Medication Policy Manual

Topic: Cinqair®, reslizumab

Date of Origin: April 8, 2016

Committee Approval: October 21, 2016

Next Review Date: October 2017

Effective Date: November 1, 2016

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medication policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Reslizumab (Cinqair) is a human monoclonal antibody used in the treatment of severe eosinophilic asthma. It is administered as an intravenous (IV) infusion by a healthcare provider.
Policy/Criteria

I. Most contracts require prior authorization approval of reslizumab (Cinqair) prior to coverage. Reslizumab (Cinqair) may be considered medically necessary when criteria A through E, below, are met.

A. A diagnosis of severe eosinophilic asthma

AND

B. A blood eosinophil count of at least 400 cells/microliter

AND

C. The patient is currently being followed by an asthma specialist (allergist, immunologist, or pulmonologist).

AND

D. Clinical documentation of poor asthma control or recurrent exacerbation requiring additional medication treatment:
   - Additional medical treatment may include any of the following: treatment with oral corticosteroids, emergency department (ED) visits, hospitalizations, or frequent office visits.
   - Poor asthma control may include (but is not limited to) clinical documentation of limitation of activities of daily living (ADLs), nighttime awakening, or dyspnea.
   - Recurrent exacerbation is defined as 2 or more acute exacerbations in a 12-month period.

AND

E. Clinical documentation that patient is compliant with high-dose inhaled corticosteroids (ICS) and long-acting inhaled beta-2 agonists (LABA) (Step 5 of the National Asthma Treatment Guidelines) and use of oral corticosteroids for exacerbation unless contraindicated.

AND

F. Underlying conditions or triggers for asthma or pulmonary disease are being maximally managed.

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx considers does not consider reslizumab to be a self-administered medication.

B. When prior authorization is approved, reslizumab may be authorized in quantities up to 3 mg/kg every 4 weeks (28 days).

C. Authorization shall be reviewed at least every 6 months to confirm that current medical necessity criteria are met and that the medication is effective, defined as sustained clinical improvement from reduced asthma symptoms (such as reduced missed days from work or school) or stable asthma control.
III. Reslizumab is considered investigational when used for all other conditions, including, but not limited to:

A. Severe allergic asthma (without documentation of severe eosinophilia)
B. Use in combination with other anti-asthma monoclonal antibodies, including omalizumab (Xolair) or mepolizumab (Nucala), (for asthma or any indication)
C. Eosinophilic esophagitis (EE)
D. Other eosinophilic conditions, such as hypereosinophilic syndrome (HES) or eosinophilic granulomatosis with polyangiitis, allergic granulomatosis, or Churg-Strauss syndrome

Position Statement

SEVERE EOSINOPHILIC ASTHMA
- Reslizumab has been studied in people with moderate and severe refractory eosinophilic asthma that is inadequately controlled despite use of high-dose corticosteroids and a controller medication. [1-4]
- Reslizumab has not been proven to be safer or more effective than preferred options recommended in treatment guidelines, nor in patients with less severe asthma or non-eosinophilic asthma. [1-4]
- High-dose inhaled corticosteroids in combination with a long-acting inhaled beta-agonist (STEP 5 therapy) are effective in the treatment of many patients with persistent asthma, along with leukotriene inhibitors and oral steroids for exacerbations. [5] Use of reslizumab add-on therapy is not included in current asthma treatment guidelines. [6]
- Reslizumab was approved as an intravenous infusion that must be administered by a health care provider.
- Reslizumab may be covered in quantities up to 3 mg/kg every 4 weeks, the dose proven to be safe and effective for management of refractory eosinophilic asthma. [1]
- The safety and efficacy of reslizumab in combination with other anti-asthma monoclonal antibodies (MAbs), such as omalizumab (Xolair) or mepolizumab (Nucala), have not been established. There are no trials of the use of anti-asthma Mabs as combination therapy.

OTHER CONDITIONS
- The safety and effectiveness of reslizumab in conditions other than severe eosinophilic asthma, such as eosinophilic esophagitis, have not been established. Trials are ongoing. [7]
Appendices 1 to 4: National Heart, Lung and Blood Institute (NHLBI) Asthma Treatment Guidelines


Appendix 1: Stepwise Approach for Managing Asthma Long-Term in Children, age 0 to 4

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4</th>
<th>Step 5</th>
<th>Step 6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intermit tent Asthma</strong></td>
<td><strong>Persistent Asthma: Requiring Daily Medication</strong></td>
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<tr>
<td><strong>Preferred:</strong></td>
<td>SABA PRN</td>
<td>low-dose ICS</td>
<td>medium-dose ICS</td>
<td>medium-dose ICS + LABA or montelukast</td>
<td>High-dose ICS + LABA or montelukast</td>
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<td></td>
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<td></td>
<td>High-dose ICS + LABA or montelukast or oral corticosteroids</td>
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<td><strong>Alternative:</strong></td>
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<tr>
<td><strong>Each step: Patient education and environmental control.</strong></td>
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</tbody>
</table>

**Quick-Relief Medication**
- Should be available for all patients.
- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms.
- With viral respiratory infection: SABA q 4–6 hours up to 24 hours (longer with physician consult). Consider short course of oral systemic corticosteroids if exacerbation is severe or patient has history of previous severe exacerbations.

