Pharmacy Management Drug Policy

SUBJECT: Xolair® (Omalizumab)
POLICY NUMBER: PHARMACY-57
EFFECTIVE DATE: 7/03
LAST REVIEW DATE: 02/10/2020

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. Medical or drug policies apply to commercial and Health Care Reform products only when a contract benefit for the specific service exists.

DESCRIPTION:

Xolair is a recombinant humanized monoclonal antibody for the management of moderate to severe asthma. Omalizumab blocks the site on free IgE that binds with mast cells, basophils, and eosinophils and hence prevents the binding of free IgE to the cell membrane high affinity receptor on effector cells and thus prevents degranulation after exposure to an allergen. Xolair is designed to interrupt the cascade of asthma events.

ASTHMA POLICY:

Based upon our criteria and review of the peer-reviewed literature, treatment with Xolair administered in accordance with FDA guidelines, has been medically proven to be effective and therefore, **medically appropriate** if **all** of the following criteria are met:

1. Patient must be at least 6 years old **AND**
2. Patient must be followed by and drug ordered by an allergist/immunologist or pulmonologist **AND**
3. Patient must have moderate to severe persistent asthma **AND**
4. Patient must be a non-smoker. Non-smoker is defined as someone who has not smoked in the past 6 months **AND**
5. Patient must have well documented use of high-dose inhaled corticosteroids (ICS) (see Tables 5 and 6) for **at least 6 months**, be compliant with existing therapy, and have followed GINA guidelines for asthma treatment including an adequate trial of a high-dose inhaled steroid in combination with a long-acting beta agonist.
    a. Compliance will be assessed based on pharmacy refill history. If the patient does not have pharmacy benefits through this health plan, a recent pharmacy profile will be requested. Progress notes documenting usage of sample medication may also be requested.
    b. If there is a contraindication to use of a long-acting beta agonist, then an alternative controller drug may be used in combination with a high-dose inhaled steroid such as a leukotriene inhibitor or long-acting muscarinic antagonist.
    c. Patient must have documentation of inadequate control with optimal therapy (above) for a period of at least 6 months **AND**
6. Patient must have documented evidence of at least 1 perennial aeroallergen [e.g.; house dust mite (*Dermatophagoides farinae, D. pteronyssinus*), animal dander (dog, cat), cockroach, feathers, mold spores] by:
    a. a skin test (i.e.; prick/puncture test) **OR**
    b. in vitro testing (i.e.; blood test for allergen-specific IgE antibodies such as the radioallergosorbent test - RAST Class 2 or greater) **AND**
7. Patient must have baseline IgE levels between 30 and 700 IU/mL

    Coverage for IgE levels outside of this range will be considered as follows:

    a. Patients with a baseline IgE level between 700 and 1300 IU/mL will be considered for Xolair therapy if all other criteria is met and as long as the dose required based on IgE

and body weight is not > 750mg per month **OR**

b. Patients with a baseline IgE level below 30 IU/mL will not be considered for coverage as there is not enough free IgE with which to bind for the drug to exert its effect. **AND**

8. Patient must have experienced 3 or more asthma exacerbations in a year that required medical management (defined as unscheduled doctor visits, urgent care visits, emergency room visits, or hospital admissions) despite existing therapy as outlined in Criterion #5 **AND**
9. Initial approval will be for 6 months. Subsequent recertifications after the initial approval period will require an objective assessment of response to therapy with Xolair (decrease in hospitalizations, decrease in ER visits, decrease in rescue medication use) by the provider as well as documentation of compliance history with the inhaled corticosteroid and controller medication. Recertification will not be granted if the patient starts or restarts smoking. See recertification statement and approval time period table in policy guidelines section of this policy.

URTICARIA POLICY:

Omalizumab is currently classified as third-line therapy in the 2017 EAACI/GA²LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria, endorsed by AAAAI/ACAAI. The following criteria are based on FDA labeling and current treatment recommendations.

