Clinical Policy: Mepolizumab (Nucala)

Reference Number: PA.CP.PHAR.200
Effective Date: 01/18
Last Review Date: 01/19

Coding Implications
Revision Log

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

FDA Approved Indication(s)
Nucala is indicated for:

- Add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype.
- Treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).

Limitation(s) of use: Nucala is not indicated for the relief of acute bronchospasm or status asthmaticus.

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania Health and Wellness that Nucala is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Severe Asthma (must meet all):

1. Diagnosis of asthma
2. Member has absolute blood eosinophil count ≥150 cells/mcL within the past 3 months;
3. Prescribed by or in consultation with a pulmonologist, immunologist, or allergist;
4. Age ≥ 12 years;
5. Member has experienced any of the following within the last 12 months
    a. Symptoms: >2 days/week
    b. Nighttime awakening:1−3x/week
    c. Interference with normal activity: some limitation
    d. Short-acting beta2-agonist use for symptom control: >2 days/week
    e. FEV1or peak flow: 60−80% predicted/personal best
    f. Validated Questionnaires
        i. ATAQ: 1-2
        ii. ACQ: ≥1.5
        iii. ACT: 16-19,

despite adherent use of controller therapy (i.e., high dose inhaled corticosteroid [ICS] plus either a long acting beta-2 agonist [LABA] or leukotriene modifier [LTRA] if LABA contraindication/intolerance);Nucala is prescribed concomitantly with an ICS plus either an LABA or LTRA;

6. Nucala is prescribed concomitantly with an ICS plus either a LABA or LTRA;
7. Dose does not exceed 100 mg every 4 weeks.

Approval duration: 6 months

B. Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss) (must meet all)**:**
1. Diagnosis of EGPA (Churg-Strauss);
2. Member has an absolute blood eosinophil count ≥150 cells/mcL within the last 3 months;
3. Prescribed by or in consultation with a pulmonologist, rheumatologist, immunologist, or nephrologist;
4. Age ≥ 18 years;
5. Failure of a 3-month trial of a glucocorticoid (*see Appendix B*), unless contraindicated or clinically significant adverse events are experienced;
6. Dose does not exceed 300 mg every 4 weeks.

Approval duration: 6 months

C. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Severe Asthma (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Demonstrated adherence to asthma controller therapy that includes an ICS plus either an LABA or LTRA;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed 100 mg every 4 weeks.

Approval duration: 12 months

B. Eosinophilic Granulomatosis with Polyangiitis (EGPA) (Churg-Strauss) (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 300 mg every 4 weeks.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PHAR.57 - Global Biopharm Policy**.**

Background

Description/Mechanism of Action:

Mepolizumab is a humanized interleukin-5 (IL-5) antagonist monoclonal antibody. Mepolizumab is produced by recombinant DNA technology in Chinese hamster ovary cells. Mepolizumab binds to IL-5 with a dissociation constant of 100 pM, inhibiting the bioactivity of IL-5 by blocking its binding to the alpha chain of the IL-5 receptor complex expressed on the eosinophil cell surface. By inhibiting IL-5 signaling, it reduces the production and survival of eosinophils; however, the mechanism of mepolizumab action in asthma has not been definitively established.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

EGPA: eosinophilic granulomatosis with polyangiitis
FDA: Food and Drug Administration
GINA: Global Initiative for Asthma
ICS: inhaled corticosteroid
LABA: Long-acting beta-agonist
LTRA: leukotriene modifier

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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Asthma - ICS (medium – high dose)		
Qvar® (beclomethasone)	> 200 mcg/day 40 mcg, 80 mcg per actuation 1-4 actuations BID	4 actuations BID
budesonide (Pulmicort®)	> 400 mcg/day 90 mcg, 180 mcg per actuation 2-4 actuations BID	2 actuations BID
Alvesco® (ciclesonide)	> 160 mcg/day 80 mcg, 160 mcg per actuation 1-2 actuations BID	2 actuations BID
Aerospan® (flunisolide)	> 320 mcg/day 80 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
Arnuity Ellipta® (fluticasone furoate)	200 mcg/day 100 mcg, 200 mcg per actuation 1 actuation QD	1 actuation QD
Asmanex® (mometasone)	>220 mcg/day HFA: 100 mcg, 200 mcg per actuation Twisthaler: 110 mcg, 220 mcg per actuation 1-2 actuations QD to BID	2 inhalations BID

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Asthma - LABA		
Serevent® (salmeterol)	50 mcg per dose 1 inhalation BID	1 inhalation BID
Asthma - Combination products (ICS + LABA)		
Dulera® (mometasone/ formoterol)	100/5 mcg, 200/5 mcg per actuation 2 actuations BID	4 actuations per day
Breo Ellipta® (fluticasone/ vilanterol)	100/25 mcg, 200/25 mcg per actuation 1 actuation QD	1 actuation QD
Advair® (fluticasone/ salmeterol)	100/50 mcg, 250/50 mcg, 500/50 mcg per actuation 1 actuation BID	1 actuation BID
Fluticasone/salmeterol (Airduo RespiClick®)	55/13 mcg, 113/14 mcg, 232/14 mcg per actuation 1 actuation BID	1 actuation BID
Symbicort® (budesonide/ formoterol)	80 mcg/4.5 mcg; 160 mcg/4.5 mcg per actuation 1-2 actuations BID	2 actuations BID
Asthma - LTRA		
Montelukast (Singulair®)	4 to 10 mg PO QD	10 mg per day
Zafirlukast (Accolate®)	10 to 20 mg PO BID	40 mg per day
zileuton ER (Zyflo® CR)	1200 mg PO BID	2400 mg per day
Zyflo® (zileuton)	1200 mg PO BID	2400 mg per day
Oral glucocorticoids		
Dexamethasone (Decadron) for asthma	0.75 to 9 mg/day PO in 2 to 4 divided doses	Varies
Methylprednisolone (Medrol) for asthma	40 to 80 mg PO in 1 to 2 divided doses	Varies
prednisolone (Millipred®, Orapred ODT®) for asthma	40 to 80 mg PO in 1 to 2 divided doses	Varies
prednisone (Deltasone®) for asthma	40 to 80 mg PO in 1 to 2 divided doses	Varies
Methylprednisolone (Medrol) for EGPA	6.0 mg/day to 0.8 mg/kg/day	Varies
Prednisone (Deltasone) for EGPA	7.5 mg/day to 1 mg/kg/day	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): hypersensitivity
- Boxed warning(s): none reported

Appendix D: General Information

- Nucala is not indicated for relief of acute bronchospasm or status asthmaticus.
- 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.
- Patients could potentially meet criteria for both Xolair and Nucala. The combination has not been studied. Approximately 30% of patients in the MENSA study also were candidates for therapy with Xolair.
- 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.
- 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.
- Positive response to therapy for EGPA is defined as a reduction of relapses or reduction in glucocorticoid dose. EULAR defines a 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

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Severe asthma	100 mg SC every 4 weeks	100 mg every 4 weeks
EGPA	300 mg SC every 4 weeks	300 mg every 4 weeks

V. Product Availability

Single-dose vial: 100 mg of lyophilized powder for reconstitution

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
J2182	Injection, mepolizumab, 1 mg

Reviews, Revisions, and Approvals	Date	Approval Date
1Q18 annual review: Removed smoking cessation program requirements as this cannot be enforced; criteria added for new FDA indication: treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EPGA); references reviewed and updated.	01.23.18	
1Q 2019 annual review: added option for immunologist prescribing for asthma; modified initial approval duration to 6 months; removed non-objective examples of positive response for continuation of therapy; references reviewed and updated.	01.19	

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