



Original Effective Date: 09/01/2016  
 Current Effective Date: 10/25/2023  
 Last P&T Approval/Version: 10/25/2023  
 Next Review Due By: 10/2024  
 Policy Number: C9704-A

## Nucala (mepolizumab)

### PRODUCTS AFFECTED

Nucala (mepolizumab)

### COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

#### **Documentation Requirements:**

Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

#### **DIAGNOSIS:**

Severe asthma with an eosinophilic phenotype, Chronic rhinosinusitis with nasal polyps, Eosinophilic granulomatosis with polyangiitis, Hypereosinophilic syndrome

#### **REQUIRED MEDICAL INFORMATION:**

This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case- by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

- A. SEVERE ASTHMA WITH EOSINOPHILIC PHENOTYPE:
1. Documented diagnosis of moderate to severe asthma  
AND

## Drug and Biologic Coverage Criteria

2. Prescriber attests or clinical reviewer has found that Nucala (mepolizumab) is NOT being prescribed as:
  - (a) Monotherapy for asthma (must be prescribed as add-on maintenance to be used in combination with other medications for long- term control of asthma)  
AND
  - (b) Concurrent therapy with other monoclonal antibodies used to treat asthma [i.e., Xolair (omalizumab) OR other IL-5 inhibitors [benralizumab (Fasenra), Cinqair (reslizumab)] OR IL- 4 agonist Dupixent (dupilumab) OR Anti-TSLP Tezspire (Tezepelumab-ekko)]  
AND
3. Documentation has eosinophilic phenotype or predominantly eosinophil- driven disease with blood eosinophil counts:  $\geq 150$  cells/microliter at initiation of therapy (within 6 weeks of request) OR  $\geq 300$  cells/microliter in the prior 12 months [DOCUMENTATION REQUIRED]:  
AND
4. Member has experienced exacerbation(s) or hospitalization(s), within the last 12 months documented by any of the following:
  - i. TWO (2) or more exacerbations requiring treatment with systemic corticosteroid (intramuscular, intravenous, or oral) despite the use of high-dose inhaled corticosteroids in the past 12 months OR
  - ii. Two-fold increase or greater in the dose of systemic corticosteroid treatment for asthma exacerbations OR
  - iii. Asthma worsens upon tapering of oral corticosteroid therapy OR
  - iv. Mechanical ventilation in the past 12 months OR
  - v. Poor symptom control indicated by Asthma Control Questionnaire (ACQ) score consistently greater than 1.5 or Asthma Control Test (ACT) score consistently less than 20 OR
  - vi. Forced expiratory volume in 1 second (FEV1)  $< 80\%$  predicted OR
  - vii. FEV1/forced vital capacity (FVC)  $< 0.80$  
AND
5. Symptoms inadequately controlled (as documented in criteria above) by the following adherent regimen of at least 3 months (within the past 90 days): (a) OR (b)
  - (a) Medium or High ICS- LABA combination product AND one additional asthma controller medication (LAMA, LTRA, Low dose azithromycin), preferably a LAMA- per GINA 2023 guideline  
OR
  - (b) Medium or High ICS- LABA combination product AND oral corticosteroids [see appendix for product classes]  
*MOLINA REVIEWER: Verify pharmacy claims for compliance with the combination therapy above within the last 90 days. For new members to Molina Healthcare, confirm medication use in medical chart history. Non-compliance, which can be documented by review of the prescription fill history, would not constitute therapeutic failure.*  
AND
6. Prescriber attestation that IF member is a smoker, the member has been counseled regarding the benefits of smoking cessation and/or connected with a program to support smoking cessation  
AND
7. Prescriber attestation that the member's underlying conditions or triggers for asthma or pulmonary disease are being maximally managed

## B. EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA):

1. Documented diagnosis of EGPA supported by both of the following [DOCUMENTATION REQUIRED]:
  - (a) Blood eosinophil level of at least 10% of leucocytes OR Absolute eosinophil count  $> 1,000$  cells/ $\mu$ L  
AND
  - (b) Presence of any of the following characteristics typical of EGPA:
    - i. Histopathological evidence of: Eosinophilic vasculitis, Perivascular eosinophilic infiltration, or Eosinophil- rich granulomatous inflammation
    - ii. Neuropathy, mono or poly (motor deficit or nerve conduction abnormality)

