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Policy Number: C23525-A

Fasenra (benralizumab) MS ONLY

PRODUCTS AFFECTED

Fasenra (benralizumab)

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

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 Fasenra (benralizumab) 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 [Cinqair (reslizumab), Nucala (mepolizumab)] OR IL-4 agonist Dupixent (dupilumab) OR Anti-TSLP Tezspire (Tezepelumab-ekko)]

AND

3. Documentation of the following [DOCUMENTATION REQUIRED]:

(a) Beneficiary 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

AND

(b) 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

4. Symptoms inadequately controlled (as documented in criteria above) by the following adherent regimen of **at least 3 months**: (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]

CONTINUATION OF THERAPY:

A. SEVERE ASTHMA WITH EOSINOPHILIC PHENOTYPE:

1. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or unacceptable toxicity from the drug [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
2. Documentation that Fasenra (benralizumab) therapy has resulted in clinical improvement as documented by ONE or more of the following from baseline [DOCUMENATION 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 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

3. Documentation beneficiary is currently treated and is compliant with standard therapy (e.g., inhaled corticosteroids, long- acting beta-2 agonist (LABA), leukotriene receptor antagonist (LTRA), long-acting muscarinic antagonist (LAMA), theophylline) within the past 90 days
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), Nucala (mepolizumab)] OR IL-4 agonist Dupixent (dupilumab) OR Anti-TSLP Tezspire (Tezepelumab- ekko)]

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of therapy: 12 months

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

AGE RESTRICTIONS:
12 years of age or older

QUANTITY:
30 mg every 4 weeks for the first 3 doses**,** then 30 mg every 8 weeks

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
Interleukin-5 Antagonists (IgG1 kappa)

FDA-APPROVED USES:
Indicated for the add-on maintenance treatment of patients with severe asthma aged 12 years and older with an eosinophilic phenotype
Limitations of use: Not indicated for treatment of other eosinophilic conditions or for the relief of acute bronchospasm or status asthmaticus

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
- 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 (list not all inclusive):
Beclometasone dipropionate (QVAR)
Budesonide DPI (Pulmicort Flexhaler)
Budesonide nebules (Pulmicort Respules)
Ciclesonide (Alvesco)
Flunisolide (Aerospan)
Fluticasone furoate (Arnuity Ellipta)
Mometasone furoate (Asmanex Twisthaler)

Fluticasone propionate (Flovent Diskus)
Mometasone furoate (Asmanex HFA)*
Fluticasone propionate (Flovent HFA)
Mometasone furoate (Asmanex HFA)*

