Clinical Policy: Omalizumab (Xolair)

Reference Number: ERX.SPA.141
Effective Date: 03.01.14
Last Review Date: 08.17

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Omalizumab (Xolair®) is an anti-immunoglobin E (IgE) antibody.

FDA approved indication
Xolair is indicated:
- For the treatment of 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
- For the treatment of chronic idiopathic urticaria (CIU) in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment

Limitations of use:
- Xolair is not indicated for the relief of acute bronchospasm or status asthmaticus.
- Xolair is not indicated for treatment of other allergic conditions.
- Xolair is not indicated for treatment of other forms of urticaria.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Synagis is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Moderate to Severe Persistent Asthma (must meet all)**:**
1. Diagnosis of moderate to severe persistent asthma;
2. Prescribed by or in consultation with an allergist or pulmonologist;
3. Age ≥ 6 years;
4. Member has experienced ≥ 2 exacerbations requiring oral/systemic corticosteroid treatment, urgent care visit or hospital admission within the last 12 months despite adherent use of controller therapy (i.e., high dose inhaled corticosteroid [ICS] plus either a long acting beta-2 agonist [LABA] or leukotriene modifier [LTRA] if LABA contraindicated/intolerance);
5. Positive immunoassay or skin test to perennial aeroallergen identified to be an asthma trigger;
6. IgE level ≥ 30 IU/mL;
7. If current smoking history, engaged in smoking cessation effort;
8. Xolair is prescribed concomitantly with an ICS plus either an LABA or LTRA;
9. Dose does not exceed 375 mg administered every 2 weeks and (a and b):
   a. Dose is based upon pre-treatment IgE level, current weight, and age;
   b. Per manufacturer, dose adjustment is recommended for significant changes in body weight during treatment.

Approval duration: 6 months

B. Chronic Idiopathic Urticaria (must meet all)**:**
1. Diagnosis of CIU;
2. Prescribed by or in consultation with a dermatologist or allergist;

3. Age ≥ 12 years;
2. Failure of both of the following unless contraindication/intolerance (a and b):
   a. Two antihistamines (including one second generation antihistamine – e.g., cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine, ranitidine, famotidine, cimetidine) at maximum indicated doses, each trialed for ≥ 4 weeks;
   b. An LTRA with an antihistamine at maximum indicated doses for ≥ 4 weeks;
3. Dose does not exceed 300 mg every 4 weeks.

Approval duration: 6 months

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Approval

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met all initial approval criteria;
2. Demonstrated adherence to asthma controller therapy that includes an ICS plus either an LABA or LTRA;
3. Member is responding positively to therapy as evidenced by reduction in exacerbations or corticosteroid dose, or improvement in FEV_1 since baseline;
4. If request is for a dose increase, new dose does not exceed 375 mg administered every 2 weeks and (a and b):
   a. Dose is based upon pre-treatment IgE level, current weight, and age;
   b. Per manufacturer, dose adjustment is recommended for significant changes in body weight during treatment.

Approval duration: 12 months

B. Chronic Idiopathic Urticaria (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 300 mg every 4 weeks.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CIU: chronic idiopathic urticarial
FDA: Food and Drug Administration
FEV: forced expiratory volume
IgE: immunoglobin E
LABA: long acting beta-2 agonist
LTRA: leukotriene modifier