## Drug and Biologic Coverage Criteria

- iii. Pulmonary infiltrates, non-fixe
- iv. Sino-nasal abnormality
- v. Cardiomyopathy (established by echocardiography or MRI)
- vi. Glomerulonephritis (hematuria, red cell casts, proteinuria)
- vii. Alveolar hemorrhage (by bronchoalveolar lavage)
- viii. Palpable purpura
- ix. Anti-neutrophil cytoplasmic antibody (ANCA) positive

AND

2. Prescriber attests that member has refractory disease defined as failure to attain remission within the prior 6 months following induction treatment with standard therapy regimens [at least 3 months of ORAL corticosteroids with or without an immunosuppressant (e.g., cyclophosphamide, azathioprine, methotrexate)] OR has a contraindication or serious side effects to oral corticosteroids and immunosuppressants

AND

3. Documentation of baseline disease severity to assess efficacy of therapy at renewal (asthma symptoms or asthma exacerbations, severity, or frequency of EGPA related symptoms, frequency and/or severity of relapses, maintenance doses of systemic corticosteroids and/or immunosuppressant, blood eosinophil count or inflammatory markers, Birmingham Vasculitis Activity Score (BVAS) score) [DOCUMENTATION REQUIRED]

AND

4. Prescriber attests or clinical reviewer has found that requested therapy is NOT prescribed for, or intended for, combination therapy or concurrent therapy with other monoclonal antibodies [i.e., Xolair (omalizumab) OR other IL-5 inhibitors [Cinqair (reslizumab), benralizumab (Fasenra)] OR IL-4 agonist Dupixent (dupilumab) OR Anti-TSLP Tezspire (Tezepelumab-ekko)]

### C. CHRONIC RHINOSINUSITIS WITH NASAL POLYPS:

1. Documentation of diagnosis of chronic rhinosinusitis with nasal polyposis

AND

2. Prescriber attests that member has a history of sino-nasal surgery or is not eligible for surgery

AND

3. Documentation that the member has experienced an inadequate response (after 3 consistent months of use) or serious side effects to ONE of the following medications unless contraindicated: preferred formulary intranasal steroids OR preferred formulary oral corticosteroids

AND

4. Documentation member is concurrently receiving treatment with one of the following: Intranasal steroids, Oral corticosteroids, Nasal saline irrigations, antibiotics, or antileukotriene agents (i.e., not to be used as monotherapy)

AND

5. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal (e.g., nasal congestion, loss of smell, sino-nasal symptoms) [DOCUMENTATION REQUIRED]

AND

6. Prescriber attests or clinical reviewer has found that requested therapy is NOT prescribed for, or intended for, combination therapy or concurrent therapy with other monoclonal antibodies [i.e., Xolair (omalizumab) OR other IL-5 inhibitors [Cinqair (reslizumab), benralizumab (Fasenra)] OR IL-4 agonist Dupixent (dupilumab) OR Anti-TSLP Tezspire (Tezepelumab-ekko)]

### D. HYPEREOSINOPHILIC SYNDROME (HES):

1. Documentation of diagnosis of hypereosinophilic syndrome for  $\geq$  6 months

AND

2. Documentation of BOTH of the following: (a) there is no identifiable non-hematologic secondary cause of the member's HES (e.g., drug hypersensitivity, parasitic helminth

## Drug and Biologic Coverage Criteria

infection, HIV infection, non- hematologic malignancy); AND (b) HES is not FIP1L1-PDGFR $\alpha$  kinase- positive  
AND

3. Documentation of baseline (pre-mepolizumab treatment) blood eosinophil level  $\geq$  1000 cells/ $\mu$ L within the past 4 weeks  
AND
4. Documentation member is currently receiving a stable dose of background HES therapy (e.g., oral corticosteroid, immunosuppressor, or cytotoxic therapy)  
AND
5. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal (e.g., frequency of HES flares, background HES therapy requirements, etc.) [DOCUMENTATION REQUIRED]  
AND
6. Prescriber attests or clinical reviewer has found that Nucala (mepolizumab) is NOT being prescribed as concurrent therapy with other monoclonal antibodies [i.e., Xolair (omalizumab) OR other IL-5 inhibitors [benralizumab (Fasenra), Cinqair (reslizumab) OR IL-4 agonist Dupixent (dupilumab) OR Anti-TSLP Tezspire (Tezepelumab-ekko)]