Caution: Frequent use of SABA may indicate the need to step up treatment. See text for recommendations on initiating daily long-term-control therapy

**Key:** Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy. EIB: exercise-induced bronchospasm; ICS: inhaled corticosteroid (See Appendix 4, for classification of ICS strength); LABA: inhaled long-acting beta2-agonist; SABA: inhaled short-acting beta2-agonist.

**Notes:**
- The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
- If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.
- If clear benefit is not observed within 4–6 weeks and patient/family medication technique and adherence are satisfactory, consider adjusting therapy or alternative diagnosis.
- Studies on children 0–4 years of age are limited. Step 2 preferred therapy is based on Evidence A. All other recommendations are based on expert opinion and extrapolation from studies in older children.
### Appendix 2: Stepwise Approach for Managing Asthma Long-Term in Children, age 5 to 11

**Intermittent Asthma**
- Consult with asthma specialist if step 3 care or higher is required.
- Consider consultation at step 2.

**Preferred:**
- SABA PRN
- low-dose ICS
- low-dose ICS + LABA, LTRA or theophylline
- medium-dose ICS + LTRA or theophylline
- High-dose ICS + LABA

**Alternative:**
- cromolyn, LTRA, nedocromil, or theophylline
- medium-dose ICS
- OR medium-dose ICS
- high-dose ICS + LTRA or theophylline
- high-dose ICS + LTRA or theophylline

**Each step: Patient education, environmental control, and management of comorbidities.**
- Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have persistent, allergic asthma (see notes).

**Quick-Relief Medication**
- Should be available for all patients.
- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Caution: Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.
- Caution: Frequent use of SABA may indicate the need to step up treatment. See text for recommendations on initiating daily long-term-control therapy.

**Step up if needed (first, check adherence, inhaler technique, and environmental control)**

**Step down if possible (and asthma is well controlled at least 3 months)**

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**Key:** Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy. EIB: exercise-induced bronchospasm; ICS: inhaled corticosteroid (See Appendix 4, for classification of ICS strength); LABA: inhaled long-acting beta2-agonist; LTRA: leukotriene receptor antagonist (montelukast or zafirlukast); SABA: inhaled short-acting beta2-agonist.

**Notes:**
- The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
- If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.
- Theophylline is a less desirable alternative due to the need to monitor serum concentration levels.
- Step 1 and step 2 medications are based on Evidence A. Step 3 ICS + adjunctive therapy and ICS are based on Evidence B for efficacy of each treatment and extrapolation from comparator trials in older children and adults—comparator trials are not available for this age group; steps 4–6 are based on expert opinion and extrapolation from studies in older children and adults.
- Immunotherapy for steps 2–4 is based on Evidence B for house-dust mites, animal danders, and pollens; evidence is weak or lacking for molds and cockroaches. Evidence is strongest for immunotherapy with single allergens.
- The role of allergy in asthma is greater in children than in adults. Clinicians who administer immunotherapy should be prepared and equipped to identify and treat anaphylaxis that may occur.
Appendix 3: Stepwise Approach for Managing Asthma in Youths ≥ 12 years old and Adults

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
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</tr>
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<td></td>
<td>Consult with asthma specialist if step 4 care or higher is required. Consider consultation at step 3.</td>
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</tbody>
</table>

**Preferred:**
- SABA PRN
- low-dose ICS
- low-dose ICS + LABA
  - OR
  - medium-dose ICS
- medium-dose ICS + LABA
- High-dose ICS + LABA
  - AND
  - Consider omalizumab for patients who have allergies
- High-dose ICS + LABA + oral corticosteroids
  - AND
  - Consider omalizumab for patients who have allergies

**Alternative:**
- cromolyn, LTRA, nedocromil, or theophylline
- low-dose ICS + LTRA, theophylline or zileuton
- medium-dose ICS + LTRA, theophylline or zileuton

**Each step: Patient education, environmental control, and management of comorbidities.**
Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

**Quick-Relief Medication**
- Should be available for all patients.
- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Caution: Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.
- Caution: Frequent use of SABA may indicate the need to step up treatment. See text for recommendations on initiating daily long-term-control therapy.

Assess control

Step down if possible (and asthma is well controlled at least 3 months)

Step up if needed (first, check adherence, inhaler technique, and environmental control)

**Key:** Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy.
EIB: exercise-induced bronchospasm; ICS: inhaled corticosteroid (See Appendix 4, for classification of ICS strength); LABA: inhaled long-acting beta2-agonist; LTRA: leukotriene receptor antagonist (montelukast or zafirlukast); SABA: inhaled short-acting beta2-agonist.

