CLINICAL MEDICATION POLICY	
Policy Name:	Interleukin-5 Inhibitors
Policy Number:	MP-025-MD-DE
Approved By:	Medical Management; Clinical Pharmacy
Provider Notice Date:	07/15/2018; 01/15/2018; 01/01/2017
Issue Date:	08/15/2018; 02/15/2018
Original Effective Date:	08/15/2018; 02/15/2018; 02/01/2017
Annual Approval Date:	06/19/2019
Revision Date:	06/19/2018; 11/08/2017; 08/09/2017
Products:	Highmark Health Options Medicaid
Application:	All participating hospitals and providers
Page Number(s):	1 of 7

Disclaimer

Health Options medical policy is intended to serve only as a general reference resource regarding coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

POLICY STATEMENT:

Highmark Health Options provides coverage under the medical benefits of the Company's Medicaid products for medically necessary intravenous administration of Interleukin-5 Inhibitors (Cinqair/Nucala/Fasenra).

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

The qualifications of the policy will meet the standards of the National Committee for Quality Assurance (NCQA) and the Delaware Department of Health and Social Services (DHSS) and all applicable state and federal regulations.

DEFINITIONS:

FEV1 – Forced expiratory volume in 1 second.

FVC – Forced vital capacity.

PEF – Peak expiratory flow.

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Mild Intermittent Asthma – defined as:

- Symptoms ≤ 2 times a week
- Asymptomatic and normal PEF between exacerbations
- Exacerbations brief (from a few hours to a few days); intensity may vary
- Nighttime symptoms ≤ 2 times a month
- FEV1 or PEF ≥ 80% predicted
- PEF variability < 20%

Mild Persistent Asthma – defined as:

- Symptoms > 2 times a week but < 1 time a day
- Exacerbations may affect activity
- Nighttime symptoms > 2 times a month
- FEV1 or PEF ≥ 80% predicted
- PEF variability 20 to 30%

Moderate Persistent Asthma – defined as:

- Daily symptoms
- Nighttime symptoms > one time a week
- Daily use of inhaled short-acting beta2-agonist
- Exacerbations may affect activity
- Exacerbations ≥ 2 times a week; may last days
- FEV1 or PEF > 60% but less than 80% predicted
- PEF variability > 30%

Severe Persistent Asthma – defined as:

- Continual symptoms (i.e., coughing, dyspnea, wheezing)
- Limited physical activity
- Frequent exacerbations
- Frequent nighttime symptoms
- FEV1 or PEF ≤ 60% predicted
- PEF variability > 30%

PROCEDURES:

1. Coverage will be provided for Interleukin-5 Inhibitor drugs when the following medical necessity criteria listed are met:
   A. The member is at least 12 years of age for Nucala OR the patient is at least 18 years of age for Cinqair; AND
   B. The medication is being prescribed by, or in consultation with, a pulmonologist, allergist, or immunologist; AND
   C. The member has a diagnosis of severe asthma; AND
   D. The member has one of the following blood eosinophil counts:
      1) For Nucala:
         a) Blood eosinophil count $\geq$ 150 cells/microliter with 6 weeks of treatment initiation; OR
         b) Blood eosinophil count $\geq$ 300 cells/microliter in the past 12 months;
            OR

      2) For Cinqair:
         a) Blood eosinophil count $\geq$ 400 cells/microliter within 4 weeks of treatment initiation; OR

      3) For Fasenra:
         a) Blood eosinophil count ≥ 150 cells/microliter within 4 weeks of treatment initiation;

         AND
   E. Symptoms have been uncontrolled despite adherence with at least a three month trial of controller medications, which includes at least a medium-dosed inhaled corticosteroid plus another agent; OR
   F. The requested medication will be used in conjunction with one of the following: standard asthma controller medications (e.g. inhaled corticosteroid, long-acting beta agonist, leukotriene receptor antagonist, etc.); AND
      1) A maximally-dosed combination inhaled corticosteroid/ling acting $beta_2$-agonist product; OR
      2) Combination therapy defined as:
         a) A high does inhaled corticosteroid; AND
         b) An additional standard asthma controller medication (e.g., long-acting beta agonist, leukotriene receptor antagonist, etc.)
   G. The requested dose and frequency is in accordance with FDA-approved package labeling, nationally recognized compendia, and/or evidence-based practice guidelines.