### CONTINUATION OF THERAPY:

#### A. SEVERE ASTHMA WITH EOSINOPHILIC PHENOTYPE:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation  
AND
2. Documentation that Nucala (mepolizumab) therapy has resulted in clinical improvement as documented by ONE or more of the following from baseline [DOCUMENTATION REQUIRED]:
  - a) Improvement in lung function (increase in percent predicted FEV1 or PEF) from pre- treatment baseline OR
  - b) Decreased utilization of rescue medications, decreased frequency of exacerbations (defined as worsening of asthma that requires increase in inhaled corticosteroid dose or treatment with systemic corticosteroids) OR
  - c) Decreased frequency of unscheduled clinic, urgent care, or emergency department visits OR
  - d) Reduction in reported symptoms: chest tightness, coughing, shortness of breath, nocturnal waking wheezing, sustained improvement in Asthma Control Test (ACT) scores OR
  - e) Decreased or stopped oral treatments (including oral corticosteroids and other add on medications, if applicable), or reduced ICS-LABA dose (to at least moderate)

MOLINA REVIEWER NOTE: For members with unclear response after initial use, see Background (GINA 2023).

AND

3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity [e.g., symptoms of anaphylaxis (bronchospasm, hypotension, syncope, urticaria, and/or angioedema), malignancy, symptoms similar to serum sickness (fever, arthralgia, and rash); parasitic (helminth) infection, eosinophilic conditions (e.g., vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy, especially upon reduction of oral corticosteroids]  
AND
4. Prescriber attests or clinical reviewer has found that requested therapy is NOT prescribed for, or intended for, combination therapy or concurrent therapy with other monoclonal antibodies used to treat asthma [i.e., Xolair (omalizumab) OR other IL-5 inhibitors [Cinqair (reslizumab), benralizumab (Fasenra)] OR IL-4 agonist Dupixent (dupilumab) OR Anti-TSLP Tezspire (Tezepelumab-ekko)]  
AND
5. Documentation member is currently treated and is compliant with standard therapy (e.g.,

## Drug and Biologic Coverage Criteria

inhaled corticosteroids, long-acting beta-2 agonist (LABA), leukotriene receptor antagonist (LTRA), long-acting muscarinic antagonist (LAMA), theophylline) within the past 90 days

### B. EOSINOPHILIA GRANULOMATOSIS WITH POLYANGIITIS (EGPA):

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation  
AND
2. Documentation Nucala (mepolizumab) therapy has resulted in clinical improvement of signs and symptoms compared to baseline as evidenced by ONE (1) or more of the following from baseline: Improvement in asthma symptoms or asthma exacerbations, Improvement in duration of remission or decrease in the rate of relapses, Decrease in severity or frequency of EGPA- related symptoms, Decrease in the frequency and/or severity of relapses, Reduction or discontinuation of maintenance doses of systemic corticosteroids and/or immunosuppressant, Decreased blood eosinophil count or inflammatory markers, Improvement in Birmingham Vasculitis Activity Score (BVAS) score compared to baseline or Member is in remission as defined by BVAS score = 0 and a prednisone/prednisolone daily dose of  $\leq 7.5$  mg [DOCUMENTATION REQUIRED]  
AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity [e.g. symptoms of anaphylaxis (bronchospasm, hypotension, syncope, urticaria, and/or angioedema), malignancy, symptoms similar to serum sickness (fever, arthralgia, and rash); parasitic (helminth) infection, eosinophilic conditions (e.g. vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy, especially upon reduction of oral corticosteroids]  
AND
4. Prescriber attests or clinical reviewer has found that requested therapy is NOT prescribed for, or intended for, combination therapy or concurrent therapy with other monoclonal antibodies [i.e., Xolair (omalizumab) OR other IL-5 inhibitors [Cinqair (reslizumab), benralizumab (Fasenra)] OR IL-4 agonist Dupixent (dupilumab) OR Anti-TSLP Tezspire (Tezepelumab-ekko)]

### C. CHRONIC RHINOSINUSITIS WITH NASAL POLYPS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation  
AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity  
AND
3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms (e.g., nasal congestion, loss of smell, sino-nasal symptoms) [DOCUMENTATION REQUIRED]  
AND
4. Prescriber attests that member continues on standard therapy (intranasal steroids, oral corticosteroids, nasal saline irrigations, antibiotics, or antileukotriene agents)  
AND
5. Prescriber attests or clinical reviewer has found that requested therapy is NOT prescribed for, or intended for, combination therapy or concurrent therapy with other monoclonal antibodies [i.e., Xolair (omalizumab) OR other IL-5 inhibitors [Cinqair (reslizumab), benralizumab (Fasenra)] OR IL-4 agonist Dupixent (dupilumab) OR Anti-TSLP Tezspire (Tezepelumab-ekko)]