Appendix B: Therapeutic Alternatives

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
High-dose ICS per National Heart, Lung, and Blood Institute Asthma Guidelines		
Beclomethasone MDI (Qvar)	Asthma *High-dose: > 480 mcg* ≥ 12 years: 4 or more inhalations (80 mcg/puff) BID *High-dose: > 320 mcg* 5-11 years: 3 or more inhalations (80 mcg/puff) BID	640 mcg/day
Budesonide DPI (Pulmicort Flexhaler)	Asthma *High-dose: > 1080 mcg* ≥ 12 years: 4 or more inhalations (180 mcg/puff) BID *High-dose: > 720 mcg* 5-11 years: 3 or more inhalations (180 mcg/puff) BID	1440 mcg/day
Ciclesonide MDI (Alvesco)	Asthma *High-dose: > 640 mcg* ≥ 12 years: 3 or more inhalations (160 mcg/puff) BID *High-dose: > 320 mcg* 5-11 years: 3 or more inhalations (80 mcg/puff) or 2 or more inhalations (160 mcg/puff) BID	640 mcg/day
Flunisolide MDI (Aerospan HFA)	Asthma *High-dose: > 640 mcg* ≥ 12 years: 5 or more inhalations (80 mcg/puff) BID *High-dose: > 480 mcg* 5-11 years: 4 or more inhalations (80 mcg/puff) BID	640 mcg/day
Fluticasone (MDI: Flovent HFA; DPI: Flovent Diskus)	Asthma MDI: *High-dose: > 440 mcg* ≥ 12 years: 3 or more inhalations (110 mcg/puff) or 2 or more inhalations (220 mcg/puff) BID *High-dose: > 352 mcg* 5-11 years: 2 or more inhalations (110 mc/puff) BID DPI: *High-dose: > 500 mcg* ≥ 12 years: 3 or more inhalations (100 mcg/puff) BID or 2 or more inhalations (250 mcg/puff) BID *High-dose: > 400 mcg* 5-11 years: 2 or more inhalations (100 mcg/puff) or 1 inhalation (250 mcg/puff) BID	MDI: 880 mcg/day DPI: 1000 mcg/day
Mometasone DPI (Asmanex Twisthaler)	Asthma *High-dose: > 440 mcg*	440 mcg/day

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
	3 or more inhalations (110 mcg/puff) BID or or more inhalations (220 mcg/puff) divided in two doses	
LABA		
Salmeterol (Serevent)	Asthma 1 inhalation (50 mcg) BID	100 mcg/day
Combination High-dose ICS + LABA		
Fluticasone/salmeterol (MDI: Advair HFA; DPI: Advair Diskus)	Asthma MDI: 2 inhalations (115 mcg and 21 mcg/puff or 230 mcg and 21 mcg/puff) BID DPI: 1 inhalation (250 mcg and 50 mcg/puff or 500 mcg and 50 mcg/puff) BID	MDI: 920 mcg and 84 mcg/day DPI: 1000 mcg and 100 mcg/day
Budesonide/salmeterol MDI (Symbicort)	Asthma 2 inhalations (160 mcg and 4.5 mcg/puff) BID	640 mcg and 18 mcg/day
Mometasone/formoterol MDI (Dulera)	Asthma 2 inhalations (200 mcg and 5 mcg/puff) BID	800 mcg and 20 mcg/day
LTRA		
Montelukast (Singulair)	Asthma ≥ 15 years: 10 mg PO QD 6-14 years: 5 mg PO QD 2-5 years: 4 mg PO QD CIU (off-label) 10 mg PO QD	10 mg/day
Zafirlukast (Accolate)	Asthma ≥ 12 years: 20 mg PO BID 5-11 years: 10 mg PO BID	40 mg/day
Zileuton (Zyflo CR)	Asthma 1200 mg PO BID	2400 mg/day
Antihistamines – 1st Generation		
Hydroxyzine (Vistaril)	CIU ≥ 6 years: 25 mg PO TID-QID < 6 years: 50 mg PO in divided doses	100 mg/day
*Antihistamines – 2nd Generation**		
Cetirizine (Zyrtec)	CIU 5-10 mg PO QD	10 mg/day
Levocetirizine (Xyzal)	CIU 2.5-5 mg PO QD	5 mg/day
Fexofenadine (Allegra)	CIU ≥ 12 years: 60 mg PO BID or 180 mg PO QD 2-11 years: 30 mg PO BID 6-23 months: 15 mg PO BID	180 mg/day
Loratadine (Claritin)	CIU 10 mg PO QD	10 mg/day
Desloratadine (Clarinex)	CIU ≥ 12 years: 5 mg PO QD 6-11 years: 2.5 mg PO QD	5 mg/day

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
	1-5 years: 1.25 mg PO QD 6-11 months: 1 mg PO QD	

**Only 2nd generation antihistamines FDA-approved for CIU are listed here*

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CIU	150 or 300 mg SC every 4 weeks	300 mg/4 weeks
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) (*see below*)	375 mg/2 weeks

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	DO NOT DOSE PER MANUFACTURER	
> 600-700		375 mg			

