Clinical Policy Title:	omalizumab
Policy Number:	RxA.316
Drug(s) Applied:	Xolair®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Xolair® is an anti-IgE antibody indicated for:

- Moderate to severe persistent asthma in patients 6 years of age and older with a positive skin test or in vitro reactivity to a perennial aeroallergen and symptoms that are inadequately controlled with inhaled corticosteroids.
- Nasal polyps in adult patients 18 years of age and older with inadequate response to nasal corticosteroids, as add-on maintenance treatment.
- Chronic idiopathic urticaria in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment.

Limitation(s) of use: Xolair® is not indicated for the relief of acute bronchospasm or status asthmaticus, treatment of other allergic conditions, or treatment of other forms of urticaria.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
omalizumab (Xolair®)	Allergic asthma	75 to 375 mg SC every 2 or 4 weeks based on serum total IgE level (IU/mL) measured before the start of treatment, and body weight (kg) Xolair® is not approved for use in patients weighing more than 150 kg. (*See Appendix E and F*). Do not administer more than 150 mg (contents of one vial) per injection site. Divide doses of more than 150 mg amongst two or more injection sites.	375 mg/4 weeks
omalizumab (Xolair®)	CIU	150 mg or 300 mg SC every 4 weeks	300 mg/4 weeks
omalizumab (Xolair®)	Nasal polyps	75 to 600 mg SC every 2 or 4 weeks. Determine	See dosing regimen

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
		dose (mg) and dosing frequency by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg). (*See Appendix G)*.	

Dosage Forms

- omalizumab (Xolair®): Single-dose vial: 150 mg.
- omalizumab (Xolair®): Single-dose prefilled syringe: 75 mg/0.5 mL, 150 mg/mL.

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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administer by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Moderate to Severe Persistent Asthma (must meet all)**:**

1. Diagnosis of asthma;
2. Prescribed by or in consultation with an allergist, immunologist, or pulmonologist;
3. Age ≥ 6 years ;
4. Member has experienced 2 or more exacerbations, within the last 12 months, requiring any of the following despite adherent use of controller therapy (i.e., medium- to high-dose inhaled corticosteroid (ICS) plus either a long acting beta-2 agonist (LABA) or leukotriene modifier (LTRA) if LABA contraindicated/intolerance):
   a. Oral/systemic corticosteroid treatment (or increase in dose if already on oral corticosteroid);
   b. Urgent care visit or hospital admission;
   c. Intubation;
5. Positive skin test or *in vitro* reactivity to a perennial aeroallergen (see *Appendix D*);
6. Immunoglobulin E (IgE) level ≥ 30 IU/mL;
7. Xolair® is prescribed concomitantly with an ICS plus either a LABA or LTRA;
8. Dose does not exceed 375 mg administered every 2 weeks (see *Appendix E* and *F* for dosing based on pre-treatment IgE level, weight, and age).

Approval duration
Commercial: 6 months
Medicaid: 6 months

B. Chronic Idiopathic Urticaria (must meet all):

1. Diagnosis of CIU;
2. Prescribed by or in consultation with a dermatologist, immunologist, or allergist;
3. Age ≥ 12 years;
4. Failure of both of the following unless contraindicated or clinically significant adverse effects are experienced (a and b):

a. Two antihistamines (including one second generation antihistamine – e.g., cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine) at maximum indicated doses, each used for ≥ 2 weeks;
b. A LTRA in combination with an antihistamine at maximum indicated doses for ≥ 2 weeks;

5. Xolair® is not prescribed concurrently with Cinqair®, Fasenra®, Nucala®, or Dupixent®.
6. Dose does not exceed 300 mg every 4 weeks.

Approval duration
Commercial: 6 months
Medicaid: 6 months

C. Nasal polyps (must meet all):
1. Diagnosis of nasal polyps;
2. Prescribed by or in consultation with a dermatologist, immunologist, or allergist;
3. Age ≥ 18 years;
4. Member have inadequate response to nasal corticosteroids and needs Xolair® for add-on maintenance treatment of nasal polyps ;
5. Xolair® is not prescribed concurrently with Cinqair®, Fasenra®, Nucala®, or Dupixent®.
6. Dose and frequency should be adjusted during therapy based on body weight and pretreatment total IgE serum levels;

Approval duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Moderate to Severe Persistent 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 either an LABA or LTRA;
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. Xolair® is not prescribed concurrently with Cinqair®, Fasenra®, Nucala®, or Dupixent®;
5. If request is for a dose increase, new dose does not exceed 375 mg administered every 2 weeks (see *Appendix E* and *F* for dosing based on pre-treatment IgE level, weight, and age).

