Reference number(s)
2546-A

STANDARD MEDICARE PART B MANAGEMENT

XOLAIR (omalizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Allergic Asthma
   Treatment of moderate to severe persistent asthma in 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

2. Chronic Spontaneous Urticaria (CSU)
   Treatment of chronic spontaneous urticaria in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment

3. Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)
   Xolair is indicated for add-on maintenance treatment of nasal polyps in adult patients 18 years of age and older with inadequate response to nasal corticosteroids.

Limitations of use
1. *Not indicated for other allergic conditions or other forms of urticaria*
2. *Not indicated for relief of acute bronchospasm or status asthmaticus*

B. Compendial Uses
1. Prophylaxis of seasonal or perennial allergic rhinitis
2. Anaphylaxis prophylaxis for patients with peanut allergies at risk for accidental exposure
3. Latex allergy prophylaxis for patients unable to avoid latex
4. Adjunct to immunotherapy for seasonal allergic rhinitis
5. Immune checkpoint inhibitor-related toxicities
6. Systemic mastocytosis

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions:

A. Asthma:
   1. Initial Requests:
      i. Member's chart notes or medical record showing pre-treatment IgE level
      ii. Chart notes, medical record documentation, or claims history supporting previous medications tried including drug, dose, frequency, and duration. If therapy is not advisable, documentation of clinical reason to avoid therapy
   2. Continuation requests: Chart notes or medical record documentation supporting benefit from therapy
B. CSU:
   1. Initial Requests: Chart notes, medical record documentation, or claims history showing prior therapy with a second-generation H1 antihistamine
   2. Continuation Requests: Chart notes or medical record documentation supporting benefit from therapy
C. CRSwNP:
   1. Initial Requests:
      i. Member's chart notes or medical record showing nasal endoscopy, anterior rhinoscopy, or computed tomography (CT) details (e.g., location, size), or Meltzer Clinical Score or endoscopic nasal polyp score (NPS) (where applicable).
      ii. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy
   2. Continuation Requests: Chart notes or medical record documentation supporting benefit from therapy
D. Immune checkpoint inhibiter-related toxicity:
   1. Initial Requests: Member's chart notes or medical record showing pre-treatment IgE level
   2. Continuation Requests: Chart notes or medical record documentation supporting benefit from therapy
E. Systemic mastocytosis:
   1. Initial Requests:
      i. Chart notes or medical record documentation supporting diagnosis of systemic mastocytosis
      ii. Chart notes, medical record documentation, or claims history of prerequisite therapies (if applicable)
   2. Continuation Requests: Chart notes or medical record documentation supporting benefit from therapy
F. Prophylaxis of seasonal or perennial allergic rhinitis
   1. Initial Requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy
   2. Continuation Requests: Chart notes or medical record documentation supporting benefit from therapy
G. Peanut allergy anaphylaxis prophylaxis and latex allergy prophylaxis:
   1. Initial Requests: Chart notes or medical record documentation of allergy
   2. Continuation Requests: Chart notes or medical record documentation supporting benefit from therapy
H. Adjunct to immunotherapy for seasonal allergic rhinitis:
   1. Initial Requests: Chart notes or medical record documentation of immunotherapy use
   2. Continuation Requests: Chart notes or medical record documentation supporting benefit from therapy

III. CRITERIA FOR INITIAL APPROVAL

A. Allergic asthma

Authorization of 12 months may be granted for treatment of allergic asthma when all of the following criteria are met:
1. Member is 6 years of age or older.
2. Member has a history of moderate to severe asthma despite current treatment with both of the following medications at optimized doses, unless the member has a clinical reason to avoid these therapies:

   i. Inhaled corticosteroid
   ii. Additional controller (i.e., long acting beta$_2$-agonist, long acting muscarinic antagonist, leukotriene modifier, or sustained-release theophylline)
3. Member has a positive skin test or in vitro reactivity to at least one perennial aeroallergen.
4. Member has a pre-treatment IgE level greater than or equal to 30 IU/mL.
5. Member will not use the requested medication concomitantly with other biologics indicated for asthma (e.g., Cinqair, Dupixent, Fasenra, Nucala, Tezspire).

