Clinical Policy: Dupilumab (Dupixent)

Reference Number: OH.PHAR.PPA.94
Effective Date: 10/2019
Last Review Date: 07/2022
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description:
Dupilumab (Dupixent®) is an interleukin-4 receptor alpha antagonist.

MONOCLONAL ANTIBODIES-ANTI-IL/ANTI-IgE

CLINICAL PA REQUIRED "PREFERRED"	PA REQUIRED "NON-PREFERRED"
FASENRA® (benralizumab) NUCALA® (mepolizumab) XOLAIR® (omalizumab)	DUPIXENT® (dupilumab)

FDA Approved Indication(s)
Dupixent is 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
- For the treatment of patients aged 6 years and older with moderate-to-severe **atopic dermatitis** whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent can be used with or without topical corticosteroids
- As an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with **nasal polyps** (CRSwNP)

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Buckeye Health Plan, an affiliate of Centene Corporation®, that Dupixent is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Atopic Dermatitis (must meet all)**:**

1. Diagnosis of moderate to severe atopic dermatitis;
2. Age ≥ 6 years;
3. Prescribed by or in consultation with a dermatologist or allergist/immunologist;
4. Prescribed in accordance with FDA-approved labeling;
5. Member has a minimum body surface area (BSA) involvement ≥ 10%;
6. Inadequate response or contraindication to at least two of the following: topical corticosteroids, topical calcineurin inhibitors (e.g., Elidel®), or topical PDE-4

inhibitors (e.g., Eucrisa) UNLESS the member meets ONE of the following (a, b, c, or d):
   a. Atopic dermatitis is severe and involves > 25% of body surface area (BSA);
   b. Allergy to medications not requiring prior approval;
   c. Contraindication to or drug interaction with medications not requiring prior approval;
   d. History of unacceptable/toxic side effects to medications not requiring prior approval.
7. Dose does not exceed the following (a or b):
   a. Initial (one-time) dose: 600 mg;
   b. Maintenance dose: 300 mg every other week.

Approval duration: 6 months.

B. Moderate-to-Severe Asthma (must meet all)**:**
1. Diagnosis of moderate to severe asthma;
2. Age ≥ 6 years;
3. Prescribed by or in consultation with an allergist/immunologist or pulmonologist;
4. Prescribed in accordance with FDA-approved labeling;
5. For members 6 to 11 years old: Documentation of uncontrolled asthma symptoms and/or exacerbations despite at least 1 month adherence to therapy with a medium dose preferred inhaled corticosteroid (ICS)/long-acting beta-agonist (LABA) inhaler UNLESS there is a reason the member cannot be changed to medications not requiring prior approval. Acceptable reasons include:
   - Allergies to all medications not requiring prior approval;
   - Contraindication to or drug-to-drug interaction with medications not requiring prior approval;
   - History of unacceptable/toxic side effects to medications not requiring prior approval;
6. For members 12 years and older: Documentation of uncontrolled asthma symptoms and/or exacerbations despite at least 1 month adherence to therapy with a medium dose preferred inhaled corticosteroid (ICS)/long-acting beta-agonist (LABA) inhaler with tiotropium OR high dose preferred ICS/LABA inhaler UNLESS there is a reason the member cannot be changed to medications not requiring prior approval. Acceptable reasons include:
   - Allergies to all medications not requiring prior approval;
   - Contraindication to or drug-to-drug interaction with medications not requiring prior approval;
   - History of unacceptable/toxic side effects to medications not requiring prior approval;
7. Documentation of uncontrolled asthma symptoms and/or exacerbations despite at least a 3 month adherent trial with a preferred monoclonal antibody agent UNLESS there is a reason the member cannot be changed to a preferred medication. Acceptable reasons include:
   - Allergies to all medications that are preferred;
   - Contraindication to or drug-to-drug interaction with medications that are preferred;
   - History of unacceptable/toxic side effects to medications that are preferred;

8. Dose does not exceed the following (a or b):
   - Initial (one-time) dose: 600 mg;
   - Maintenance dose: 300 mg every other week.

Approval duration: 6 months.

