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Policy Number: C11152-A

Dupixent (dupilumab)

PRODUCTS AFFECTED

Dupixent (dupilumab)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Moderate to severe Atopic Dermatitis, Moderate-to-severe asthma with an eosinophilic phenotype or with oral corticosteroid dependent, Nasal polyposis, Eosinophilic esophagitis, Prurigo nodularis, Chronic Obstructive Pulmonary Disease, Chronic Spontaneous Urticaria, Bullous pemphigoid

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

Drug and Biologic Coverage Criteria

A. ALL INDICATIONS:

1. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Dupixent (dupilumab) include: Known hypersensitivity to dupilumab or any of its excipients, avoid use of live vaccines with Dupixent]
   AND
2. IF THIS IS A NON-FORMULARY/NON-PREFERRED PRODUCT: Documentation of trial/failure of or serious side effects to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. Submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s).

B. MODERATE TO SEVERE ATOPIC DERMATITIS:

1. Documented diagnosis of moderate to severe chronic atopic dermatitis (eczema)
   AND
2. Documentation of ONE of the following:
   i. Member has atopic dermatitis involvement estimated to be ≥10% of the body surface area (BSA) according to the prescribing physician
   ii. Member has atopic dermatitis involvement estimated to be <10 % of the BSA affecting face, eyes/eyelids, skin folds, and/or genitalia according to the prescribing physician
   AND
3. Documentation of inadequate response, serious side effects, or contraindication to TWO of the following: topical corticosteroids or preferred/formulary topical calcineurin inhibitor (tacrolimus, pimecrolimus)
   AND
4. Documentation of inadequate response, serious side effects, or contraindication to ONE of the following: Eucrisa (crisaborole), Opzelura (ruxolitinib), Vtama (tapinarof), or Zoryve (roflumilast)
   AND
5. Documentation of prescriber baseline assessment of disease activity (e.g., erythema, induration/papulation/edema, excoriations, lichenification, pruritus, BSA affected, topical requirement, etc.)

C. MODERATE TO SEVERE ASTHMA:

1. Documented diagnosis of moderate to severe asthma
   AND
2. Documentation that Dupixent (dupilumab) is NOT being used as monotherapy for asthma (must be prescribed as add-on maintenance to be used in combination with other medications for long-term control of asthma)
   AND
3. Documentation member has eosinophilic phenotype or predominantly eosinophil-driven disease with blood eosinophil counts ≥150 cells/microliter at initiation of therapy (within 6 weeks of request) or ≥300 cells/microliter in the prior 12 months OR member requires chronic maintenance oral corticosteroid treatment [DOCUMENTATION REQUIRED]
   AND
4. Documentation member has experienced exacerbation(s) or hospitalization(s), within the last 12 months as evidenced by any of the following:
   i. TWO or more exacerbations requiring treatment with systemic corticosteroid (intramuscular, intravenous, or oral) despite the use of high-dose inhaled corticosteroids in the past 12 months
      OR
   ii. One or more exacerbation requiring hospitalization in the past 12 months
      OR
   iii. Two-fold increase or greater in the dose of systemic corticosteroid treatment for asthma exacerbations

OR

iv. Asthma worsens upon tapering of oral corticosteroid therapy
OR
v. Mechanical ventilation in the past 12 months
OR
vi. Poor symptom control indicated by Asthma Control Questionnaire (ACQ) score consistently greater than 1.5 or Asthma Control Test (ACT) score consistently less than 20
OR
vii. Forced expiratory volume in 1 second (FEV1) < 80% predicted OR FEV1/forced vital capacity (FVC) < 0.80

AND

5. Documentation of adherence to ONE of the following regimens of at least 3 months (within the last 90 days) and symptoms inadequately controlled (as documented in criteria above):
   a. Medium or High dose ICS-LABA combination product AND one additional asthma controller medication (LAMA, LTRA, low dose azithromycin), preferably a LAMA per GINA 2024 guideline
   OR
   b. Medium or High dose ICS-LABA combination product AND oral corticosteroids [see Appendix for product classes]