1. Patient must be followed by and drug ordered by an allergist/immunologist **AND**
2. Patients must be at least 12 years old with at least a 6-week history of urticaria and the presence of hives associated with itching despite adequate trials (minimum of four weeks) of:
   a. A second generation H_1-antihistamine at standard dosing **AND**
   b. A second-generation H_1-antihistamine trialed at two to four times the standard dose
3. Initial approval will be for 150mg or 300 mg SQ every 4 weeks for 6 months (see approval time period table in policy guidelines section of this policy).
   a. Total doses above 300 mg per 4-week interval will not be allowed for urticaria
4. Subsequent recertifications will require documentation that the patient has responded to or continues to benefit from therapy (i.e.; decreased severity of itching, or size/number of hives). See recertification statement in policy guidelines section of this policy.

POLICY GUIDELINES

1. Prior-authorization is contract dependent.
2. Xolair is administered by a healthcare professional and is covered under the medical benefit.
3. Xolair will be covered only if administered in the prescriber's office or a supervised medical treatment facility. Because of the risk of anaphylaxis, patients should be closely observed for an appropriate period of time after Xolair administration, and health care providers administering Xolair should be prepared to manage anaphylaxis, which can be life-threatening. Patients should also be informed of the signs and symptoms of anaphylaxis and instructed to seek immediate medical care should symptoms occur.
4. According to GINA 2007 guidelines, addition of anti-IgE treatment to other controller medications has been shown to improve control of allergic asthma when control has not been achieved on combinations of other controllers including high-doses of inhaled corticosteroids, long-acting beta agonists, leukotriene modifiers, or theophylline.
5. Asthma dosing is based on patient weight and pretreatment IgE levels as shown below.

6. Dosing of Xolair in CIU patients is not dependent upon serum IgE level (free or total) or body weight.
7. The appropriate duration of therapy for CIU has not been evaluated. Periodically reassess the need for continued therapy.
8. Xolair is not recommended for patients who require more than 750mg per month according to the manufacturer's dosing table below. Doses greater than 750mg per month would require more than two injection schedules per month. See policy guideline #12 below for further information.

Table 1. Subcutaneous Xolair Doses Every 4 Weeks for Patients 12 Years of Age and Older with Asthma

Pre-treatment Serum IgE	Body Weight			
	30–60 kg	> 60–70 kg	> 70–90 kg	> 90–150 kg
≥ 30–100 IU/mL	150 mg	150 mg	150 mg	300 mg
> 100–200 IU/mL	300 mg	300 mg	300 mg	
> 200–300 IU/mL	300 mg			
> 300–400 IU/mL	SEE TABLE 2			
> 400–500 IU/mL				
> 500–600 IU/mL				

Table 2. Subcutaneous Xolair Doses Every 2 Weeks for Patients 12 Years of Age and Older with Asthma

Pre-treatment Serum IgE	Body Weight			
	30–60 kg	> 60–70 kg	> 70–90 kg	> 90–150 kg
≥ 30–100 IU/mL	SEE TABLE 1			
> 100–200 IU/mL				225 mg
> 200–300 IU/mL		225 mg	225 mg	300 mg
> 300–400 IU/mL	225 mg	225 mg	300 mg	
> 400–500 IU/mL	300 mg	300 mg	375mg	
> 500–600 IU/mL	300 mg	375 mg	DO NOT DOSE	
> 600–700 IU/mL	375 mg			

Table 3. Subcutaneous Xolair Doses Every 2 or 4 Weeks for Pediatric Patients with Asthma Who Begin Xolair Between the Ages of 6 to <12 Years

Pre-treatment Serum IgE (IU/mL)	Dosing Freq.	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
		Dose (mg)									
30-100	Every 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	DO NOT DOSE	
>400-500		225	300	225	225	300	300	375	375		
>500-600		300	300	225	300	300	375	DO NOT DOSE			
>600-700		300	225	225	300	375	DO NOT DOSE				
>700-800	Every 2 weeks	225	225	300	375	DO NOT DOSE					
>800-900		225	225	300	375						
>900-1000		225	300	375	DO NOT DOSE						
>1000-1100		225	300	375							
>1100-1200		300	300	DO NOT DOSE							
>1200-1300		300	375								