C. Chronic Rhino-Sinusitis with Nasal Polyps (must meet all)**:**

1. Diagnosis of chronic rhinosinusitis with nasal polyposis;
2. Age ≥ 18 years;
3. Prescribed by or in consultation with an allergist/immunologist, pulmonologist, or otolaryngologist;
4. Prescribed in accordance with FDA-approved labeling;
5. Member has had an inadequate response, intolerance or contraindication to one oral corticosteroid;
6. Member had a 1 month trial to one nasal corticosteroid spray;
7. Documentation of a 3 month adherent trial with a preferred monoclonal antibody agent UNLESS there is a reason the member cannot be changed to a preferred medication. Acceptable reasons include:
   - Allergies to all medications that are preferred;
   - Contraindication to or drug-to-drug interaction with medications that are preferred;
   - History of unacceptable/toxic side effects to medications that are preferred;
8. Dose does not exceed 300 mg every other week.

Approval duration: 12 months.

D. Other diagnoses/indications:

1. There are no pharmacy and therapeutic committee approved off-label use criteria for the diagnosis;
2. Use is supported by one of the following (a, b, or c):
   a. The National Comprehensive Cancer Network (NCCN) Drug Information and Biologics Compendium level of evidence 1 or 2A;
   b. Evidence from at least two high-quality, published studies in reputable peer-reviewed journals or evidence-based clinical practice guidelines that provide all of the following (i – iv):
      i. Adequate representation of the member's clinical characteristics, age, and diagnosis;
      ii. Adequate representation of the prescribed drug regimen;
      iii. Clinically meaningful outcomes as a result of the drug therapy in question;
      iv. Appropriate experimental design and method to address research questions;
   c. Micromedex DrugDex® with strength of recommendation Class I, IIa, or IIb;
3. Prescribed by or in consultation with an appropriate specialist for the diagnosis;
4. Failure of an adequate trial of at least two FDA-approved drugs for the indication and/or drugs that are considered the standard of care, when such agents exist for the same indication at maximum indicated doses, unless no such drugs exist, at maximum indicated doses, unless contraindicated or clinically significant adverse effect are experienced;
5. Dosing regimen and duration are within dosing guidelines recommended by clinical practice guidelines and/or medical literature.

Approval duration: 112 days.

II. Continued Therapy

A. Atopic Dermatitis (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy (e.g., reduced BSA affected);
3. If request is for a dose increase, new dose does not exceed 300 mg given every other week.

Approval duration: 12 months.

B. Moderate-to-Severe Asthma (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member demonstrates improvement in condition with therapy (e.g., improvement in pulmonary function tests [PFTs]);
3. If request is for a dose increase, new dose does not exceed 300 mg every other week.

Approval duration: 12 months.

C. Chronic Rhino-Sinusitis with Nasal Polyps (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Dose does not exceed 300 mg every other week.

Approval duration: 12 months.

III. Diagnoses/Indications for which coverage is NOT authorized:

Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
ACQ: Asthma Control Questionnaire
BSA: Body Surface Area
FDA: Food and Drug Administration
PA: Prior Authorization
PDE-4 Inhibitor: Phosphodiesterase-4 Inhibitor