D. NASAL POLYPOSIS:
1. Documented diagnosis of chronic rhinosinusitis with nasal polyposis
   AND
2. Documentation that Member has a history of sino-nasal surgery or is not eligible for surgery
   AND
3. Documentation the member has experienced an inadequate response (after 3 consistent months of use) or serious side effects to ONE of the following medications unless contraindicated: preferred formulary/PDL intranasal steroids OR preferred formulary/PDL oral corticosteroids
   AND
4. Documentation member is concurrently receiving treatment with one of the following agents: intranasal steroids, oral corticosteroids, nasal saline irrigations, antibiotics, or leukotriene agents (i.e., not to be used as monotherapy)
   AND
5. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal (e.g., nasal congestion, loss of smell, sino-nasal symptoms) [DOCUMENTATION REQUIRED]

E. EOSINOPHILIC ESOPHAGITIS:
1. Documented diagnosis of eosinophilic esophagitis (EoE)
   AND
2. Documentation of inadequate response, or labeled contraindication to ALL of the following: elimination diet, proton-pump inhibitor, and topical glucocorticoids (fluticasone or budesonide)
   AND
3. Member weighs at least 15 kg

F. PRURIGO NODULARIS:
1. Documented diagnosis of prurigo nodularis
   AND
2. Documentation that member has widespread disease (greater than or equal to 20 nodular lesions) or has failed to respond to topical or intralesional corticosteroids (minimum of a 6 week trial)

G. CHRONIC OBSTRUCTIVE PULMONARY DISEASE:
1. Documented diagnosis of chronic obstructive pulmonary disease (COPD)
   AND
2. Documentation member has eosinophilic phenotype or predominantly eosinophil-driven disease

with blood eosinophil count ≥ 300 cells/mcL [DOCUMENTATION REQUIRED]
AND

3. Documentation member has experienced exacerbation(s) or hospitalizations, within the last 12 months as evidenced by either of the following:
    i. Two or more moderate exacerbations that meet three of the following AND no evidence of acidosis:
        a. Dyspnea VAS ≥ 5
        b. Respiratory rate ≥ 24 breaths/min
        c. Heart rate ≥ 95 beats/min
        d. Resting SaO2 < 92% (on room air or member's usual oxygen) and/or change > 3%
        e. CRP ≥ 10 mg/L

    OR

    ii. One or more severe exacerbation that meet three of the following AND there is evidence of new onset or worsening hypercapnia and acidosis:
        a. Dyspnea VAS ≥ 5
        b. Respiratory rate ≥ 24 breaths/min
        c. Heart rate ≥ 95 beats/min
        d. Resting SaO2 < 92% (on room air or member's usual oxygen) and/or change > 3%
        e. CRP ≥ 10 mg/L

AND

4. Symptoms are inadequately controlled (as documented in criteria above) after an adherent regimen of at least 3 months of triple therapy that includes a long-acting muscarinic antagonist (LAMA), long-acting beta agonist (LABA), and inhaled corticosteroid (ICS)
AND
5. Documentation that Dupixent (dupilumab) is NOT being used as monotherapy for COPD (must be prescribed as add-on maintenance to be used in combination with other medications for long-term control of COPD)
AND
6. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal (e.g., baseline symptomatology [dyspnea, wheezing, cough, sputum], exacerbations, etc.)

H. CHRONIC SPONTANEOUS URTICARIA (CSU):

1. Documented diagnosis of Chronic Spontaneous Urticaria (CSU) documented by the presence of urticaria (hives) that has been continuously or intermittently present for more than 6 weeks
AND
2. Prescriber attests that other underlying causes of member's condition have been ruled out, including bradykinin-related angioedema and interleukin-1 associated urticarial syndromes (auto-inflammatory disorders, urticarial vasculitis)
AND
3. Prescriber attests that possible conditions or triggers for urticaria are being maximally managed without improvement
AND
4. Documented baseline score from an objective clinical evaluation tool within the past 30 days (e.g., Urticaria Control Test (UCT), Urticaria Activity Score (UAS7), Angioedema Activity Score (AAS), Dermatology Life Quality Index (DLQI), Angioedema Quality of Life (AE-QoL), or Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL)) [DOCUMENTATION REQUIRED]
AND
5. Documentation that member continues to experience hives associated with itching despite adequate, adherent trials (minimum 4 weeks) of ALL of the following treatments (See Appendix 2) (Reference: AAAAI/ACAAI guideline on diagnosis and management acute and chronic urticaria [J Allergy Clin Immunol 2014 May;133(5):1270] see BACKGROUND) [DOCUMENTATION REQUIRED of trial/failure with dates of therapy]:
    i. Two different H1-antihistamines at the maximally tolerated doses (up to 4 times standard daily

