Omalizumab

ACG: A-0315 (AC)
Link to Codes

Clinical Indications

Omalizumab may be indicated for 1 or more of the following(1)(2)(3):

- Allergic asthma (moderate to severe), as indicated by 1 or more of the following:
  - Initial course, as indicated by ALL of the following:
    - Age 6 years or older
    - Asthma present for 1 year or more
    - Need for treatment escalation, as indicated by 1 or more of the following:
      - Remains uncontrolled despite treatment with medium or high-dose inhaled corticosteroids plus long-acting beta-agonist
      - Requires maintenance treatment with medium or high-dose inhaled corticosteroids plus long-acting beta-agonist to achieve asthma symptom control
    - Omalizumab not being used as monotherapy for asthma
    - Prebronchodilator FEV1 of 80% predicted or less
    - Specific allergen sensitivity documented, as indicated by 1 or more of the following:
      - Positive skin testing for perennial aeroallergen (eg, cat, cockroach, dust mite, dog, mice, mold)
      - Positive specific IgE level for at least one perennial aeroallergen (eg, cat, cockroach, dust mite, dog, mice, mold)
    - Total serum IgE of 30 International Units per milliliter (IU/mL) (kIU/L) or greater at baseline
  - Subsequent course, as indicated by ALL of the following:
    - Age 6 years or older
    - Omalizumab not being used as monotherapy for asthma
    - Favorable response to prior administration of omalizumab

- Chronic idiopathic urticaria, as indicated by ALL of the following:
  - Age 12 years or older
  - History of chronic idiopathic urticaria for at least 6 months
  - Persistent hives with itching for at least 8 consecutive weeks despite adequate trial of H1-antihistamines

Evidence Summary

Background

Omalizumab is a recombinant monoclonal antibody that selectively binds human IgE, reducing free circulating IgE and subsequent release of inflammatory mediators.(1)(4)(5)(6) (EG 2)

Criteria

For allergic asthma (moderate to severe), evidence demonstrates at least moderate certainty of at least moderate net benefit. (RG A1)
A systematic review of 24 nonrandomized effectiveness studies (with a total of 4117 adult patients with severe allergic asthma) found that the use of omalizumab resulted in significant improvement in asthma exacerbations, steroid use, emergency department visits, hospital admissions and length of stay, and overall quality of life.(43) (EG 2) A systematic review and meta-analysis of 19 studies found that omalizumab reduced the probability of acute exacerbation from 26% (with placebo) to 16% over 16 to 60 weeks and reduced the probability of hospitalization from 3% (with placebo) to 0.5% over 28 to 60 weeks.(44) (EG 1) Systematic reviews demonstrated that adding omalizumab to baseline therapy significantly reduced corticosteroid use and decreased the risk of asthma exacerbations in adult, adolescent, and pediatric patients age 6 years and older.(45)(46) (EG 1) A multicenter, randomized, double-blind, placebo-
controlled trial of 850 patients ranging from 12 to 75 years of age with severe allergic asthma inadequately controlled with high-dose corticosteroids and inhaled long-acting beta-agonists, with elevated IgE levels between 30 to 700 International Units per milliliter (IU/mL) (kIU/L), reported that omalizumab conferred a 25% relative reduction in asthma exacerbations, decreased rescue beta-agonist use, and improved quality of life. (47) (EG 1) For an inner city pediatric and young adult population (age 6 to 20 years) with persistent allergic asthma treated with guideline-based therapy, a randomized double-blind placebo-controlled trial reported that the addition of omalizumab resulted in a significant decrease in asthma-related symptoms, a reduction in the number of participants experiencing at least one exacerbation, fewer hospitalizations, and a reduced need for inhaled corticosteroids. (48) (EG 1) Information from a large registry of patients receiving omalizumab for atopic asthma indicates a significant reduction in overall healthcare utilization as well as absentee days from work or school related to asthma exacerbations. (49) (EG 2) A review article noted that randomized controlled trials have shown that omalizumab reduces asthma exacerbations; however, its impact on health-related quality of life and pulmonary function are not consistent. (50) (EG 2) In a retrospective study, 26 asthma patients with total serum IgE levels greater than 700 International Units per milliliter (IU/mL) (kIU/L) who received omalizumab were matched with 26 asthma patients who received omalizumab for total serum IgE levels between 30 and 700 International Units per milliliter (IU/mL) (kIU/L); similar improvements in asthma control and frequency of systemic steroid use were noted in the 2 groups during the 6 months post omalizumab initiation without an increase in the frequency of adverse events. (51) (EG 2) An evidence-based practice guideline supports the use of omalizumab for patients age 6 years and older who have moderate or severe allergic asthma that is not controlled on moderate to high-dose inhaled corticosteroids plus a long-acting beta-agonist, with or without additional controllers. (52) (EG 2)