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ATOPIC DERMATITIS		
Very High Potency Topical Corticosteroids		
clobetasol propionate 0.05% (Clobex, Olux, Temovate®) cream, foam, lotion, ointment, gel, solution, spray, shampoo	Apply topically to the affected area(s) BID	varies
High Potency Topical Corticosteroids		
amcinonide ointment, cream, lotion	Apply topically to the affected area(s) BID	varies
diflorasone 0.05% (Florone®, Florone E®, Maxiflor®,Psorcon E®) cream, ointment		
fluocinonide acetonide 0.05% (Lidex®, Lidex E®) cream, ointment, gel, solution		
betamethasone valerate (Valisone) ointment		
Medium Potency Topical Corticosteroids		
betamethasone dipropionate-calcipotriene ointment	Apply topically to the affected area(s) BID	varies
betamethasone valerate cream, lotion (generic of Valisone®)		
fluticasone propionate cream, ointment (generic of Cutivate®)		
mometasone 0.1% (Elocon®) cream, ointment, solution		
prednicarbate (Dermatop) cream		
triamcinolone acetonide 0.025%, 0.1% (Aristocort®, Kenalog®) cream, ointment, lotion		
Low Potency Topical Corticosteroids		
fluocinolone body oil, scalp oil (generic of Derma-Smoothe/ FS®)	Apply topically to the affected area(s) BID	varies
desonide 0.05% (Desowen®) cream, ointment		
fluocinolone acetonide 0.01% (Synalar®) cream, solution		
hydrocortisone 2.5% (Hytone®) cream, ointment, lotion		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Other Classes of Agents		
Protopic® (tacrolimus), Elidel® (pimecrolimus labeler 68682)	Children ≥ 2 years and adults: Apply a thin layer topically to affected skin BID. Treatment should be discontinued if resolution of disease occurs.	varies
cyclosporine	3-6mg/kg/day PO BID	300 mg/day
azathioprine	1-3mg/kg/day PO once daily	Weight-based
methotrexate	7.5-25mg/wk PO once weekly	25 mg/week
mycophenolate mofetil	1-1.5 PO BID	3 g/day
Systemic corticosteroids (e.g. prednisone, prednisolone, triamcinolone)	PO, IM, or parenteral; dose varies	varies
ASTHMA		
ICS (medium – high dose)		
budesonide (Pulmicort® Flexhaler)	> 400 mcg/day 90 mcg, 180 mcg per actuation 2-4 actuations BID	2 actuations BID
budesonide nebulizer solution (generic of Pulmicort®) (no PA required for age 6 or under)	0.5 mg once daily or 0.25 mg twice daily via nebulizer	0.5 mg/day
Flovent® Diskus and HFA (fluticasone propionate)	> 250 mcg/day 44-250 mcg per actuation 2-4 actuations BID	2 actuations BID
Asmanex® (mometasone)	Twisthaler: 110 mcg, 220 mcg per actuation 1-2 actuations QD to BID	2 inhalations BID
LABA		
Serevent® (salmeterol)	50 mcg per dose 1 inhalation BID	1 inhalation BID
Combination products (ICS + LABA)		
Dulera® (mometasone/ formoterol)	100/5 mcg, 200/5 mcg per actuation 2 actuations BID	4 actuations per day
salmeterol/fluticasone (generic of Advair Diskus®) [Labeler 66993]	Diskus: 100/50 mcg, 250/50 mcg, 500/50 mcg per actuation HFA: 45/21 mcg, 115/21 mcg, 230/21 mcg per actuation 1 actuation BID	1 actuation BID
Symbicort® (budesonide/ formoterol)	80 mcg/4.5 mcg, 160 mcg/4.5 mcg per actuation 2 actuations BID	2 actuations BID
LTRA		
montelukast (Singulair®)	4 to 10 mg PO QD	10 mg per day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Oral corticosteroids		
dexamethasone (Decadron®)	0.75 to 9 mg/day PO in 2 to 4 divided doses	Varies
methylprednisolone (Medrol®)	40 to 80 mg PO in 1 to 2 divided doses	Varies
prednisolone (Millipred®, Orapred ODT®)	40 to 80 mg PO in 1 to 2 divided doses	Varies
prednisone (Deltasone®)	40 to 80 mg PO in 1 to 2 divided doses	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known hypersensitivity to Dupixent or any of its excipients
- Boxed warning(s): none reported

Appendix D: General Information

- The Phase III pivotal studies (SOLO 1 and SOLO 2) of Dupixent showed no significant difference in clinical outcomes between dosing of Dupixent every week and every other week for the treatment of atopic dermatitis.
- During clinical trials (LIBERTY ASTHMA QUEST), among patients with a baseline blood eosinophil count of < 150 per cubic millimeter, the exacerbation rate was similar with dupilumab and with placebo: 0.47 (95% CI, 0.36 to 0.62) with lower-dose dupilumab and 0.51 (95% CI, 0.35 to 0.76) with matched placebo, and 0.74 (95% CI, 0.58 to 0.95) with higher-dose dupilumab and 0.64 (95% CI, 0.44 to 0.93) with matched placebo.
- Positive response to therapy for asthma may include reduction in exacerbations or corticosteroid dose, improvement in forced expiratory volume over one second since baseline, or reduction in the use of rescue therapy.
- Lab results for blood eosinophil counts can be converted into cells/mcL using the following unit conversion calculator: https://www.fasenrahcp.com/m/fasenra-eosinophil-calculator.html

