RXADVANCE
2 Park Central Drive
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Clinical Policy Title:	mepolizumab
Policy Number:	RxA.600
Drug(s) Applied:	Nucala®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

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

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Mepolizumab (Nucala®)	Severe asthma	Age 6 to 11 years: 40 mg every 4 weeks; Age ≥ 12 years: 100 mg SC every 4 weeks	100 mg every 4 weeks
	EGPA	300 mg SC once every 4 weeks	300 mg every 4 weeks

Dosage Forms

- Single-dose vial: 100 mg of lyophilized powder for reconstitution
- Single-dose prefilled glass syringe with needle for injection: 100 mg/mL
- Single-dose prefilled autoinjector with needle for injection: 100 mg/mL

Clinical Policy

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

I. Initial Approval Criteria

A. Severe Asthma (must meet all)**:**

1. Diagnosis of asthma;
2. Member has an absolute blood eosinophil count ≥150 cells/mcL within the past 3 months or blood eosinophil count ≥300 cells/mcL within the past 12 months;

3. Prescribed by or in consultation with a pulmonologist, immunologist, or allergist;
4. Age 6 years of age or older;
5. Member has experienced ≥ 2 exacerbations with in the last 12 months, requiring any of the following despite adherent use of controller therapy (i.e., medium- to high-dose inhaled corticosteroid (ICS) plus either a long acting beta-2 agonist (LABA) or leukotriene modifier (LTRA) if LABA contraindication/intolerance):
   a. Oral/systemic corticosteroid treatment (or increase in dose if already on oral corticosteroid);
   b. Urgent care visit or hospital admission;
   c. Intubation;
6. Nucala® is prescribed concomitantly with an ICS plus either a LABA or LTRA;
7. Nucala® is not prescribed concurrently with Cinqair®, Fasenra®, Dupixent®, or Xolair®
8. 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
Commercial: 6 months
Medicaid: 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 of age or older;
5. Failure of a 3-month trial of a glucocorticoid (*see Appendix B*), unless contraindicated or clinically significant adverse events are experienced;
6. Nucala is not prescribed concurrently with Cinqair®, Fasenra®, Dupixent® or Xolair®;
7. Dose does not exceed 300 mg every 4 weeks.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Severe Asthma (must meet all)**:**
1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Demonstrated adherence to asthma controller therapy that includes an ICS plus either an LABA or LTRA;
3. Member is responding positively to therapy (examples may include but are not limited to a reduction in exacerbations or corticosteroid dose, improvement in forced expiratory volume over one second since baseline; reduction in the use of rescue therapy);
4. Nucala is not prescribed concurrently with Cinqair®, Fasenra®, Dupixent® or Xolair®;
5. 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
Commercial: 6 months
Medicaid: 12 months

B. Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss) (must meet all):

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;;
2. Member is responding positively to therapy;
3. Nucala® is not prescribed concurrently with Cinqair®, Fasenra®, Dupixent®, or Xolair®;
4. If request is for a dose increase, new dose does not exceed 100 mg every 4 weeks.

Approval Duration
Commercial: 6 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

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

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

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
Alvesco® (ciclesonide)	> 160 mcg/day 80 mcg, 160 mcg per actuation 1-2 actuations BID	2 actuations BID
Arnuity Ellipta® (fluticasone furoate)	200 mcg/day 100 mcg, 200 mcg per actuation 1 actuation once daily	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 once daily to BID	2 inhalations BID
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 once daily	1 actuation once daily
Advair® (fluticasone/ salmeterol)	100/50 mcg, 250/50 mcg, 500/50 mcg per actuation 1 actuation BID	1 actuation BID

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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 once daily	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

References

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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	02/2020	03/06/2020
Policy was reviewed: 1. Clinical policy title was updated 2. Line of business policy applies to was updated to All lines of business 3. For Severe Asthma: Dose criteria updated based on age for Initial & continued therapy approval criteria 4. Concurrent therapy criteria added for all indication under both Initial therapy approval & Continued therapy approval criteria 5. Currently receiving medication that has been authorized by RxAdvance..." 6. Appendix B was reviewed and updated 7. Reference reviewed and updated.	09/23/2020	12/07/2020