### D. HYPEREOSINOPHILIC SYNDROME (HES):

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation

## Drug and Biologic Coverage Criteria

AND

2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity  
AND
3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms (i.e., Reduction in frequency of HES flares, Maintenance, or reduction in background HES therapy requirements)  
[DOCUMENTATION REQUIRED]  
AND
4. Prescriber attests or clinical reviewer has found that requested therapy is NOT prescribed for, or intended for, combination therapy or concurrent therapy with other monoclonal antibodies [i.e., Xolair (omalizumab) OR other IL-5 inhibitors [Cinqair (reslizumab), benralizumab (Fasenra)] OR IL-4 agonist Dupixent (dupilumab) OR Anti-TSLP Tezspire (Tezepelumab-ekko)]

### **DURATION OF APPROVAL:**

Initial authorization: 6 months, Continuation of treatment: 12 months

### **PRESCRIBER REQUIREMENTS:**

Prescribed by, or in consultation with, a board-certified asthma specialist (allergist, immunologist, pulmonologist), or physician experienced in the management of asthma, cardiologist, or otorhinolaryngologist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

### **AGE RESTRICTIONS:**

Severe Asthma, add on maintenance in patients with eosinophilic phenotype: 6 years of age and older

Eosinophilic Granulomatosis with Polyangiitis: 18 years of age and older

Hypereosinophilic syndrome: 12 years of age and older

Chronic rhinosinusitis with nasal polyps: 18 years of age and older

### **QUANTITY:**

Severe asthma (eosinophilic phenotype): Children 6 years to 11 years: 40 mg once every 4 weeks

Children and adults (12 years and older): 100 mg once every 4 weeks

Eosinophilic granulomatosis with polyangiitis: 300 mg (as 3 separate 100-mg injections) once every 4 weeks

Hypereosinophilic syndrome: 300 mg (as 3 separate 100-mg injections) once every 4 weeks

Chronic rhinosinusitis with nasal polyps: 100 mg once every 4 weeks

### **PLACE OF ADMINISTRATION:**

The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the subcutaneous injectable products administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

**Note:** Site of Care Utilization Management Policy applies for Nucala (mepolizumab). For information on site of care, see

[Specialty Medication Administration Site of Care Coverage Criteria \(molinamarketplace.com\)](https://www.molinamarketplace.com)

## **DRUG INFORMATION**

### **ROUTE OF ADMINISTRATION:**

Molina Healthcare, Inc. confidential and proprietary © 2023

*This document contains confidential and proprietary information of Molina Healthcare and cannot be reproduced, distributed, or printed without written permission from Molina Healthcare. This page contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with Molina Healthcare.*

**DRUG CLASS:**

Interleukin-5 Antagonists (IgG1 kappa)

**FDA-APPROVED USES:**

NUCALA is indicated for:

- Add-on maintenance treatment of adult and pediatric patients aged 6 years and older with severe asthma and with an eosinophilic phenotype.
- Add-on maintenance treatment of adult patients 18 years and older with chronic rhinosinusitis with nasal polyps (CRSwNP).
- The treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).
- The 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.

*Limitations of use: Not for relief of acute bronchospasm or status asthmaticus*

**COMPENDIAL APPROVED OFF-LABELED USES:**

None

**APPENDIX**

**APPENDIX:**

Asthma Controller medications: suppress the inflammatory causes of asthma to provide clinical control over the long term, whereas reliever medications relieve bronchoconstriction quickly. Controller medications include inhaled glucocorticoids, long-acting beta-agonists (LABAs) and Leukotriene receptor antagonists (LTRA). Theophylline (Theo-24, Uniphyll, TheoChron ER, generics) is also a controller agent, however, it is not as efficacious as LABAs.

**Anticholinergic (LAMA)**

Tiotropium bromide monohydrate (Spiriva Respimat)

**Inhaled Corticosteroids (ICS) (list not all inclusive):**

*Beclometasone dipropionate (QVAR)*

*Fluticasone furoate (Arnuity Ellipta)*

*Budesonide DPI (Pulmicort Flexhaler)*

*Fluticasone propionate (Flovent Diskus)*

*Budesonide nebulules (Pulmicort Respules)*

*Fluticasone propionate (Flovent HFA)*

*Ciclesonide (Alvesco)*

*Fluticasone propionate (ArmonAir Digihaler)*

*Flunisolide (Aerospan)*

*Mometasone furoate (Asmanex Twisthaler)*

*Mometasone furoate (Asmanex HFA\*)*

*\*HFA: hydrofluoroalkane propellant metered dose inhaler*

*\*DPI: dry powder inhaler*

**Combination Long-Acting Bronchodilator and Corticosteroid (ICS+ LABA) (list not all inclusive):**

*Budesonide/formoterol fumarate dihydrate (Symbicort)*

*Fluticasone propionate/salmeterol (Advair Diskus/ Adair HFA/ AirDuo/ AirDuo RespiClick/Wixela Inhub)*