**Notes:**
- The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
- If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.
- Zileuton is a less desirable alternative due to limited studies as adjunctive therapy and the need to monitor liver function.
- Theophylline requires monitoring of serum concentration levels.
- In step 6, before oral systemic corticosteroids are introduced, a trial of high-dose ICS + LABA + either LTRA, theophylline, or zileuton may be considered, although this approach has not been studied in clinical trials.
- Step 1, 2, and 3 preferred therapies are based on Evidence A; step 3 alternative therapy is based on Evidence A for LABA, Evidence B for theophylline, and Evidence D for zileuton. Step 4 preferred therapy is based on Evidence B, and alternative therapy is based on Evidence B for LTRA and theophylline and Evidence D for zileuton. Step 5 preferred therapy is based on Evidence B. Step 6 preferred therapy is based on (EPR-2 1997) and Evidence B for omalizumab.
- Immunotherapy for steps 2–4 is based on Evidence B for house-dust mites, animal danders, and pollens; evidence is weak or lacking for molds and cockroaches. Evidence is strongest for immunotherapy with single allergens. The role of allergy in asthma is greater in children than in adults.
- Clinicians who administer immunotherapy or omalizumab should be prepared and equipped to identify and treat anaphylaxis that may occur.

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## Appendix 4: NHBLI Estimated Comparative Daily Dosages for Inhaled Corticosteroids (ICS) in Adults

<table>
<thead>
<tr>
<th>Drug</th>
<th>Low Daily Dose</th>
<th>Medium Daily Dose</th>
<th>High Daily Dose</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Child</td>
<td></td>
<td>Child</td>
</tr>
<tr>
<td></td>
<td>0–4 yo 5–11yo</td>
<td>0–4 yo 5–11yo</td>
<td>0–4 yo 5–11yo</td>
</tr>
<tr>
<td>Beclomethasone HFA 40 or 80 mcg/puff</td>
<td>NA</td>
<td>80–160 mg MCg</td>
<td>80–240 mg MCg</td>
</tr>
<tr>
<td>Budesonide DPI 90, 180, 200 mcg/inhalation *</td>
<td>NA</td>
<td>180–400 mg MCg</td>
<td>180–600 mg MCg</td>
</tr>
<tr>
<td>Budesonide Inhaled Inhalation suspension for nebulization</td>
<td>0.25–0.5 mg NA</td>
<td>&gt;0.5–1.0 mg NA</td>
<td>1.0 mg NA</td>
</tr>
<tr>
<td>Flunisolide 250 mcg/puff</td>
<td>NA</td>
<td>500–750 mg MCg</td>
<td>500–1000 mg MCg</td>
</tr>
<tr>
<td>Flunisolide HFA 80 mcg/puff</td>
<td>NA</td>
<td>160 mg NA</td>
<td>320 mg NA</td>
</tr>
<tr>
<td>Fluticasone HFA/MDI: 44, 110, 220 mcg/puff</td>
<td>176 mcg</td>
<td>88–176 mg MCg</td>
<td>88–264 mg MCg</td>
</tr>
<tr>
<td>DPI: 50, 100, or 250 mcg/inhalation</td>
<td>NA</td>
<td>100–200 mg MCg</td>
<td>100–300 mg MCg</td>
</tr>
<tr>
<td>Mometasone DPI 200 mcg/inhalation</td>
<td>NA</td>
<td>200 mg NA</td>
<td>400 mg NA</td>
</tr>
<tr>
<td>Triamcinolone acetonide 75 mcg/puff</td>
<td>NA</td>
<td>300–600 mg MCg</td>
<td>300–750 mg MCg</td>
</tr>
</tbody>
</table>

Key: DPI: dry power inhaler; HFA: hydrofluoroalkane; MDI: metered-dose inhaler; NA: not available (either not approved, no data available, or safety and efficacy not established for this age group)

\* Maximum daily dose of budesonide from Symbicort (budesonide/formoterol) is 640 mcg/day, a medium dose of ICS.
Cross References

<table>
<thead>
<tr>
<th>Cross References</th>
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<tbody>
<tr>
<td>Allergy Testing lab01, TRG Medical Policy Manual, Laboratory</td>
</tr>
<tr>
<td>Xolair®, omalizumab, Medication Policy Manual, Policy No. dru087</td>
</tr>
<tr>
<td>Nucala™, mepolizumab, Medication Policy Manual, Policy No. dru428</td>
</tr>
</tbody>
</table>

References

1. Center for Drug Evaluation and Research (CDER). FDA Pulmonary-Allergy Drugs Advisory Committee - December 9, 2015 Meeting Materials (Briefing Information, Minutes) for NDA 761033: Cinqair (reslizumab). [cited 8/24/2016]; Available at: http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Pulmonary-AllergyDrugsAdvisoryCommittee/ucm433815.htm


7. Clinicaltrials.gov [cited 8/24/2016]

Revision History

<table>
<thead>
<tr>
<th>Revision Date</th>
<th>Revision Summary</th>
</tr>
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<tbody>
<tr>
<td>10/21/2016</td>
<td>No changes with this annual update.</td>
</tr>
<tr>
<td>4/8/2016</td>
<td>New policy</td>
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