Clinical Policy: Respiratory Agents: Monoclonal Antibodies-Anti-IL/Anti-IgE (Self-Administered)

Reference Number: OH.PHAR.PPA.101
Effective Date: 01/01/2021
Last Review Date: 11.21
Line of Business: Medicaid

Coding Implications
Revision Log

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

Description:
Benralizumab (Fasenra™) is an interleukin (IL)-5 receptor alpha-directed cytolytic monoclonal antibody.

Mepolizumab (Nucala®) is an interleukin-5 antagonist monoclonal antibody (IgG1 kappa).

Omalizumab (Xolair® is an immunoglobulin E (IgE) inhibitor.

MONOCLONAL ANTIBODIES-ANTI-IL/ANTI-IgE (SELF-ADMINISTERED)

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

FDA Approved Indication(s)
Fasenra is indicated for:
- Add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype.

Nucala is indicated for:
- Add-on maintenance treatment of patients with severe asthma aged 6 years and older, and with an eosinophilic phenotype.
- Treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).

Xolair is indicated for:
- Add-on maintenance treatment of patients with moderate to severe persistent asthma aged 6 years and older.
- Treatment of chronic idiopathic urticaria in patients aged 12 years and older who remain symptomatic despite H1 antihistamine treatment.
- Add-on maintenance treatment of nasal polyps in adults with inadequate response to nasal corticosteroids.

Limitation(s) of use:
- Fasenra is not indicated for treatment of other eosinophilic conditions.
- Fasenra is not indicated for the relief of acute bronchospasm or status asthmaticus.

- Nucala is not indicated for the relief of acute bronchospasm or status asthmaticus.
- Xolair is not indicated for the relief of acute bronchospasm or status asthmaticus, treatment of other allergic conditions, or treatment of other forms of urticaria.

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 Fasenra and Nucala are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. For Fasenra (benralizumab) (must meet all)**:**

1. Diagnosis of asthma (moderate to severe);
2. Age ≥ 12 years;
3. Prescribed by or in consultation with a/an allergist, immunologist, or pulmonologist;
4. Documentation that there has been a therapeutic failure to no less than a 1 month adherent trial 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;
5. Dose does not exceed 30 mg every 4 weeks for the first 3 doses, then 30 mg every 8 weeks thereafter.

Approval duration: 12 months.

B. For Nucala (mepolizumab) (must meet all)**:**

1. Diagnosis of asthma (moderate to severe);
2. Age ≥ 6 years;
3. Prescribed by or in consultation with a/an allergist, immunologist, or pulmonologist;
4. For members 6 to 11 years old: Documentation that there has been a therapeutic failure to no less than a 1 month adherent trial 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;
5. For members 12 years and older: Documentation that there has been a therapeutic failure to no less than a 1 month adherent trial 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;

6. Dose does not exceed (a or b):
   a. Age 6 to 11 years: 40 mg every 4 weeks;
   b. Age ≥ 12 years: 100 mg every 4 weeks.

Approval duration: 12 months.

C. For Xolair (omalizumab) (must meet all):
1. For diagnosis of moderate to severe asthma, all the of the following must be met (a, b, c, d, and e):
   a. Age ≥ 6 years;
   b. Prescribed by or in consultation with a/an allergist, immunologist, or pulmonologist;
   c. For members 6 to 11 years old: Documentation that there has been a therapeutic failure to no less than a 1 month adherent trial 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:
      i. Allergies to all medications not requiring prior approval.
      ii. Contraindication to or drug-to-drug interaction with medications not requiring prior approval.
      iii. History of unacceptable/toxic side effects to medications not requiring prior approval;
   d. For members 12 years and older: Documentation that there has been a therapeutic failure to no less than a 1 month adherent trial 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:
      i. Allergies to all medications not requiring prior approval.
      ii. Contraindication to or drug-to-drug interaction with medications not requiring prior approval.
      iii. History of unacceptable/toxic side effects to medications not requiring prior approval;
   e. Dose does not exceed 375 mg every 2 weeks.