For chronic idiopathic urticaria, evidence demonstrates at least moderate certainty of at least moderate net benefit. (RG A1) Uncontrolled retrospective study data from 51 patients showed that treatment with omalizumab led to complete remission in 83% of patients with chronic spontaneous (idiopathic) urticaria. (73) (EG 2) A phase III, multicenter, randomized, double-blind study involving 323 patients with moderate to severe chronic idiopathic urticaria with persistent symptoms despite antihistamine therapy concluded that omalizumab significantly decreased signs and symptoms at week 12 as compared with placebo. (74)(75) (EG 1) Similar efficacy was noted in another phase III randomized trial with 336 patients. (76) (EG 1) A systematic review of 5 studies with 1117 patients indicates that the use of omalizumab in patients with chronic idiopathic urticaria refractory to H1-antihistamines is associated with significant improvement in weekly scores of urticarial activity and in percentage of angioedema-free days. (77) (EG 1) A systematic review of omalizumab in antihistamine-refractory chronic idiopathic urticaria identified 29 studies (5 randomized controlled trials) and concluded that omalizumab appears to be a safe and effective treatment for this condition; however, the authors called for confirmation in larger, longer-term studies that include children and pregnant women before omalizumab becomes the preferred treatment in antihistamine-refractory cases. (78) (EG 1) Review articles note that omalizumab is a safe and effective treatment for chronic idiopathic urticaria. (79) (80) (EG 2) European consensus guidelines concluded that there is strong evidence for omalizumab as a third-level treatment for chronic urticaria refractory to standard therapy. (66)(80)(81) (EG 2)

Inconclusive or Non-Supportive Evidence

For allergic bronchopulmonary aspergillosis in cystic fibrosis, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. (RG B) Review articles suggest a potential role for omalizumab in allergic bronchopulmonary aspergillosis in cystic fibrosis; however, efficacy in many reported cases was only partial and transitory, and review articles conclude that additional randomized studies are necessary. (7)(8)(9)(10) (EG 2) A systematic review and meta-analysis studying the use of anti-IgE therapy for patients with allergic bronchopulmonary aspergillosis in cystic fibrosis found only a single study with 14 patients and concluded that evidence is currently lacking for assessing both efficacy and safety of omalizumab for this indication. (11) (EG 1) A randomized controlled study of 13 patients with allergic bronchopulmonary aspergillosis featured a crossover design for all patients between omalizumab and placebo. While on omalizumab, patients had significantly fewer disease exacerbations, as well as significantly improved exhaled nitric oxide and basophil immunologic parameters, although the authors cautioned that this was a small study. (12) (EG 1)

For allergic rhinitis, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. (RG B) Review articles have concluded that despite favorable outcomes of omalizumab as compared with placebo in nonasthmatic patients with allergic rhinitis, further studies are needed. (7)(9)(13) (EG 2) Another review article endorses the use of omalizumab for allergic rhinitis only for those age 12 years and older with concomitant allergic asthma. (14) (EG 2) A consensus-based specialty guideline noted that omalizumab should not be used as monotherapy for allergic rhinitis. (15) (EG 2)

For asthma (nonatopic), evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. (RG B) Several studies suggest that either inflammatory markers or symptoms may mildly improve in patients with nonatopic asthma who receive omalizumab, but strong outcome data from randomized controlled studies are lacking. (7)(16)(17) (EG 1) A review article concludes that while some evidence suggests that patients with nonatopic asthma may benefit from omalizumab, the evidence is not strong enough to systematically recommend its use. (18) (EG 2) A systematic review and meta-analysis of interventions to reduce asthma exacerbations requiring hospitalizations or oral corticosteroid use in autumn in children identified one study evaluating omalizumab vs placebo or inhaled corticosteroid boost. Omalizumab started 4 to 6 weeks prior to school return was associated with a reduction in oral steroid use or hospitalization during the first 90 days after school return compared with placebo (11% vs 21%, respectively); however, in children with milder asthma (ie, requiring step 2 to step 4 therapy), omalizumab treatment was comparable to inhaled corticosteroid boost and placebo. The authors called for further research to be performed. (19) (EG 1)
For atopic dermatitis, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. (RG B) A double-blind randomized controlled pilot study of 20 patients comparing omalizumab with placebo reported that omalizumab did not improve clinical disease parameters despite a reduction in serum IgE and improvement in atopy patch testing. The authors concluded that the lack of clinical efficacy points to the complexity of the disease, which may not be solely IgE dependent. (20) (EG 1) A randomized controlled study of 8 patients with severe refractory atopic dermatitis found comparable clinical outcome improvement in both placebo and active treatment groups. (21) (EG 1) Uncontrolled case series suggest possible efficacy of omalizumab alone or with other agents such as rituximab, but additional confirmatory randomized controlled studies are required. (9)(22)(23)(24) (EG 2)

