Xolair (Omalizumab)
Policy Number: C8757-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
	10/9/2019	10/9/2020
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
J2357	RxPA	Q2 2019

PRODUCTS AFFECTED:
Xolair (omalizumab)

DRUG CLASS:
Monoclonal Antibody, Anti-Asthmatic

ROUTE OF ADMINISTRATION:
Subcutaneous

PLACE OF SERVICE:
Specialty Pharmacy or Buy and Bill
The recommendation is that medications in this policy will be for pharmacy benefit coverage and the subcutaneous product is administered in a place of service that is a non-hospital facility based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless the therapy/patient meets the Site of Care exceptions. (See appendix for excerpt from Specialty Medication Administration Site of Care Policy)

AVAILABLE DOSAGE FORMS:
Xolair 150mg Powder for Injection; Xolair 150mg/mL Prefilled Syringe Solution for Injection; Xolair 75mg/0.5mL Prefilled Syringe Solution for Injection

FDA-APPROVED USES:
Chronic idiopathic urticaria: Treatment of chronic idiopathic urticaria in adults and adolescents 12 years and older who remain symptomatic despite H1 antihistamine treatment Not for treating other forms of urticaria.

Asthma: Treatment of moderate to severe persistent asthma in adults and patients 6 years and older who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids

COMPENDIAL APPROVED OFF-LABELED USES:
None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS: Chronic idiopathic urticarial, moderate to severe persistent asthma

REQUIRED MEDICAL INFORMATION:
A. CHRONIC IDIOPATHIC URTICARIA
Documentation of ALL of the following criteria required:

1. Diagnosis of Chronic Idiopathic Urticaria (CIU) documented by the presence of urticaria (hives) that has been continuously or intermittently present for more than 6 weeks
   AND
2. Other underlying causes of member's condition has been ruled out, including bradykinin-related angioedema and interleukin-1-associated urticarial syndromes (auto-inflammatory disorders, urticarial vasculitis); AND if applicable, possible conditions or triggers for urticaria are being maximally managed without improvement
   AND
3. Documented baseline score from an objective clinical evaluation tool within the past 30 days [e.g. urticaria activity score (UAS7), angioedema activity score (AAS), Dermatology Life Quality Index (DLQI), Angioedema Quality of Life (AE-QoL), or Chronic Urticaria Quality of Life Questionnaire(CU-Q2oL)]
   AND
4. Documentation that member continues to experience hives associated with itching despite adequate trials, minimum 4 weeks, of ALL of the following treatments. Prescriber to submit documentation of trial/failure with dates to drug therapy:
   (a) Two (2) different H1-antihistamines at the maximally tolerated doses (up to 4 times normal dose daily dose], unless medically contraindicated AND A LTRA (montelukast, zafirlukast) in combination with an antihistamine NOTE: First generation H1 antihistamine (doxepin, hydroxyzine, cyproheptadine), second generation H1 antihistamine (cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine), H2 antihistamine (ranitidine, famotidine, cimetidine)
   - MOLINA REVIEWER: If denying for prior utilization at high doses, please enter override for antihistamine quantity limits (Reference: AAAAI/ACAAI guideline on diagnosis and management acute and chronic urticaria (J Allergy Clin Immunol 2014 May;133(5):1270)
   AND
   (b) A H1-antihistamine in combination with leukotriene receptor antagonist [(LTRA): montelukast (Singulair), zafirlukast (Accolate), zileuton (Zyflo)] at the maximally tolerated doses (up to 4 times normal dose daily dose), unless medically contraindicated
   AND
   (c) A H1-antihistamine at the maximally tolerated doses (up to 4 times normal dose daily dose) in combination with:H2-Antihistamines [e.g. cimetidine (Tagamet), famotidine (Pepcid), nizatidine (Axid), ranitidine (Zantac)] OR an anti-inflammatory agent (e.g. dapsone, hydroxychloroquine, sulfasalazine) OR an immunosuppressant agent (e.g. cyclosporine, mycophenolate)
   AND
   (d) Xolair dosing requested is in accordance with the FDA-approved labeling for member's treatment of chronic idiopathic urticaria

B. MODERATE-TO-SEVERE PERSISTENT ALLERGIC ASTHMA

1. Documentation of Diagnosis of moderate to severe persistent asthma as defined by the National Asthma Education and Prevention Program (NAEPP) (Step 5 or Step 6) or moderate to severe persistent as defined by the National Heart, Lung and Blood Institute (NHLBI) criteria asthma
   AND
2. Allergic asthma confirmed by positive skin testing (i.e. prick/puncture test, intracutaneous test) or in vitro reactivity (i.e. RAST, MAST, FAST, ELISA) to at least one perennial aeroallergen
   AND
3. (a) Age 6 to <12 years: (a) Body weight between 20 kg (44 lbs) and 150 kg (330 lbs), AND (b) Pre-treatment serum total IgE levels (measured prior to start of treatment): 30 to 1500 IU/mL.