2. For diagnosis of chronic urticaria, all of the following must be met (a, b, c, and d):
   a. Age ≥ 12 years;
   b. Member has tried and failed two ≥14 day trials with two different antihistamines;
   c. Prescribed by or in consultation with a dermatologist or allergist/immunologist;

d. Dose does not exceed 300 mg every 4 weeks.

3. For diagnosis of chronic rhinosinusitis with nasal polyposis, all of the following must be met (a, b, c, and d):
   a. Age ≥ 18 years;
   b. Member had an inadequate response, intolerance, or contraindication to one oral corticosteroid;
   c. Member had a ≥ 30-day trial and experienced an inadequate response, intolerance, or contraindication to one nasal corticosteroid spray;
   d. Dose does not exceed 600 mg every 2 weeks.

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;
1. 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;
2. 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. Moderate-to-Severe Asthma (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Demonstrated adherence to asthma controller therapy;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed (a, b, or c);
   a. For Fasenra: 30 mg every 8 weeks;
   b. For Nucala (age 6 to 11 years): 40 mg every 4 weeks;
   c. For Nucala (age ≥ 12 years): 100 mg every 4 weeks.

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
BEC: Blood Eosinophil Count
EGPA: Eosinophilic Granulomatosis with Polyangiitis
FDA: Food and Drug Administration
GINA: Global Initiative for Asthma
ICS: Inhaled Corticosteroid
IL: Interleukin
LABA: Long-Acting Beta-Agonist
LTRA: Leukotriene Modifier
PA: Prior Authorization

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
ASTHMA		
ICS (medium – high dose)		
budesonide (Pulmicort®)	> 400 mcg/day 90 mcg, 180 mcg per actuation 2-4 actuations BID	2 actuations BID
Flovent® (fluticasone propionate)	> 250 mcg/day 44-250 mcg per actuation 2-4 actuations BID	2 actuations BID
Asmanex® (mometasone)	Twisthaler: 110 mcg, 220 mcg 1-2 actuations QD to BID	2 inhalations BID
budesonide (Pulmicort®) nebulizer solution (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
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	4 actuations per day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	2 actuations BID	
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
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 Fasenra or Nucala or any of its excipients
- Boxed warning(s): none reported

Appendix D: General Information

- The pivotal trials defined severe asthma as two or more exacerbations of asthma despite regular use of high-dose inhaled corticosteroids plus an additional controller with or without oral corticosteroids. Clinically significant exacerbation was defined as a worsening of asthma leading to the doubling (or more) of the existing maintenance dose of oral glucocorticoids for three or more days or hospital admission or an emergency department visit for asthma treatment.
- Controller medications are: inhaled glucocorticoids (Flovent, Pulmicort, Qvar, Asmanex), long-acting beta-agonists (LABAs) such as salmeterol, formoterol, or vilanterol, and antileukotriene agents (montelukast [Singulair], zafirlukast [Accolate] or Zyflo [zileuton]). Theophylline is also a controller agent; however, it is not as efficacious as LABAs.
- In the pivotal trial for treatment of EGPA, patients with a baseline blood eosinophil count < 150 cells/mcL did not have a statistically significant improvement in the primary endpoint, total accrued weeks of remission, when mepolizumab was compared to placebo (odds ratio, 0.95; 95% CI 0.28 to 3.24). Total number of weeks of remission was

significantly greater in patients with a baseline eosinophil count ≥ 150 cells/mcL (odds ratio, 26.10; 95% CI 7.02 to 97.02).

- Standard of care for EGPA is oral glucocorticoids. Induction therapy of prednisone 1 mg/kg/day is recommended for 2-3 weeks followed by gradual tapering to the minimal effective dose. Patients with stable doses of prednisone ≤ 7.5 mg/day are considered to be in remission, as defined by the European League Against Rheumatism (EULAR) and in the pivotal trial. The EGPA Consensus Task Force recommends that patients who are

  unable to taper prednisone to < 7.5 mg/day after 3-4 months of therapy should be considered for additional immunosuppressant therapy.
- EULAR defines an EGPA relapse as the appearance of new or worsening clinical manifestations, not including asthma and/or ear, nose, and throat.
- Lab results for blood eosinophil counts can be converted into cells/mcL using the following unit conversion calculator: https://www.gsksource.com/pharma/content/micro-sites/nucala-eos-calc/index.html

