Dupixent (dupilumab)

Policy/Coverage:

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug for the same indication.

Note: If the member is a current smoker or vaper, they should be counseled on the harmful effects of smoking and vaping on pulmonary conditions and available smoking and vaping cessation options.

Dupilumab meets member benefit certificate primary coverage criteria that there be scientific evidence of effectiveness in improving health outcomes when ALL the following criteria are met:

ASTHMA, MODERATE TO SEVERE

INITIAL APPROVAL STANDARD REVIEW for up to 6 months:

1. Individual is 6 years or older (FDA, Dupixent, 2019); **AND**
2. Individual has a diagnosis of moderate to severe eosinophilic asthma; **AND**
3. *Evidence of asthma is demonstrated by both of the following (GINA, 2022):
    a. A pretreatment forced expiratory volume in 1 second (FEV1) < 80% predicted for adults or ≤ 90% for children (<18 years of age); **AND**
    b. Positive bronchodilator responsiveness test evidenced by an increase in FEV1 of > 12% and > 200 mL for adults and >12% for children (<18 years of age); **AND**

4. Documentation of inadequate control of symptoms with use of one of the following combination therapies (ERS/ATS, 2014), unless the individual is intolerant of, or has a medical contraindication to these agents:
    a. 3 months of high-dose inhaled corticosteroid (ICS) (equivalent to those defined in the policy guidelines) given in combination with a minimum of 3 months of controller medication (either a long-acting beta2-agonist [LABA], **OR** leukotriene receptor antagonist [LTRA], or theophylline); **OR**
    b. 6 months of high-dose ICS with additional controller (i.e., long-acting beta-agonist, long-acting muscarinic antagonist, leukotriene modifier, or theophylline) and daily oral glucocorticoids equivalent to at least 5 mg per day of prednisone/prednisolone (only applicable to a diagnosis of severe eosinophilic asthma); **AND**
5. Individual has one of the following (ERS/ATS, 2014):
    a. A history of 2 or more exacerbations in the previous year, requiring bursts of systemic steroids (> 3 days each); **OR**
    b. At least one exacerbation requiring hospitalization, ICU stay or mechanical ventilation in the previous year; **AND**

6. Individual has a blood eosinophil count of ≥ 150 cells/microliter at baseline prior to other eosinophil lowering therapy (e.g., systemic corticosteroids) and in the absence of other potential causes of eosinophilia, including hypereosinophilic syndromes, neoplastic disease, and known or suspected parasitic infection (FDA, Dupixent, 2019); **AND**
7. Individual is not being treated concurrently with another biologic agent for the same or similar condition (such as benralizumab, mepolizumab, omalizumab, reslizumab or

tezepelumab); **AND**
8. Individual will continue to use maintenance asthma treatments (e.g., inhaled corticosteroid, LABA, LTRA or theophylline) in combination with dupilumab (GINA, 2022); **AND**
9. Must be prescribed by or in consultation with an Allergist/Immunologist or Pulmonologist.
10. Must be dosed in accordance with the FDA label.

CONTINUED APPROVAL for up to 1 year:
1. Treatment with dupilumab has resulted in clinical improvement as documented by one or more of the following:
   a. Decreased utilization of rescue medications, OR
   b. Decreased frequency of exacerbations (defined as worsening of asthma that requires an increase in inhaled corticosteroid dose or treatment with systemic corticosteroids), hospitalizations, and/or ER/urgent visits or ER visit or hospitalization); **OR**
   c. Increase in predicted FEV1 from pretreatment baseline; **AND**
2. Member will continue to use maintenance asthma treatments (i.e., inhaled corticosteroid and additional controller) in combination with the requested medication **AND**
3. Individual is not being treated concurrently with another biologic agent for the same or similar condition (such as benralizumab, mepolizumab, omalizumab, reslizumab or tezepelumab); **AND**
4. Must be dosed in accordance with the FDA label.