dose), unless medically contraindicated as monotherapy
MOLINA REVIEWER NOTE: If denying for prior utilization at high doses, please enter override for antihistamine quantity limits
AND

ii. One H1-antihistamine IN COMBINATION with leukotriene receptor antagonist (LTRA) at the maximally tolerated doses (up to 4 times standard daily dose), unless medically contraindicated
AND

iii. One H1-antihistamine at the maximally tolerated doses (up to 4 times standard daily dose) in combination with ANY of the following: H2-Antihistamines OR an anti- inflammatory agent (e.g., dapsone, hydroxychloroquine, sulfasalazine) OR an immunosuppressant agent (e.g., cyclosporine, mycophenolate), unless medically contraindicated

I. BULLOUS PEMPHIGOID:
1. Documented diagnosis of bullous pemphigoid
AND
2. Documentation diagnosis was confirmed with biopsy or serum testing (indirect immunofluorescence [IIF] assay or enzyme-linked immunosorbent assay [ELISA])
AND
3. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal (e.g., vesicles and bullae, erythema, pruritus)
AND
4. Documentation of inadequate response, serious side effects, or contraindication to corticosteroids (oral or topical) AND a steroid-sparing agent (i.e., doxycycline, dapsone, azathioprine, mycophenolate, methotrexate)

CONTINUATION OF THERAPY:

A. FOR ALL INDICATIONS:
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
AND
2. (a) MODERATE TO SEVERE ASTHMA: Documentation of clinical improvement as evidenced by improvement in lung function (increase in percent predicted FEV1 or PEF) from pre-treatment baseline, or decreased utilization of rescue medication, or decreased frequency of exacerbations (defined as worsening of asthma that requires increase in inhaled corticosteroid dose or treatment with systemic corticosteroids), or decreased frequency of unscheduled clinic or urgent care or emergency department visits, or reduction in reported symptoms (chest tightness, coughing, shortness of breath, nocturnal wakening, wheezing, sustained improvement in Asthma Control Text scores), or decreased or stopped oral treatments including oral corticosteroids and other add on medication if applicable, or reduced ICS-LABA dose to at least moderate
OR
(b) MODERATE TO SEVERE ATOPIC DERMATITIS: Member has responded to Dupixent therapy as determined by the prescribing physician (e.g., marked improvements in erythema, induration/ papulation/edema, excoriations, and lichenification; reduced pruritus; decreased requirement for other topical or systemic therapies; reduced body surface area (BSA) affected with atopic dermatitis; or other responses observed
OR
(c) NASAL POLYPOSIS: Documentation of significant reduction in nasal congestion, loss of smell or sino-nasal symptoms reported at initial authorization
OR
(d) EOSINOPHILIC ESOPHAGITIS: Documentation of positive clinical response as demonstrated by low EoE disease activity and/or improvements in the condition's signs and symptoms
OR
(e) PRURIGO NODULARIS: Documentation of positive clinical response as demonstrated by an

improvement in itching
OR
(f) COPD: Documentation of positive clinical response as demonstrated by improvement in symptoms (e.g., dyspnea, wheezing, cough, sputum), or decreased severity or frequency of exacerbations
OR
(g) CHRONIC SPONTANEOUS URTICARIA: Clinical improvement as documented by improvement from baseline using objective clinical evaluation tools [e.g., Urticaria Control Test (UCT), Urticaria Activity Score (UAS7), Angioedema Activity Score (AAS), Dermatology Life Quality Index (DLQI), Angioedema Quality of Life (AE- QoL), or Chronic Urticaria Quality of Life Questionnaire (CU- Q2oL)]. [DOCUMENTATION REQUIRED]
OR
(h) BULLOUS PEMPHIGOID: Documentation of positive clinical response as demonstrated by improvement in symptoms (e.g., vesicles and bullae, erythema, pruritus)
AND

