Clinical Policy: Omalizumab (Xolair), Omalizumab-igec (Omlyclo)

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Line of Business: Commercial, HIM

Coding Implications
Revision Log

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

Description

Omalizumab (Xolair®) and its biosimilar omalizumab-igec (Omlyclo®) are anti-immunoglobulin E (IgE) antibodies.

FDA Approved Indication(s)

Xolair and Omlyclo are indicated for:

- Moderate to severe persistent asthma in adults and pediatric 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
- Chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids, as add-on maintenance treatment
- Chronic spontaneous urticaria (CSU) in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment
- Reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods in adult and pediatric patients aged 1 year and older with IgE-mediated food allergy. Xolair and Omlyclo are to be used in conjunction with food allergen avoidance

Limitation(s) of use: Xolair and Omlyclo are not indicated for the relief of acute bronchospasm or status asthmaticus, treatment of other forms of urticaria, or emergency treatment of allergic reactions including anaphylaxis.

Policy/Criteria

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

It is the policy of health plans affiliated with Centene Corporation® that Xolair and Omlyclo are **medically necessary** when the following criteria are met:

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 exacerbations within the last 12 months, requiring one of the following (a or b) 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 contraindication/intolerance):
   a. Oral/systemic corticosteroid treatment (or increase in dose if already on oral corticosteroid);
   b. Urgent care/emergency room (ER) visit or hospital admission;
5. Positive skin test or in vitro reactivity to a perennial aeroallergen (*see Appendix D*);
6. IgE level ≥ 30 IU/mL;
7. Xolair/Omlyclo is prescribed concurrently with an ICS plus either a LABA or LTRA;
8. Xolair/Omlyclo is not prescribed concurrently with Cinqair®, Fasenra®, Nucala®, Dupixent®, or Tezspire®;
9. 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: 6 months

B. Chronic Spontaneous Urticaria (must meet all)**:**
1. Diagnosis of CSU (formerly known as chronic idiopathic urticaria [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 clinically significant adverse effects are experienced or all are contraindicated (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/Omlyclo is not prescribed concurrently with Cinqair, Fasenra, Nucala, Dupixent, or Tezspire;
6. Dose does not exceed 300 mg every 4 weeks.

Approval duration: 6 months

C. Chronic Rhinosinusitis with Nasal Polyps (must meet all)**:**
1. Diagnosis of CRSwNP with documentation of all of the following (a, b, and c):
   a. Presence of nasal polyps;
   b. Disease is bilateral;
   c. Member has experienced signs and symptoms (e.g., nasal congestion/blockage/ obstruction, loss of smell, rhinorrhea) for ≥ 12 weeks;
2. Prescribed by or in consultation with an allergist, immunologist, or otolaryngologist;
3. Age ≥ 18 years;
4. Member has required the use of systemic corticosteroids for symptom control within the last 2 years, unless contraindicated or clinically significant adverse effects are experienced *(see Appendix B for examples)*;
5. Failure of maintenance therapy with at least two intranasal corticosteroids, one of which must be Xhance™, each used for ≥ 4 weeks, unless contraindicated or clinically significant adverse effects are experienced (see *Appendix B for examples*);

6. Xolair/Omlyclo is prescribed concurrently with an intranasal corticosteroid, unless contraindicated or clinically significant adverse effects are experienced (see *Appendix B for examples*);
7. Xolair/Omlyclo is not prescribed concurrently with Cinqair, Fasenra, Nucala, Dupixent, or Tezspire;
8. Dose does not exceed 600 mg every 2 weeks (*see Appendix G for dosing based on pre-treatment IgE level and weight*).

