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Medication Policy Manual

Policy No: dru087

Topic: Xolair[®], omalizumab

Date of Origin: July 20, 2003

Revised/Effective Date: July 17, 2009

Next Review Date: July 2010

IMPORTANT REMINDER

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Xolair[®] (omalizumab) is a human monoclonal antibody used in allergic asthma. Omalizumab binds to IgE antibodies and prevents IgE from attaching to mast cells, therefore preventing the activation of the allergic cascade and decreasing airway inflammation.

Policy/Criteria

I. Most contracts require prior authorization approval of omalizumab prior to coverage. Omalizumab may be considered medically necessary in patients with asthma when all criteria A through F below are met.

A. Patient is currently followed by an asthma specialist (allergist, immunologist, or pulmonologist).

AND

B. Positive skin prick test or in-vitro specific IgE test (such as RAST, MAST, FAST, ELISA) to one or more allergens, (or is currently receiving specific immunotherapy like allergy shots) which support the patient's clinical history.

AND

C. Total serum IgE level is equal or greater than 30 IU/ml and less than or equal to 700 IU/ml.

AND

D. Clinical documentation of poor asthma control or recurrent exacerbation requiring additional medication treatment:

- Additional medical treatment may include any of the following: treatment with oral corticosteroids, ER visits, hospitalizations, or frequent office visits.
- Poor asthma control may include (but is not limited to) clinical documentation of limitation of activities of daily living (ADLs), nighttime awakening, or dyspnea.
- Recurrent exacerbation is defined as 2 or more acute exacerbations in a 12-month period.

AND

E. Clinical documentation that patient is compliant with high-dose inhaled corticosteroids and long-acting inhaled beta-2 agonists (Step 5 of the National Asthma Treatment Guidelines) and use of oral corticosteroids for exacerbation unless contraindicated.

AND

F. Underlying conditions or triggers for asthma or pulmonary disease are being maximally managed.

II. Administration, Quantity Limitations, and Authorization Period

- A. Regence does not consider omalizumab to be a self-administered medication.
- B. When prior authorization is approved, omalizumab may be authorized in quantities that **do not exceed** administration of greater than 375mg every 2 weeks for up to 6 months.
- C. Authorization may be reviewed at least every 6 months to confirm that current medical necessity criteria are met and that the medication is effective (defined as sustained clinical improvement or stable asthma control).

III. Omalizumab is considered not medically necessary when used for the following conditions:

- A. Allergic rhinitis.
- B. Prevention of peanut or other food allergies.

IV. Omalizumab is considered investigational when used for all other conditions.

Position Statement

Summary

- Omalizumab is approved for adolescents (12 years and above) and adults with moderate-to-severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.
- Omalizumab is only covered under the medical benefit. Omalizumab is not considered a self-injectable medication due to product labeling indicating that medical observation for hypersensitivity reactions is necessary following administration.
- Omalizumab increases the number of patients who are able to reduce or withdraw their inhaled steroids and is effective in reducing asthma. ^[1, 2, 4, 7]
- Efficacy and dosing of omalizumab in patients with IgE levels greater than 700 have not been established. ^[24]
 - * IgE levels after administration of Xolair are relatively insignificant in trying to quantify because there are no labs to differentiate between bound and unbound (free) IGE.

- * The relevance of serum free IgE suppression is unclear, since the release of histamine and other mediators from IgE-receptor-bearing cells is more dependent upon bound IgE than on free IgE, and the relation of bound to free IgE is complex. ^[25]
- The National Heart, Lung, and Blood Institute (NHLBI) defines asthma as a chronic inflammatory disorder of the airways in which many cells and cellular elements (multiple cytokines and mediators, as well as potentially IgE-mediated events involving mast cells and basophils) play a role (in particular, mast cells, eosinophils, T lymphocytes, macrophages, neutrophils and epithelial cells).
- IgE may be in the inflammatory cascade of some events leading to asthmatic airway inflammation, it is only one part of the picture.
- Efficacy and dosing of omalizumab in patients whose weight is outside the range provided in the standard dosing table for omalizumab has not been established (weight-IgE level combinations yielding doses greater than 750 mg every 4 weeks were excluded from clinical trials). ^[24, 25]
- There are no available data demonstrating that omalizumab is superior to preferred options recommended in national treatment guidelines for moderate-to-severe persistent asthma. ^[14, 15, 20]
- Strict compliance with omalizumab is necessary because there is a 6 to 12 week lag before beneficial effects are apparent. (Effects are not immediate and explain the various phases that are included in study protocols.)
- Phase II results (suggesting benefits of another anti-IgE compound-TNX-901) cannot be extrapolated to the use of omalizumab to protect against anaphylaxis in patients with peanut allergy. ^[16]

