Clinical Policy Title:	reslizumab
Policy Number:	RxA.69
Drug(s) Applied:	Cinqair®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Reslizumab (Cinqair®) is a humanized interleukin-5 antagonist monoclonal antibody (IgG1 kappa). Cinqair® is indicated for add-on maintenance treatment of patients with severe asthma aged 18 years and older, and with an eosinophilic phenotype. It should be administered in a healthcare setting by a healthcare professional prepared to manage anaphylaxis.

Limitation(s) of use: Cinqair® is not indicated for treatment of other eosinophilic conditions. It is not indicated for the relief of acute bronchospasm or status asthmaticus.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
reslizumab (Cinqair®)	Severe asthma	3 mg/kg IV every 4 weeks	3 mg/kg every 4 weeks

Dosage Forms

- Single-use vial: 100 mg/10 mL solution

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Severe Asthma (must meet all):

1. Diagnosis of asthma;
2. Member has an absolute blood eosinophil count ≥ 400 cells/mcL within the past 3 months;
3. Prescribed by or in consultation with an allergist, immunologist, or pulmonologist;
4. Age 18 years of age and older;
5. Member has experienced 2 or more exacerbations within 12 months, requiring any of the following despite adherent use of controller therapy (i.e., medium- to high-dose inhaled corticosteroid (ICS) plus long acting beta-2 agonist (LABA) or leukotriene modifier (LTRA) unless there is contraindication/intolerance to both):
   a. Oral/systemic corticosteroid treatment (or increase in dose if already on oral corticosteroid);

b. Urgent care visit or hospital admission;
c. Intubation (FEV1 of ≥ 20%);

6. Cinqair® is prescribed concomitantly with an ICS plus LABA or LTRA unless there is contraindication/intolerance to both;
7. Dose does not exceed 3 mg/kg once every 4 weeks.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Severe Asthma (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Demonstrated adherence to asthma controller therapy that includes an ICS plus LABA or LTRA unless there is contraindication/intolerance to both;
3. Member is responding positively to therapy (examples may include but are not limited to a reduction in exacerbations or corticosteroid dose, improvement in forced expiratory volume over one second) since baseline; reduction in the use of rescue therapy);
4. If request is for a dose increase, new dose does not exceed 3 mg/kg once every 4 weeks.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
GINA: Global Initiative for Asthma
ICS: inhaled corticosteroid
FDA: Food and Drug Administration
LABA: long-acting beta-agonist
LTRA: leukotriene modifier

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ICS (medium – high dose)		
Qvar® (beclomethasone)	> 200 mcg/day 40 mcg, 80 mcg per actuation; 1-4 actuations BID	4 actuations BID
Budesonide (Pulmicort®)	> 400 mcg/day 90 mcg, 180 mcg per actuation; 2-4 actuations BID	2 actuations BID
Alvesco® (ciclesonide)	> 160 mcg/day 80 mcg, 160 mcg per actuation; 1-2 actuations BID	2 actuations BID

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Aerospan® (flunisolide)	> 320 mcg/day 80 mcg per actuation; 2-4 actuations BID	2 actuations BID
Flovent® (fluticasone propionate)	> 250 mcg/day 44-250 mcg per actuation; 2-4 actuations BID	2 actuations BID
Arnuity Ellipta® (fluticasone furoate)	200 mcg/day 100 mcg, 200 mcg per actuation; 1 actuation once daily	1 actuation once daily
Asmanex® (mometasone)	>220 mcg/day HFA: 100 mcg, 200 mcg per actuation Twisthaler: 110 mcg, 220 mcg per actuation 1-2 actuations once daily to BID	2 inhalations BID
LABA		
Serevent® (salmeterol)	50 mcg per dose 1 inhalation BID	1 inhalation BID
Combination products (ICS + LABA)		
Dulera® (mometasone/ formoterol)	100/5 mcg, 200/5 mcg per actuation 2 actuations BID	4 actuations per day
Breo Ellipta® (fluticasone/vilanterol)	100/25 mcg, 200/25 mcg per actuation 1 actuation once daily	1 actuation once daily
Advair® (fluticasone/ salmeterol)	Diskus: 100/50 mcg, 250/50 mcg, 500/50 mcg per actuation HFA: 45/21 mcg, 115/21 mcg, 230/21 mcg per actuation 1 actuation BID	1 actuation BID
fluticasone/salmeterol (Airduo RespiClick®)	55/13 mcg, 113/14 mcg, 232/14 mcg per actuation 1 actuation BID	1 actuation BID
Symbicort® (budesonide/ formoterol)	80 mcg/4.5 mcg, 160 mcg/4.5 mcg per actuation 2 actuations BID	2 actuations BID
LTRA		
montelukast (Singulair®)	4 to 10 mg PO once daily	10 mg per day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
zafirlukast (Accolate®)	10 to 20 mg PO BID	40 mg per day
zileuton ER (Zyflo® CR)	1200 mg PO BID	2400 mg per day
Zyflo® (zileuton)	600 mg PO QID	2400 mg per day
Oral corticosteroids		
dexamethasone (Decadron®)	0.75 to 9 mg/day PO in 2 to 4 divided doses	Varies
methylprednisolone (Medrol®)	40 to 80 mg PO in 1 to 2 divided doses	Varies
prednisolone (Millipred®, Orapred ODT®)	40 to 80 mg PO in 1 to 2 divided doses	Varies
prednisone (Deltasone®)	40 to 80 mg PO in 1 to 2 divided doses	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Hypersensitivity to reslizumab or any of its excipients.