Approval duration: 6 months

D. IgE-Mediated Food Allergy (must meet all)**:**

1. Diagnosis of IgE-mediated food allergy;
2. Prescribed by or in consultation with an allergist or immunologist;
3. Age ≥ 1 year;
4. Confirmation of one of the following (a, b, or c):
   a. Positive skin prick test with wheal diameter ≥ 4 mm greater than control;
   b. Food-specific serum IgE ≥ 6 kU_A/L;
   c. Positive oral food challenge test;
5. Member has history of significant allergic reaction(s) to the food (e.g., hives, swelling, wheezing, hypotension, gastrointestinal symptoms) that meets both of the following (a and b):
   a. Prescriber deemed past allergic reaction to the food significant enough to require a prescription for injectable epinephrine;
   b. Xolair/Omlyclo is prescribed concurrently with injectable epinephrine;
6. Medical justification supports necessity for Xolair/Omlyclo despite food allergen avoidance (e.g., member lacks sufficient mental capacity to effectively avoid food allergens);
7. Xolair/Omlyclo is not prescribed concurrently with Palforzia™, Cinqair, Fasenra, Nucala, Dupixent, or Tezspire;
8. Dose does not exceed 600 mg every 2 weeks (*see Appendix H for dosing based on pre-treatment IgE level and weight*).

Approval duration: 6 months

E. NCCN Compendium Indications (off-label) (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. Systemic mastocytosis;
   b. Immune checkpoint inhibitor-related severe (G3; *see Appendix I*) pruritus;
2. Prescribed by or in consultation with an oncologist;
3. For systemic mastocytosis, prescribed in one of the following settings (a, b, c, or d):
   a. As stepwise prophylactic treatment for chronic mast cell mediator-related cardiovascular and pulmonary symptoms when the member has tried both of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Antihistamine (i.e., H1 blocker, H2 blocker);
      ii. Corticosteroid;
   b. For prevention of unprovoked anaphylaxis;

c. For prevention of hymenoptera (e.g., bees, wasps, hornets) or food-induced anaphylaxis, and one of the following (i or ii):
   i. Member has negative specific IgE;
   ii. Member has negative skin test;
d. To improve tolerability of immunotherapy;

4. For immune checkpoint inhibitor-related severe pruritis, all of the following (a, b, and c):
   a. Pruritus is refractory;
   b. Member has an increased IgE level;
   c. Member has not responded to a gabapentinoid (e.g., gabapentin, pregabalin) after 1 month of therapy;
5. Xolair/Omlyclo is not prescribed concurrently with Cinqair, Fasenra, Nucala, Dupixent, or Tezspire;
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.33 for health insurance marketplace; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.103 for health insurance marketplace; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and HIM.PA.154 for health insurance marketplace.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Demonstrated adherence to asthma controller therapy (an ICS plus either a LABA or LTRA) as evidenced by proportion of days covered (PDC) of 0.8 in the last 6 months

(i.e., member has received asthma controller therapy for at least 5 of the last 6 months);
3. Member is responding positively to therapy (examples may include but are not limited to: 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/Omlyclo is not prescribed concurrently with Cinqair, Fasenra, Nucala, Dupixent, or Tezspire;
5. If request is for a dose increase, new dose does not exceed 375 mg every 2 weeks (*see Appendix E and F for dosing based on pre-treatment IgE level, weight, and age*).

Approval duration:
HIM – 12 months
Commercial – 6 months or member's renewal period, whichever is longer

B. Chronic Spontaneous Urticaria (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. Xolair/Omlyclo is not prescribed concurrently with Cinqair, Fasenra, Nucala, Dupixent, or Tezspire;
4. If request is for a dose increase, new dose does not exceed 300 mg every 4 weeks.

Approval duration:
HIM – 12 months
Commercial – 6 months or member's renewal period, whichever is longer

C. Chronic Rhinosinusitis with Nasal Polyps (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Demonstrated adherence to an intranasal corticosteroid, unless contraindicated or clinically significant adverse effects are experienced;
3. Member is responding positively to therapy (examples may include but are not limited to: reduced nasal polyp size, reduced need for systemic corticosteroids, improved sense of smell, improved quality of life);
4. Xolair/Omlyclo is not prescribed concurrently with Cinqair, Fasenra, Nucala, Dupixent, or Tezspire;
5. If request is for a dose increase, new dose does not exceed 600 mg every 2 weeks (*see Appendix G for dosing based on pre-treatment IgE level and weight*).