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Moderate-to-severe atopic dermatitis	Adults: Initial dose of 600 mg SC followed by 300 mg SC every other week Adolescents 12-17 years of age: Body weight < 30 kg: Initial dose of 600 mg SC followed by 300 mg SC every other 4 weeks Body weight 30-59 kg: Initial dose of 400 mg SC followed by 200 mg SC every other week	600 mg initially, then 300 mg every other week

Indication	Dosing Regimen	Maximum Dose
	Body weight ≥ 60 kg: Initial dose of 600 mg SC followed by 300 mg SC every other week Children 6-11 years of age: Body weight < 30 kg: Initial dose of 600 mg SC followed by 300 mg SC every other 4 weeks Body weight 30-59 kg: Initial dose of 400 mg SC followed by 200 mg SC every other week Body weight ≥ 60 kg: Initial dose of 600 mg SC followed by 300 mg SC every other week	
Moderate-to-severe asthma	Adults: Initial dose of 400 mg SC followed by 200 mg SC every other week; or Initial dose of 600 mg SC followed by 300 mg SC every other week Adolescents 12-17 years of age: Initial dose of 400 mg SC followed by 200 mg SC every other week; or Initial dose of 600 mg SC followed by 300 mg SC every other week Children 6-11 years of age: Body weight < 30 kg: 100 mg SC every other week OR 300 mg SC every 4 weeks Body weight ≥ 30 kg: 200 mg SC every other week For patients requiring concomitant oral corticosteroids or with co-morbid moderate-to-severe atopic dermatitis for which Dupixent is indicated, start with an initial dose of 600 mg SC followed by 300 mg SC every other week	600 mg initially, then 300 mg every other week
Chronic rhino-sinusitis with nasal polyps	300 mg SC every other week	300 mg SC every other week

VI. Product Availability

Pre-filled syringe with needle shield for injection: 200 mg/1.4 mL, 300 mg/2 mL

VII. References

1. Dupixent Prescribing Information. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; March 2019. Available at: www.dupixent.com. Accessed March 21, 2019.

2. Simpson EL, Bieber T, Guttman-Yassky E, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. New England Journal of Medicine. 2016; 375: 2335-48.
3. Eichenfield F, Tom WL, Chamlin SL, et al. Guidelines of Care for the Management of Atopic Dematitis. *J Am Acad Dermatol*. 2014 February; 70(2): 338–351.
4. Leshem YA, Hajar T, Hanifin JM, et al. What the Eczema Area and Severity Index score tells us about the severity of atopic dermatitis: an interpretability study. British Journal of Dermatology 2015; 172(5):1353-1357.
5. National Asthma Education and Prevention Program: Expert panel report III: Guidelines for the diagnosis and management of asthma. Bethesda, MD: National Heart, Lung, and Blood Institute, 2007. (NIH publication no. 08-4051). Available at http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines. Accessed November 13, 2018.
6. Global Initiative for Asthma: Global strategy for asthma management and prevention (2018 update). Available at: https://ginasthma.org/2018-gina-report-global-strategy-for-asthma-management-and-prevention/. Accessed November 13, 2018.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9399; J3590	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created.	10.19	N/A
Policy updated.	11.20	N/A
Under Asthma diagnosis – removed criteria point indicating member must have had asthma-related emergency treatment within the last 180 days	02.21	N/A
Added Xolair to PA required, preferred.	11.21	N/A
ODM Q2 P&T update. Updated asthma indication to include 6 years of age and up. Added "prescribed in accordance with its FDA approved labeling" to all indications. Updated initial authorization for atopic dermatitis indication from 112 days to 6 months. Added criteria for inhaler trial with asthma indication. Updated initial authorization for asthma indication from 12 months to 6 months. Added prescriber specialty criteria for nasal polyp indication. Added criteria for preferred monoclonal antibody agent trial with nasal polyps indication. Added documentation of improvement in PFTs to continuation criteria for asthma. Updated dosing chart for moderate-to-severe asthma.	07.22	N/A

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.