Clinical Efficacy

- Omalizumab reduces seasonal and perennial allergic rhinitis symptoms, ^[3, 9, 22, 23] but has not been shown to have better efficacy than first-line alternatives (such as nasal corticosteroids, antihistamines, or allergen desensitization therapy). ^[13]
- The efficacy of omalizumab in patients with a history of smoking has not been established (patients with a smoking history in the previous two years or who had a previous history of greater than or equal to 10 pack-years were excluded from omalizumab clinical trials). ^[25]

Safety

- There is a black box warning for anaphylaxis.
 - * Anaphylaxis in patients after treatment with omalizumab. These reactions generally occur within two hours of receiving omalizumab.
 - * Delayed anaphylaxis—with onset two to 24 hours or even longer—after receiving omalizumab treatment.
 - * Anaphylaxis can occur after any dose.
 - * It is recommended that patients be observed for at least two hours after omalizumab is administered.
- Urticaria is the most frequent adverse effect reported with short-term therapy. ^[12]
- There have been some initial concerns with elevated risks of cancer with omalizumab; however, an independent committee of oncologists reviewed available data and were unable to establish a direct correlation. ^[18, 19]
- The FDA is evaluating interim long-term safety data that suggest a risk of cardiovascular and cerebrovascular adverse events. ^[34]

Appendices

Appendix 1: National Heart, Lung and Blood Institute (NHLBI) Asthma Treatment Guidelines for Managing Infants and Young Children (4 years of age and younger) with Acute or Chronic Asthma.

[Click here for a printable version of Appendix 1.](#)

Appendix 2: National Heart, Lung and Blood Institute (NHLBI) Asthma Treatment Guidelines for Managing Asthma in Children 5 -11 years of Age.

[Click here for a printable version of Appendix 2.](#)

Appendix 3: National Heart, Lung and Blood Institute (NHLBI) Asthma Treatment Guidelines for Managing Asthma in Adults and Children older than 12 years of Age.

[Click here for a printable version of Appendix 3.](#)

Appendix 4: Estimated Comparative Daily Dosages for Inhaled Steroids (Adults).

[Click here for a printable version of Appendix 4.](#)

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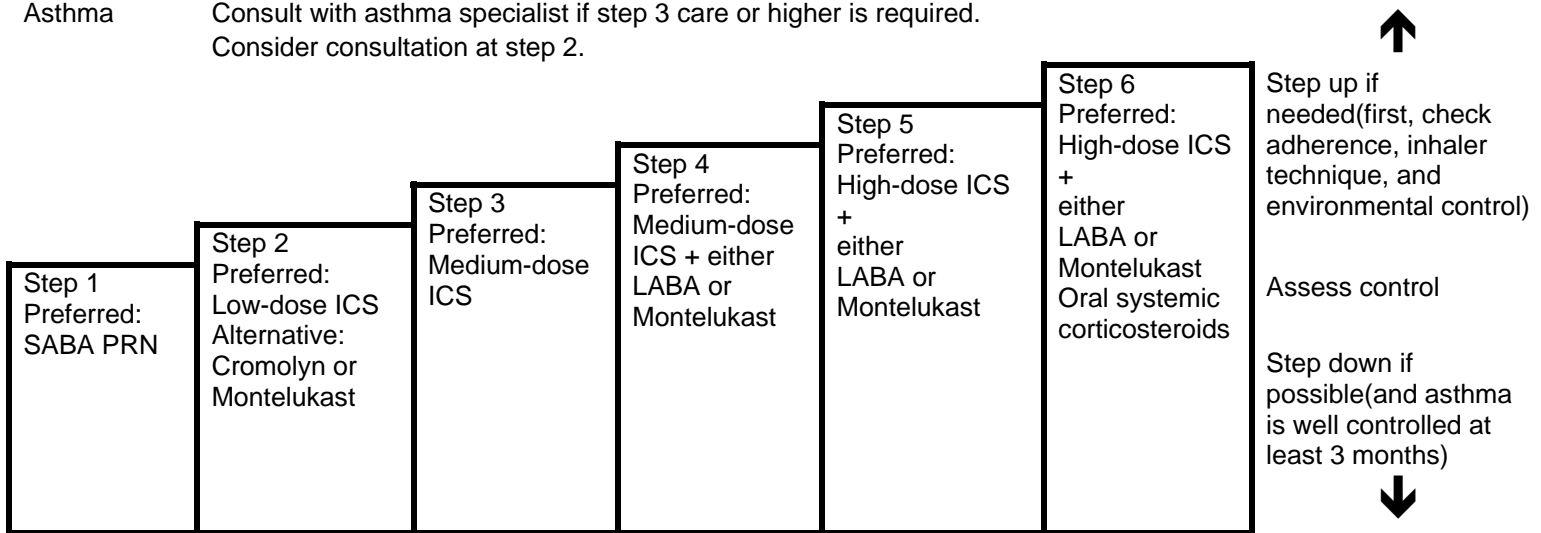
Cross References
Allergy Testing lab01, TRG Medical Policy Manual, Laboratory