9. Xolair will not be covered for patients who have had previous anaphylaxis to Xolair.
10. Xolair will not be covered for food allergies, latex allergy, atopic dermatitis, or seasonal allergic rhinitis (hay fever).
11. Authorization will not be granted for patients <6 years of age as there is insufficient data to support the use of Xolair in these patients.
12. Although not FDA approved, based on current study data we may allow for doses above 750mg per month on a case by case basis. The dosing utilized in this study and found to be safe and effective is listed below for reference.

Table 4. Omalizumab dosage based on body weight and serum total IgE levels at baseline

Body Weight (kg)	Omalizumab 450mg every 2 weeks	Omalizumab 525mg every 2 weeks	Omalizumab 600mg every 2 weeks
>125-150	**n/a**	**>300-400**	**>400-2000**
>90-125	**>300-400**	**>400-500**	**>500-2000**
>80-90	**>500-600**	**>600-700**	**>700-2000**
>70-80	**>500-700**	**>700-800**	**>800-2000**
>60-70	**>600-800**	**>800-900**	**>900-2000**
>50-60	**>700-900**	**>900-1000**	**>1000-2000**
>40-50	**>900-1100**	**>1100-1300**	**>1300-2000**

13. For either diagnosis, if Xolair therapy is initiated with samples and the member does not meet our criteria for coverage (as outlined above) before the start of Xolair therapy, upon completion of the samples, coverage of Xolair will not be granted.
14. Unless otherwise stated above within the individual drug criteria, **approval time periods** are listed in the table below.
    - Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e.; generics, biosimilars, or other guideline-supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.

Line of Business	Initial approval	Continued approval
Medicaid Managed Care (MMC) / Child Health Plus (CHP)	6 months	12 months
Commercial / Exchange	Outpatient Hospital – 6 months	Outpatient Hospital – 6 months
	Home Care or Office Based – 6 months	Home Care or Office Based – 2 years
Medicare	Outpatient Hospital – 6 months	Outpatient Hospital – 2 years
	Home Care or Office Based – 6 months	Home Care or Office Based – 2 years

15. **Tables 5 and 6. Estimated comparative daily doses for inhaled glucocorticoids in adolescents and adults; Usual doses of combination inhaled glucocorticoids and long-acting beta-agonists for the treatment of asthma in adolescents age 12 and older and adults**

Estimated comparative daily doses for inhaled glucocorticoids in adolescents and adults