OR
(b) Age ≥ 12 years: (a) Body weight between 30 kg (66 lbs) and 150 kg (330 lbs), AND (b) Pre-treatment serum total IgE levels (measured prior to start of treatment): 30 to 700 IU/mL, AND baseline FEV1 <80% predicted.
AND

4. Asthma symptoms have not been adequately controlled by inhaled corticosteroids after at least 3 months of therapy as documented by 1 or more of the following: (a) Requirement for systemic (oral, parenteral) corticosteroids to control exacerbations of asthma, (b) Excessive use of rescue medications and/or oral steroids OR increasing need for short-acting inhaled beta2 agonists, (c) Frequent severe exacerbations that often require emergency room visits, unscheduled office visits and/or hospitalizations, (d) Limitations or impairment in activities of daily living, such as work, school, exercise and/or sleep, (e) Lung function (PEF or FEV1) < 80% predicted or personal best (without administration of bronchodilator or after bronchodilator withhold), (g) Measures of asthma control indicate uncontrolled asthma (e.g., Asthma Control Test [ACT] score ≤ 19)
   AND
5. Inadequate symptom control (as documented in criterion above) demonstrated by a compliant, trial of at least 3 months of 1 of the following:
   a. Combination controller therapy of medium- to high- dose inhaled corticosteroids plus long-acting beta-2 agonists (LABA) or leukotriene receptor antagonists (LTRA)-- (GINA 2018), OR
   b. LABA plus either a LTRA, Long-acting muscarinic antagonist (LAMA), or theophylline, OR
   c. Member has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the standard therapies (in #5a and #5b)
   AND
6. Member is a non-smoker OR smoking cessation has been at least 6 months
   AND
7. Underlying conditions or triggers for asthma or pulmonary disease are being maximally managed
   AND
8. Xolair is prescribed concomitantly with an ICS plus either a LABA or LTRA
   AND
9. Not prescribed for concurrent use with either of the following: Anti-interleukin 4 therapy [e.g. Dupixent (dupilumab)], OR Anti-interleukin 5 therapy [e.g. Nucala (mepolizumab), Cinqair (resilizumab), Fasenra (benralizumab)]
   AND
10. Xolair dosing requested is within the defined dosing of the FDA-approved labeling based on pre-treatment serum IgE level and member's body weight

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of therapy: 6 months

QUANTITY:
Options for dosing quantity limits:
Dose (75mg) = 1x 75mg syringe ONLY
Dose (150mg) = 1x150mg syringe OR 150mg vial
Dose (225mg) = 1x 75mg syringe+ 1x 150mg syringe ONLY
Dose (300mg) = 2 x 150mg syringe OR 2x 150mg vials
Dose (375mg) = 1x75mg syringe + 2

PRESCRIBER REQUIREMENTS:

Prescribed by, or in consultation with, an allergy/asthma specialist (allergist, immunologist, or pulmonologist) or dermatologist (for CIU). Consultation notes must be submitted for initial request and for continuation of treatment requests at least ONCE annually

AGE RESTRICTIONS:
Chronic idiopathic urticaria: 12 years of age or older; Asthma: 6 years of age or older

GENDER:
Male and female

CONTINUATION OF THERAPY:
A. FOR ALL INDICATIONS:

