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Last P&T Approval/Version: N/A
Last Reviewed Date: 04/2024
Policy Number: C23838-A

Nucala (mepolizumab) MS ONLY

PRODUCTS AFFECTED

Nucala (mepolizumab)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the beneficiary'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 beneficiary 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 beneficiary, 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:

A. SEVERE ASTHMA WITH EOSINOPHILIC PHENOTYPE:
   1. Documented diagnosis of moderate to severe asthma
      AND
   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: ≥150 cells/microliter at initiation of therapy (within 6 weeks

of request) OR ≥ 300 cells/microliter in the prior 12 months [DOCUMENTATION REQUIRED]
AND

4. Beneficiary 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]

B. EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA):
1. Documented diagnosis of EGPA
AND
2. Prescriber attests that beneficiary has refractory disease defined as failure to attain remission within the prior 6 months following induction treatment with standard therapy regimens [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. 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 beneficiary has a history of sino-nasal surgery or is not eligible for surgery
AND

3. Documentation that the beneficiary has experienced an inadequate response (after 3 consistent months of use) or serious side effects to ONE of the following medications unless contraindicated: preferred intranasal steroids OR preferred oral corticosteroids
   AND
4. Documentation beneficiary 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. 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 ≥ 6 months
   AND
2. Documentation of BOTH of the following: (a) there is no identifiable non-hematologic secondary cause of the beneficiary's HES (e.g., drug hypersensitivity, parasitic helminth infection, HIV infection, non- hematologic malignancy); AND (b) HES is not FIP1L1-PDGFRαkinase- positive
   AND
3. Documentation of baseline (pre-mepolizumab treatment) blood eosinophil level ≥ 1000 cells/μL within the past 4 weeks
   AND
4. Documentation beneficiary is currently receiving a stable dose of background HES therapy (e.g., oral corticosteroid, immunosuppressor, or cytotoxic therapy)
   AND
5. 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. Documentation that Nucala (mepolizumab) therapy has resulted in clinical improvement as documented by ONE or more of the following from baseline:
   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 wakening 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 beneficiaries with unclear response after initial use, see Background (GINA 2023).

   AND
2. 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

3. 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)]

B. EOSINOPHILIA GRANULOMATOSIS WITH POLYANGIITIS (EGPA):

1. 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 beneficiary is in remission as defined by BVAS score = 0 and a prednisone/prednisolone daily dose of ≤ 7.5 mg
AND
2. 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
3. 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. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
AND
2. 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)
AND
3. 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. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
AND
2. 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)
AND

3. 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: up to 12 months, Continuation of treatment: up to 12 months at a time

PRESCRIBER REQUIREMENTS:
Prescribed by, or in consultation with, an asthma specialist (allergist, immunologist, pulmonologist), or physician experienced in the management of asthma, cardiologist, or otorhinolaryngologist.

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

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

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, Uniphyl, 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 nebules (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*