3. Documentation Dupixent (dupilumab) will not be used as monotherapy for asthma or nasal polyps or COPD
AND
4. Prescriber attests or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
MODERATE TO SEVERE ATOPIC DERMATITIS, CHRONIC SPONTANEOUS URTICARIA, BULLOUS PEMPHIGOID: Prescribed by or in consultation with an allergist, immunologist, or dermatologist.
MODERATE TO SEVERE ASTHMA: Prescribed by, or in consultation with, a board-certified asthma specialist (allergist, immunologist, pulmonologist) or physician experienced in the management of asthma.
NASAL POLYPOSIS: Prescribed by or in consultation with an otolaryngologist, or allergist/immunologist
EOSINOPHILIC ESOPHAGITIS: Prescribed by or in consultation with a gastroenterologist or physician experienced in the management of eosinophilic esophagitis
PRURIGO NODULARIS: Prescribed by or in consultation with a dermatologist or physician experienced in the management of prurigo nodularis
COPD: Prescribed by or in consultation with an allergist/immunologist or pulmonologist
[If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
ATOPIC DERMATITIS: 6 months of age and older
MODERATE TO SEVERE ASTHMA: 6 years of age and older
NASAL POLYPOSIS, CHRONIC SPONTANEOUS URTICARIA: 12 years of age and older
EOSINOPHILIC ESOPHAGITIS: 1 year of age and older
PRURIGO NODULARIS, COPD, BULLOUS PEMPHIGOID: 18 years of age and older

QUANTITY:
ATOPIC DERMATITIS:
Adults: 600mg (2x300mg) followed by 300mg every 2 weeks

Pediatrics (6 months to 5 years of age):
5kg to <15kg: 200mg every 4 weeks
15kg to <30kg: 300mg every 4 weeks

Pediatrics (6 years to 17 years of age):
15 to <30kg: 600mg (2x300mg) followed by 300mg every 4 weeks
30 to <60kg: 400mg (2x200mg) followed by 200mg every 2 weeks

60kg or greater: 600 mg (2x300mg) followed by 300 mg every 2 weeks

MODERATE TO SEVERE ASTHMA:
Adults and Pediatrics 12 years and older: 400mg (2x200mg) followed by 200mg every 2 weeks OR 600mg (2x300mg) followed by 300mg every 2 weeks

Pediatrics 6 to 11 years of age:
15kg to < 30kg: 300mg every 4 weeks
30kg or greater: 200mg every 2 weeks
NOTE: For pediatric patients 6 to 11 years of age with asthma and co-morbid moderate-to-severe AD, follow the recommended dosage for AD which includes an initial loading dose.

NASAL POLYPOSIS: 300 mg given every 2 weeks.

EOSINOPHILIC ESOPHAGITIS:
15 to <30kg: 200mg every 2 weeks
30 to <40kg: 300mg every 2 weeks
40kg or greater: 300 mg given every week

PRURIGO NODULARIS: 600 mg (2x300mg), followed by 300 mg given every 2 weeks

COPD: 300 mg given every 2 weeks

CSU:
Adults: 600mg (2x300mg) followed by 300mg every 2 weeks

Pediatrics 12 to 17 years of age:
30 to <60kg: 400mg (2x200mg) followed by 200mg every 2 weeks
60kg or greater: 600 mg (2x300mg) followed by 300 mg every 2 weeks

BULLOUS PEMPHIGOID: 600 mg (2x300mg), followed by 300 mg given every 2 weeks

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
Atopic Dermatitis - Monoclonal Antibodies

FDA-APPROVED USES:
Dupixent is indicated:

- for the treatment of adult and pediatric patients aged 6 months and older with moderate-to-severe atopic dermatitis (AD) 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.
- as an add-on maintenance treatment of adult and pediatric patients aged 6 years and older with moderate- to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma.
- as an add-on maintenance treatment in adult and pediatric patients aged 12 years and older with inadequately controlled chronic rhinosinusitis with nasal polyps (CRSwNP)
- for the treatment of adult and pediatric patients aged 1 year and older, weighing at least 15 kg, with

eosinophilic esophagitis (EoE)
- for the treatment of adult patients with prurigo nodularis
- as an add-on maintenance treatment of adult patients with inadequately controlled chronic obstructive pulmonary disease (COPD) and an eosinophilic phenotype
- for the treatment of adult and pediatric patients aged 12 years and older with chronic spontaneous urticaria (CSU) who remain symptomatic despite H1 antihistamine treatment
- for the treatment of adult patients with bullous pemphigoid (BP)

