled, multicenter, parallel-group trials (PRIME (NCT04183335) and PRIME 2 (NCT04202679)) in 311 adult subjects 18 years of age and older with pruritus (WI-NRS ≥ 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.

In these trials, the mean age was 49.5 years, the median weight was 71 kg, 65% of subjects were female, 57% were White, 6% were Black, and 34% were Asian. 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). Eleven percent (11%) of subjects were taking stable doses of antidepressants at baseline and were instructed to continue taking these medications during the trial. Forty-three percent (43%) had a history of atopy (defined as having a medical history of AD, allergic rhinitis/rhinoconjunctivitis, asthma, or food allergy).

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

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

HCPCS Code

HCPCS Code	Description
J3490/J3590	Dupilumab inj

Diagnosis Codes

Diagnosis Code	Description
L20	Atopic dermatitis
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
K20.0	Eosinophilic esophagitis
J45.0	Moderate persistent asthma
J45.40	Moderate persistent asthma, uncomplicated
J45.41	Moderate persistent asthma with (acute) exacerbation
J45.5	Severe persistent asthma
J45.50	Severe persistent asthma, uncomplicated
J45.51	Severe persistent asthma with (acute) exacerbation
J45.9	Other and unspecified asthma
J45.90	Unspecified asthma
J45.901	Unspecified asthma with (acute) exacerbation
J82.83	Eosinophilic asthma
J33	Nasal polyp
J33.0	Polyp of the nasal cavity
J33.1	Polypoid sinus degeneration
J33.8	Other polyp of sinus
J33.9	Nasal polyp, unspecified

Dosage Form & Route of Administration

Concentration	Route
300mg/2ml PFS	subcutaneous
200mg/1.14ml PFS	subcutaneous
100mg/0.67ml PFS	subcutaneous
300mg/2ml pre-filled pen	subcutaneous
200mg/1.14ml pre-filled pen	subcutaneous

Acronyms

FEV = Forced Expiratory Volume

FVC = Forced Vital Capacity

ICS = Inhaled Corticosteroid

LABA = Long-acting Beta Agonist

CRSwNP = Chronic Rhinosinusitis with Nasal Polyposis

CT = Computed tomography, HPF=High power field

LD = Loading dose, PN=Prurigo Nodularis

EoE = Eosinophilic esophagitis

OCS = Oral corticosteroid

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