*Fluticasone furoate/vilanterol (Breo Ellipta)*

*Mometasone furoate/formoterol fumarate dihydrate (Dulera)*

**Combination Anticholinergic and Corticosteroid and long-acting bronchodilator (ICS+ LAMA+ LABA)**

*Fluticasone/umeclidinium/vilanterol (Trelegy Ellipta)*

**Leukotriene receptor antagonist (LTRA) (list not all inclusive):**

*Montelukast (Singulair), Zafirlukast (Accolate), Zileuton (Zyflo)*

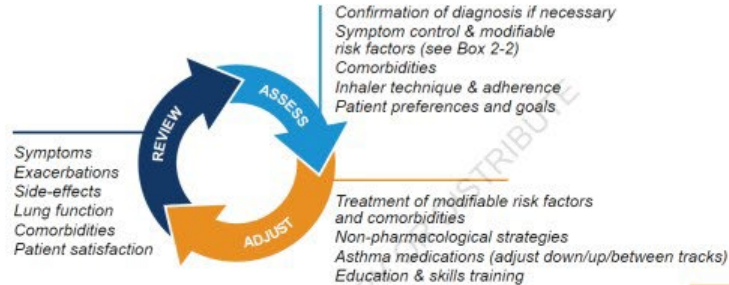
## Drug and Biologic Coverage Criteria

- FEV1 (forced expiratory volume in 1 second): A measure of airway obstruction determined using spirometry. Individual FEV1 values are compared to predicted values based on age, height, sex and race.
- PEF (peak expiratory flow): PEF is often described as a percent of personal best measurement. Personal best PEF is the highest PEF value attained after 2 to 3 weeks of testing when asthma is in good control.

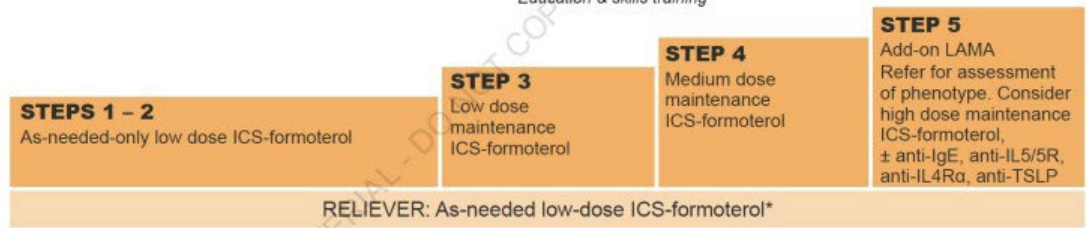
## APPENDIX 1: Managing Asthma in Adults and Adolescents 12+ Years

### GINA 2023 – Adults & adolescents 12+ years

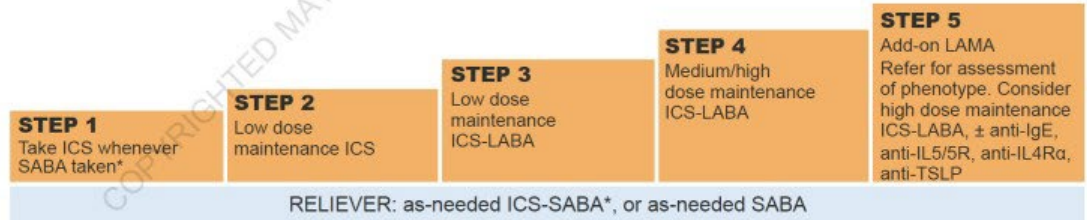
**Personalized asthma management**  
Assess, Adjust, Review  
for individual patient needs



**TRACK 1: PREFERRED CONTROLLER and RELIEVER**  
Using ICS-formoterol as the reliever\* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen



**TRACK 2: Alternative CONTROLLER and RELIEVER**  
Before considering a regimen with SABA reliever, check if the patient is likely to adhere to daily controller treatment



Other controller options (limited indications, or less evidence for efficacy or safety – see text)

	Low dose ICS whenever SABA taken*, or daily LTRA, or add HDM SLIT	Medium dose ICS, or add LTRA, or add HDM SLIT	Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS	Add azithromycin (adults) or LTRA. As last resort consider adding low dose OCS but consider side-effects
--	---	---	--	--