Approval duration:
HIM – 12 months
Commercial – 6 months or member's renewal period, whichever is longer

D. IgE-Mediated Food Allergy (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy;
3. Xolair/Omlyclo is prescribed concurrently with injectable epinephrine;
4. Xolair/Omlyclo is not prescribed concurrently with Palforzia, Cinqair, Fasenra, Nucala, Dupixent, or Tezspire;
5. If request is for a dose increase, new dose does not exceed 600 mg every 2 weeks (*see Appendix H for dosing based on pre-treatment IgE level and weight*).

Approval duration:
HIM – 12 months
Commercial – 6 months or member's renewal period, whichever is longer

E. NCCN Compendium Indications (off-label) (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Xolair/Omlyclo for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 6 months

F. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.33 for health insurance marketplace; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.103 for health insurance marketplace; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line

of business: CP.CPA.09 for commercial and HIM.PA.154 for health insurance marketplace.

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 policies – CP.CPA.09 for commercial and HIM.PA.154 for health insurance marketplace, or evidence of coverage documents;

B. Acute bronchospasm or status asthmaticus.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AAAAI: American Academy of Allergy, Asthma, and Immunology
ADL: activity of daily living
CIU: chronic idiopathic urticaria
CRSwNP: chronic rhinosinusitis with nasal polyps
CSU: chronic spontaneous urticaria
EAACI: European Academy of Allergy and Clinical Immunology
EDF: European Dermatology Forum
EPR3: Expert Panel Report 3
FDA: Food and Drug Administration
GA2LEN: Global Allergy and Asthma European Network
GINA: Global Initiative for Asthma
ICS: inhaled corticosteroids
IgE: immunoglobulin E
kU_A/L: kilounits of allergen-specific IgE per liter
LABA: long-acting beta-agonist
LTRA: leukotriene modifier
PDC: proportion of days covered
WAO: World Allergy Organization

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Asthma – ICS (medium – high dose)		
Qvar® (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
fluticasone propionate (Flovent®)	> 100 mcg/day 44-250 mcg per actuation 2-4 actuations BID	2 actuations BID
Arnuity Ellipta® (fluticasone furoate)	≥ 50 mcg/day	1 actuation QD