CHRONIC RHINOSINUSITIS WITH NASAL POLYPOSIS (CRSwNP)

INITIAL APPROVAL STANDARD REVIEW for up to 6 months:

1. Individual is 12 years of age or older; **AND**
2. Individual is diagnosed with CRSwNP; **AND**
3. Dupilumab is prescribed by a physician with expertise in the treatment of CRSwNP, e.g., an otolaryngologist [ear, nose, and throat (ENT) specialist] **OR** an allergist/immunologist; **AND**
4. Individual has moderate to severe symptoms of nasal obstruction; **AND**
5. Individual has symptoms of nasal blockage, congestion, or obstruction plus one of the following additional symptoms:
a. Rhinorrhea; **OR**
b. Decreased sense of smell for at least 12 weeks; **AND**

6. Individual has bilateral sinonasal polyposis reaching the lower border of the middle turbinate or beyond, which has been confirmed by nasal endoscopy, anterior rhinoscopy, or sinus CT scan (AAO-HNSF, 2015); **AND**
7. Individual has had at least one prior sinonasal surgery for CRSwNP or is not a candidate for sinonasal sinus surgery to remove polyps – reason(s) for non-candidacy must be provided (AAO-HNS, 2015); **AND**
8. Individual has tried and failed systemic corticosteroids, unless contraindicated, in the past 2 years (AAAAI/ACAAI 2014); **AND**
9. Individual has tried and failed (e.g., lack of significant reduction in size or resolution of nasal polyps), within the past 6 months, to at least 8 weeks of continuous treatment with an intranasal corticosteroid post-sinonasal surgery (individuals who are ineligible for sinonasal surgery are still required to have tried intranasal corticosteroids) (AAO-HNS, 2015); **AND**
10. Individual will be using a daily intranasal corticosteroid during treatment with dupilumab, unless contraindicated or not tolerated; **AND**

11. Individual is not being treated concurrently with a biologic agent for the same or similar condition (such as benralizumab, mepolizumab, or omalizumab); **AND**
12. Must be dosed in accordance with the FDA label.

CONTINUED APPROVAL for up to 1 year:

Requirement of documentation in the medical records that the member has achieved and maintains a clinically meaningful benefit as defined below:

1. Individual has had clinical improvement in clinical signs and symptoms of the disease (including but not limited to improvement in nasal polyp score or nasal congestion score); **AND**
2. Individual meets all of the following initial approval criteria:
    a. Dupilumab is prescribed by a physician with expertise in the treatment of CRSwNP, e.g., an otolaryngologist [ear, nose, and throat (ENT) specialist] **OR** an allergist/immunologist; **AND**
    b. The individual will be using a daily intranasal corticosteroid during treatment with dupilumab, unless contraindicated or not tolerated; **AND**
    c. Individual is not being treated concurrently with a biologic agent for the same or similar condition (such as benralizumab, mepolizumab, or omalizumab); **AND**
4. Individual is not being treated concurrently with a biologic agent for the same or similar condition (such as benralizumab, mepolizumab, or omalizumab) **AND**
3. Must be dosed in accordance with the FDA label.

<u>ATOPIC DERMATITIS</u>

INITIAL APPROVAL STANDARD REVIEW for up to 6 months:

1. Individual has a confirmed diagnosis of moderate to severe atopic dermatitis supported by the submitted medical records; **AND**
2. Individual is ≥ 6 months of age; **AND**
3. Individual has chronic or relapsing history that has been present for at least 6 months **AND**
4. Individual has a history of pruritus associated with atopic dermatitis (Boguniewicz, 2018); **AND**
5. Individual has at least one of the following (Boguniewicz, 2018):
    a. Early age of onset (≤ 5 years of age) (Lyons, 2015); **OR**
    b. Atopy; **OR**
    c. Family history; **OR**
    d. Xerosis; **AND**

6. Individual has involvement of >10% of body surface area **OR** involvement of critical areas (e.g., palms, face, etc) (FDA, 2021) **AND**
7. Individual must have documentation of one of the following (Boguniewicz, 2018):
    a. For infants and children: facial, neck or extensor involvement; **OR**
    b. For any age group: current or previous flexural lesions; sparing of groin and axillary regions; **AND**

8. Individual has a skin biopsy consistent with the diagnosis of atopic dermatitis OR documentation is provided that other skin conditions have been excluded or adequately treated

