Cinqair (reslizumab injection for IV use)

Prior Approval Criteria
March 2017

OVERVIEW
Cinqair, an interleukin (IL)-5 antagonist immunoglobulin G (IgG)4κ monoclonal antibody, is indicated for add-on maintenance treatment of patients with severe asthma aged ≥ 18 years who have an eosinophilic phenotype. 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, Cinqair decreases the production and survival of eosinophils. However, the exact mechanism of action of Cinqair in asthma has not been established. Cinqair should be administered as a 3 mg/kg intravenous (IV) infusion once every 4 weeks by a healthcare professional.

POLICY STATEMENT
Prior authorization is recommended for prescription benefit coverage of Cinqair. Because of the specialized skills required for evaluation and diagnosis of patients treated with Cinqair as well as the monitoring required for adverse events and long-term efficacy, approval requires Cinqair to be prescribed by or in consultation with a physician who specializes in the condition being treated. Refer to criteria below for approval durations.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Cinqair (reslizumab) is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

1. Asthma in Patients with Severe Disease and an Eosinophilic Phenotype.
   1) Initial Therapy. Approve for 6 months if the patient meets the following criteria (A, B, C, D and E):
      A. Patient is ≥ 18 years of age; AND
      B. Cinqair is prescribed by or in consultation with an allergist, immunologist, or pulmonologist; AND
      C. Patient has a peripheral blood eosinophil count of ≥ 400 cells per microliter within the previous 4 weeks (prior to treatment with an interleukin [IL]-5 antagonist monoclonal antibody); AND
      D. Patient has received at least 3 consecutive months of combination therapy with BOTH of the following (i and ii):
         i. An inhaled corticosteroid (ICS) [e.g. Flovent® HFA {fluticasone inhalation aerosol}, Flovent® Diskus® {fluticasone inhalation powder}, Arnuity™ Ellipta® {fluticasone furoate inhalation powder}, Asmanex® Twisthaler® {mometasone inhalation powder}, Asmanex® HFA {mometasone inhalation...}]
      
      ii. An inhaled long-acting β2 agonist (LABA) [e.g. Symbicort® HFA {budesonide and formoterol inhalation powder for powdermist dosage form}, Symbicort® Ellipta® {budesonide and formoterol inhalation powder}], Asma...
aerosol}, Aersopan® [flunisolide HFA inhalation aerosol], Alvesco® [ciclesonide inhalation powder], Pulmicort Flexhaler® [budesonide inhalation powder], QVAR® [beclomethasone HFA inhalation aerosol]; AND

ii. At least ONE of the following (a, b, c or d):
   a. Inhaled long-acting beta-agonist (LABA) [e.g., Serevent® Diskus® {salmeterol xinafoate inhalation powder}]; OR
      NOTE: Use of a combination inhaler containing both an ICS and a LABA would fulfill the requirement for both criteria i and ii (e.g., Advair® Diskus/HFA [fluticasone propionate and salmeterol inhalation powder/aerosol], Symbicort® [budesonide and formoterol fumarate inhalation aerosol], Breo® Ellipta® [fluticasone furoate and vilanterol inhalation powder], and Dulera® [mometasone furoate and formoterol fumarate inhalation aerosol])
   b. Inhaled long-acting muscarinic antagonist (LAMA) [e.g., Spiriva® Respimat® {tiotropium bromide inhalation spray}]; OR
   c. Leukotriene receptor antagonist (LTRA) [e.g. montelukast tablets/granules {Singulair®, generics}, Accolate® {zafirlukast tablets}]; OR
   d. Theophylline (Theo-24, TheoChron ER, generics); AND

E. Patient’s asthma continues to be uncontrolled as defined by ONE of the following (i, ii, iii, iv or v):
   i. The patient experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year; OR
   ii. The patient experienced one or more asthma exacerbation requiring hospitalization or an Emergency Department (ED) visit in the previous year; OR
   iii. Patient has a forced expiratory volume in 1 second (FEV<sub>1</sub>) < 80% predicted; OR
   iv. Patient has an FEV<sub>1</sub>/forced vital capacity (FVC) < 0.80; OR
   v. The patient’s asthma worsens upon tapering of oral corticosteroid therapy.

2) Patients Continuing Cinqair Therapy. Approve for 1 year if the patient meets the following criteria (A, B, C and D):
   A. Patient is ≥ 18 years of age; AND
   B. Cinqair is prescribed by or in consultation with an allergist, immunologist, or pulmonologist; AND
   C. Patient continues to receive therapy with one inhaled corticosteroid (ICS) or one ICS-containing combination inhaler (e.g., Flovent® Diskus/HFA [fluticasone inhalation powder/aerosol], Arnuity™ Ellipta® [fluticasone furoate inhalation powder], Asmanex™ Twisthaler®/HFA [mometasone inhalation powder/aerosol], Aersopan™ [flunisolide HFA inhalation aerosol], Alvesco® [ciclesonide inhalation aerosol], Pulmicort Flexhaler® [budesonide inhalation powder], budesonide suspension for inhalation [Pulmicort Respules™, generics], QVAR®
[beclomethasone HFA inhalation aerosol], Advair® Diskus/HFA [fluticasone propionate and salmeterol inhalation powder/aerosol], Symbicort® [budesonide and formoterol fumarate inhalation aerosol], Breo® Ellipta® [fluticasone furoate and vilanterol inhalation powder], and Dulera® [mometasone furoate and formoterol fumarate inhalation aerosol]); AND

D. The patient has responded to Cinqair therapy as determined by the prescribing physician (e.g., decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, emergency department (ED)/urgent care, or physician visits due to asthma; decreased requirement for oral corticosteroid therapy).