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Severe asthma (Fasenra)	30 mg SC every 4 weeks for the first 3 doses, followed by once every 8 weeks thereafter	30 mg/dose
Severe asthma (Nucala)	Age 6 to 11 years: 40 mg every 4 weeks Age ≥ 12 years: 100 mg SC every 4 weeks	100 mg every 4 weeks
Allergic asthma (Xolair)	75 to 375 mg SC every 2 or 4 weeks based on serum total IgE level (IU/mL) measured before the start of treatment, and body weight (kg) Xolair is not approved for use in patients weighing more than 150 kg Do not administer more than 150 mg (contents of one vial) per injection site. Divide doses of more than 150 mg amongst two or more injection sites.	375mg/2weeks
CIU (Xolair)	150 mg or 300 mg SC every 4 weeks	300 mg/4 weeks
Nasal polyps (Xolair)	75 to 600 mg SC every 2 or 4 weeks based on serum total IgE level (IU/mL) measured before the start of treatment, and body weight (kg)	600 mg/2 weeks

VI. Product Availability

- Single-dose prefilled syringe with solution for injection (Fasenra): 30 mg/mL
- Single-dose autoinjector Pen with solution for injection (Fasenra): 30 mg/mL
- Single-dose vial (Nucala): 100 mg of lyophilized powder for reconstitution
- Single-dose prefilled glass syringe with needle for injection (Nucala): 100 mg/mL
- Single-dose prefilled autoinjector with needle for injection (Nucala): 100 mg/mL

- Single-dose vial (Xolair): 150 mg
- Single-dose prefilled syringes (Xolair): 75mg/0.5 ml, 150 mg/ml

VII. References

1. Nucala Prescribing Information. Philadelphia, PA: GlaxoSmithKline LLC; September 2019. Available at: http://www.nucala.com. Accessed November 7, 2019.
2. 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 7, 2019.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: http://www.clinicalpharmacology.com. Accessed November 7, 2019.
4. Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. N Engl J Med 2014; 371:1198-207.
5. Bel EH, Wenzel SE, Thompson PH, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. New Engl J Med 2014; 371:1189-97.
6. Pavord ID, Korn S, Howarth P et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicenter, double-blind, placebo-controlled trial (Abstract). Lancet 2012; 380(9842):651-59.
7. Wechsler ME, Akuthota P, Jayne D, et al. Mepolizumab or placebo for eosinophilic granulomatosis with polyangiitis. N Engl J Med. 2017 May 18;376(20):1921-1932.
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9. Hellmich B, Flossmann O, Gross WL, et al. EULAR recommendations for conducting clinical studies and/or clinical trials in systemic vasculitis: focus on anti-neutrophil cytoplasm antibody-associated vasculitis. Ann Rheum Dis. 2007 May;66(5):605-17.
10. Mukhtyar C, Guillevin L, Cid MC, et al. EULAR recommendations for the management of primary small and medium vessel vasculitis. Ann Rheum Dis. 2009;68(3):310-7.
11. Global Initiative for Asthma. Global strategy for asthma management and prevention, 2019. Available at: www.ginasthma.org. Published June 2019. Accessed November 5, 2019.
12. Fasenra Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; October 2019. Available at: www.fasenra.com. Accessed November 7, 2019.
13. 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 7, 2019.
14. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: http://www.clinicalpharmacology.com. Accessed November 7, 2019.
15. Global Initiative for Asthma. Global strategy for asthma management and prevention, 2019. Available at: www.ginasthma.org. Published June 2019. Accessed November 5, 2019.

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
J0517	Injection, benralizumab, 1 mg
J2182	Injection, mepolizumab, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created.	11.20	N/A
Removed criteria point requiring that member has had asthma-related emergency treatments within the last 180 days; removed criteria point requiring that member has an absolute blood eosinophil count ≥ 150 cells/mcL within the past 3 months	02.21	N/A
Added Xolair to PA required, preferred. Added criteria for Xolair for asthma, chronic urticaria, and nasal polyps. For Fasenra, removed criteria that absolute blood eosinophil count ≥ 150 cells/mcL within the past 3 months must be met.	11.21	

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.