Limitation of Use: Not for the relief of acute bronchospasm or status asthmaticus or other forms of urticaria

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Appendix 1:
Asthma Control Questionnaire (ACQ): A validated, patient-centered tool for evaluating asthma control developed using expert opinion and originally contained seven items; however, a five-item version (ACQ- 5) has been validated for use in clinical trials and epidemiological surveys. The ACQ score has been shown to correlate with a measure of control based on the GINA/NIH criteria. The ACQ assesses 7 items, which include asking patients to recall their experiences in the previous week and to respond to questions about nighttime waking, symptoms on waking, activity limitations, shortness of breath, wheezing, required use of short-acting b2-agonists for rescue, and FEV1 percent predicted before bronchodilator on a 7-pointscale. All of these items are equally weighted, and the ACQ score is the mean of the 7 items and ranges from 0 (totally controlled) to 6 (severely uncontrolled). The final score is generated by averaging the total scores for the 7 items. Higher scores indicate worse asthma control.[9] May be accessed via: https://www.qoltech.co.uk/questionnaires.htm
Asthma Control Test (ACT): The ACT contains 5 questions that are related to the frequency of both asthma symptoms and required rescue medication use during the previous 4 weeks. The scores in the ACT range from 5 (worse control) to 25 (total control).[10]May be accessed via: https://www.asthma.com/additional-resources/asthma-control-test.html https://www.memphischildrens.org/Asthma_Control-12-and-older.pdf

LONG-ACTING BETA2-AGONIST
- salmeterol xinafoate Serevent Diskus

MAST CELL STABILIZER
- cromolyn sodium

STEROID + LONG-ACTING BETA2-AGONIST
- budesonide/ formoterol fumarate dihydrate Symbicort 80mcg/4.5mcg, 160mcg/4.5mcg MDI
- fluticasone furoate/ vilanterol Breo Ellipta 100mcg/25mcg, 200mcg/25mcg DPI
- fluticasone propionate/ salmeterol Advair Diskus 100mcg/50mcg, 250mcg/50mcg, 500mcg/50mcg DPI, Advair HFA 45mcg/21mcg, 115mcg/21mcg, 230mcg/21mcg MDI, AirDuo Digihaler/RespiClick 55mcg/14mcg, 113mcg/14mcg, 232mcg/14mcg DPI, Wixela Inhub 100mcg/50mcg,250mcg/50mcg,500mcg/50mcg DPI
- mometasone furoate/formoterol fumarate dihydrate Dulera 50mcg/5mcg, 100mcg/5mcg, 200mcg/5mcg MDI

ANTICHOLINERGIC
- tiotropium bromide monohydrate Spiriva Respimat 1.25mcg, 2.5mcg soln

STEROID
- beclomethasone diproprionate Qvar Redihaler 40mcg, 80mcg MDI
- budesonide Pulmicort Flexhaler 90mcg, 180mcg DPI
- ciclesonide Alvesco 80mcg, 160mcg MDA
- fluticasone furoate Arnuity Ellipta 50mcg, 100mcg, 200mcg DPI

- fluticasone propionate ArmonAir Digihaler 55mcg, 113mcg, 232mcg DPI, Flovent Diskus 50mcg, 100mcg,250mcg DPI, Flovent HFA 44mcg, 110mcg, 220mcg MDI
- mometasone furoate Asmanex HFA 50mcg, 100mcg, 200mcg MDI, Asmanex Twisthaler 110mcg, 220mcgDPI

STEROID + ANTICHOLINERGIC + LONG-ACTING BETA2-AGONIST

- fluticasone + umeclidinium + vilanterol Trelegy Ellipta 100/62.5/25mcg, 200/62.5/25mcg DPI
- budesonide + glycopyrrolate + formoterol Breztri Aerosphere MDI 160/9/4.8 mcg

Appendix 2:
First generation H1 antihistamine: hydroxyzine, cyproheptadine
Second generation H1 antihistamine: cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine
Leukotriene receptor antagonist (LTRA): montelukast (Singulair), zafirlukast (Accolate), zileuton (Zyflo)
H2-Antihistamines: cimetidine (Tagamet), famotidine (Pepcid), nizatidine (Axid), ranitidine (Zantac)

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Dupixent is indicated for the treatment of adult patients with moderate to severe atopic dermatitis (AD) whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent is a human monoclonal antibody that binds to the interleukin- 4receptoralpha (IL-4Rα) subunit shared by the interleukin (IL)-4 and IL-13 receptor complexes, thereby inhibiting IL-4 and IL-13 signaling. This inhibition limits IL-4 and IL-13 cytokine-induced responses, including the release of proinflammatory cytokines, chemokines, and IgE. Following a one-time loading dose of 600 mg (administered as two 300 mg subcutaneous [SC] injections), the recommended dose of Dupixent is 300 mg SC once every other week (QOW). Dupixent may be administered by the patient or caregiver following appropriate training.