(such as scabies, seborrheic dermatitis, contact dermatitis (irritant or allergic), ichthyoses, cutaneous T-cell lymphoma, psoriasis, photosensitivity dermatoses, immune deficiency disease, and erythroderma of other causes) (Boguniewicz, 2018) **AND**
9. The drug is authorized and managed by a physician with expertise in the treatment of atopic dermatitis (e.g., allergist/immunologist or dermatologist) **AND**
10. Topical therapy failure (FDA, 2021). The patient has either failed a trial, proved intolerant of a medication, or has contraindications to both below topical treatments (in accordance with AAD Guidelines (Eichenfield, 2014) (Howe, 2022):
    a. A topical calcineurin inhibitor (excluding patients < 2 years of age) [i.e., pimecrolimus (Elidel) or tacrolimus (Protopic)] **(For pediatric patients ≥ 2 to <12 years old - use of appropriate pediatric formulation)** with an inadequate response to maintenance therapy that includes intermittent use (at least 2 days per week) for at least 12 weeks; **AND**
    b. A topical corticosteroid **(For pediatric patients ≥ 6 months to <12 years old - use of appropriate pediatric formulation with precautions for adrenal suppression)** with an inadequate response to maintenance therapy that includes intermittent use (at least 2 days per week) for at least 12 weeks of a moderate-to-high-potency topical corticosteroid, unless involvement is limited to the face and intertriginous areas in which a lower-potency corticosteroid may be used; **AND**
11. The drug will NOT be used in combination with a janus kinase (JAK) inhibitor or another biologic agent for the treatment of atopic dermatitis [e.g., omalizumab (e.g., Xolair), mepolizumab (e.g., Nucala), reslizumab (e.g., Cinqair), tralokinumab (e.g., Adbry) and rituximab (e.g., Rituxan)] or another atopic condition; **AND**
12. Individual has an Investigator's Global Assessment (IGA) score ≥ 3 (FDA, 2021); **AND**
13. Individual has at least one of the following:
    a. Eczema Area and Severity Index (EASI) score ≥ 21 (Simpson, 2016; Simpson 2020); **OR**
    b. Weekly-average baseline worst itch score (Peak, Pruritus Numerical Rating Scale [NRS]) ≥ 4 (Efficacy, 2022); **AND**

14. Must be dosed in accordance with the FDA label.

CONTINUED APPROVAL for up to 1 year:
Requirement of documentation in the medical records that the member has achieved and maintains a clinically meaningful benefit as defined below:

1. Reduction in disease severity (e.g., erythema, dryness, edema/papulation, excoriations, lichenification, oozing/crusting); **AND**
2. Reduction in the frequency or intensity of pruritus associated with atopic dermatitis; **AND**
3. Reduction in the frequency of disease exacerbations/flairs; **AND**
4. Reduction in the amount of Body Surface Area involvement relative to pretreatment baseline; **AND**
5. Improvement in overall patient quality of life (e.g., improved sleep, less depression or anxiety, etc.); **AND**
6. The drug will NOT be used in combination with a janus kinase (JAK) inhibitor or another biologic agent for the treatment of atopic dermatitis [e.g., omalizumab (e.g., Xolair), mepolizumab (e.g., Nucala), reslizumab (e.g., Cinqair), tralokinumab (e.g., Adbry) and rituximab (e.g., Rituxan)] or another atopic condition **AND**
7. 7. Must be dosed in accordance with the FDA label.

EOSINOPHILIC ESOPHAGITIS

INITIAL APPROVAL STANDARD REVIEW for up to 6 months:

1. Individual has a confirmed diagnosis of eosinophilic esophagitis supported by the submitted medical records; **AND**
2. Individual is ≥ 1 years of age (Study, 2022); **AND**
3. Individual weighs ≥ 15 kg (Study, 2022); **AND**
4. Member meets either of the following:
    - Member is 1 year of age to less than 11 years of age and has clinical manifestations of disease (e.g., vomiting, heartburn, abdominal pain, food refusal, failure to thrive).
    - Member is 11 years of age or older and has history of an average of at least 2 episodes of dysphagia (with intake of solids) per week.