**HFA: hydrofluoroalkane propellant metered dose inhaler*
**DPI: dry powder inhaler*

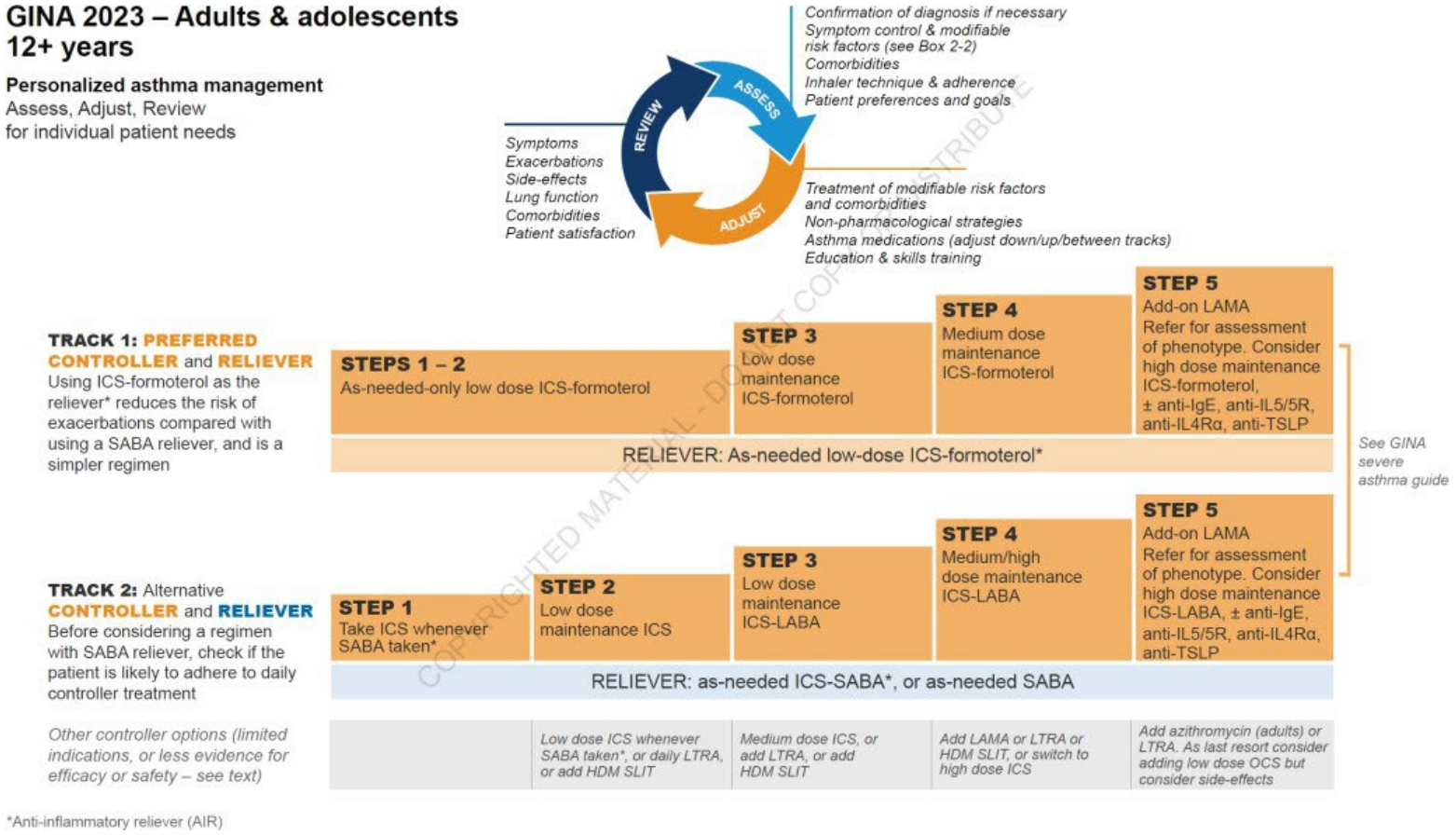
Combination Long-Acting Bronchodilator and Corticosteroid (list not all inclusive):
Budesonide/formoterol (Symbicort)
Fluticasone/salmeterol (Advair Diskus)
Fluticasone/salmeterol (Advair HFA)
Fluticasone/vilanterol(Breo Ellipta)
Mometasone/formoterol (Dulera)

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)

- 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

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

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Asthma is a heterogeneous syndrome that might be better described as a constellation of phenotypes, each with distinct cellular and molecular mechanisms, rather than as a singular disease. One of these phenotypes is eosinophilic asthma. Eosinophilic asthma is a sub phenotype of severe asthma characterizedby elevated sputum and blood eosinophil levels as well as increased asthma severity, atopy, late-onset disease, and steroid refractoriness. Severe asthma is defined as “asthma that requires treatment with high dose inhaled corticosteroids (ICS) plus a second controller and/or systemic corticosteroids to prevent it from becoming ‘uncontrolled’ or which remains ‘uncontrolled’ despite this therapy.” Several biomarkers including blood eosinophilic counts and sputum eosinophilic counts are used in diagnosing severe asthma with an eosinophilic phenotype. Development of eosinophilic inflammation is dependent on the biological activity of Interleukin-5 (IL-5), an inflammatory cytokine. IL-5 is responsible for growth, differentiation, recruitment, activation, and survival of eosinophils. Nucala (mepolizumab), Cinqair (reslizumab), and Fasenra (benralizumab), IL-5 antagonist monoclonal antibodies, antagonize the IL- 5/eosinophil inflammatory pathway. Nucala and Cinqair binds to IL-5, and Fasenra binds directly through the IL-5 surface receptors on eosinophils. Similar to other severe forms of asthma, the Gold Standard/International Guidelines treatment for severe asthma, including eosinophilic asthma, is high dose ICS plus a long acting beta-2 agonist (LABA), leukotriene modifier or theophylline and/or continuous systemic corticosteroids as background therapy. Cinqair (reslizumab), Fasenra (benralizumab), and Nucala (mepolizumab) are FDA indicated for severe eosinophilic asthma. Fasenra (benralizumab)