Codes	Number	Description
HCPCS	J2357	Injection, omalizumab, 5 mg
ICD-9	493.00	Extrinsic asthma, unspecified

NHLBI STEPWISE APPROACH FOR MANAGING ASTHMA LONG TERM IN CHILDREN, 0–4 YEARS OF AGE

Appendix 1

Intermittent Asthma Persistent Asthma: Daily Medication
 Consult with asthma specialist if step 3 care or higher is required.
 Consider consultation at step 2.



Patient Education and Environmental Control at Each Step

Quick-Relief Medication for All Patients

- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms.
- With viral respiratory infection: SABA q 4–6 hours up to 24 hours (longer with physician consult). Consider short course of oral systemic corticosteroids if exacerbation is severe or patient has history of previous severe exacerbations.
- Caution: Frequent use of SABA may indicate the need to step up treatment. See text for recommendations on initiating daily long-term-control therapy

Key: Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy. ICS, inhaled corticosteroid; LABA, inhaled long-acting beta2-agonist; SABA, inhaled short-acting beta2-agonist

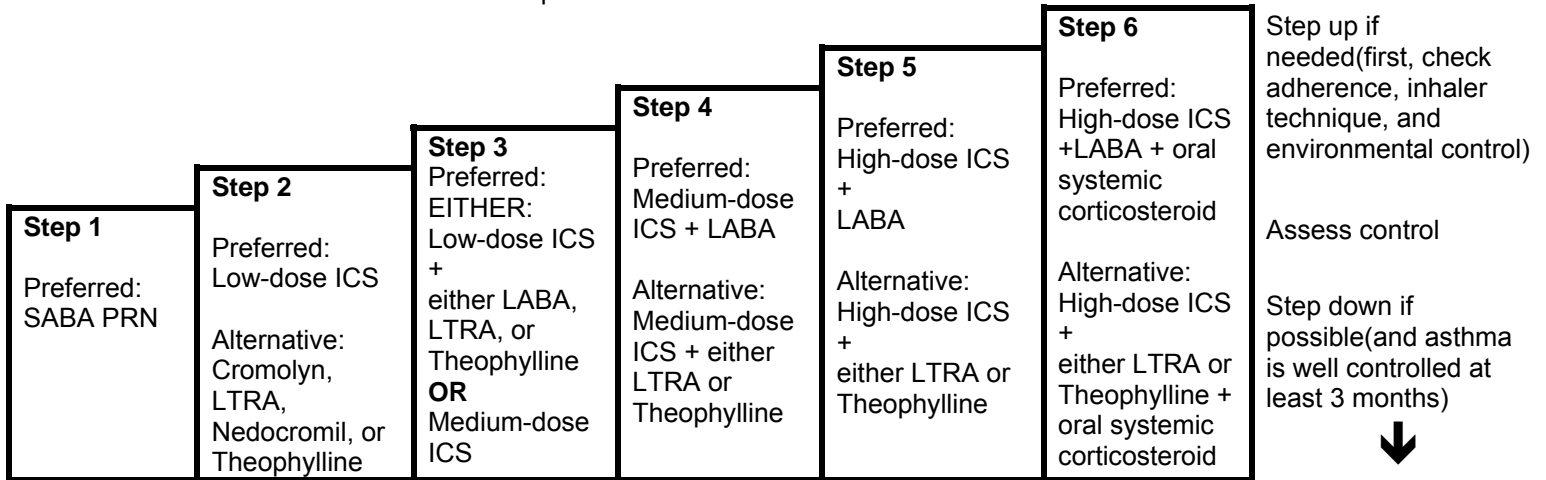
Notes:

- The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
- If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.
- If clear benefit is not observed within 4–6 weeks and patient/family medication technique and adherence are satisfactory, consider adjusting therapy or alternative diagnosis.
- Studies on children 0–4 years of age are limited. Step 2 preferred therapy is based on Evidence A. All other recommendations are based on expert opinion and extrapolation from studies in older children

NHLBI STEPWISE APPROACH FOR MANAGING ASTHMA LONG TERM IN CHILDREN 5–11 YEARS OF AGE

Appendix 2

Intermittent Asthma Persistent Asthma: Daily Medication
 Consult with asthma specialist if step 3 care or higher is required.
 Consider consultation at step 2.