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	100 mcg, 200 mcg per actuation 1 actuation QD	
Asmanex® (mometasone)	≥ 100 mcg/day HFA: 100 mcg, 200 mcg per actuation Twisthaler: 110 mcg, 220 mcg per actuation 1-2 actuations QD to BID	2 inhalations 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 QD	1 actuation QD
fluticasone/salmeterol (Advair®)	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
budesonide/formoterol (Symbicort®)	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 QD	10 mg per day
zafirlukast (Accolate®)	10 to 20 mg PO BID	40 mg per day
zileuton ER (Zyflo® CR)	1,200 mg PO BID	2,400 mg per day
Zyflo® (zileuton)	600 mg PO QID	2,400 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 (Deltasone®)	40 to 80 mg PO in 1 to 2 divided doses	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
CSU		
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
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 QD	10 mg/day
levocertirizine (Xyzal®)	2.5 mg to 5 mg PO QD	5 mg/day
loratadine (Claritin®)	10 mg PO QD	10 mg/day
desloratadine (Clarinex®)	5 mg PO QD	Will vary according to condition
fexofenadine (Allegra®)	60 mg PO BID or 180 mg QD	180 mg/day
Nasal polyps		
Oral corticosteroids		
dexamethasone (Decadron®)	0.75 to 9 mg/day PO in 2 to 4 divided doses	Varies
methylprednisolone (Medrol®)	4 to 48 mg PO in 1 to 2 divided doses	Varies
prednisolone (Millipred®, Orapred ODT®)	5 to 60 mg PO in 1 to 2 divided doses	Varies
prednisone (Deltasone®)	5 to 60 mg PO in 1 to 2 divided doses	Varies
Intranasal corticosteroids		
beclomethasone (Beconase AQ®, Qnasl®)	1-2 sprays IN BID	2 sprays/nostril BID
budesonide (Rhinocort® Aqua, Rhinocort®)	128 mcg IN QD or 200 mcg IN BID	1-2 inhalations/nostril/ day
flunisolide	2 sprays IN BID	2 sprays/nostril TID
fluticasone propionate (Flonase®)	1-2 sprays IN BID	2 sprays/nostril BID
mometasone (Nasonex®)	2 sprays IN BID	2 sprays/nostril BID
Omnaris®, Zetonna® (ciclesonide)	Omnaris: 2 sprays IN QD Zetonna: 1 spray IN QD	Omnaris: 2 sprays/ nostril/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
		Zetonna: 2 sprays/ nostril/day
triamcinolone (Nasacort®)	2 sprays IN QD	2 sprays/ nostril/day
Xhance™ (fluticasone propionate)	1 to 2 sprays (93 mcg/spray) to nostril IN BID	744 mcg/day
Systemic mastocytosis, Immunotherapy-related pruritus		
antihistamines, H1 blockers: examples – diphenhydramine, chlorpheniramine, hydroxyzine, cetirizine, loratadine, fexofenadine	Varies	Varies
antihistamines, H2 blockers: examples – cimetidine, famotidine	Varies	Varies
corticosteroids: examples – betamethasone, dexamethasone, methylprednisolone, prednisolone, prednisone	Varies	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
- Boxed warning(s): anaphylaxis

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 FEV1 between 40% and 80% of predicted. No patients were enrolled with an FEV1 greater than 80% of predicted.
  - Omalizumab has been shown to be marginally effective in decreasing the incidence of asthma exacerbations in patients who have met all the criteria described above.
  - Omalizumab 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 2007 National Heart, Lung and Blood Institute's Expert Panel Report 3 (EPR3) Guidelines for the Diagnosis and Management of Asthma recommend omalizumab 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) guidelines recommend omalizumab be considered as adjunct therapy for patients 6 years of age and older with exacerbations or poor symptom control despite taking at least high dose ICS/LABA and who have allergic biomarkers or need maintenance oral corticosteroids.
  - 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 omalizumab have been reported. Usually these reactions occur within two hours of receiving an omalizumab subcutaneous injection. However, these new reports include patients who had delayed anaphylaxis—with onset two to 24 hours or even longer- after receiving omalizumab treatment. Anaphylaxis may occur after any dose of omalizumab (including the first dose), even if the patient had no allergic reaction to the first dose.
  - Patients could potentially meet asthma criteria for both omalizumab and Nucala, though there is insufficient data to support the combination use of multiple asthma biologics. The combination has not been studied. Approximately 30% of patients in the Nucala MENSA study also were candidates for therapy with omalizumab.
  - PDC is a measure of adherence. PDC is calculated as the sum of days covered in a time frame divided by the number of days in the time frame. To achieve a PDC of 0.8, a member must have received their asthma controller therapy for 144 days out of the last 180 days, or approximately 5 months of the last 6 months.
- CSU:
  - CSU 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 omalizumab 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 omalizumab 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 omalizumab 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.

- Omalizumab is the first medicine in its class approved for CSU since non-sedating antihistamines.
- The use of over-the-counter H_1 antihistamines may not be a benefit to the treatment of CIU. Credit will be given for their use, but will not be covered under plan.
- Anaphylaxis has occurred as early as after the first dose of omalizumab, but also occurred beyond 1 year after beginning regularly administered treatment.