AND

5. Individual has had one or more esophageal biopsies that have shown eosinophil predominant inflammation consisting of a peak value of ≥ 15 eosinophils per high power field (or 60 eosinophils per mm2) (FDA, 2022); **AND**

6. Must include documentation of diagnosis, dietary counseling (registered dietician) and compliance with appropriate dietary changes and adequate treatment interval to allow assessment of response (Wechsler, 2021); **AND**

7. Individual has a documented inadequate response (8-week trial) to both of the following:
    a. High-dose PPI therapy (defined as 1-2 mg/kg total daily dose for children or a daily dose equivalent to omeprazole 40 mg twice daily for adults – see dose conversion chart in policy guidelines) (FDA, 2022; Lucendo, 2015); **AND**
    b. Topical glucocorticoid therapy (budesonide oral viscous slurry) (Muir, 2021) **AND**

8. Medication is prescribed by a gastroenterologist or prescribed by an allergist in consultation with a gastroenterologist; **AND**
9. Must be dosed in accordance with the FDA label.

CONTINUED APPROVAL for up to 1 year:

1. Requirement of documentation in the medical records that the member has achieved and maintains a clinically meaningful benefit as defined by any of the following (Bonis-Diagnosis, 2022; Study, 2022):
    a. Reduction in symptoms and associated complications, such as – symptom frequency, food impaction or hospitalization; **OR**
    b. Endoscopic features, such as – edema, furrows, exudates, rings, strictures; **OR**
    c. Reduction in eosinophil burden per high power field relative to pretreatment baseline; **AND**

2. Medication is prescribed by a gastroenterologist or prescribed by an allergist in consultation with a gastroenterologist; **AND**
3. Must be dosed in accordance with the FDA label.

PRURIGO NODULARIS (PN)

INITIAL APPROVAL STANDARD REVIEW for up to 6 months:

1. Individual must have documentation of confirmed diagnosis of PN by a dermatologist (PRIME2, 2022); **AND**
2. Individual has been diagnosed with PN a least 3 months prior to initiation of dupilumab (PRIME2, 2022); **AND**
3. Individual is ≥ 18 years of age (PRIME2, 2022); **AND**
4. Individual has presence of chronic pruritus lasting longer than 6 weeks as documented by both of the following (Stander, 2020):
   a. An average worst itch numeric rating scale (WI-NRS) score ≥ 7, (PRIME2, 2022); **AND**
   b. History and/or signs of repeated scratching (e.g., excoriations and scars) (Stander, 2020); **AND**

5. Individual has at least 20 PN lesions in total located on at least two of the following (PRIME2, 2022):
   a. Both legs (bilaterally symmetric lesions); **OR**
   b. Both arms (bilaterally symmetric lesions); **OR**
   c. Trunk; **AND**

6. Individual has failed at least a 2-week course (or for the maximum duration recommended by the product prescribing information, whichever is shorter) or has a contraindication to a medium- to super high-potency topical corticosteroid (PRIME2, 2022); **AND**
7. Individual has failed at least one systemic therapy (e.g. UV phototherapy, gabapentin, cyclosporine, methotrexate, etc); **AND**
8.Medication is ordered by or in consultation with a dermatologist; **AND**
9.Member is not treated concurrently with any other biologic drug or targeted synthetic drug for the same indication **AND**
10. Must be dosed in accordance with the FDA label.

CONTINUED APPROVAL for up to 1 year:
1. Individual has confirmed diagnosis of PN by a dermatologist; **AND**
2. Individual is ≥ 18 years of age; **AND**
3. Individual has documented clinical improvement as demonstrated by a decrease from baseline in the number of lesions and their WI-NRS score; **AND**
4. Medication is ordered by or in consultation with a dermatologist; **AND**
5. Member is not treated concurrently with any other biologic drug or targeted synthetic drug for the same indication **AND**
6. Must be dosed in accordance with the FDA label.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

INITIAL APPROVAL STANDARD REVIEW for up to 6 months:

1. Member has a confirmed diagnosis of moderate or severe COPD supported by the submitted medical records.
2. Member is ≥ 18 years of age
3. Physician diagnosed COPD for at least 12 months
4. Member does not have significant pulmonary disease other than COPD (e.g., lung fibrosis, sarcoidosis, interstitial lung disease, pulmonary hypertension, bronchiectasis, Churg-Strauss Syndrome, etc)

