Clinical Policy: Mepolizumab (Nucala)

Reference Number: ERX.SPA.214
Effective Date: 07.01.16
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

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

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 6 years and older, and with an eosinophilic phenotype.
- Add-on maintenance treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids.
- Treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).
- Treatment of adult and pediatric patients aged 12 years and older with hypereosinophilic syndrome (HES) for ≥ 6 months without an identifiable non-hematologic secondary cause.

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

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 an 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 ≥ 6 years;
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 concurrently with an ICS plus either an 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: 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 past 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. Nucala is not prescribed concurrently with Cinqair, Fasenra, Dupixent, or Xolair;
7. Dose does not exceed 300 mg every 4 weeks.

Approval duration: 6 months

C. Hypereosinophilic Syndrome (must meet all)**:**
1. Diagnosis of HES with all of the following characteristics (a, b, and c):
   a. FIP1L1-PDGFRα negative;
   b. Does not have a non-hematologic secondary cause (e.g., drug sensitivity, parasite helminth infection, HIV infection, non-hematological malignancy);
   c. Uncontrolled, defined as a history of ≥ 2 flares (*see Appendix D*) within the past 12 months;
2. Prescribed by or in consultation with a hematologist, dermatologist, or immunologist;
3. Age ≥ 12 years;
4. Member has a blood eosinophil count ≥ 1,000 cells/mcL within the past 3 months;
5. Failure of a 2-month trial of a corticosteroid (*see Appendix B*) within one of the following timeframes (a or b), unless contraindicated or clinically significant adverse events are experienced:
   a. Within the last 6 months:
   b. Within the last year if the member's current HES baseline therapy includes interferon-alfa, cyclosporine, azathioprine, hydroxyurea, or imatinib;
6. Nucala is prescribed concurrently with baseline HES therapy (e.g., oral corticosteroids, immunosuppressive therapy);
7. Nucala is not prescribed concurrently with Cinqair, Fasenra, Dupixent, or Xolair;
8. Dose does not exceed 300 mg every 4 weeks.

Approval duration: 6 months

D. Chronic Rhinosinusitis with Nasal Polyps (must meet all)**:**
1. Diagnosis of CRSwNP with documentation of all of the following (a, b, and c):
   a. Presence of nasal polyps;
   b. Disease is bilateral;
   c. Member has experienced signs and symptoms (e.g., nasal congestion/blockage/obstruction, loss of smell, rhinorrhea) for ≥ 12 weeks;
2. Prescribed by or in consultation with an allergist, immunologist, or otolaryngologist;
3. Age ≥ 18 years;
4. Member has required the use of systemic corticosteroids for symptom control within the last 2 years, unless contraindicated or clinically significant adverse effects are experienced *(see Appendix B for examples)*;
5. Failure of maintenance therapy with at least three intranasal corticosteroids, one of which must be Xhance™, each used for ≥ 4 weeks, unless contraindicated or clinically significant adverse effects are experienced *(see Appendix B for examples)*;
6. Nucala is prescribed concurrently with an intranasal corticosteroid, unless contraindicated or clinically significant adverse effects are experienced *(see Appendix B for examples)*;
7. Nucala is not prescribed concurrently with Cinqair, Dupixent, Fasenra, or Xolair;
8. Dose does not exceed 100 mg every 4 weeks.

Approval duration: 6 months

E. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Severe Asthma (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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: 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. If request is for a dose increase, new 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

B. Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss) (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy (examples may include but are not limited to: reduction of relapses or reduction in glucocorticoid dose);
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 300 mg every 4 weeks.

Approval duration: 12 months

C. Hypereosinophilic Syndrome (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy with reduction in flares from baseline or reduction in maintenance HES therapy dose from baseline (*see Appendix D*);
3. Nucala is prescribed concurrently with baseline HES therapy (e.g., oral corticosteroids, immunosuppressive therapy);
4. Nucala is not prescribed concurrently with Cinqair, Fasenra, Dupixent, or Xolair;
5. If request is for a dose increase, new dose does not exceed 300 mg every 4 weeks.

Approval duration: 12 months

D. Chronic Rhinosinusitis with Nasal Polyps (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Demonstrated adherence to an intranasal corticosteroid, unless contraindicated or clinically significant adverse effects are experienced;
3. Member is responding positively to therapy (examples may include but are not limited to: reduced nasal polyp size, reduced need for systemic corticosteroids, improved sense of smell, improved quality of life);
4. Nucala is not prescribed concurrently with Cinqair, Dupixent, Fasenra, or Xolair;
5. If request is for a dose increase, new dose does not exceed 100 mg every 4 weeks.