See GINA severe asthma guide

\*Anti-inflammatory reliever (AIR)

ABBREVIATIONS: HDM: house dust mite; ICS: inhaled corticosteroid; LABA: long-acting beta2-agonist; LAMA: long-acting muscarinic antagonist; LTRA: Leukotriene Receptor Antagonist; OCS: oral corticosteroids; SABA: short-acting beta2-agonist; SLIT: sublingual immunotherapy

REFERENCE: Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2023. Available from: [www.ginasthma.org](http://www.ginasthma.org)



**Managing Asthma in Children 6-11 Years**

**GINA 2023 – Children 6–11 years**

**Personalized asthma management:**

Assess, Adjust, Review

Symptoms  
Exacerbations  
Side-effects  
Lung function  
Comorbidities  
Child (and parent/ caregiver) satisfaction



Confirmation of diagnosis if necessary  
Symptom control & modifiable risk factors (see Box 2-2)  
Comorbidities  
Inhaler technique & adherence  
Child and parent/caregiver preferences and goals

Treatment of modifiable risk factors & comorbidities  
Non-pharmacological strategies  
Asthma medications (adjust down or up)  
Education & skills training

**STEP 5**  
Refer for phenotypic assessment ± higher dose ICS-LABA or add-on therapy, e.g. anti-IgE, anti-IL4Rα, anti-IL5

**STEP 4**  
Medium dose ICS-LABA, OR low dose ICS-formoterol maintenance and reliever therapy (MART). Refer for expert advice

**STEP 3**  
Low dose ICS-LABA, OR medium dose ICS, OR very low dose ICS-formoterol maintenance and reliever (MART)

**STEP 2**  
Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)

**STEP 1**  
Low dose ICS taken whenever SABA taken\*

**PREFERRED CONTROLLER**  
to prevent exacerbations and control symptoms

Other controller options (limited indications, or less evidence for efficacy or safety)

Consider daily low dose ICS

Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken\*

Low dose ICS + LTRA

Add tiotropium or add LTRA

As last resort, consider add-on low dose OCS, but consider side-effects

**RELIEVER**

As-needed SABA (or ICS-formoterol reliever\* in MART in Steps 3 and 4)

\*Anti-inflammatory relievers (AIR)

ABBREVIATIONS: BUD-FORM: budesonide-formoterol; ICS: inhaled corticosteroid; LABA: long-acting beta2-agonist; LTRA: Leukotriene Receptor Antagonist; MART: maintenance and reliever therapy with ICS-formoterol; OCS: oral corticosteroids; SABA: short-acting beta2-agonist; SLIT: sublingual immunotherapy  
REFERENCE: Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2023. Available from: www.ginasthma.org

**APPENDIX 2: SUGGESTED TOTAL DAILY DOSAGES for INHALED CORTICOSTEROIDS (ICS) IN ADULTS AND ADOLESCENTS (12 years and older):**

Inhaled Corticosteroid	Low Dose ICS (mcg)	Medium Dose ICS (mcg)	High Dose ICS (mcg)
Beclometasone dipropionate (pMDI, standard particle, HFA)	200-500	>500-1000	>1000
Beclometasone dipropionate (DPI or pMDI, extrafine particle, HFA)	100-200	>200-400	>400
Budesonide (DIP, or pMDI, standard particle, HFA)	200-400	>400-800	>800
Ciclesonide (pMDI, extrafine particle, HFA)	80-160	>160-320	>320
Fluticasone furoate (DPI)	100	100	200
Fluticasone propionate (DPI)	100-250	>250-500	>500
Fluticasone propionate (pMDI, standard particle, HFA)	100-250	>250-500	>500
Mometasone furoate (DPI)	Depends on DPI device – see product information		
Mometasone furoate (pMDI, standard particle, HFA)	200-400	200-400	>400

Reference: Box 3-14. Low, medium, and high daily metered doses of inhaled corticosteroids (alone or with LABA) Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2023. Available from: [www.ginasthma.org](http://www.ginasthma.org)