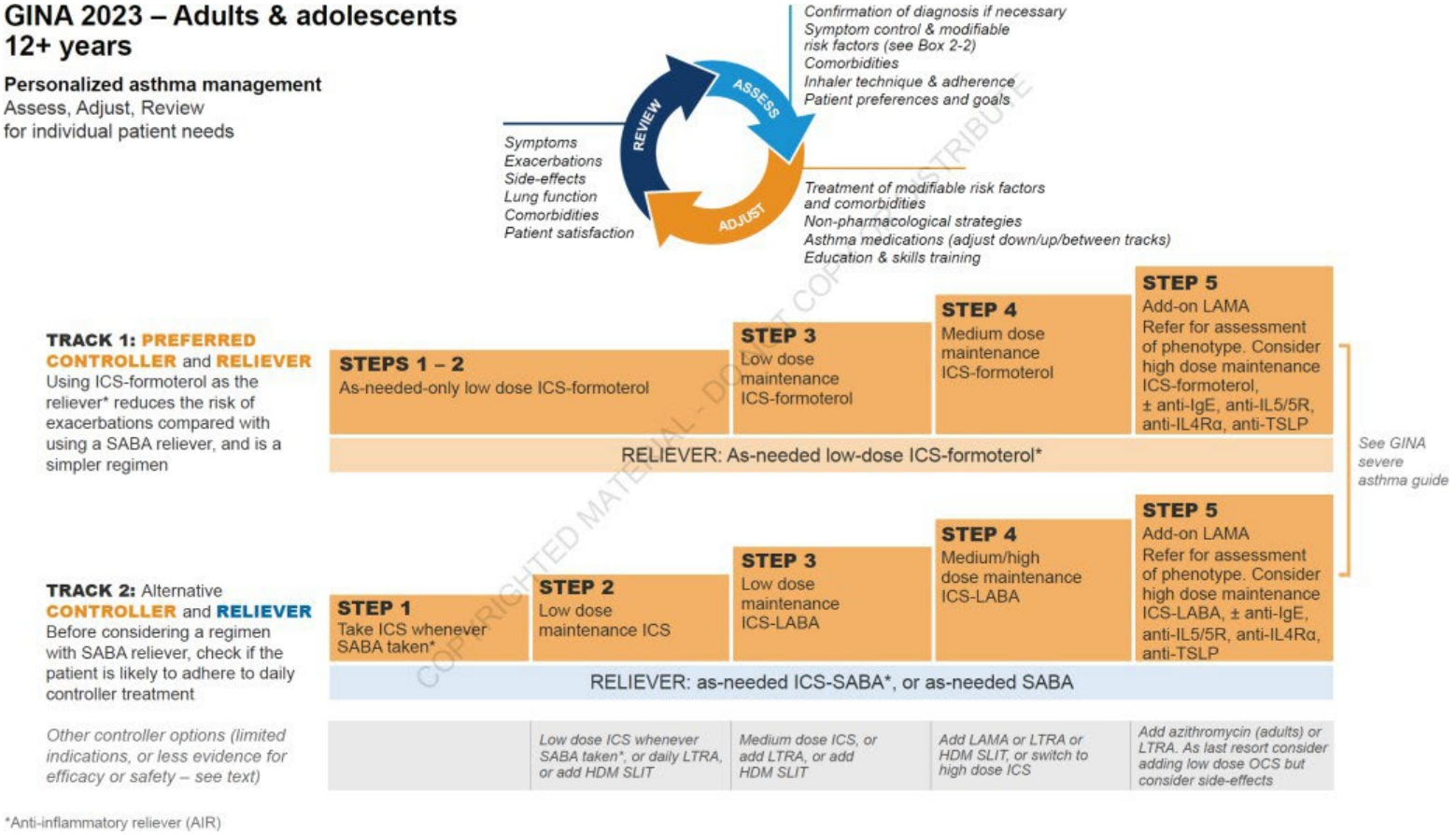
Combination Long-Acting Bronchodilator and Corticosteroid (ICS+ LABA) (list not all inclusive):
Budesonide/formoterol fumarate dihydrate (Symbicort)
Fluticasone propionate/salmeterol (Advair Diskus/ Adair HFA/ AirDuo/ AirDuo RespiClick/Wixela Inhub) Fluticasone furoate/vilanterol(Breo Ellipta)
Mometasone furoate/formoterol fumarate dihydrate (Dulera)

Combination Anticholinergic and Corticosteroid and long-acting bronchodilator (ICS+ LAMA+ LABA)
Fluticasone/umeclidnium/vilanterol (Trelegy Elipta)

Leukotriene receptor antagonist (LTRA) (list not all inclusive):
Montelukast (Singulair), Zafirlukast (Accolate), Zileuton (Zyflo)

- 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.