Drug	Low dose	Medium dose	High dose
Beclomethasone HFA (Qvar and Qvar RediHaler products available in United States)*	80 to 160 mcg	>160 to 320 mcg	>320 mcg
40 mcg per puff	2 to 4 puffs	¶	¶
80 mcg per puff	1 to 2 puffs	3 to 4 puffs	>4 puffs
Beclomethasone HFAΔ (Qvar product available in Canada, Europe, and elsewhere)	100 to 200 mcg	>200 to 400 mcg	>400 mcg
50 mcg per puff	2 to 4 puffs	¶	¶
100 mcg per puff	1 to 2 puffs	3 to 4 puffs	>4 puffs
Budesonide DPI (Pulmicort Flexhaler product available in United States)*	180 to 360 mcg	>360 to 720 mcg	>720 mcg
90 mcg per inhalation	2 to 4 inhalations	¶	¶
180 mcg per inhalation	1 to 2 inhalations	3 to 4 inhalations	>4 inhalations
Budesonide DPIΔ (Pulmicort Turbuhaler product available in Canada, Europe, and elsewhere)	200 to 400 mcg	>400 to 800 mcg	>800 mcg
100 mcg per inhalation	2 to 4 inhalations	¶	¶
200 mcg per inhalation	1 to 2 inhalations	3 to 4 inhalations	¶
400 mcg per inhalation	1 inhalation	2 inhalations	>2 inhalations
Ciclesonide HFA (Alvesco product available in United States, Europe, and elsewhere)*	80 to 160 mcg	>160 to 320 mcg	>320 mcg
80 mcg per puff	1 to 2 puffs	3 to 4 puffs	¶
160 mcg per puff	1 puff	2 puffs	>2 puffs
Ciclesonide HFAΔ (Alvesco product available in Canada)	100 to 200 mcg	>200 to 400 mcg	>400 mcg
100 mcg per puff	1 to 2 puffs	3 to 4 puffs	¶
200 mcg per puff	1 puff	2 puffs	>2 puffs
Flunisolide MDI (Aerospan product available in United States)*	320 mcg	>320 to 640 mcg	Insufficient data
80 mcg per puff	4 puffs	5 to 8 puffs	Insufficient data
Fluticasone propionate HFA (Flovent HFA product available in United States)*	88 to 220 mcg	>220 to 440 mcg	>440 mcg
44 mcg per puff	2 to 5 puffs	¶	¶
110 mcg per puff	1 to 2 puffs	3 to 4 puffs	¶
220 mcg per puff	◊	2 puffs	>2 puffs
Fluticasone propionate HFAΔ (Flovent HFA product available in Canada, Europe, and elsewhere)	100 to 250 mcg	>250 to 500 mcg	>500 mcg
50 mcg per puff	2 to 5 puffs	¶	¶
125 mcg per puff	1 to 2 puffs	3 to 4 puffs	¶
250 mcg per puff	◊	2 puffs	>2 puffs
Fluticasone propionate DPI (Flovent Diskus product available in United States and Canada)*	100 to 250 mcg	>250 to 500 mcg	>500 mcg
50 mcg per inhalation	2 to 5 inhalations	¶	¶
100 mcg per inhalation	1 to 2 inhalations	3 to 5 inhalations	¶
250 mcg per inhalation	1 inhalation	2 inhalations	>2 inhalations
500 mcg per inhalation (strength not available in United States)	◊	1 inhalation	>1 inhalation
Fluticasone propionate DPI (Armonair Respiclick product available in United States)*	100 to 250 mcg	>250 to 500 mcg	>500 mcg
55 mcg per inhalation	2 to 4 inhalations	¶	¶
113 mcg per inhalation	1 to 2 inhalations	3 to 4 inhalations	>4 inhalations
232 mcg per inhalation	1 inhalation	2 inhalation	>2 inhalations
Fluticasone furoate DPI (Arnuity Ellipta product available in United States)* **NOTE:** Inhaled fluticasone furoate has a greater anti-inflammatory potency per microgram than fluticasone propionate inhalers. Thus, fluticasone furoate is administered at a lower daily dose and used only once daily.	50 mcg (by use of pediatric DPI, which is off-label in adolescents and adults)	100 mcg	200 mcg
50 mcg per inhalation	1 inhalation	¶	¶
100 mcg per inhalation	◊	1 inhalation	2 inhalations
200 mcg per actuation	◊	◊	1 inhalation
Mometasone DPI§ (Asmanex DPI product available in United States)*	110 to 220 mcg	>220 to 440 mcg	>440 mcg
110 mcg per inhalation	1 to 2 inhalations	¶	¶
220 mcg per inhalation	1 inhalation	2 inhalations	>2 inhalations
Mometasone HFA§ (Asmanex HFA product available in United States)*	100 to 200 mcg	>200 to 400 mcg	>400 mcg
100 mcg per actuation	1 to 2 inhalations	¶	¶
200 mcg per actuation	1 inhalation	2 inhalations	>2 inhalations
Mometasone DPI§§ (Asmanex Twisthaler product available in Canada, Europe, and elsewhere)	200 mcg	>200 to 400 mcg	>400 mcg
200 mcg per inhalation	1 inhalation	2 inhalations	>2 inhalations
400 mcg per inhalation	◊	1 inhalation	>1 inhalation

- **The most important determinant of appropriate dosing is the clinician's judgment of the patient's response to therapy.** The clinician must monitor the patient's response on several clinical parameters and adjust the dose accordingly. The stepwise approach to therapy emphasizes that once control of asthma is achieved, the dose of medication should be carefully titrated to the minimum dose required to maintain control, thus reducing the potential for adverse effects.
- Depending on the specific product, total daily doses are administered once or twice daily.
- Some doses are outside the approved product information recommendations.

DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant metered dose inhaler.
* Doses shown and strengths (ie, mcg per puff or inhalation) are based upon product descriptions approved in the United States which may differ from how strengths are described for products available in other countries. Consult local product information before use.
¶ Select alternate preparation with higher mcg/puff to improve convenience.
Δ Products shaded in light blue color are not available in the United States but are available widely elsewhere.
◊ Select preparation with fewer mcg/puff.
§ Approved for once-daily dosing in mild asthma in some countries.

National Heart, Blood, and Lung Institute Expert Panel Report 3 (EPR 3): Guidelines for the Diagnosis and Management of Asthma; 2007. NIH Publication 08-4051 available at http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/full-report; updated with additional data from Global Initiative for Asthma (GINA); Global Strategy for Asthma Management and Prevention; 2017. Available at www.ginasthma.org

Usual doses of combination inhaled glucocorticoids and long-acting beta-agonists for the treatment of asthma in adolescents age 12 and older and adults

Medication	Low dose	Medium dose	High dose
Budesonide-formoterol HFA (Brand name: Symbicort)			
80 mcg-4.5 mcg	2 puffs twice a day		
160 mcg-4.5 mcg		2 puffs twice a day	
Fluticasone furoate-vilanterol DPI (Brand name: Breo Ellipta)*			
NOTE: Inhaled fluticasone furoate has a greater anti-inflammatory potency per microgram than fluticasone propionate inhalers. Thus, fluticasone furoate is administered at a lower daily dose and used only **once** daily.			
100 mcg-25 mcg		1 inhalation once daily	
200 mcg-25 mcg			1 inhalation once daily
Fluticasone propionate-salmeterol DPI (Brand name: Advair Diskus)			
100 mcg-50 mcg	1 inhalation twice a day		
250 mcg-50 mcg		1 inhalation twice a day	
500 mcg-50 mcg			1 inhalation twice a day
Fluticasone propionate-salmeterol HFA (Brand name: Advair HFA)			
45 mcg-21 mcg	2 puffs twice a day		
115 mcg-21 mcg		2 puffs twice a day	
230 mcg-21 mcg			2 puffs twice a day
Fluticasone propionate-salmeterol DPI (Brand name: AirDuo RespiClick)¶			
55 mcg-14 mcg	1 inhalation twice a day		
113 mcg-14 mcg	1 inhalation twice a day	1 inhalation twice a day	
232 mcg-14 mcg			1 inhalation twice a day
Mometasone-formoterol HFA (Brand name: Dulera)			
100 mcg-5 mcg		2 puffs twice a day	
200 mcg-5 mcg			2 puffs twice a day

Do not exceed the maximum number of inhalations/puffs per day listed in the table due to the risk of toxicity from an excess dose of long acting beta-agonist (ie, salmeterol, formoterol, or vilanterol). Brand names and dose per puff or per inhalation of commercially available fixed dose combinations are according to United States licensed product information. Consult local product information before use.

HFA: metered dose inhaler with hydrofluoroalkane propellant; DPI: dry powder inhaler.
* Not approved for use in patients <18 years old.
¶ In AirDuo inhalers the daily dose of salmeterol is approximately one-fourth of the dose in Advair, and the daily dose of fluticasone is approximately one-half that of the comparable low, medium, and high dose strengths of Advair. AirDuo contains lactose.

UpToDate®

RATIONALE:

CODES: Number

Description

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).

HCPCS: J2357 Xolair

UPDATES:

Date:	Revision:
2/20	Revised
1/20	Revised
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4/14	Revised
6/13	Revised
4/13	Revised
4/12	Reviewed
1/10	Revised
7/09	Revised
4/08	Revised

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