5. Diagnosis has been confirmed by spirometry showing:
    a. Forced expiratory volume in one second (FEV_1)/forced vital capacity (FVC) less than 0.7 post-bronchodilation.
    b. Postbronchodilator FEV1 of 30 to 70% of the predicted normal value
6. Member demonstrates classic signs or symptoms of COPD (e.g., dyspnea, wheezing, chest tightness, fatigue, activity limitation, cough with or without sputum production, chronic bronchitis).
7. Member has an absolute blood eosinophil count of at least 300 cells per microliter prior to initiating therapy with the requested medication.
8. Member has inadequately controlled COPD as demonstrated by experiencing either of the following in the last year:
    a. At least two moderate exacerbations resulting in treatment with systemic glucocorticoids, antibiotics, or both.
    b. One or more severe exacerbation(s) requiring hospitalization or an emergency medical care visit.
9. Member meets either of the following:
    a. Member is currently receiving (for at least 3 months) maintenance inhaled triple therapy (i.e., inhaled corticosteroid [ICS], long-acting muscarinic antagonist [LAMA], and long-acting $beta_2$-agonist [LABA]).
    b. Member is currently receiving (for at least 3 months) a LAMA and LABA, and has a contraindication to ICS.
10. Member will continue to use maintenance COPD treatments (e.g., ICS with LAMA and LABA, LAMA and LABA) in combination with the requested medication
11. Medication is ordered by or in consultation with a pulmonologist or an allergist/immunologist
12. Member is not treated concurrently with any other biologic drug or targeted synthetic drug for the same indication
13. Must be dosed in accordance with the FDA label

CONTINUED APPROVAL for up to 1 year:
1.Member is ≥ 18 years of age
2. Member has achieved or maintained a positive clinical response from baseline as evidenced by improvement in signs and symptoms of COPD (e.g., decrease in exacerbations, improvement in pre-bronchodilator FEV_1) or stabilization of disease.
3. Member continues to use maintenance COPD treatments (e.g., ICS with LAMA and LABA, LAMA and LABA) in combination with the requested medication.
4. Medication is ordered by or in consultation with a pulmonologist or an allergist/immunologist
5. Member is not treated concurrently with any other biologic drug or targeted synthetic drug for the same indication
6. Must be dosed in accordance with the FDA label

CHRONIC SPONTANEOUS URTICARIA

INITIAL APPROVAL STANDARD REVIEW for up to 6 months:

1. Individual is 12 years of age or older ; **AND**
2. Other etiologies of urticaria have been excluded and there is no diagnosis of a more specific etiology (e.g., allergic, contact, vibratory, thermal or cholinergic urticaria); **AND**
3. Individual has the presence of recurrent urticaria, angioedema or both for a period of at least

6 weeks (Saini, 2021); **AND**
4. There must be a clear documentation of physical findings characteristic of CSU (see policy guidelines (Zuberbier, 2018); **AND**
5. Individual is not being treated concurrently with another biologic agent for the same or similar condition (such as omalizumab, benralizumab, mepolizumab, reslizumab or tezepelumab); **AND**
6. Individual has had an inadequate response to at least four weeks of treatment with a second-generation antihistamine (e.g., cetirizine, desloratadine, fexofenadine, levocetirizine, loratadine) used in combination with an H2-antihistamine (e.g., cimetidine, famotidine) and a leukotriene modifier (e.g., montelukast, zafirlukast) (Bernstein, 2014); **AND**
7. Must be dosed in accordance with the FDA label.