B. Chronic spontaneous urticaria (CSU)

Authorization of 12 months may be granted for treatment of chronic spontaneous urticaria when all of the following are met:

1. Member is 12 years of age or older.
2. Member has experienced a spontaneous onset of wheals (hives), angioedema, or both, for at least 6 weeks.
3. Member remains symptomatic despite treatment with a second-generation H_1 antihistamine (e.g., cetirizine, fexofenadine, levocetirizine, loratadine) for at least 2 weeks.
4. Member has been evaluated for other causes of urticaria, including bradykinin-related angioedema and interleukin-1-associated urticarial syndromes (auto-inflammatory disorders, urticarial vasculitis).

C. Chronic rhinosinusitis with nasal polyps (CRSwNP)

Authorization of 12 months may be granted for treatment of CRSwNP when all of the following criteria are met:

1. Member is 18 years of age or older.
2. Member has bilateral nasal polyposis and chronic symptoms of sinusitis despite intranasal corticosteroid treatment for at least 2 months unless contraindicated or not tolerated.
3. Member has one of the following:
   i. A bilateral nasal endoscopy, anterior rhinoscopy, or computed tomography (CT) showing polyps reaching below the lower border of the middle turbinate or beyond in each nostril
   ii. Meltzer Clinical Score of 2 or higher in both nostrils
   iii. A total endoscopic nasal polyp score (NPS) of at least 5 with a minimum score of 2 for each nostril
4. Member has symptoms of nasal blockage, congestion or obstruction plus one of the following additional symptoms:
   i. Rhinorrhea (anterior/posterior)
   ii. Reduction or loss of smell
   iii. Facial pain or pressure
5. Member will continue to use a daily intranasal corticosteroid while being treated with the requested medication, unless contraindicated or not tolerated.
6. Member will not use the requested medication concomitantly with other biologics indicated for nasal polyps (e.g., Dupixent, Nucala).

D. Immune checkpoint inhibitor-related toxicity

Authorization of 1 month may be granted for treatment of immune checkpoint inhibitor-related toxicity when both of the following are met:

1. The member has a refractory case of immune-therapy related severe (G3) pruritus.
2. The member has elevated IgE levels.

E. Systemic mastocytosis

Authorization of 12 months may be granted for the treatment of systemic mastocytosis when both of the following are met:

1. The major and at least one minor diagnostic criterion for systemic mastocytosis are present or three or more minor diagnostic criteria are present (see Appendix).
2. The requested medication will be used in any of the following treatment settings:
   i. Used as stepwise prophylactic treatment for chronic mast cell mediator-related cardiovascular and pulmonary symptoms when the member has tried both of the following:
      a. H1 blockers and H2 blockers
      b. Corticosteroids
   ii. Used for prevention of unprovoked anaphylaxis
   iii. Used for prevention of hymenoptera or food-induced anaphylaxis, with negative specific IgE or negative skin test
   iv. Used improve tolerability of venom immunotherapy

F. Prophylaxis of seasonal or perennial allergic rhinitis
Authorization of 12 months may be granted for prophylaxis of seasonal or perennial allergic rhinitis in patients who previously had inadequate symptom control with a combination of intranasal steroids and an intranasal antihistamine.

G. Peanut allergy anaphylaxis prophylaxis
Authorization of 12 months may be granted for prophylaxis of anaphylaxis due to a peanut allergy in patients with a history of immediate hypersensitivity.

H. Latex allergy prophylaxis
Authorization of 12 months may be granted for the prophylaxis of latex allergy symptoms in patients with a proven latex allergy and who are unable to avoid occupational latex (e.g., healthcare workers).

I. Adjunct to immunotherapy
Authorization of 3 months may be granted as an adjunct to immunotherapy for seasonal allergic rhinitis.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization of 12 months may be granted when all of the following criteria are met:
A. The member is currently receiving therapy with the requested medication.
B. The requested medication is being used to treat an indication enumerated in Section III.
C. The member is receiving benefit from therapy.
D. Member will not use the requested medication concomitantly with other biologics indicated for asthma or CRSwNP (e.g., Cinqair, Dupixent, Fasenra, Nucala, Tezspire).