- Benralizumab is the third anti-IL-5 antibody to be approved for treatment of severe eosinophilic asthma; mepolizumab (Nucala) and reslizumab (Cinqair), which target IL-5 itself, were approved earlier
- FDA approved in combination with other asthma medications as add-on maintenance treatment of severe asthma in patients 12 years and older with an eosinophilic phenotype
- Benralizumab is not approved for the treatment of other eosinophilic conditions or for the relief of acute bronchospasm or status asthmaticus
- Administered via subcutaneous injection [similar to Nucala (mepolizumab)]; while Cinqair (reslizumab) is administered via IV infusion only
- FDA Approval was based on results obtained from Phase III clinical trials SIROCCO, CALIMA, and ZONDA from the WINDWARD program [which included six phase III trials SIROCCO, CALIMA, ZONDA, BISE, BORA, and GREGALE]
- The SIROCCO and CALIMA trials were powered for efficacy analysis in patients with baseline blood eosinophil count (BEC) ≥ 300 cells/μL. In addition, the ZONDA trial found Fasenra to significantly reduce oral corticosteroid dose in patients with baseline BEC ≥ 150 cells/μL.

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.

European Respiratory Society (ERS)/American Thoracic Society (ATS)

- The guidelines recommend “While the anti-IL5 antibody, mepolizumab, was not beneficial in unselected adult patients with moderate asthma, when studied in severe asthma patients with persistent sputum eosinophilia, two anti- IL-5 antibodies, mepolizumab and reslizumab, have been shown to decrease exacerbations and oral corticosteroid use, as well as improve symptoms and lung function to varying degrees.”
- Asthma is classified as severe when it requires treatment with high-dose inhaled corticosteroids plus a second asthma controller therapy (e.g., long-acting β2-agonist), and/or systemic corticosteroids to prevent asthma from becoming or remaining uncontrolled despite this therapy.
  - Although there are no widely accepted definitions for specific asthma phenotypes, an eosinophilic phenotype (i.e., eosinophilic asthma) is generally characterized by blood

and sputum eosinophilia and eosinophilic inflammation, recurrent exacerbations, and, frequently, responsiveness to corticosteroids.

- Sputum eosinophil counts are used as a reliable biomarker for eosinophilic lung inflammation; ATS and ERS currently recommend treatment of severe asthma guided by sputum eosinophil counts in addition to clinical criteria in adults, and treatment guided by clinical criteria alone in pediatric patients. However, sputum eosinophil counts are difficult to use in routine practice because testing must be performed in specialized centers experienced in using the technique.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Fasenra (benralizumab) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Fasenra (benralizumab) include: known hypersensitivity to benralizumab or excipients, previous anaphylactic reaction to benralizumab, treatment of other eosinophilic conditions or for the relief of acute bronchospasm or status asthmaticus.