- Idiopathic anaphylaxis: A randomized, double-blind, placebo-controlled study in 19 patients with frequent episodes (≥ 6/year) of idiopathic anaphylaxis found omalizumab to have no significant difference compared to placebo in the number of anaphylactic episodes at 6 months (Carter MC et al).
- Atopic dermatitis: A double-blind, placebo-controlled study in 62 pediatric patients with severe atopic dermatitis found omalizumab to have a statistically significant difference compared to placebo in the Scoring Atopic Dermatitis [SCORAD] index at 24 weeks; however, the clinical significance of this is unknown (Chan S et al). Another randomized, double-blind, placebo-controlled study found that while omalizumab reduced serum levels of free IgE and decreased surface-bound IgE, it did not significantly alter several measures of clinical disease activity (i.e., atopy patch test results in single patients) (Heil PM et al). The 2023 American Academy of Dermatology atopic dermatitis guidelines state that there are insufficient data to make a recommendation regarding the use of omalizumab.

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	Insufficient Data to Recommend a Dose	
> 600-700		375 mg			

†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 Freq-uency	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					

Pre-treatment serum IgE IU/mL	Dosing Frequency	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
> 700-800	Q 2 weeks	225	225	300	375	Insufficient Data to Recommend a Dose					
> 800-900		225	225	300	375						
> 900-1,000		225	300	375							
> 1,000-1,100		225	300	375							
> 1,100-1,200		300	300								
> 1,200-1,300		300	375								

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

Appendix G: Age ≥ 18 Years: CRSwNP Dosing Based on Pre-treatment IgE and Body Weight†

Pre- treatment serum IgE IU/mL	Dosing Frequency	Body Weight							
		> 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	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
> 500-600		450	600	600	375	450	450	600	Insufficient Data to Recommend a Dose
> 600-700		450	600	375	450	450	525		
> 700-800	Q 2 weeks	300	375	450	450	525	600		
> 800-900		300	375	450	525	600			
> 900-1,000		375	450	525	600				
> 1,000-1,100		375	450	600					
> 1,100-1,200		450	525	600					
> 1,200-1,300		450	525						
> 1,300- 1,500		525	600						

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

Appendix H: Age ≥ 1 Year: IgE-Mediated Food Allergy Dosing Based on Pre-treatment IgE and Body Weight†

Pre-treatment serum IgE IU/mL	Dosing Frequency	Body Weight (continued on next table)						
		≥ 10-12 kg	> 12-15 kg	> 15-20 kg	> 20-25 kg	> 25-30 kg	> 30-40 kg	> 40-50 kg
≥ 30-100	Q 4 weeks	75	75	75	75	75	75	150
> 100-200		75	75	75	150	150	150	300
> 200-300		75	75	150	150	150	225	300
> 300-400		150	150	150	225	225	300	450
> 400-500		150	150	225	225	300	450	450
> 500-600		150	150	225	300	300	450	600
> 600-700		150	150	225	300	225	450	600
> 700-800	Q 2 weeks	150	150	150	225	225	300	375
> 800-900		150	150	150	225	225	300	375
> 900-1,000		150	150	225	225	300	375	450
> 1,000-1,100		150	150	225	225	300	375	450
> 1,100-1,200		150	150	225	300	300	450	525
> 1,200-1,300		150	225	225	300	375	450	525
> 1,300-1,500		150	225	300	300	375	525	600

Pre-treatment serum IgE IU/mL	Dosing Frequency	Body Weight (continued on next table)						
		≥ 10-12 kg	> 12-15 kg	> 15-20 kg	> 20-25 kg	> 25-30 kg	> 30-40 kg	> 40-50 kg
> 1,500-1,850		*	225	300	375	450	600	*

†*The manufacturer recommends dose adjustments for significant body weight changes during treatment.*
** Insufficient data to recommend a dose*