V. APPENDIX

2017 WHO Diagnostic Criteria for Systemic Mastocytosis
A. Major Criteria: multifocal, dense infiltrates of mast cells (at least 15 mast cells in aggregates) detected in sections of bone marrow and/or other extracutaneous organs
B. Minor Criteria
   1. In biopsy sections of bone marrow or other extracutaneous organs, greater than 25% of mast cells in the infiltrate are spindle-shaped or have atypical morphology, or greater than 25% of all mast cells in bone marrow aspirate smears are immature or atypical

2. Detection of an activating point mutation at codon 816 of KIT in the bone marrow, blood, or another extracutaneous organ
3. Mast cells in bone marrow, blood, or other extracutaneous organs express CD25, with or without CD2, in addition to normal mast cell markers
4. Serum total tryptase persistently greater than 20 ng/mL (unless there is an associated myeloid neoplasm, in which case this parameter is not valid)

VI. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:

1. The prescribing information for Xolair.
2. The available compendium
   A. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
   B. Micromedex DrugDex
   C. American Hospital Formulary Service- Drug Information (AHFS-DI)
   D. Lexi-Drugs
3. Global Initiative for Asthma (GINA): Global Strategy for Asthma Management and Prevention
4. Managing asthma in adolescents and adults: 2020 asthma guideline update from the National Asthma Education and Prevention Program
5. Clinical Practice Guideline: Allergic Rhinitis

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Xolair are covered in addition to the following:

1. Prophylaxis of seasonal or perennial allergic rhinitis
2. Anaphylaxis prophylaxis for patients with peanut allergies at risk for accidental exposure
3. Adjunct to immunotherapy for seasonal allergic rhinitis
4. Immune checkpoint inhibitor-related toxicities
5. Systemic mastocytosis

VII. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Xolair for allergic asthma can be found in the manufacturer's prescribing information, the Global Initiative for Asthma (GINA): Global strategy for asthma management and prevention guidelines, and the guideline update from the National Asthma Education and Prevention Program. The prescribing information indicates the minimum labeled age for Xolair is six years of age. Xolair should be used in patients whose symptoms are inadequately controlled with inhaled corticosteroids. According to the 2022 update of the GINA Global Strategy for asthma management and prevention, Xolair should be considered as an add-on therapy that is uncontrolled on other medications such as long-acting beta2-agonists, leukotriene receptor antagonists, tiotropium, or inhaled corticosteroids-formoterol maintenance and reliever therapy (MART).

Support for the above criteria for using Xolair to treat chronic spontaneous urticaria can be found in the manufacturer's prescribing information, the 2014 guidelines for the diagnosis and management of acute and chronic urticaria (Bernstein et al), and the EAACI/GA(2) LEN/EDF/WAO guideline for the definition, classification, diagnosis, and management of urticaria. The guidelines differentiate between several different causes of urticaria (autoinflammatory disorders, urticarial vasculitis, HAE) and the treatment for these

indications differ from the treatment for chronic spontaneous urticaria. Zuberbier et al suggest using 2nd generation H1 antihistamines over 1st generation H1 antihistamines for the treatment of chronic urticaria. Bernstein et al indicate patients with episodes of urticaria that last greater than six weeks meet the definition of chronic urticaria. The first step for treating chronic urticaria is monotherapy with second generation antihistamines and avoidance of triggers and relevant physical factors if physical urticaria/angioedema syndrome is present. The second step is dose advancement of the second-generation antihistamine, addition of another antihistamine, addition of an H2-antagonist, addition of a leukotriene antagonist or addition of a 1st generation antihistamine at bedtime. The guideline indicates omalizumab should be used in chronic urticaria refractory to these therapies.