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 (CSNP Trial 1 and CSNP Trial 2) in 724subjects aged 18 years 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. Patients with chronic rhinosinusitis without nasal polyposis were not included in these trials. Rescue with systemic corticosteroids or surgery was allowed during the studies at the investigator's discretion.
In CSNP Trial 1, a total of 276 subjects were randomized to receive either 300 mg DUPIXENT (N=143) or placebo (N=133) every other week for 24 weeks. In CSNP Trial 2, 448 subjects were randomized to receive either 300 mg DUPIXENT (N=150) every other week for 52 weeks, 300 mg DUPIXENT (N=145) every other week until week 24 followed by 300 mg DUPIXENT every 4 weeks until week 52, or placebo (N=153). All subjects had evidence of sinus opacification on the Lund Mackay (LMK) sinus CT scan and 73% to 90% of subjects had opacification of all sinuses. Subjects were stratified based on their histories of prior surgery and co- morbid asthma/nonsteroidal anti- inflammatory drug exacerbated respiratory disease (NSAID- ERD). A total of 63% of subjects reported previous sinus surgery, with a mean number of 2.0 prior surgeries, 74% used systemic corticosteroids in the previous 2 years with a mean number of 1.6 systemic corticosteroid courses in the previous 2 years, 59% had co-morbid asthma, and 28% had NSAID-ERD. The co-primary efficacy endpoints were change from baseline to Week 24 in bilateral endoscopic nasal polyps score (NPS; 0-8 scale) as graded by central blinded readers, and change from baseline to Week 24 in nasal congestion/obstruction score averaged over 28 days (NC; 0-3 scale), as determined by subjects using a daily diary. For NPS, polyps on each side of the nose were graded on a categorical scale (0=no polyps; 1=small polyps in the middle meatus not reaching below the inferior border of the middle turbinate; 2=polyps reaching below the lower border of the middle turbinate; 3=large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle turbinate; 4=large polyps causing complete obstruction of the inferior nasal cavity). The total score was the sum of the right and left scores. Nasal

congestion was rated daily by the subjects on a 0 to 3 categorical severity scale (0=no symptoms; 1=mild symptoms; 2=moderate symptoms; 3=severe symptoms).