2. Coverage may be provided for eosinophilic granulomatosis with polyangiitis for Nucala ONLY when all the following are met:
   A. Member has a documented diagnosis of eosinophilic granulomatosis with polyangiitis based on the presence of at least four of the following diagnostic criteria:
      1) Asthma;
      2) Eosinophilia (>10% eosinophils on the differential leukocyte count);
      3) Mononeuropathy or polyneuropathy;
      4) Migratory or transient pulmonary infiltrates on chest x-rays;
      5) Paranasal sinus abnormalities;

6) Biopsy containing a blood vessel with extravascular eosinophils;

B. Must be prescribed by, or in consultation with, an allergist, immunologist, pulmonologist, or rheumatologist;
C. The member is at least 18 years of age or older;
D. The member has been stable on corticosteroids for at least 4 weeks or the prescriber has indicated clinical inappropriateness of corticosteroid therapy

3. Contraindications
   - The safety and efficacy in pediatric individuals younger than 12 years of age have not been established.
   - Known hypersensitivity to Nucala/Cinqair/Fasenra or excipients in the formulation.

4. When Nucala, Cinqair, and Fasenra are not covered
   All other conditions not listed above are considered experimental/investigational. Scientific evidence has not been established to support the use of Interleuken-5 Inhibitors for any other indication. Services are considered not medically necessary.

   Coverage may be provided for any non-FDA labeled indication or a medically accepted indication that is supported by nationally recognized pharmacy compendia or peer-reviewed medical literature for treatment of the diagnosis for which it is prescribed and will be reviewed on a case-by-case basis to determine medical necessity.

5. Length of Coverage
   The initial length of coverage will be 6 months. Reauthorization will be granted for 12 months when the member meets the reauthorization criteria described above.

6. Post-payment Audit Statement
   The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Highmark Health Options at any time pursuant to the terms of your provider agreement.

7. Place of Service
   The place of service for administration of Nucala, Cinqair or Fasenra is outpatient.

GOVERNING BODIES APPROVAL

On November 4, 2015, the U.S. Food and Drug Administration approved Mepolizumab (Nucala®) for use with other asthma medicines for the maintenance treatment of asthma in patients age 12 years and older. Mepolizumab (Nucala®) is approved for patients who have a history of severe asthma attacks (exacerbations) despite receiving their current asthma medicines.

Mepolizumab (Nucala®) is administered once every four weeks by subcutaneous injection by a health care professional into the upper arm, thigh, or abdomen. Mepolizumab (Nucala®) is a humanized interleukin-5 antagonist monoclonal antibody produced by recombinant DNA technology in Chinese hamster ovary cells. Mepolizumab reduces severe asthma attacks by reducing the levels of blood eosinophils, a type of white blood cell that contributes to the development of asthma.
On March 28, 2016, the U.S. Food and Drug Administration approved reslizumab (Cinqair) for use with other asthma medicines for the maintenance treatment of asthma in patients age 18 years and older.

Reslizumab (Cinqair) is approved for patients who have a history of severe asthma attacks (exacerbations) despite receiving their current asthma medicines.

Reslizumab (Cinqair) is administered once every four weeks by intravenous infusion in a clinical setting prepared to manage anaphylaxis. Reslizumab (Cinqair) is a humanized interleukin-5 antagonist monoclonal antibody produced by recombinant DNA technology in murine myeloma non-secreting 0 (NS0) cells. Reslizumab (Cinqair) reduces severe asthma attacks by reducing the levels of blood eosinophils, a type of white blood cell that contributes to the development of asthma.

Benralizumab (Fasenra) was FDA approved on November 14, 2017 for the treatment of severe eosinophilic asthma. Benralizumab is administered subcutaneously via prefilled syringe every four weeks for the first 3 doses then every 8 weeks thereafter.