The prescribing information for Xolair as well as the European Forum for Research and Education in Allergy and Airway Diseases (Bachert et al) support using Xolair to treat nasal polyps. The prescribing information indicates Xolair should be used to treat chronic rhinosinusitis with nasal polyps in patients 18 years of age and older with inadequate response to nasal corticosteroids (e.g., mometasone). In the CRSwNP Trial cited in the package insert, patients used nasal mometasone for a 5 week run in period as well as during the treatment period with Xolair. Prior to randomization, patients were required to have evidence of bilateral polyps as determined by a nasal polyp score (NPS) ≥ 5 with NPS of 2 in each nostril, despite use of nasal mometasone during the run-in period. NPS was measured via endoscopy and scored (range 0-4 per nostril: 0= no polyps; 1=small polyps in the middle meatus not reaching below the inferior border of the middle turbinate; 2=polyps reaching below the lower border of the middle turbinate; 3=large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle turbinate; 4=large polyps causing complete obstruction of the inferior nasal cavity) for a total NPS (range 0-8). Patients were furthermore required to have a weekly average of nasal congestion score (NCS) > 1 prior to randomization, despite use of nasal mometasone. The co-primary endpoints in Trials 1 and 2 were NPS and average daily NCS at Week 24. In both trials, patients who received XOLAIR had a statistically significant greater improvement from baseline at Week 24 in NPS and weekly average NCS, than patients who received placebo. The greater improvements in NPS and NCS in the XOLAIR group compared to the placebo group were observed as early as the first assessment at Week 4 in both studies cited in the prescribing information. XOLAIR had statistically significant improvements on sense of smell score compared to placebo. Sense of smell was measured by a daily assessment on a 0 to 3 point severity scale (0=no symptoms, 1=mild symptoms, 2=moderate symptoms, 3=severe symptoms). The LS mean difference for change from baseline at Week 24 in sense of smell score in XOLAIR compared to placebo was -0.3 (95% CI: -0.6, -0.1) in Trial 1 and -0.5 (95% CI: -0.7, -0.2) in Trial 2. XOLAIR had statistically significant improvements on post-nasal drip compared to placebo. The LS mean difference for change from baseline at Week 24 in post-nasal drip score in XOLAIR compared to placebo was -0.6 (95% CI: -0.8, -0.3) in Trial 1 and -0.5 (95% CI: -0.8, -0.3) in Trial 2. XOLAIR had statistically significant improvements on runny nose compared to placebo. The LS mean difference for change from baseline at Week 24 in runny nose score in XOLAIR compared to placebo was -0.4 (95% CI: -0.7, -0.2) in Trial 1 and -0.6 (95% CI: -0.9, -0.4) in Trial 2.

Support for using Xolair for prophylaxis of season or perennial allergic rhinitis can be found in a multicenter, open-label study by Nayak et al, conducted during ragweed season, 287 patients (aged 12 to 75) received subQ omalizumab 300 mg every 3 (IgE greater than 150 international units/mL or 4 weeks (IgE less than or equal to 150 international units/mL) for 12 weeks beginning 2 weeks prior to ragweed season. Chlorpheniramine 4 mg and fexofenadine 60 mg was permitted as rescue medicine. Overall use of rescue medicine in both groups was very low, 84 of 287 (29.3%). At least one adverse event occurred in 47.4% of patients; headache, upper respiratory tract infection and viral infection were most commonly reported. There were no severe adverse events related to omalizumab therapy.
In a phase 3, randomized, double-blind, parallel-group design by Chervinsky et al, efficacy and safety of subQ omalizumab (minimum dose 0.016 mg/kg/IgE (international units/mL) per 4 weeks) was investigated in 289 patients with moderate-to-severe PAR. All patients had a positive skin prick test, total serum IgE level of 30 to 700 international units/mL, and were chronically exposed to dust mites, dog or cat allergens. Patients ranged