In both studies, key secondary endpoints at Week 24 included change from baseline in: LMK sinus CT scan score, daily loss of smell, and 22-item sino-nasal outcome test (SNOT-22). The LMK sinus CT scan score evaluated the opacification of each sinus using a 0 to 2 scale (0=normal; 1=partial opacification; 2=total opacification) deriving a maximum score of 12 per side and a total maximum score of 24 (higher scores indicate more opacification). Loss of smell was scored reflectively by the patient every morning on a 0-3 scale (0=no symptoms, 1=mild symptoms, 2=moderate symptoms, 3=severe symptoms). SNOT- 22 includes 22 items assessing symptoms and symptom impact associated with CRSwNP with each item scored from 0 (no problem) to 5 (problem as bad as it can be) with a global score ranging from 0 to 110. SNOT-22 had a 2-week recall period. In the pooled efficacy results, the reduction in the proportion of subjects rescued with systemic corticosteroids and/or sino-nasal surgery (up to Week 52) were evaluated. At Week 52, the LS mean difference for nasal congestion in the DUPIXENT group versus placebo was -
0.98 (95% CI -1.17, -0.79). In both studies, significant improvements in nasal congestion were observed as early as the first assessment at Week 4. The LS mean difference for nasal congestion at Week 4 in the DUPIXENT group versus placebo was -0.41 (95% CI: -0.52, -0.30) in CSNP Trial 1and -0.37 (95% CI: -0.46, -0.27) in CSNP Trial 2. A significant decrease in the LMK sinus CT scan score was observed. The LS mean difference for LMK sinus CT scan score at Week 24 in the DUPIXENT group versus placebo was -7.44 (95% CI: -8.35, -6.53) in CSNP Trial 1 and -5.13 (95% CI: -5.80, -4.46) in CSNP Trial 2 At Week52, in CSNP Trial 2 the LS mean difference for LMK sinus CT scan score in the DUPIXENT group versus placebo was -6.94 (95% CI: -7.87, -6.01). Dupilumab significantly improved the loss of smell compared to placebo. The LS mean difference for loss of smell at Week 24 in the DUPIXENT group versus placebo was -1.12 (95% CI: -1.31, -0.93) in CSNP Trial 1 and -0.98 (95% CI: - 1.15, -0.81) in CSNP Trial 2. At Week 52, the LS mean difference for loss of smell in the DUPIXENT group versus placebo was -1.10 (95% CI 1.31, -0.89). In both studies, significant improvements in daily loss of smell severity were observed as early as the first assessment at Week 4. Dupilumab significantly decreased sino-nasal symptoms as measured bySNOT-22 compared to placebo. The LS mean difference for SNOT-22 at Week 24 in the DUPIXENT group versus placebo was -21.12 (95% CI: -25.17, -17.06) in CSNP Trial 1 and -17.36 (95% CI: - 20.87, -13.85) in CSNP Trial 2. At Week 52, the LS mean difference in the DUPIXENT group versus placebo was -20.96 (95% CI -25.03, -16.89). In the pre- specified multiplicity-adjusted pooled analysis of two studies, treatment with DUPIXENT resulted in significant reduction of systemic corticosteroid use and need for sino-nasal surgery versus placebo (HR of 0.24; 95% CI: 0.17, 0.35) (see Figure 9). 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).

Chronic Obstructive Pulmonary Disease (COPD)

Dupixent is approved for us in adult patients with inadequately controlled chronic obstructive pulmonary disease (COPD) and an eosinophilic phenotype. Efficacy and safety were evaluated in two randomized, double-blind, multicenter, parallel-group, placebo-controlled trials (BOREAS [NCT03930732] and NOTUS [NCT04456673]) of 52 weeks duration. The two trials enrolled a total of 1874 adult subjects with COPD. Both trials enrolled subjects with a diagnosis of COPD with moderate to severe airflow limitation and a minimum blood eosinophil count of 300 cells/mcL at screening. Trial enrollment required an exacerbation history of at least 2 moderate or 1 severe exacerbation in the previous year despite receiving maintenance triple therapy consisting of a long-acting muscarinic antagonist (LAMA), long- acting beta agonist (LABA), and inhaled corticosteroid (ICS), and symptoms of chronic productive cough for at least 3 months in the past year. In both trials, subjects were randomized to receive DUPIXENT 300 mg subcutaneously every two weeks (Q2W) or placebo in addition to their background maintenance therapy for 52 weeks. The primary endpoint for BOREAS and NOTUS trials was the annualized rate of moderate or severe COPD exacerbations during the 52-week treatment period. In both trials, DUPIXENT demonstrated a significant reduction in the annualized rate of moderate or severe COPD exacerbations compared to placebo when added to background maintenance therapy [BOREAS rate ratio vs placebo 0.71 (95% CI 0.58, 0.86), NOTUS rate ratio vs placebo 0.66 (95% CI 0.54, 0.82)]. Treatment with Dupixent also decreased time to first exacerbation when compared with placebo in BOREAS (HR: 0.80; 95% CI: 0.66, 0.98) and NOTUS (HR: 0.71; 95% CI: 0.57, 0.89).

The 2024 GOLD guidelines mention dupilumab as a drug with potential to reduce exacerbations that requires confirmation in further studies.
The 2025 GOLD guidelines list dupilumab as treatment for patients treated with LABA+LAMA+ICS who still have exacerbations, with eosinophils 300 cellls/mcL or greater, and with symptoms of chronic bronchitis.