**SUGGESTED TOTAL DAILY DOSAGES for INHALED CORTICOSTEROIDS (ICS) IN CHILDREN 6-11 YEARS:**

<b>Inhaled Corticosteroid</b>	<b>Low Dose ICS (mcg)</b>	<b>Medium Dose ICS (mcg)</b>	<b>High Dose ICS (mcg)</b>
Beclometasone dipropionate (pMDI, standard particle, HFA)	100-200	>200-400	>400
Beclometasone dipropionate (pMDI, standard particle, HFA)	50-100	>100-200	>200
Budesonide (DPI, or pMDI, standard particle, HFA)	100-200	>200-400	>400
Budesonide (nebulas)	250-500	>500-1000	>1000
Ciclesonide (pMDI, extrafine particle, HFA)	80	>80-160	>160
Fluticasone furoate (DPI)	50	50	NA
Fluticasone propionate (DPI)	50-100	>100-200	>200
Fluticasone propionate (pMDI, standard particle, HFA)	50-100	>100-200	>200
Mometasone furoate (pMDI, standard particle, HFA)	100	100	200

Reference: Box 3-14. Low, medium and high daily metered doses of inhaled corticosteroids (alone or with LABA) Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2023. Available from: [www.ginasthma.org](http://www.ginasthma.org)

**BACKGROUND AND OTHER CONSIDERATIONS**

**BACKGROUND:**

Nucala, an interleukin (IL)-5 antagonist immunoglobulin G (IgG)1κ monoclonal antibody, is indicated for add-on maintenance treatment of patients with severe asthma aged ≥ 6 years who have an eosinophilic phenotype.<sup>1</sup> Nucala is also indicated for treatment of Eosinophilic Granulomatosis with Polyangiitis (EGPA) in patients aged ≥ 12 years. Nucala is also indicated for Rhinosinusitis with nasal polyps in adult patients. Limitations of Use: Nucala is not indicated for the treatment of other eosinophilic conditions or for the relief of acute bronchospasm/status asthmaticus. Nucala is a human IL-5 antagonist; IL-5 is the main cytokine involved in the growth, differentiation, recruitment, activation, and survival of eosinophils. The most important factor in the pathogenesis of asthma is inflammation, which involves multiple mediators and cell types, including eosinophils. By inhibiting the signaling of IL- 5, Nucala decreases the production and survival of eosinophils. However, the exact mechanism of action of Nucala in asthma has not been established. Nucala is not indicated for intravenous (IV) use; it should be administered as a 100 mg subcutaneous (SC) injection once every 4 weeks by a healthcare professional.

Global Initiative for Asthma (GINA, 2023)

Add-on biologic therapy: options recommended by GINA for patients with uncontrolled severe asthma despite optimized maximal therapy include:

- Add-on anti-immunoglobulin E treatment (omalizumab[Xolair]) for patients age ≥ 6 years with **severe allergic asthma** (Evidence A)

## Drug and Biologic Coverage Criteria

- Add-on anti-interleukin- 5/5R treatment (SC mepolizumab[Nucala] for patients age  $\geq 6$  years; IV reslizumab[Cinqair] for ages 18 years or SC benralizumab[Fasenra] for ages  $\geq 12$  years), with **severe eosinophilic asthma** (Evidence A)
- Add-on anti-interleukin-4R $\alpha$  treatment (SC dupilumab[Dupixent]) for patients aged  $\geq 6$  years with **severe eosinophilic/type 2 asthma** or for **adults or adolescents requiring treatment with maintenance OCS** (Evidence A)
- Add-On anti-thymic stromal lymphopoietin (anti TSLP) treatment (subcutaneous tezepelumab[Tezspire]) for patients aged  $\geq 12$  years with **severe asthma** (Evidence A)
- Suggested initial trial of add-on anti-IL5 for severe eosinophilic asthma is at least 4 months. At that point, response to initial trial of add-on therapy should be reviewed. There are no well-defined criteria for good response, but exacerbations, symptom control, lung function, side effects, treatment intensity, and patient satisfaction should be considered. If the response is unclear, consider extending the trial to 6-12 months. If there is no response, stop the biologic therapy and consider switching to a different targeted therapy, if available.

### CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Nucala (mepolizumab) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Nucala (mepolizumab) include: history of hypersensitivity to mepolizumab or excipients in the formulation.

### OTHER SPECIAL CONSIDERATIONS:

None

## CODING/BILLING INFORMATION

*Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement*

HCPCS CODE	DESCRIPTION
J2182	Injection, mepolizumab, 1 mg

### AVAILABLE DOSAGE FORMS:

Nucala SOLR 100MG single-dose vial  
Nucala SOAJ 100MG/ML (auto-injector)  
Nucala SOSY 100MG/ML (pre-filled syringe)  
Nucala SOSY 40MG/0.4ML (pre-filled syringe)