from 12 to 75 years of age and had the following relevant comorbid conditions: 26% with history of asthma; 17% with history of atopic dermatitis; 58% with history of intranasal steroid use; 37% had attempted desensitizing immunotherapy. Using a mean daily nasal severity score (range, 0 to 3; mean of 4-point scores for sneezing, itchy, runny, and stuffy nose) as the primary efficacy variable and compared to placebo, omalizumab was associated with larger improvements in symptoms at each of the 4-week visits and for the overall 16-week treatment period (p less than 0.001 for each). In addition, treated patients were more likely to shift to a less severe symptom category compared to the established baseline severity rating (p=0.001); symptoms were considered controlled in 28% of those on active treatment vs 10% of those on placebo. In post hoc analysis in subgroups of patients who had either previously failed desensitization or intranasal steroids, the favorable effects of omalizumab on nasal symptoms persisted. Furthermore, treated patients required antihistamines on statistically significantly fewer days than those on placebo (p=0.005), although the clinical and economic merits of the small reduction may be questioned (maximum difference between the range of days of rescue medication use was 1.2 days per month, and the proportion of rescue days reached statistically significant difference only during week 8). Other secondary measures that showed favorable improvements in the omalizumab group were quality of life measures, including larger differences deemed clinically important, and patients' global evaluation of treatment efficacy. About half of treated patients reported complete control or marked improvement in symptoms, in contrast to that degree of control in only 34% of those on placebo. Omalizumab treatment was well tolerated with the following notable occurrences: 1 patient discontinued the study due to urticaria and 1 patient experienced infectious mononucleosis, although the latter was not attributed to drug therapy. No anti-omalizumab antibodies were detected in patients' sera, and no adverse events suggested drug-induced immunologic reactions.

Support for using Xolair as anaphylaxis prophylaxis for patients with peanut allergies at risk for accidental exposure can be found in a randomized trial (n=82) by Leung et al, omalizumab 450 mg significantly increased the threshold of peanut sensitivity following an oral food challenge, compared with placebo in patients with a history of peanut allergy. Patients (12 to 60 years) with a history of immediate hypersensitivity to peanut were randomized to receive either placebo or omalizumab 150 mg, 300 mg, or 450 mg subQ every 4 weeks for 4 doses. Within 2 to 4 weeks after the last dose, patients underwent an oral food challenge with peanut flour. Among the groups, the mean baseline threshold of sensitivity to peanut flour was 178 to 436 mg. Following oral food challenge, the mean increases in sensitivity thresholds were 710 mg, 913 mg, 1650 mg, and 2627 mg in the placebo group, omalizumab 150-mg group, 300-mg group, and 450-mg group, respectively. Compared with placebo, the mean increase in peanut sensitivity threshold was only significant in the omalizumab 450-mg group; however, a strong trend was associated with increasing doses. In the omalizumab 450-mg group, the results equate to an increase in the threshold of sensitivity to peanut from approximately half a peanut (178 mg) to nearly 9 peanuts (2805 mg). Omalizumab was well tolerated, with similar incidence and spectrum of adverse events in omalizumab and placebo groups. Since the average amount of peanut ingested in an accidental exposure is believed to be no more than 1 or 2 peanuts, the sensitivity thresholds achieved in the omalizumab 300-mg and 450-mg groups (6 and 8 peanuts, respectively) should provide considerable protection in most patients.

Support for using Xolair as latex allergy prophylaxis in healthcare workers exposed to latex on a daily basis can be found in a randomized study conducted by Leynadier and colleagues. Sixteen healthcare workers with documented allergy (positive skin prick test response; elevated Ig E serum levels [30 to 700 international units/mL]) were randomized to receive either placebo or omalizumab subcutaneously every 2 to 4 weeks for 16 weeks, after which all patients could continue or start omalizumab therapy for another 16 weeks. Omalizumab was dosed according to body weight and serum IgE levels and ranged from 150 to 750 mg monthly. Efficacy was measured by mean conjunctival challenge test total score, which is the sum (rated from 0, absent to 3, severe) of physician-evaluated eye redness, eyelid swelling, chemosis, and tearing and patient-rated itching (1, mild to 4, incapacitating). A score of 7 or less is considered normal. Mean score from baseline to week 16 decreased significantly in patients receiving omalizumab compared with placebo (from 10 to 5 vs

from 9.67 to 9). Overall ocular response rate after 32 weeks, was 93.8% (15 of 16 patients). Furthermore, 11 of 15 patients had negative response to a latex glove challenge after 32 weeks of treatment, with the remaining 4 having a mild response.