Chronic Spontaneous Urticaria:
In 2014, the Joint Task Force on Practice Parameters (JTFPP), representing the American Academy of Allergy, Asthma & Immunology (AAAAI); the American College of Allergy, Asthma & Immunology (ACAAI); and the Joint Council of Allergy, Asthma & Immunology updated the practice parameter for the diagnosis and management of acute and chronic urticaria (CU). The practice parameter established a step-care approach to the treatment of chronic urticaria and angioedema. The task force recommended the following step-care treatment approach:
• Monotherapy with second-generation antihistamines: H1-antagonists are effective in the majority of patients with CU but might not achieve complete control in all patients.
• Dose advancement of H1-antihistamine therapy, combining first- and second-generation agents and adding an H2-antihistamine and/or an antileukotriene agent: Higher doses of second-generation antihistamines can provide greater efficacy when control is not achieved with conventional doses of these agents.
• Therapeutic trial of potent antihistamine (e.g., hydroxyzine or doxepin): First-generation antihistamines should be prescribed cautiously in the elderly or patients with occupations (e.g., machine operators, airline pilots, or alpine skiers) for which alertness is essential.
• Add an immunosuppressant or biologic agent: Omalizumab and cyclosporine have the greatest published experience documenting efficacy in patients with CU compared with all other alternative agents. The EAACI/GA2LEN/EDF/AAAAI/WAO Guideline for the Management of Urticaria include Xolair in combination with H1-antihistamines as a third line treatment option in patients who have failed to respond to higher doses of H1-Antihistamines.
The Joint Task Force on Practice Parameters representing various American allergy organizations include biologics in combination with H1-antihistamines as a fourth line treatment option following a stepwise approach starting with a second-generation antihistamine. This is followed by one or more of the following: a dose increases of the second-generation antihistamine, or the addition of another second- generation antihistamine, H2-antagonist, LTRA, or first-generation antihistamine. Treatment with hydroxyzine or doxepin can be considered in patients whose symptoms remain poorly controlled. Dupixent was not yet FDA approved for urticaria at the time of this publication.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Dupixent (dupilumab) are considered experimental/investigational and therefore will follow the Molina Healthcare, Inc. off-label policy. Contraindications to Dupixent (dupilumab) include: Known hypersensitivity to dupilumab or any of its excipients, avoid use of live vaccines with Dupixent.

Exclusions/Discontinuation:
Do not use Dupixent concurrently with other monoclonal antibodies: Xolair (omalizumab), Cinqair (reslizumab), Nucala (mepolizumab), Fasenra (benralizumab), or Tezspire (tezepelumab).

OTHER SPECIAL CONSIDERATIONS:
If a weekly dose is missed, administer the dose as soon as possible, and start a new weekly schedule from the date of the last administered dose. If an every other week dose is missed, administer the injection within 7 days from the missed dose and then resume the patient's original schedule. If the missed dose is not administered within 7 days, wait until the next dose on the original schedule. If an every 4 week dose is missed, administer the injection within 7 days from the missed dose and then resume the patient's original schedule. If the missed dose is not administered within 7 days, administer the dose, starting a new schedule based on this date.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-*

inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Dupixent SOAJ 200MG/1.14ML prefilled pen
Dupixent SOAJ 300MG/2ML prefilled pen
Dupixent SOSY 100MG/0.67ML prefilled syringe
Dupixent SOSY 200MG/1.14ML prefilled syringe
Dupixent SOSY 300MG/2ML prefilled syringe

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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION-Notable Revisions: Required Medical Information Continuation of Therapy Prescriber Requirements Age Restrictions Quantity FDA-Approved Uses Appendix Background References	Q3 2025
REVISION-Notable Revisions: Required Medical Information Continuation of Therapy Quantity Background Contraindications/Exclusions/ Discontinuation References	Q2 2025

REVISION-Notable Revisions: Diagnosis Required Medical Information Continuation of Therapy Prescriber Requirements Age Restrictions Quantity FDA-Approved Uses Appendix Background References	Q4 2024
REVISION-Notable Revisions: Required Medical Information Continuation of Therapy Prescriber Requirements Quantity Other Special Considerations References	Q2 2024
REVISION-Notable Revisions: Diagnosis Required Medical Information Continuation of Therapy Duration of Approval Quantity Available Dosage Forms References	Q2 2023
REVISION-Notable Revisions: Required Medical Information Continuation of Therapy Prescriber Requirements Age Restrictions Quantity FDA-Approved Uses	Q4 2022
REVISION-Notable Revisions: Required Medical Information Prescriber Requirements Quantity FDA Approved Uses Appendix	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file