Approval duration
Commercial: 6 months
Medicaid: 12 months

B. Chronic Idiopathic Urticaria (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. Member is responding positively to therapy;
3. Xolair® is not prescribed concurrently with Cinqair®, Fasenra®, Nucala®, or Dupixent®;
4. If request is for a dose increase, new dose does not exceed 300 mg every 4 weeks.

Approval duration
Commercial: 6 months
Medicaid: 12 months

C. Nasal polyps (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. Member is responding positively to therapy;
3. Xolair® is not prescribed concurrently with Cinqair®, Fasenra®, Nucala®, or Dupixent®;

Approval duration
Commercial: 6 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

AAAAI: American Academy of Allergy, Asthma, and Immunology
CIU: Chronic Idiopathic Urticaria
EAACI: European Academy of Allergy and Clinical Immunology
EDF: European Dermatology Forum
EPR3: Expert Panel Report 3
GA2LEN: Global Allergy and Asthma European Network
GINA: Global Initiative for Asthma
ICS: Inhaled Corticosteroids
LABA: Long-Acting Beta-Agonist
LTRA: Leukotriene Modifier
WAO: World Allergy Organization

APPENDIX B: Therapeutic Alternatives

This 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
Asthma – ICS (medium – high dose)		
beclomethasone	> 100 mcg/day 40 mcg, 80 mcg per actuation 1-4 actuations BID	4 actuations BID
budesonide (Pulmicort®)	> 200 mcg/day 90 mcg, 180 mcg per actuation 2-4 actuations BID	2 actuations BID
Alvesco® (ciclesonide)	> 80 mcg/day 80 mcg, 160 mcg per actuation 1-2 actuations BID	2 actuations BID
flunisolide	≥ 320 mcg/day 80 mcg per actuation 2-4 actuations BID	2 actuations BID
fluticasone propionate	>176 mcg/day 44-250 mcg per actuation 2-4 actuations BID	2 actuations BID
Arnuity Ellipta® (fluticasone furoate)	200 mcg/day (≥ 12 years only) 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	2 inhalations BID

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
	1-2 actuations once daily to BID	
Asthma - LABA		
Serevent® (salmeterol)	50 mcg per dose; 1 inhalation BID	1 inhalation BID
Asthma - 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
Asthma - LTRA		
montelukast (Singulair®)	4 to 10 mg PO once daily	10 mg per day
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
Asthma - 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	40 to 80 mg PO in 1 to 2 divided doses	Varies
CIU		
hydroxyzine (Vistaril®)	Adult: 25 mg PO TID to QID Age ≥ 6 years: 50 mg-100 mg/day in divided doses	Adult: Will vary according to condition Age ≥ 6 years: 50 mg-100 mg/day in divided doses

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
diphenhydramine (Benadryl®)	Adult: 25 mg to 50 mg PO TID to QID Pediatric: 12.5 mg to 25 mg PO TID to QID or 5 mg/kg/day or 150 mg/m²/day	Adult: Will vary according to condition Children: 300 mg/day
chlorpheniramine (Aller- Chlor®)	Immediate Release: 4 mg PO every 4 to 6 hours Extended Release: 12 mg PO every 12 hours	Do not exceed 24 mg/day
cetirizine (Zyrtec®)	5 to 10 mg PO once daily	10 mg/day
levocertirizine (Xyzal®)	2.5 mg to 5 mg PO once daily	5 mg/day
loratadine (Claritin®)	10 mg PO once daily	10 mg/day
desloratadine (Clarinex®)	5 mg PO once daily	Will vary according to condition
fexofenadine	60 mg PO BID or 180 mg once daily	180 mg/day

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):
  - Severe hypersensitivity reaction to Xolair® or any ingredient of Xolair®.