Pre-treatment serum IgE IU/mL	Dosing Frequency	Body Weight (continued from previous table)					
		> 50- 60 kg	> 60- 70 kg	> 70-80 kg	> 80-90 kg	> 90-125 kg	> 125-150 kg
≥ 30-100	Q 4 weeks	150	150	150	150	300	300
> 100-200		300	300	300	300	450	600
> 200-300		300	450	450	450	600	375
> 300-400		450	450	600	600	450	525
> 400-500		600	600	375	375	525	600
> 500-600		600	375	450	450	600	
> 600-700		375	450	450	525		
> 700-800	Q 2 weeks	450	450	525	600		
> 800-900		450	525	600			
> 900-1,000		525	600				
> 1,000-1,100		600					
> 1,100-1,200		600					
> 1,200-1,300							
> 1,300-1,500							
> 1,500-1,850							

Insufficient Data to Recommend a Dose

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

Appendix I: Immunotherapy-related Pruritus

- Immunotherapy refers to immune checkpoint inhibitors. Immune checkpoint inhibitors comprise a class of agents that target immune cell checkpoints, such as programmed cell death-1 (PD-1; e.g., Opdivo®, Keytruda®) and PD-1 ligand (PD-L1; e.g., Tecentriq®, Bavencio®, Imfinzi®), as well as cytotoxic T-lymphocyte–associated antigen 4 (e.g., Yervoy®, Imjudo®).
- NCCN grading of pruritus
  - G1: Mild or localized
  - G2: Moderate. Intense or widespread; intermittent; skin changes from scratching (e.g., edema, papulation, excoriations, lichenification, oozing/crusts); limiting instrumental activities of daily living (ADLs)
  - G3: Severe. Intense or widespread; constant; limiting self-care ADLs or sleep

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
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). Adjust doses for significant changes in body weight during treatment	375 mg/2 weeks

Indication	Dosing Regimen	Maximum Dose
	Xolair and Omlyclo are 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	
CSU	150 mg or 300 mg SC every 4 weeks	300 mg/4 weeks
CRSwNP*	75 to 600 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). Adjust doses for significant changes in body weight during treatment	600 mg/2 weeks
IgE-mediated food allergy*	75 mg to 600 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). Adjust doses for significant changes in body weight during treatment	600 mg/2 weeks

**For patients with a combination of either asthma, CRSwNP, and/or IgE-mediated food allergy, dosing determination should be based on the primary diagnosis for which Xolair/Omlyclo is being prescribed.*

VI. Product Availability

Drug Name	Availability
Omalizumab (Xolair)	• Single-dose vial: 150 mg • Single-dose prefilled syringes: 75 mg/0.5 mL, 150 mg/mL, 300 mg/2 mL • Single-dose prefilled autoinjectors: 75 mg/0.5 mL, 150 mg/mL, 300 mg/2 mL
Omalizumab-igec (Omlyclo)	Single-dose prefilled syringes: 75 mg/0.5 mL, 150 mg/mL

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Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2357	Injection, omalizumab, 5 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created per November SDC (adapted from CP.PHAR.01). Template changes applied to other diagnoses/indications and continued therapy section.	11.18.22	02.23
Per February SDC, for nasal polyps modified requirement from three intranasal steroids to require only two; RT4: revised FDA labeled indication from “nasal polyps” to “CRSwNP” per updated prescribing information.	04.03.23	05.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2024 annual review: added off-label indications and criteria for systemic mastocytosis and immunotherapy-related pruritus per NCCN; updated formulations to include strengths of prefilled syringe and autoinjectors; references reviewed and updated.	11.06.23	02.24
RT4: added new FDA-labeled indication of IgE-mediated food allergy; corrected continued therapy section for NCCN Compendium indications to allow for continued therapy for an approval duration of 6 months; moved immunotherapy-related pruritus appendix information to Appendix I.	04.09.24	05.24
1Q 2025 annual review: for asthma initial approval criteria, added allowance for ER visit, removed intubation option for alignment purposes as a hospital admission would encompass intubation; for immune checkpoint inhibitor-related severe pruritis, added requirement for no response to 1 month of gabapentinoid therapy per NCCN; updated Appendix D to include information about atopic dermatitis; references reviewed and updated.	11.14.24	02.25
RT4: added newly approved biosimilar Omlyclo.	03.25.25	

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or

regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. 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 clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.