For chronic rhinosinusitis, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. (RG B) A randomized controlled trial of 14 patients with chronic rhinosinusitis found evidence that IgE may play a small role, at best, in the pathogenesis of disease, but the authors stated that larger studies are needed. (25) (EG 1) Review articles state that while initial studies did not find any significant improvement after treatment with omalizumab, further studies in patients with concomitant allergic asthma found significant improvement in nasal polyposis, CT scan results, and chronic rhinosinusitis symptoms, suggesting the possible existence of different disease subtypes for which additional research is needed to determine which patients might benefit the most from treatment. (26)(27) (EG 2)

For eosinophil-associated gastrointestinal disorders, including food allergy, eosinophilic esophagitis, gastroenteritis, or colitis, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. (RG B) In a double-blind randomized controlled study of 57 patients with an allergy to cow's milk who were also receiving oral immunotherapy, administration of omalizumab over a period of 28 months was associated with a significant improvement in safety (adverse event rate during escalation of concomitant oral immunotherapy), but not in efficacy (desensitization and sustained unresponsiveness). The authors indicated that further study is needed. (28) (EG 1) A case series of 13 children with severe peanut allergy found that omalizumab appeared to be effective in facilitating rapid oral desensitization, but the authors cautioned that additional randomized studies are required. (29) (EG 2) Review articles have noted that studies suggest possible efficacy of omalizumab for treatment of food allergy, but indicated that large multicenter confirmatory studies are needed, especially in order to identify patient subgroups that may benefit the most. (30)(31)(32)(33)(34) (EG 2) A review article identified one small randomized controlled trial and one small open-label single-arm study of omalizumab for eosinophilic esophagitis and concluded that omalizumab was not beneficial for these patients. (35) (EG 2)

For use during immunotherapy, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. (RG B) In a study randomizing 248 patients with allergic asthma to either omalizumab or placebo for 11 weeks followed by specific immunotherapy for the offending allergens, significantly fewer of those receiving omalizumab had systemic allergic reactions to immunotherapy (14% vs 26%), and more of those receiving omalizumab were able to reach the target maintenance immunotherapy dose (87% vs 72%). However, antihistamine use was at investigator discretion, which may have introduced bias. Further study is required. (36) (EG 1) Review articles indicate that while omalizumab may be effective and well tolerated in some patients during immunotherapy, additional randomized studies are required. (37)(38)(39)(40) (EG 2) A consensus-based specialty society guideline noted that omalizumab in combination with allergen immunotherapy may be considered for highly poly-allergen-sensitive allergic rhinitis patients at increased risk of anaphylaxis; however, the authors note that this treatment is not routinely performed in clinical practice. (15) (EG 2)

For chronic inducible urticaria, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. (RG B) A systematic review of treatment options for chronic inducible urticaria (including cold urticaria, symptomatic dermographism, and delayed pressure urticaria) identified one randomized controlled trial that evaluated omalizumab to treat symptomatic dermographism; heterogeneity of outcomes, small sample sizes, and poor reporting quality hindered the conclusions that could be drawn for the various interventions, including omalizumab. (41) (EG 1) A systematic review of omalizumab for chronic inducible urticaria identified 2 randomized controlled trials (86 patients) and concluded that there is evidentiary support for the use of omalizumab in therapy-refractory inducible chronic urticaria. Limitations include the small numbers of patients, study design, significant bias, and heterogeneity; further study was recommended. (42) (EG 1)

References

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Footnotes

[A] For allergic asthma, Omalizumab is administered as a subcutaneous injection every 2 to 4 weeks, with dosing based on body weight and serum IgE level. (1) Due to the potential for uncommon anaphylactic reaction, patients should be observed for at least 2 hours after each of the first 3 injections and for at least 30 minutes after each subsequent injection. (53) [A in Context Link 1]

[B] If a patient is at high risk for intestinal helminth infection (including Ascaris lumbricoides, Trichuris trichiura, hookworm, and Strongyloides stercoralis) due to prolonged exposure in an endemic area or a history of Strongyloides stercoralis infection with ongoing exposure, screening should be considered before the initiation of therapy and continued in an ongoing fashion, given the presumed role of IgE in protecting against helminths. (1)(54) [B in Context Link 1, 2, 3]
For chronic idiopathic urticaria, Omalizumab is administered as a subcutaneous injection every 4 weeks. Due to the potential for uncommon anaphylactic reaction, patients should be observed for at least 2 hours after each of the first 3 injections and for at least 30 minutes after each subsequent injection.

**Codes**

**HCPCS:** J2357