Each step: Patient education, environmental control, and management of comorbidities.
 Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

Quick-Relief Medication for All Patients

- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Caution: Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.

Key: Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy. ICS, inhaled corticosteroid; LABA, inhaled long-acting beta2-agonist, LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta2-agonist.

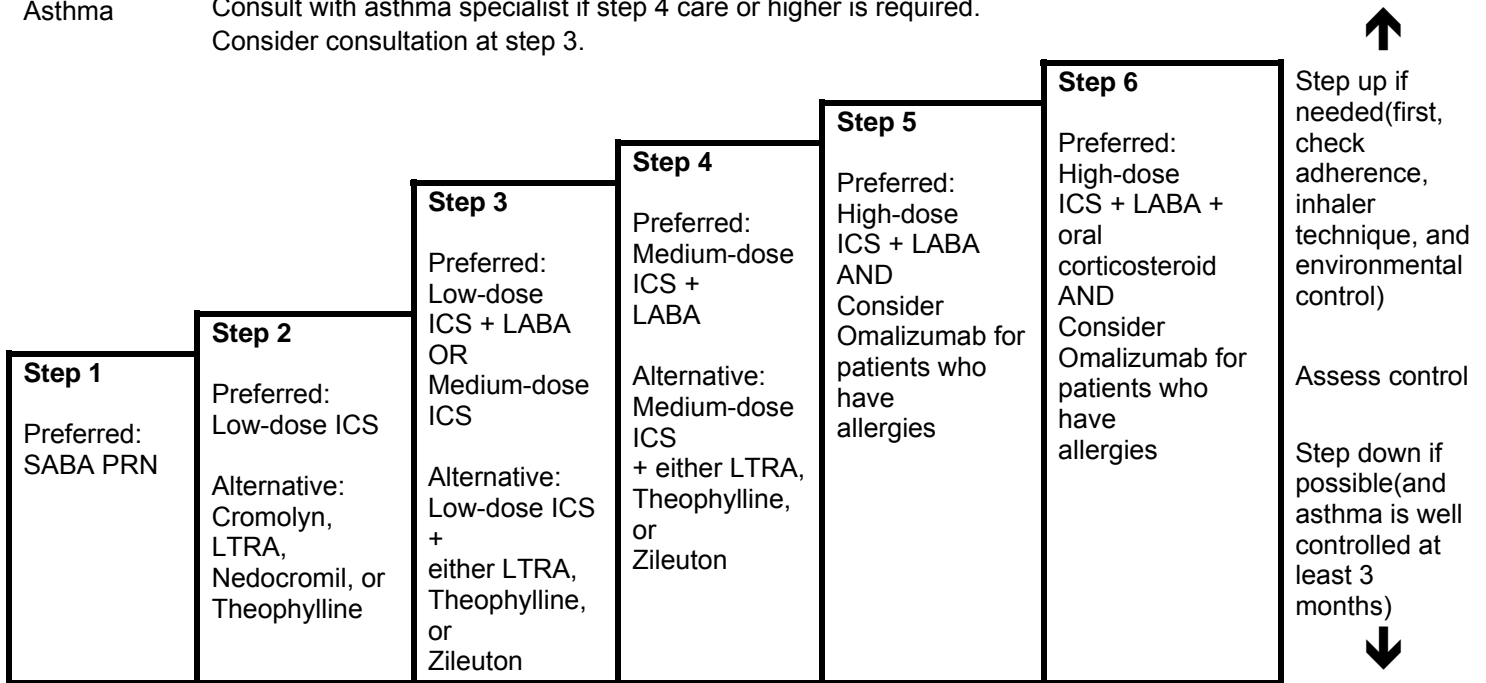
Notes:

- The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
- If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.
- Theophylline is a less desirable alternative due to the need to monitor serum concentration levels.
- Step 1 and step 2 medications are based on Evidence A. Step 3 ICS + adjunctive therapy and ICS are based on Evidence B for efficacy of each treatment and extrapolation from comparator trials in older children and adults—comparator trials are not available for this age group; steps 4–6 are based on expert opinion and extrapolation from studies in older children and adults.
- Immunotherapy for steps 2–4 is based on Evidence B for house-dust mites, animal danders, and pollens; evidence is weak or lacking for molds and cockroaches. Evidence is strongest for immunotherapy with single allergens.
- The role of allergy in asthma is greater in children than in adults. Clinicians who administer immunotherapy should be prepared and equipped to identify and treat anaphylaxis that may occur.