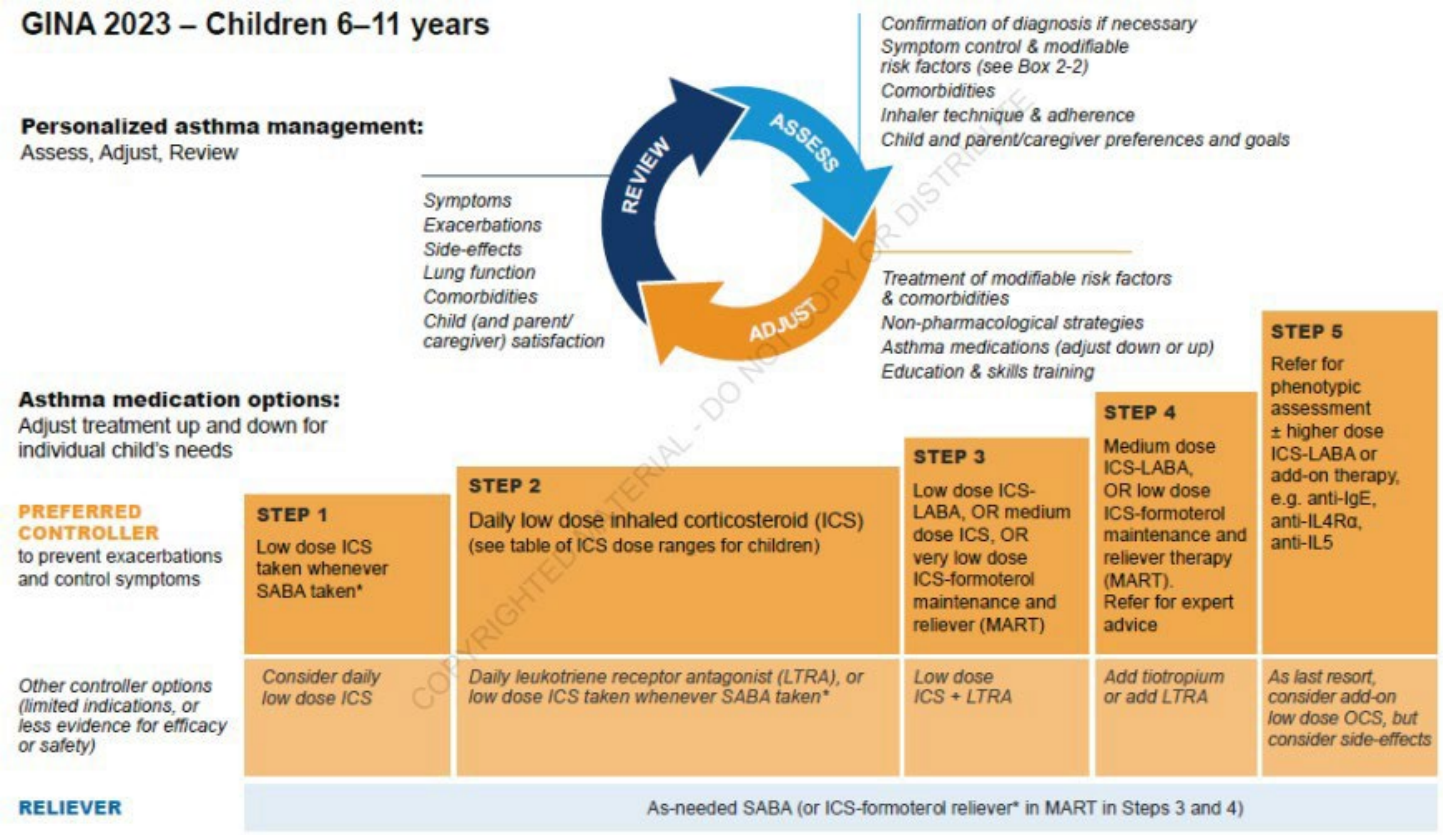
APPENDIX 1: Managing Asthma in Adults and Adolescents 12+ Years



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

Managing Asthma in Children 6-11 Years



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

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

Inhaled Corticosteroid	Low Dose ICS (mcg)	Medium Dose ICS (mcg)	High Dose ICS (mcg)
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 (nebules)	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

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 ≥ 12 years who have an eosinophilic phenotype.1 Nucala is also indicated for treatment of Eosinophilic Granulomatosis with Polyangiitis (EGPA).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)
- Add-on anti-interleukin- 5/5R treatment (SC mepolizumab [Nucala] for patients age ≥

6 years; IV reslizumab [Cinqair] for ages 18 years or SC benralizumab [Fasenra] for ages ≥12 years), with **severe eosinophilic asthma** (Evidence A)

- Add-on anti-interleukin-4Rα treatment (SC dupilumab [Dupixent]) for patients aged ≥ 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 ≥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)

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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