## REFERENCES

1. Nucala® injection for subcutaneous use [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; March 2023.
2. Global Initiative for Asthma. Global strategy for asthma management and prevention. Updated March 2021 Available at: <http://www.ginasthma.org>.
3. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2014;43:343-373.
4. Bel EH, Wenzel SE, Thompson PJ, Prazma CM, et al. Oral Glucocorticoid-Sparing Effect of Mepolizumab in Eosinophilic Asthma. *New Eng J Med*. 2014 Sept;371(13):1189-97
5. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2021. Available at <http://www.ginasthma.org>.
6. Parameswaran KN, Dasgupta A, et al. Mepolizumab in COPD with Eosinophilic Bronchitis: A Randomized Clinical Trial. Poster session presented at the Annual Meeting of the American Academy of Allergy, Asthma and Immunology, Los Angeles, CA. March 6, 2016
7. Wechsler ME, Akuthota P, Jayne D, et al. Mepolizumab or placebo for eosinophilic granulomatosis with polyangiitis. *N Engl J Med* 2017; 376: 1921-32.
8. Steinfeld J, Bradford ES, Brown J, et al. Evaluation of clinical benefit from treatment with mepolizumab for patients with eosinophilic granulomatosis with polyangiitis. *J Allergy Clin Immunol*. 2019 Jun;143(6):2170-2177.
9. Hypereosinophilic Syndrome (HES). American Academy of Allergy, Asthma & Immunology. Available at <http://www.aaaai.org>.
10. Wenzel S. Severe asthma in adults. *Am J Respir Crit Care Med*. 2005;172(2):149–160.
11. Pavord ID, Korn S, Howarth P, et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo-controlled trial. *Lancet*. 2012;380:651-659.
12. Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. *N Engl J Med*. 2014;371:1198-1207.
13. Bel EH, Wenzel SE, Thompson PJ, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. *N Engl J Med*. 2014;371(13):1189-1197
14. Severe asthma (eosinophilic phenotype) for add-on maintenance treatment HG Ortega et al. Mepolizumab treatment in patients with severe eosinophilic asthma. *N Engl J Med* 2014; 371:1198.
15. HG Ortega et al. Severe eosinophilic asthma treated with mepolizumab stratified by baseline eosinophilic thresholds: a secondary analysis of the DREAM and MENSA studies. *Lancet Respir Med* 2016; 4:549.
16. EH Bel et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. *N Engl J Med* 2014; 371:1189.
17. Pavord ID, Korn S, Howarth P, et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicenter, double-blind, placebo-controlled trial. *Lancet* 2012; 380: 651-59. <https://clinicaltrials.gov/ct2/show/NCT01000506>
18. Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. *N Engl J Med* 2014; 371: 1198-1207.
19. Eosinophilic granulomatosis with polyangiitis (EGPA) Wechsler ME, Akuthota P, Jayne D, et al; EGPA Mepolizumab Study Team. Mepolizumab or placebo for eosinophilic granulomatosis with polyangiitis. *NEngl J Med*. 2017;376(20):1921-1932.[PubMed 28514601]10.1056/NEJMoa1702079
20. Institute for Clinical and Economic Review/The California Technology Assessment Forum Mepolizumab (Nucala®, GlaxoSmithKline plc.) for the Treatment of Severe
21. Asthma with Eosinophilia: Effectiveness, Value, and Value-Based Price Benchmarks. March 14, 2016. Available at <http://icer-review.org/material/asthma-final-report/>.
22. Eosinophilic granulomatosis with polyangiitis (EGPA) Masi AT, Hunder GG, Lie JT; Michel BA,

**Drug and Biologic Coverage Criteria**

et al. The American College of Rheumatology 1990 criteria for the classification of Churg- Strauss syndrome (allergic granulomatosis and angiitis). *Arthritis Rheum.* 1990; 33(8):1094- 100 (ISSN: 0004-3591)

23. National Asthma Education and Prevention Program (NAEPP): 2020 Focused updates to the asthma management guidelines. Bethesda, MD: National Heart, Lung, and Blood Institute, 2020. (NIH publication no. 20-HL-8140). Available at <https://www.nhlbi.nih.gov/resources/2020-focused-updates-asthma-management-guidelines>. Accessed September 2022.
24. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2022. Available from: [www.ginasthma.org](http://www.ginasthma.org)
25. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2023. Available from: [www.ginasthma.org](http://www.ginasthma.org)

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Quantity Appendix Background Contraindications/Exclusions/Discontinuation References	Q4 2023
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Prescriber Requirements Appendix Background Contraindications/Exclusions/Discontinuation Available Dosage Forms References	Q4 2022
Q2 2022 Established tracking in new format	Historical changes on file