STEPWISE APPROACH FOR MANAGING ASTHMA IN YOUTHS ≥ 12 YEARS OF AGE AND ADULTS

Appendix 3

Intermittent Asthma Persistent Asthma: Daily Medication
 Consult with asthma specialist if step 4 care or higher is required.
 Consider consultation at step 3.



Each step: Patient education, environmental control, and management of comorbidities.
 Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

Quick-Relief Medication for All Patients

- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment

Key: Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy. EIB, exercise-induced bronchospasm; ICS, inhaled corticosteroid; LABA, long-acting inhaled beta2-agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta2-agonist.

Notes:

- The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
- If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.
- Zileuton is a less desirable alternative due to limited studies as adjunctive therapy and the need to monitor liver function. Theophylline requires monitoring of serum concentration levels.
- In step 6, before oral systemic corticosteroids are introduced, a trial of high-dose ICS + LABA + either LTRA, theophylline, or zileuton may be considered, although this approach has not been studied in clinical trials.
- Step 1, 2, and 3 preferred therapies are based on Evidence A; step 3 alternative therapy is based on Evidence A for LTRA, Evidence B for theophylline, and Evidence D for zileuton. Step 4 preferred therapy is based on Evidence B, and alternative therapy is based on Evidence B for LTRA and theophylline and Evidence D for zileuton. Step 5 preferred therapy is based on Evidence B. Step 6 preferred therapy is based on (EPR□2 1997) and Evidence B for omalizumab.
- Immunotherapy for steps 2–4 is based on Evidence B for house-dust mites, animal danders, and pollens; evidence is weak or lacking for molds and cockroaches. Evidence is strongest for immunotherapy with single allergens. The role of allergy in asthma is greater in children than in adults.
- Clinicians who administer immunotherapy or omalizumab should be prepared and equipped to identify and treat anaphylaxis that may occur.

NHLBI ESTIMATED COMPARATIVE DAILY DOSAGES FOR INHALED CORTICOSTEROIDS

Appendix 4

Drug	Low Daily Dose			Medium Daily Dose			High Daily Dose		
	Child 0–4 yo	Child 5–11yo	≥12 Years & Adults	Child 0–4 yo	Child 5–11yo	≥12 Years & Adults	Child 0–4 yo	Child 5–11yo	≥12 Years & Adults
Beclomethasone HFA 40 or 80 mcg/puff	NA	80–160 mcg	80–240 mcg	NA	>160–320 mcg	>240–480 mcg	NA	>320 mcg	>480 mcg
Budesonide DPI 90, 180, 200 mcg/inhalation	NA	180–400 mcg	180–600 mcg	NA	>400–800 mcg	>600–1,200 mcg	NA	>800 mcg	>1,200 mcg
Budesonide Inhaled Inhalation suspension for nebulization	0.25–0.5 mg	0.5 mg	NA	>0.5–1.0 mg	1.0 mg	NA	>1.0 mg	2.0 mg	NA
Flunisolide 250 mcg/puff	NA	500–750 mcg	500–1,000 mcg	NA	1,000–1,250 mcg	>1,000–2,000 mcg	NA	>1,250 mcg	>2,000 mcg
Flunisolide HFA 80 mcg/puff	NA	160 mcg	320 mcg	NA	320 mcg	>320–640 mcg	NA	≥640 mcg	>640 mcg
Fluticasone HFA/MDI: 44, 110, 220 mcg/puff	176 mcg	88–176 mcg	88–264 mcg	>176–352 mcg	>176–352 mcg	>264–440 mcg	>352 mcg	>352 mcg	>440 mcg
DPI: 50, 100, or 250 mcg/inhalation	NA	100–200 mcg	100–300 mcg	NA	>200–400 mcg	>300–500 mcg	NA	>400 mcg	>500 mcg
Mometasone DPI 200 mcg/inhalation	NA	NA	200 mcg	NA	NA	400 mcg	NA	NA	>400 mcg
Triamcinolone acetonide 75 mcg/puff	NA	300–600 mcg	300–750 mcg	NA	>600–900 mcg	>750–1,500 mcg	NA	>900 mcg	>1,500 mcg

Key: DPI, dry power inhaler; HFA, hydrofluoroalkane; MDI, metered-dose inhaler; NA, not available (either not approved, no data available, or safety and efficacy not established for this age group)