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Medication Policy Manual

Policy No: dru456

Topic: Cinqair®, reslizumab

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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.

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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. Regence Pharmacy Services consider 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.

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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]

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Appendices 1 to 4: National Heart, Lung and Blood Institute (NHLBI) Asthma Treatment Guidelines

Adapted from: NHLBI, NIH: National Asthma Education and Prevention Program Expert Panel Report 3 Guidelines for the Diagnosis and Management of Asthma October 2007. Available at: http://www.nhlbi.nih.gov/guidelines/asthma/asthsumm.pdf

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

	Step 1	Step 2	Step 3	Step 4	Step 5	Step 6	
	Intermit-tent Asthma	**Persistent Asthma: Requiring Daily Medication** Consult with asthma specialist if step 3 care or higher is required. Consider consultation at step 2.					↑
Preferred:	SABA PRN	low-dose ICS	medium-dose ICS	medium-dose ICS + LABA *or* montelukast	High-dose ICS + LABA *or* montelukast	High-dose ICS + LABA *or* montelukast *or* oral corticosteroids	Step up if needed (first, check adherence, inhaler technique, and environmental control)
Alternative:		cromolyn *or* montelukast					Assess control
	Each step: Patient education and environmental control.						
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						Step down if possible (and asthma is well controlled at least 3 months) ↓

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.

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Appendix 2: Stepwise Approach for Managing Asthma Long-Term in Children, age 5 to 11

	Step 1	Step 2	Step 3	Step 4	Step 5	Step 6	
	Intermittent Asthma	**Persistent Asthma: Requiring Daily Medication** 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 + LABA	High-dose ICS + LABA	High-dose ICS + LABA + oral corticosteroids	Step up if needed (first, check adherence, inhaler technique, and environmental control)
Alternative:		cromolyn, LTRA, nedocromil, *or* theophylline	*OR* medium-dose ICS	medium-dose ICS + LTRA *or* theophylline	high-dose ICS + LTRA *or* theophylline	high-dose ICS + LTRA *or* theophylline + oral corticosteroids	
	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).						Assess control
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 down if possible (and asthma is well controlled at least 3 months) ↓

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.

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Appendix 3: Stepwise Approach for Managing Asthma in Youths ≥ 12 years old and Adults

	Step 1	Step 2	Step 3	Step 4	Step 5	Step 6	
	Intermittent Asthma	**Persistent Asthma: Requiring Daily Medication** Consult with asthma specialist if step 4 care or higher is required. Consider consultation at step 3.					↑
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	Step up if needed (first, check adherence, inhaler technique, and environmental control)
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).						Assess control
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 down if possible (and asthma is well controlled at least 3 months) ↓

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 LTRA, 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 [a]

	Low Daily Dose			Medium Daily Dose			High Daily Dose		
	Child			Child			Child		
Drug	0–4 yo	5–11yo	≥12 Years	0–4 yo	5–11yo	≥12 Years	0–4 yo	5–11yo	≥12 Years
Beclomethasone HFA 40 or 80 mcg/puff	NA	80–160 mcg	80–240 mcg	NA	>160–320 mcg	>240–480 mcg	NA	>320 mcg	>480 mcg
Budesonide DPI 90, 180, 200 mcg/DPI [b]	NA	180–400 mcg	180–600 mcg	NA	>400–800 mcg	>600–1,200 mcg [a]	NA	>800 mcg	>1,200 mcg [b]
Budesonide inhalation suspension for nebulization	0.25–0.5 mg	0.5 mg	NA	>0.5–1.0 mg	1.0 mg	NA	>1.0 mg	2.0 mg	NA
Flunisolide 250 mcg/puff	NA	500–750 mcg	500–1,000 mcg	NA	1,000–1,250 mcg	>1,000–2,000 mcg	NA	>1,250 mcg	>2,000 mcg
Flunisolide HFA 80 mcg/puff	NA	160 mcg	320 mcg	NA	320 mcg	>320–640 mcg	NA	≥640 mcg	>640 mcg
Fluticasone furoate DPI:100, or 200 mcg/DPI [a]	NA	NA	NA	NA	NA	NA	100 mcg	NA	200 mcg
Fluticasone propionate HFA/MDI: 44, 110, 220 mcg/puff	176 mcg	88–176 mcg	88–264 mcg	>176–352 mcg	>176–352 mcg	>264–440 mcg	>352 mcg	>352 mcg	>440 mcg
Fluticasone propionate DPI: 50, 100, or 250 mcg/DPI	NA	100–200 mcg	100–300 mcg	NA	>200–400 mcg	>300–500 mcg	NA	>400 mcg	>500 mcg
Mometasone DPI 200 mcg/DPI	NA	NA	200 mcg	NA	NA	400 mcg	NA	NA	>400 mcg
Triamcinolone acetonide 75 mcg/puff	NA	300–600 mcg	300–750 mcg	NA	>600–900 mcg	>750–1,500 mcg	NA	>900 mcg	>1,500 mcg

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)

[a] NHLBI Estimated Comparative Daily Dose except as noted. Other dose comparisons are supported by GINA (2017).

[b] Maximum daily dose of budesonide from Symbicort (budesonide/formoterol) is 640 mcg/day, a medium dose of ICS.

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Inhaled Corticosteroid/Long-acting Beta-agonist (ICS/LABA) Combinations

Product	Dosing	Max puff/day	Available strength [a]
fluticasone propionate / salmeterol DPI (Advair Diskus®)	Twice daily	2 (1,000 mcg)	100/50 250/50 500/50
fluticasone propionate/ salmeterol MDI (Advair HFA®)	Twice daily	4 (920 mcg)	45/21 115/21 230/21
budesonide + formoterol MDI (Symbicort®)	Twice daily	4 (640 mcg)	80/4.5 160/4.5
fluticasone propionate / salmeterol DPI (AirDuo™ RespiClick®)	Twice daily	2 (464 mcg)	55/14 113/14 232/14
mometasone/ formoterol MDI (Dulera®)	Twice daily	4 (800 mcg)	100/5 200/5
fluticasone furoate/vilanterol DPI (Breo Ellipta®)	Once daily	1 (200 mcg)	100/25 200/25

Cross References
Allergy Testing lab01, TRG Medical Policy Manual, Laboratory
Xolair®, omalizumab, Medication Policy Manual, Policy No. dru087
Nucala™, mepolizumab, Medication Policy Manual, Policy No. dru428
Non-Preferred Inhaled Corticosteroid-Containing Medications, Medication Policy Manual, Policy No. dru380

References

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

Revision History

Revision Date	Revision Summary
10/13/2017	No changes with this annual update.
10/21/2016	No changes with this annual update.
4/8/2016	New policy

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