CODING REQUIREMENTS:

Procedure Codes

HCPCS Codes	Description
J2182	Injection, mepolizumab, 1 mg (new code effective 1/1/2017)
J2786	Injection, reslizumab, 1 mg (new code effective 1/1/2017)
J3590	Unclassified biologics
C9466	Injection, benralizumab, 1 mg

Diagnosis Codes

ICD-10 Codes	Description
J45.50	Severe persistent asthma, uncomplicated [add-on maintenance treatment of patients aged 12 years and older]
J45.51	Severe, persistent asthma with (acute) exacerbation [add-on maintenance treatment of patients aged 12 years and older[
J45.52	Severe persistent asthma with status asthmaticus [add-on maintenance treatment of patients aged 12 years and older]
J82	Pulmonary eosinophilia, not elsewhere classified [add-on maintenance treatment of patients aged 12 years and older] [eosinophilic asthma]

REIMBURSEMENT:

Participating facilities will be reimbursed per their Highmark Health Options contract.

POLICY SOURCE(S):

Mepolizumab (Nucala®) Prescribing Information. Accessed on September 13, 2016 from http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/125526Orig1s000Lbl.pdf.

American Academy of Allergy Asthma and Immunology (AAAAI). Practice Parameters: Allergy Diagnostic Testing. Available at: http://www.aaaai.org. Accessed on August 25, 2016.

FDA approves Reslizumab (Cinqair) to treat severe asthma [news release]. Silver Spring, MD U.S. Food and Drug Administration March 23, 2016. Accessed on April 8, 2016 from: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm491980.htm.

Reslizumab (Cinqair) Prescribing Information. Accessed on March 28, 2016 from http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/761033lbl.pdf.

FDA approves Nucala to treat severe asthma [news release]. Silver Spring, MD U.S. Food and Drug Administration November 4, 2015. Accessed on January 7, 2016 from: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm471031.htm.

American Academy of Allergy Asthma and Immunology (AAAAI). Conditions and treatments. Asthma. Available at: http://www.aaaai.org/. Accessed on September 13, 2016.

American Academy of Allergy Asthma and Immunology (AAAAI). AAAAI allergy & asthma medication guide. Available at: http://www.aaaai.org/conditions-and-treatments/treatments/drug-guide/inhaled-corticosteroids.aspx. Accessed on September 13, 2016.

Fasenra [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals, LP; November 2017.

Treatment and prognosis of eosinophilic granulomatosis with polyangiitis (Churg-Strauss). UptoDate. https://www.uptodate.com/contents/treatment-and-prognosis-of-eosinophilic-granulomatosis-with-polyangiitis-churg-strauss#H16. Accessed March 8, 2018.

Nair P, Wenzel S, Rabe K, et al. Oral Glucocorticoid–Sparing Effect of Benralizumab in Severe Asthma. N Engl J Med. 2017 Jun;376:2248-2458.

Policy History:

Date	Action
10/17/2016	Initial document developed
12/06/2016	QI/UM committee approval
02/01/2017	Provider effective date
08/09/2017	Added new procedure codes J2182 and J2786. Removed procedure codes J3490, J3590 and C9473.
11/08/2017	Revisions: Annual review, reformatted into combined medical/pharmacy template; revised specific diagnostic criteria for asthma to require "diagnosis of severe asthma;" removed statement regarding pharmacy claims; moved requirement for at least medium-dosed inhaled corticosteroids to sections 1.F. and 1.G.; removed combination of anti-asthma monoclonal antibody requirement; revised reauthorization criteria; removed chart of comparative daily doses for inhaled glucocorticoids; removed ruling out of other causes of eosinophilia; and updated references
12/12/2017	QI/UM committee review approval
02/15/2018	New provider effective date
06/19/2018	Annual Review: Removed the word 'Covered' from the procedure and diagnosis code tables in Attachments A & B; Added coverage guidelines, coding for new drug Fasenra; deleted nonrelated CPT codes 96372 & 96401; combined specified therapy requirements; removed specific dosing with general dosing statement, removed parasitic infection criteria; removed Attachment C, Estimated Clinical Comparability of Daily Doses of Inhaled Corticosteroids; updated references.
06/19/2018	QI/UM Committee Review Approval
08/15/2018	New Provider effective date