- Boxed warning(s):
  - Anaphylaxis, presenting as bronchospasm, hypotension, syncope, urticaria, and/or angioedema of the throat or tongue, has been reported to occur after administration of Xolair®. Anaphylaxis has occurred after the first dose of Xolair but also has occurred beyond 1 year after beginning treatment. Closely observe patients for an appropriate period of time after Xolair® administration and be prepared to manage anaphylaxis that can be life-threatening. Inform patients of the signs and symptoms of anaphylaxis and have them seek immediate medical care should symptoms occur.

APPENDIX D: General Information

- Allergic asthma:
  - The definition of moderate to severe allergy varied among the clinical trials. The definition most often used was a patient who required oral systemic steroid bursts or unscheduled physician office visits for "uncontrolled" asthma exacerbations despite maintenance inhaled steroid use. Patients in the clinical trials most often were required to have an FEV_1 between 40% and 80% of predicted. No patients were enrolled with an FEV_1 greater than 80% of predicted.
  - Xolair® has been shown to be marginally effective in decreasing the incidence of asthma exacerbations in patients who have met all the criteria described above.
  - Xolair® provides little therapeutic benefit over existing therapies. Use in patients on inhaled corticosteroids or chronic oral steroids plus or minus a second controller agent decreased asthma exacerbation by 0.5 to 1 per year. Use of rescue beta- agonists declined by 1 inhalation per day. Small changes in pulmonary function tests were also seen. An analysis of unpublished data indicated that hospital admissions declined by 3 per hundred patient years, emergency department (ED) visits by 2 per hundred patient years, and unscheduled physician office visits by 14 per one hundred patient years.
  - The National Heart, Lung and Blood Institute's Expert Panel Report 3 (EPR3) Guidelines for the Diagnosis and Management of Asthma recommend Xolair® may be considered as adjunct therapy for patients 12

years and older with allergies and Step 5 or 6 (severe) asthma whose symptoms have not been controlled by ICS and LABA.
  - The four perennial aeroallergens most commonly tested for in the clinical trials were dog dander, cat dander, cockroach, and house dust mite.
  - Serious and life-threatening allergic reactions (anaphylaxis) in patients after treatment with Xolair® have been reported. Usually these reactions occur within two hours of receiving a Xolair® subcutaneous injection. However, these new reports include patients who had delayed anaphylaxis—with onset two to 24 hours or even longer- after receiving Xolair® treatment. Anaphylaxis may occur after any dose of Xolair®
    (including the first dose), even if the patient had no allergic reaction to the first dose.
  - 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.

- CIU:
  - CIU is classified as spontaneous onset of wheals, angioedema, or both, for more than 6 weeks due to an unknown cause.
  - Clinical studies have shown that Xolair® 150 mg and 300 mg significantly improved the signs and symptoms of chronic idiopathic urticaria compared to placebo in patients who had remained symptomatic despite the use of approved dose of H_1- antihistamine.
  - The Joint Task Force on Practice Parameters representing various American allergy organizations include Xolair® in combination with H1-antihistamines as a fourth line treatment option following a stepwise approach starting with a second generation antihistamine. This is followed by one or more of the following: a dose increase of the second generation antihistamine, or the addition of another second generation antihistamine, H2-antagonist, LTRA, or first generation antihistamine. Treatment with hydroxyzine or doxepin can be considered in patients whose symptoms remain poorly controlled.
  - The EAACI/GA2LEN/EDF/AAAAI/WAO Guideline for the Management of Urticaria include Xolair® in combination with H_1-antihistamines as a third line treatment option in patients who have failed to respond to higher doses of H_1- Antihistamines.
  - Xolair® is the first medicine in its class approved for CIU since non-sedating antihistamines.
  - The use of over-the-counter H1 antihistamines may not be a benefit to the treatment of chronic idiopathic urticaria. Credit will be given for its use, but will not be covered under plan.
  - Anaphylaxis has occurred as early as after the first dose of Xolair®, but also occurred beyond 1 year after beginning regularly administered treatment.

APPENDIX E: Age ≥ 12 years: Asthma dosing based on pre-treatment IgE and body weight†

Pre-treatment serum IgE IU/mL	Dosing Frequency	Body Weight			
		30-60 kg	>60-70 kg	>70-90 kg	>90-15 kg
≥ 30-100	Q 4 weeks	150 mg	150 mg	150 mg	300 mg
> 100-200		300 mg	300 mg	300 mg	225 mg
> 200-300		300 mg	225 mg	225 mg	300 mg
>300-400	Q 2 weeks	225 mg	225 mg	300 mg	
>400-500		300 mg	300 mg	375 mg	
> 500-600		300 mg	375 mg		
> 600-700		375 mg	Insufficient Data to Recommend a Dose		

†The manufacturer recommends dose adjustments for significant body weight changes during treatment.