Approval duration: 12 months

E. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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

A. 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 policy – ERX.PA.01 or evidence of coverage documents;

B. Acute bronchospasm or status asthmaticus.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CRSwNP: chronic rhinosinusitis with nasal polyps
EGPA: eosinophilic granulomatosis with polyangiitis
FDA: Food and Drug Administration
FIP1L1-PDGFRα: Fip1-like1-platelet-derived growth factor receptor alpha
GINA: Global Initiative for Asthma
HES: hypereosinophilic syndrome
ICS: inhaled corticosteroid
LABA: long acting beta-2 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
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
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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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)	1,200 mg PO BID	2,400 mg per day
Zyflo® (zileuton)	1,200 mg PO BID	2,400 mg per day
Oral Glucocorticoids		
dexamethasone (Decadron®)	Refer to prescribing information	Refer to prescribing information
methylprednisolone (Medrol®) for asthma		
prednisolone (Millipred®, Orapred ODT®)		
prednisone (Deltasone®)		
methylprednisolone (Medrol®) for EGPA	6.0 mg/day to 0.8 mg/kg/day	Refer to prescribing information
prednisone (Deltasone®) for EGPA	7.5 mg/day to 1 mg/kg/day	Refer to prescribing information
HES		
oral corticosteroids: prednisolone, prednisone (off-label)	0.5 – 1 mg/kg/day	Varies
interferon alfa-2b (Intron-A®) (off-label)	1 – 6.25 million IU subcutaneously daily	20 million IU/m^2/day
imatinib (Gleevec®)	100 – 400 mg PO QD	400 mg/day
cyclosporine (off-label)	150 – 500 mg PO QD	Varies
azathioprine (off-label)	1 – 3 mg/kg PO QD	Varies
hydroxyurea (off-label)	0.5 – 3 gm PO QD with or without corticosteroid	80 mg/day
CRSwNP		
Oral corticosteroids		
dexamethasone (Decadron®)	0.75 to 9 mg/day PO in 2 to 4 divided doses	Varies
methylprednisolone (Medrol®)	4 to 48 mg PO in 1 to 2 divided doses	Varies
prednisolone (Millipred®, Orapred ODT®)	5 to 60 mg PO in 1 to 2 divided doses	Varies
prednisone (Deltasone®)	5 to 60 mg PO in 1 to 2 divided doses	Varies
Intranasal corticosteroids		
beclomethasone (Beconase AQ®, Qnasl®)	1-2 sprays IN BID	2 sprays/nostril BID
budesonide (Rhinocort® Aqua, Rhinocort®)	128 mcg IN QD or 200 mcg IN BID	1-2 inhalations/nostril/ day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
flunisolide	2 sprays IN BID	2 sprays/nostril TID
fluticasone propionate (Flonase®)	1-2 sprays IN BID	2 sprays/nostril BID
mometasone (Nasonex®)	2 sprays IN BID	2 sprays/nostril BID
Omnaris®, Zetonna® (ciclesonide)	Omnaris: 2 sprays IN QD Zetonna: 1 spray IN QD	Omnaris: 2 sprays/ nostril/day Zetonna: 2 sprays/ nostril/day
triamcinolone (Nasacort®)	2 sprays IN QD	2 sprays/ nostril/day
Xhance™ (fluticasone propionate)	1 to 2 sprays (93 mcg/spray) to nostril IN BID	744 mcg/day

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

- 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.
- The 2019 Global Initiative for Asthma (GINA) guidelines for difficult-to-treat and severe asthma recommend Nucala be considered as adjunct therapy for patients 18 years of age and older with exacerbations or poor symptom control despite taking at least high dose ICS/LABA and who have allergic or eosinophilic biomarkers or need maintenance oral corticosteroids. Per 2020 GINA guidelines, Nucala may also be considered if the patient is uncontrolled on Step 4 treatment (medium dose ICS/LABA).
- Patients could potentially meet asthma criteria for both Xolair and Nucala, though data is insufficient to support combination use of multiple asthma biologics. 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.
- 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
- Flares defined as a worsening of HES related clinical symptoms (e.g., pain, pruritus, skin lesions, nasal congestion, polyposis, dysphagia, or fatigue). An increase in blood eosinophil count

requiring an escalation in therapy or above the predefined threshold level. An increase in maintenance oral corticosteroid dose by greater than or equal to 10 mg for 5 days or increase in/addition of any cytotoxic and/or immunosuppressive HES therapy.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Asthma	Age 6 to 11 years: 40 mg SC every 4 weeks Age ≥ 12 years: 100 mg SC every 4 weeks	100 mg every 4 weeks
EGPA, HES	300 mg SC every 4 weeks	300 mg every 4 weeks
CRSwNP	100 mg SC every 4 weeks	100 mg every 4 weeks

Product Availability

- 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

VI. References

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q17 Annual Review Converted to new template. Added requirement related to smoking cessation efforts for current smokers per guidelines. Increased initial/continued approval duration from 3/6 months to 6/12 months. Added positive response to therapy on re-auth. Added acute bronchospasm and status asthmaticus as indications for which coverage is not authorized per PI.	09.25.17	11.17
1Q18 annual review: Removed smoking cessation requirements as this cannot be enforced. Added requirement for blood eosinophil count within the past 3 months.	11.06.17	02.18
Criteria added for new FDA indication: treatment of adult patients with EPGA.	01.23.18	05.18
1Q 2019 annual review: modified ICS requirement to include medium dose ICS per GINA 2018 recommendations; added option for immunologist prescribing for asthma; references reviewed and updated.	10.11.18	02.19
RT4: added new 100 mg/mL self-administered PFS and auto-injector formulations.	07.07.19	
1Q 2020 annual review: criteria updated to include asthma pediatric expansion for age 6-11 years; added requirement that Nucala is not prescribed concurrently with other biologic therapies for asthma; references reviewed and updated.	11.07.19	02.20
1Q 2021 annual review: criteria added for new FDA indication: hypereosinophilic syndrome indication (HES); updated Appendix B and D; references reviewed and updated.	10.30.20	02.21
RT4: criteria added for newly FDA-approved indication of CRSwNP.	08.15.21	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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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