OTHER SPECIAL CONSIDERATIONS:

Fasenra should be administered via subcutaneous injection only by a healthcare professional. Monitoring of patients after administration for hypersensitivity-type reactions (e.g., anaphylaxis, angioedema, urticaria, rash) after each injection is recommended. One trial found that most patients and caregivers could administer benralizumab using the prefilled syringe in their home environment (Ferguson GT, et al. 2017). No formal drug interaction studies have been conducted and none are anticipated based on benlizumab's mechanism of action. Cytochrome P450 enzymes, efflux pumps, and protein-binding mechanisms are not involved in the clearance of benralizumab.
Safety of concurrent use of Nucala, Cinqair, Fasenra, and Dupixent with other monoclonal antibodies used to treat inflammation (TNF-inhibitors, interleukin antagonists, etc.) has not been established. Warnings and precautions include hypertensive reactions (e.g., anaphylaxis, angioedema), parasitic (Helminth) infection, and reduction in corticosteroid dosage (not to discontinue systemic or inhaled corticosteroid abruptly upon initiation of therapy, must decrease gradually, if appropriate).

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
J0517	Injection, benralizumab, 1 mg

AVAILABLE DOSAGE FORMS:
Fasenra SOSY 30MG/ML (prefilled syringe)
Fasenra Pen SOAJ 30MG/ML (auto-injector)

REFERENCES

1. Fasenra (benralizumab) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; February 2021.
2. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2022. Available from www.ginasthma.org
3. Bleecker ER, FitzGerald JM, Chanez P, et al; SIROCCO Study Investigators. Efficacy andsafety of benralizumab for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β2-agonists (SIROCCO): a randomized, multicenter, placebo-controlled phase 3 trial. Lancet. 2016; 388(10056):2115- 2127.[PubMed27609408]
4. FitzGerald JM, Bleecker EG, Nair P, et al; CALIMA Study Investigators. Benralizumab,an anti-interleukin-5 receptor α monoclonal antibody, as add-on treatment for patientswith severe, uncontrolled, eosinophilic asthma (CALIMA): a randomized, double-blind,placebo-controlled phase 3 trial. Lancet. 2016; 388(10056):2128-2141.[PubMed 27609406]
5. Ferguson GT, Mansur AH, Jacobs JS, et al. Functionality, reliability, and performanceof an accessorized pre-filled syringe with home-administered subcutaneous benralizumab for adult patients with severe asthma [abstract]. Am J Resp Crit Care Med. 2017;195:A3194.
6. Goldman M, Hirsch I, Zangrilli JG, Newbold P, Xu X. The association between blood eosinophil count and benralizumab efficacy for patients with severe, uncontrolled asthma: subanalyses of the phase III SIROCCO and CALIMA studies. Curr Med Res Opin. 2017; 33(9):1605- 1613.[PubMed 286440104]10.1080/03007995.2017.1347091
7. Nair P, Wenzel S, Rabe KF, et al; ZONDA Trial Investigators. Oral glucocorticoid-sparingeffect of benralizumab in severe asthma. N Engl J Med. 2017; 376(25):2448-2458.[PubMed 28530840]10.1056/NEJMoa1703501
8. Lieberman P, Nicklas RA, Randolph C, et al. Anaphylaxis--a practice parameter update2015. Ann Allergy Asthma Immunol. 2015;115(5):341-384.[PubMed 26505932]10.1016/j.anai.2015.07.019
9. Walford H and Doherty T. Diagnosis and management of eosinophilic asthma: a USperspective. Journal of Asthma and allergy 2014:7 53-65.
10. European Respiratory Society (ERS)/American Thoracic Society (ATS). Chung KF,Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ et al. International ERS/ATS guidelines on definition, evaluation, and treatment of severe asthma. Eur Respir J 2014;43:343-373.
11. National Asthma Education and Prevention Program (NAEPP): Expert panel report III: Guidelines for the diagnosis and management of asthma. Bethesda, MD: National Heart,Lung, and Blood Institute, 2007. (NIH publication no. 08-4051). Available at: http://www.nhlbi.nih.gov/healthpro/guidelines/current/asthma-guidelines. Accessed April2019.
12. 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.

13. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2022. Available from: www.ginasthma.org
14. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2023. Available from: www.ginasthma.org

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