CONTINUED APPROVAL for up to 12 months:

For **ALL** individuals:

1. Must be dosed in accordance with the FDA label; **AND**
2. Individual is not being treated concurrently with another biologic agent for the same or similar condition (such as omalizumab, benralizumab, mepolizumab, reslizumab or tezepelumab).
3. Individual is 12 years of age or older **AND**
4. Individual has experienced a positive clinical response compared to baseline (e.g.,reduction in exacerbations, itch severity, hives, decrease in weekly urticaria activity score [UAS7] since initiation of therapy)
5. Medication is ordered by or in consultation with a dermatologist or allergist/immunologist

<u>BULLOUS PEMPHIGOID</u>

INITIAL APPROVAL STANDARD REVIEW for up to 6 months

1. Member is 18 years of age or older
2. Diagnosis has been confirmed by either of the following:
    a. Direct immunofluorescence (DIF) study
    b. Immune serological test(s) (e.g., Indirect immunofluorescence microscopy [IIF], ELISA)
6. Member demonstrates characteristic clinical features of bullous pemphigoid (e.g., urticarial or eczematous or erythematous plaques, bullae, pruritus)
7. Member has moderate to severe disease
8. Member meets either of the following:
    a. Member has had an inadequate treatment response with either of the following:
        i. A super-high potency topical corticosteroid
        ii. An oral corticosteroid
    b. The use of super-high potency topical corticosteroid or oral corticosteroid is not advisable for the member (e.g., contraindications, prior intolerances)
9. Member is not treated concurrently with any other biologic drug or targeted synthetic drug for the same indication

CONTINUED APPROVAL for up to 12 months:

1. Member is ≥ 18 years old
2. Member has achieved or maintained a positive clinical response as evidenced by either of

the following:

1. Low disease activity (e.g., absence of new or established lesions)
2. Reduction in pruritus intensity and improvement in extent and severity of lesions

3. Member is not treated concurrently with any other biologic drug or targeted synthetic drug for the same indication

Policy Guidelines

The ERS/ATS definition of high doses of various inhaled glucocorticoids in relation to patient age (in mcg/day):

Age 6 to 12 years

Beclomethasone ≥ 320 (HFA MDI)
Budesonide ≥ 800 (MDI or DPI); (≥ 720 mcg/day of US labeled budesonide DPI)
Ciclesonide ≥ 160 (HFA MDI)
Fluticasone propionate ≥ 500 (HFA MDI or DPI); (≥ 440 mcg/day of US labeled fluticasone HFA MDI)
Fluticasone furoate: 50 (DPI)
Mometasone ≥ 500 (DPI); (≥ 550 mcg/day of US labeled mometasone DPI)

Age >12 years

Beclomethasone ≥ 1000 (HFA MDI)
Budesonide ≥ 1600 (MDI or DPI) ;(≥ 1440 mcg/day of US labeled budesonide DPI)
Ciclesonide ≥ 320 (HFA MDI)
Fluticasone propionate ≥ 1000 (HFA MDI or DPI); (≥ 880 mcg/day of US labeled fluticasone HFA MDI)
Fluticasone furoate 200 (DPI)
Mometasone ≥ 800 (DPI); (≥ 880 mcg/day of US labeled mometasone DPI

Note: Designation of high doses is provided from manufacturers' recommendations where possible. Equivalent high doses may be expressed differently between countries and some products (e.g., beclomethasone) are available in multiple formulations with different dosing recommendations. Medication inserts should be carefully reviewed by the clinician for the equivalent high daily dosage.

PPI dose conversion chart (Clinical resource, 2022; Dusky, 2006)

Drug	**Approximate Oral Daily Dose Providing Similar Effects on Gastric pH**
Dexlansoprazole (e.g., Dexilant)	60 mg
Esomeprazole (e.g., Nexium)	40 mg
Lansoprazole (e.g., Prevacid)	30 mg
Omeprazole (e.g., Prilosec)	40 mg
Pantoprazole (e.g., Protonix)	40 mg
Rabeprazole (e.g., Aciphex)	20 mg

Please refer to a separate policy on Site of Care or Site of Service Review (policy #2018030) for pharmacologic/biologic medications.

Does Not Meet Primary Coverage Criteria Or Is Investigational For Contracts Without Primary Coverage Criteria

Dupilumab, for any indication or circumstance not described above does not meet member benefit certificate primary coverage criteria that there be scientific evidence of effectiveness in improving health outcomes.

For members with contracts without primary coverage criteria, dupilumab, for any indication or circumstance not described above, is considered **investigational**. **Investigational** services are specific contract exclusions in most member benefit certificates of coverage.