1. Member currently meets ALL initial coverage criteria
   AND
2. Consultation notes must be submitted for initial request and for continuation of treatment requests at least ONCE annually. The prescribing physician should periodically reassess the need for continuation of therapy based on the member's disease severity and level of asthma control. Continuation of therapy requires submission of relevant medical records or chart notes documenting continued efficacy of Xolair.
   AND
3. Member compliance with therapy as verified by Prescriber and member's medication fill history (review Rx history for compliance)
   AND
4. Member has not experienced ANY of the following: Intolerable adverse effects or absence of unacceptable toxicity from the drug [e.g. symptoms of anaphylaxis (bronchospasm, hypotension, syncope, urticaria, and/or angioedema), malignancy, symptoms similar to serum sickness (fever, arthralgia, and rash); parasitic (helminth) infection, eosinophilic conditions (e.g. vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy, especially upon reduction of oral corticosteroids]; Poor response to treatment as evidenced by physical findings and/or clinical symptoms
   AND
5. Xolair dosing requested is in accordance with the FDA-approved labeling for member's treatment

B. CHRONIC IDIOPATHIC URTICARIA

Clinical improvement as documented by improvement from baseline using objective clinical evaluation tools within the past 30 days [e.g. urticaria activity score (UAS7), angioedema activity score (AAS), Dermatology Life Quality Index (DLQI), Angioedema Quality of Life (AE-QoL), or Chronic Urticaria Quality of Life Questionnaire(CU-Q2oL)]. Documentation of current UAS7, AAS, DLQI, AE-QoL, or Cu-Q2oL must be submitted.

C. MODERATE-TO-SEVERE PERSISTENT ALLERGIC ASTHMA

1. Positive clinical improvement (from pre-Xolair treatment baseline) as documented by 1 or more of the following: (a) Improvement in lung function (increase in percent predicted FEV1 or PEF) from pre-treatment baseline, (b) Decreased utilization of rescue medications, (c) Decreased frequency of exacerbations (defined as worsening of asthma that requires increase in inhaled corticosteroid dose or treatment with systemic corticosteroids), (d) Decreased frequency of unscheduled clinic, urgent care or emergency department visits, (e) Reduction in reported symptoms: chest tightness, coughing, shortness of breath, nocturnal wakening wheezing, sustained improvement in ACT scores; (f) Reduction use of ICS, leukotriene or beta agonist therapy, (g) Reduction in severity or frequency of asthma-related symptoms (e.g., wheezing/heavy breathing, coughing, chest tightness or heaviness,

shortness of breath, sleep disturbance, night wakening, fatigue, sleep disturbance, or asthmatic symptoms upon awakening)
AND

2. Xolair is used in combination with other medications for long-term control of asthma [e.g. inhaled corticosteroids, long acting beta-2 agonists (LABA), leukotriene receptor antagonists (LTRA), Long-acting muscarinic antagonist (LAMA), theophylline], OR Member has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the standard therapies
AND
3. Xolair is not used in combination with either of the following: Anti-interleukin 4 therapy [e.g. Dupixent (dupilumab)], OR Anti-interleukin 5 therapy [e.g. Nucala (mepolizumab), Cinqair (resilizumab), Fasenra (benralizumab)]

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Xolair are considered experimental/investigational and therefore, will follow Molina's Off-Label policy; Severe hypersensitivity reaction to omalizumab or any component of the formulation; Treatment to relieve acute bronchospasm or status asthmaticus

DISCONTINUATION: Poor response to treatment as evidenced by physical findings and/or clinical symptoms; Intolerable adverse effects or drug toxicity; Persistent and uncorrectable problems with adherence to treatment

EXCLUSION: Xolair is not used in combination with either of the following: Anti-interleukin 4 therapy [e.g. Dupixent (dupilumab)], OR Anti-interleukin 5 therapy [e.g. Nucala (mepolizumab), Cinqair (resilizumab), Fasenra (benralizumab)]

OTHER SPECIAL CONSIDERATIONS:
Boxed warning Anaphylaxis, presenting as bronchospasm, hypotension, syncope, urticaria, and/or angioedema of the throat or tongue, has been reported to occur after administration of omalizumab. Anaphylaxis has been reported after the first dose of Xolair but also beyond one year after beginning treatment. Individuals should be closely observed after Xolair administration as well as informed of signs and symptoms of anaphylaxis and to seek care immediately should symptoms occur.

BACKGROUND:
<u>ASTHMA</u>
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 Global Initiative for Asthma (GINA, 2018) recommends that patients 6 years and older may be treated with omalizumab as follows (Evidence A: Randomized controlled trials and meta-analyses. Rich body of evidence):
• Suggested add-on treatment for patients ≥ 6 years with moderate or severe allergic asthma that is uncontrolled on Step 4 treatment (Evidence A)
• Patients with severe asthma, uncontrolled on Step 4 treatment, may benefit from phenotyping into categories such as severe allergic, aspirin-exacerbated or eosinophilic asthma. Patients ≥6 years

with severe allergic asthma with elevated IgE levels may benefit from omalizumab (anti-IgE) therapy (Evidence A).