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

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

Pre-treatment serum IgE IU/mL	Dosing Frequency	Body Weight									
		20-25 kg	**>25-30 kg**	**>30-40 kg**	**>40-50 kg**	**>40-50 kg**	**>40-50 kg**	**>40-50 kg**	**>40-50 kg**	**>40-50 kg**	**>40-50 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	300	375							
>900-1000		225	300	375							
>1100-1200		300	300								
>1200-1300		300	375								

DO NOT DOSE PER MANUFACTURER

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

VI. Product Availability

Single-use vial: 150 mg

VII. References

1. Xolair Prescribing Information. Irvine, CA: Spectrum Pharmaceuticals, Inc.; June 2017. Available at https://www.gene.com/download/pdf/xolair_prescribing.pdf. Accessed July 5, 2017.
2. National Asthma Education and Prevention Program. Expert Panel Report e (EPR-3): guidelines for the diagnosis and management of asthma-summary report 2007. J *Allergy Clin Immunol.* November 2007; 120(5 Suppl): S94-138. (NIH publication no. 08-4051). Available at http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines.
3. Wenzel S. Evaluation of severe asthma in adolescents and adults. In: UpToDate, Waltham, MA: Wolters Kluwer Health; 2017. Available at uptodate.com. Accessed July 6, 2017.
4. Wenzel S. Treatment of severe asthma in adolescents and adults. In: UpToDate, Waltham, MA: Wolters Kluwer Health; 2017. Available at uptodate.com. Accessed July 6, 2017.
5. Bernstein JA, Lang DM, Khan DA, et al. The diagnosis and management of acute and chronic urticaria: 2014 update. *J Allergy Clin Immunol*. 2014; 133(5); 1270-1277.
6. Khan DA. Chronic urticarial: Standard management and patient education. In: UpToDate, Waltham, MA: Wolters Kluwer Health; 2017. Available at uptodate.com. Accessed July 6, 2017.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	02/14	03/14
Reworded FDA-approved indication to mirror package insert. Modified wording in figure 1 to read “Chart notes support adequate ICS dose titration or use of oral steroid therapy w/asthma exacerbation?”. Added figure 3 & 4 for new indication of chronic urticaria. Modified Appendix B to require the use of high dose corticosteroids along with leukotriene modifiers, rather than by itself. Added a safety section that discusses the boxed warning.	04/15	06/15
Policy converted to new template. All documentation requests removed; modified requirement for 3 months of adherent use to requirement for at least 2 exacerbations in the last 12 months despite adherent use of controller medication; changed “RAST” to “immunoassay.” Changed requirement for nonsmoker and nonsmoking home to engaged in smoking cessation efforts if smoker. Added requirement for concomitant use of maintenance therapy in asthma. Added failure or contraindication to step therapy for CIU. Removed criteria regarding response to therapy and rescuer inhaler use from asthma renewal criteria; removed questions about adverse reaction to Xolair for continuation of therapy requirement for both asthma and CIU; added maximum allowed dose to asthma and CIU criteria; added “positive response” to CIU continuation criteria; added definition of positive response to asthma continuation criteria. Modified age restriction in asthma from ≥ 12 years to ≥ 6 years based on FDA labeling update.	08/16	09/16
Modified initial/continued approval durations from 3/6 months to 6/12 months. Asthma step therapy edited to require LABAs before LTRAs unless contraindicated or intolerant. Added positive response to therapy under continued approval. CIU: Examples of second-generation antihistamines added. Initial criteria: IgE level between 30-700 IU/mL is edited to read “between 30-1300 IU/mL” per PI.	06/17	08/17
Converted to new template. FEV1 < 80% is removed from the asthma criteria leaving a history of at least 2 exacerbations despite step 5 therapy as	07/17	08/17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
evidence of moderate to severe persistent asthma that is not well controlled. References updated.		

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

This policy is the property of Envolve Pharmacy Solutions. Unauthorized copying, use, and distribution of this Policy or any information contained herein is strictly prohibited. By accessing this policy, you agree to be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.

©2014 Envolve Pharmacy Solutions. All rights reserved. All materials are exclusively owned by Envolve Pharmacy Solutions and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Envolve Pharmacy Solutions. You may not alter or remove any trademark, copyright or other notice contained herein.