APPENDIX F: Age 6 to < 12 years: Asthma dosing based on pre-treatment IgE and body weight†

Pre-treatment serum IgE IU/mL	Dosing Fre-quency	Body Weight									
		20-25 kg	>25-30 kg	>30-40 kg	>40-50 kg	>50-60 kg	>60-70 kg	>70-80 kg	>80-90 kg	>90-125 kg	>125- 150 kg
≥ 30-100	Q 4 weeks	75	75	75	150	150	150	150	150	300	300
>100-200		150	150	150	300	300	300	300	300	225	300
>200-300		150	150	225	300	300	225	225	225	300	375
>300-400		225	225	300	225	225	225	300	300		
>400-500		225	300	225	225	300	300	375	375		
>500-600		300	300	225	300	300	375				
>600-700		300	225	225	300	375					
>700-800	Q 2 weeks	225	225	300	375						
>800-900		225	225	300	375						
>900-1000		225	300	375	Insufficient Data to Recommend a Dose						
>1000-1100		225	300	375							
>1100-1200		300	300								
>1200-1300		300	375								

†The manufacturer recommends dose adjustments for significant body weight changes during treatment.

APPENDIX G: Subcutaneous Xolair® Doses Every 2 or 4 Weeks* for Adult Patients with Nasal Polyps.

Pre-treatment serum IgE IU/mL	Dosing Fre-quency	Bodyweight							
		>30-40 kg	>40-50 kg	>50-60 kg	>60-70 kg	>70-80 kg	>80-90 kg	>90-125 kg	> 125-150 kg
		Dose (mg)							
30 - 100	Q 4 weeks	75	150	150	150	150	150	300	300
>100 - 200		150	300	300	300	300	300	450	600
>200 - 300		225	300	300	450	450	450	600	375
>300 - 400		300	450	450	450	600	600	450	525
>400 - 500		450	450	600	600	375	375	525	600

Pre-treatment serum IgE IU/mL	Dosing Fre-quency	Bodyweight							
		>30-40 kg	>40-50 kg	>50-60 kg	>60-70 kg	>70-80 kg	>80-90 kg	>90-125 kg	> 125-150 kg
>500 - 600		450	600	600	375	450	450	600	
>600 - 700	Q 2 weeks	450	600	375	450	450	525		
>700 - 800		300	375	450	450	525	600		
>800 - 900		300	375	450	525	600			
>900 - 1000		375	450	525	600				
>1000 - 1100		375	450	600	Insufficient Data to Recommend a Dose				
>1100 - 1200		450	525	600					
>1200 - 1300		450	525						
>1300 - 1500		525	600						

Dosing Frequency	
	Subcutaneous doses to be administered every 2 weeks.
	Subcutaneous doses to be administered every 4 weeks.

References

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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was revised 1. Initial Therapy I.A.1 was updated to ''Diagnosis to Asthma'' 2. Initial Therapy & Continued Therapy-One criteria added: ''Xolair® is not prescribed concurrently with Cinqair®, Fasenra®, Nucala, or Dupixent®''. 3. Continued Therapy II.A.1. was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 4. Reference reviewed and updated	07/07/2020	09/14/2020
Policy was revised 1. Last review date was updated. 2. Background, dosing regimen, initial and continuation therapy criteria updated for new indication “Nasal polyp”. 3. Appendix B: Allegra®, Deltasone®, Zyflo® CR, Flovent®, Aerospan®, Qvar® brand names were removed. 4. Appendix B: Therapeutic Alternatives verbiage was updated to "Below are suggested therapeutic alternatives based on clinical guidance...." 5. Appendix C: updated for Contraindication and box warning to “Severe hypersensitivity reaction…” and “Anaphylaxis, presenting as bronchospasm, hypotension, syncope…”. 6. Appendix G added for new indication dosing regimen “Nasal polyp”. 7. Continued Therapy II.A.1.,B.1.,C..1., was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 8. References were reviewed and updated.		