- Boxed Warning(s):
  - Anaphylaxis occurred with Cinqair® infusion in 0.3% of patients in placebo controlled studies.
  - Patients should be observed for an appropriate period of time after Cinqair® infusion; healthcare professionals should be prepared to manage anaphylaxis that can be life-threatening.

APPENDIX D: General Information

- Asthma exacerbations (primary endpoint) was defined as 1) use of systemic steroid, or ≥ 2-fold increase in the use of ICS for 3 or more days; 2) asthma related emergency treatment by nebulizer, a visit to the emergency department (ED) or asthma related hospitalization.
- Controller medications are: inhaled glucocorticoids (Flovent®, Pulmicort®, Qvar®, Asmanex®), long-acting beta-agonists (LABAs) such as salmeterol, formoterol, or vilanterol, and antileukotriene agents (montelukast [Singulair®], zafirlukast [Accolate®] or Zyflo® [zileuton]). Theophylline is also a controller agent; however, it is not as efficacious as LABAs.
- Patients could potentially meet criteria for both Xolair® and Cinqair®. The combination has not been studied. Approximately 30% of patients in the Nucala study also were candidates for therapy with Xolair®.
- Positive response to therapy for asthma may include reduction in exacerbations or corticosteroid dose, improvement in forced expiratory volume over one second since baseline, or reduction in the use of rescue therapy.

References

1. Cinqair prescribing information. Teva Pharmaceuticals. February 2020. Available at: https://www.cinqair.com/globalassets/cinqair/prescribinginformation.pdf . Accessed February 02, 2021.

2. National Asthma Education and Prevention Program: 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/health- pro/guidelines/current/asthma-guidelines. Accessed February 02, 2021.
3. Corren J, Weinstein S, Janka L, Zangrilli J, Garin M. Phase 3 study of reslizumab in patients with poorly controlled asthma: effects across a broad range of eosinophil counts. *Chest.* 2016; 150(4): 799-810. Accessed February 02, 2021.
4. Maselli DJ, Velez MI, Rogers L. Reslizumab in the management of poorly controlled asthma: The data so far. *Journal of Asthma and Allergy.* August 31, 2016; 9: 155-162. Accessed February 02, 2021.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. Available at: http://www.clinicalpharmacology.com. Accessed February 02, 2021.
6. Global Initiative for Asthma: Global strategy for asthma management and prevention (2018 update). Available at: https://ginasthma.org/2018-gina-report-global-strategy-for-asthma- management-and-prevention/. Accessed February 02, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Updated references	05/2020	05/21/2020
1. Policy was reviewed:Line of Business Policy Applies to was updated to “All lines of business”. 2. Continuation therapy criteria II.A.1. rephrased to “Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy” 3. Approval duration for commercial plans continued therapy was changed from 6 months to 12 months. 4. Appendix B language updated to ‘’Below are suggested therapeutic alternatives….’’. 5. Appendix C updated with boxed warning. 6. References were reviewed and updated.	02/02/2021	03/09/2021