CHRONIC URTICARIA

In 2014, the Joint Task Force on Practice Parameters (JTFPP), representing the American Academy of Allergy, Asthma & Immunology (AAAAI); the American College of Allergy, Asthma & Immunology (ACAAI); and the Joint Council of Allergy, Asthma & Immunology updated the practice parameter for the diagnosis and management of acute and chronic urticaria (CU). The practice parameter established a step-care approach to the treatment of chronic urticaria and angioedema. The task force recommended the following step-care treatment approach:

• Monotherapy with second-generation antihistamines: H1-antagonists are effective in the majority of patients with CU but might not achieve complete control in all patients.

• Dose advancement of H1-antihistamine therapy, combining first- and second-generation agents and adding an H2-antihistamine and/or an antileukotriene agent: Higher doses of second-generation antihistamines can provide greater efficacy when control is not achieved with conventional doses of these agents.

• Therapeutic trial of potent antihistamine (e.g., hydroxyzine or doxepin): First-generation antihistamines should be prescribed cautiously in the elderly or patients with occupations (e.g., machine operators, airline pilots, or alpine skiers) for which alertness is essential.

• Add an immunosuppressant or biologic agent: Omalizumab and cyclosporine have the greatest published experience documenting efficacy in patients with CU compared with all other alternative agents.

The EAACI/GA2LEN/EDF/AAAAI/WAO Guideline for the Management of Urticaria include Xolair in combination with H1-antihistamines as a third line treatment option in patients who have failed to respond to higher doses of H1-Antihistamines

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.

APPENDIX:

Dermatology Life Quality Index (DLQI): A self-administered 10-item questionnaire that rates the impact of skin disease on symptoms and feelings, daily activities, leisure, work and school, personal relationships and treatment. The average completion time of 2 minutes. The DLQI may be used for routine clinical use by clinicians in order to assist the clinical consultation, patient evaluation and monitoring and to help with clinical decision making process.

Urticaria Activity Score (UAS): A patient reported CIU measure which captures intensity of pruritus and number of hives. Daily intensity of pruritus (range: 0 = none to 3 = severe) and number of hives ratings (range: 0 = none to 3 = more than 12 hives) are summed over a week to create the UAS7 (range: 0–42) score.

FEV1 (forced expiratory volume in 1 second): A measure of airway obstruction determined using spirometry. Individual FEV1 values are compared to predicted values based on age, height, sex and race.
'Estimated Comparative Daily Dosages for ICSs in Children' from the National Asthma Educational Prevention Program (NAEPP)-- EPR 3 Guidelines on Asthma by NAEPP. Figure 4–4b. Available at: https://www.nhlbi.nih.gov/sites/default/files/media/docs/asthgdln_1.pdf

Molina Healthcare, Inc. covers injectable/infused treatment in a hospital outpatient setting or at a hospital-affiliated infusion suite* when the level of care is determined to be medically necessary. Considerations used to determine if an alternative level of care is not suitable may include the following findings:

1. The patient is clinically unstable based on documented medical history and susceptible to complication with drug administration (e.g., cardiopulmonary or renal dysfunction, risk for fluid overload)
2. The requested medication is administered as part of a chemotherapy regimen (e.g., anti-neoplastic agent, colony stimulating factor, erythropoiesis-stimulating agent, anti-emetic) for treatment of cancer or with dialysis
3. The patient exhibits physical or cognitive impairment and a capable caregiver is not available to assist with safe administration of prescribed medication in the home
4. It is the patient's first dose of the medication or it is being re-initiated after at least 12 months*
5. The patient has experienced adverse events with past administration of the drug and cannot be managed by premedication or resources available at an non-hospital facility based location (NHFBL)
6. Documented history of difficulty establishing and maintaining patent vascular access, or is not a candidate for a mode of long term vascular access during the duration of prescribed treatment

Note: a hospital outpatient setting or a hospital-affiliated infusion suite is expected to have immediate access to specific services of a medical center/hospital setting, including having emergency resuscitation equipment and personnel (ACLS protocol), emergency services, and inpatient admission or intensive care, if necessary

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

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