**Dosing:** 3 mg/kg intravenous (IV) infusion every 4 weeks

**Approval Duration**
Initial Approval = 180 days (6 months)
Re-authorization = 365 days (1 year)

**CONDITIONS NOT RECOMMENDED FOR APPROVAL**
Cinqair has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Concurrent use of Cinqair with another interleukin (IL)-5 antagonist monoclonal antibody.** Nucala is another IL-5 antagonist recombinant IgG1κ monoclonal antibody indicated for add-on maintenance treatment of patients with severe asthma aged ≥ 12 years who have an eosinophilic phenotype. The efficacy and safety of Cinqair in combination with Nucala or any other IL-5 antagonist have not been established.

2. **Concurrent use of Cinqair with Xolair® (omalizumab injection for subcutaneous use).** Xolair is a recombinant humanized IgG1κ monoclonal antibody indicated for use in adults and adolescents (aged ≥ 6 years) with moderate to severe persistent asthma and who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with ICSs. The efficacy and safety of Cinqair in combination with Xolair have not been established.

3. **Eosinophilic Esophagitis (EoE) or Eosinophilic Gastroenteritis.** One pilot study (available as abstract) [n = 4] examined the effects of Cinqair on peripheral blood and gastrointestinal eosinophils in patients with eosinophilic gastroenteritis. Following one IV infusion of Cinqair 1 mg/kg, blood eosinophil counts declined quickly in all patients, but symptom scores were not improved. One additional randomized, double-blind, placebo controlled study (published) [n =226] evaluated the efficacy of Cinqair in pediatric and adolescent patients with EoE. In this study, patients were randomly assigned to receive Cinqair IV infusions of 1 mg/kg, 2 mg/kg, or 3 mg/kg, or placebo at Weeks 0, 4, 8, and 12. At Week 15, peak esophageal eosinophil counts were reduced by a median 24%, 59%, 67%, and 64%, with placebo, Cinqair 1 mg/kg, 2 mg/kg, 3 mg/kg, respectively; all reductions with Cinqair were significant compared with placebo (P < 0.001). Improvements in physician’s global assessment scores were also observed in all groups (including placebo), but the difference between Cinqair and placebo was not statistically significant. Additional, well-
controlled trials are needed to determine the role of Cinqair in the treatment of EoE and eosinophilic gastroenteritis.

4. **Hypereosinophilic Syndrome (HES), Idiopathic.** One small pilot study (published) \([n = 4]\) evaluated the safety and efficacy of Cinqair in patients with HES who were refractory to or intolerant of treatment with conventional therapy. A single 1 mg/kg dose of Cinqair resulted in a response in two of four patients. In the two responders, blood eosinophil counts dropped to within the normal range within 48 hours of the Cinqair infusion and this was accompanied by an improvement in clinical signs and symptoms. Additional, well-controlled trials are needed to determine the role of Cinqair in the treatment of HES.

5. **Nasal Polyps.** Cinqair was studied in one double-blind, placebo-controlled, randomized safety and pharmacokinetic study (published) \([n = 24]\) in patients with nasal polyps. Patients received a single infusion of either Cinqair 3 mg/kg, Cinqair 1 mg/kg, or placebo. It was reported that blood eosinophil counts and concentrations of eosinophil cation protein were reduced for up to 8 weeks following the Cinqair infusion. Nasal polyp scores improved for approximately 4 weeks in one-half of patients receiving active treatment. Additionally, a pooled subgroup analysis from the two pivotal Cinqair asthma exacerbation trials found that in patients with inadequately controlled asthma and chronic sinusitis with nasal polyps \((n = 150)\) Cinqair demonstrated enhanced efficacy. Patients in this subgroup experienced an 83% reduction the CAE rate with Cinqair vs. placebo (rate ratio \([RR]\) 0.17; \(P = 0.0002\)). The magnitude of this reduction was greater than that observed with the overall study population. However, additional, well-controlled trials are needed to determine the role of Cinqair in the treatment of patients with nasal polyps who do not have asthma.

6. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

References

- Cinqair® injection for intravenous use [prescribing information]. Frazer, PA: Teva Respiratory, LLC; May 2016.
- Xolair® subcutaneous injection [prescribing information]. South San Francisco, CA and East Hanover, NJ: Genentech, Inc. and Novartis Pharmaceuticals Corporation; September 2014.