Support for using Xolair as an adjunct to immunotherapy for seasonal allergic rhinitis can be found in a 4-arm, double-blind, parallel-group, placebo-controlled trial by Casale et al found pretreatment with omalizumab significantly decreases the adverse effects associated with rush immunotherapy. Adult patients (n=159; ages 18 to 50 years) with a minimum 2-year history of ragweed allergic rhinitis and no recent immunotherapy were randomized to receive either immunotherapy and omalizumab, placebo immunotherapy and omalizumab, immunotherapy and placebo omalizumab, or placebo immunotherapy and placebo omalizumab. The dose of omalizumab was 0.016 mg/kg/IgE (international units/mL)/month subQ every 2 to 4 weeks, depending on weight and baseline IgE levels. Rush immunotherapy consisted of ragweed extract in increasing doses up to a maximal dose of 1.2 to 4 mcg Amb a 1 within a 3-hour period, one time. Immunotherapy consisted of weekly short ragweed extract injections in increasing doses over 4 weeks, then 8 weeks of a maintenance dose. Patients in each arm underwent 9 weeks of pretreatment with omalizumab or placebo, followed by rush immunotherapy or placebo. Each arm then underwent 12 weeks in 1 of the 4 treatment arms. Patients that received omalizumab in addition to rush immunotherapy had less adverse effects than patients receiving immunotherapy by itself. In post hoc analysis of the groups receiving rush immunotherapy, the addition of omalizumab was associated with an odds ratio of 0.17 (p=0.026) for anaphylaxis compared to groups not receiving omalizumab. Severity scores during the ragweed season were significantly improved in patients that received both omalizumab and immunotherapy compared to those who received immunotherapy by itself (0.69 vs 0.86; p=0.044)

Support for using Xolair for systemic mastocytosis can be found in the National Comprehensive Cancer Network's guideline for systemic mastocytosis. The NCCN Guideline for systemic mastocytosis supports the use of Xolair as a stepwise prophylactic treatment for chronic mast cell mediator-related cardiovascular and pulmonary symptoms. Xolair can also be used for the prevention of the following: unprovoked anaphylaxis, hymenoptera or food-induced anaphylaxis with negative specific IgE or negative skin test, or to improve tolerance while on immunotherapy.

Support for using Xolair for the management of immunotherapy-related toxicities can be found in the National Comprehensive Cancer Network's guideline for management of immunotherapy-related toxicities. The NCCN Guideline supports the use of Xolair for the management of refractory cases of immunotherapy-related severe (G3) pruritus with increased IgE levels.

VIII. REFERENCES

1. Xolair [package insert]. South San Francisco, CA: Genentech, Inc.; March 2023.
2. Micromedex (electronic version). IBM Watson Health. Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/ (March 16, 2023).
3. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2022 update. Available at: https://ginasthma.org/wp-content/uploads/2022/07/GINA-Main-Report-2022-FINAL-22-07-01-WMS.pdf. Accessed March 1, 2023.
4. Cloutier MM, Dixon AE, Krishnan JA, et al. Managing asthma in adolescents and adults: 2020 asthma guideline update from the National Asthma Education and Prevention Program. *JAMA.* 2020;324(22): 2301-2317.
5. Maurer M, Rosen K, Hsieh HJ, et al. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. *N Engl J Med*. 2013;368(10):924-935.
6. Seidman MD, Gurgel RK, Lin SY, et al. Clinical Practice Guideline: Allergic Rhinitis. *Otolaryngology – Head and Neck Surg*. 2015;151(IS):S1-S43.

7. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed March 16, 2023.
8. Bernstein DI, Blessing-Moore J, Cox L, et al. The diagnosis and management of acute and chronic urticaria: 2014 update. American Academy of Allergy, Asthma & Immunology Practice Parameter. http://www.aaaai.org/practice-resources/statements-and-practice-parameters/practice-parameter-guidelines.aspx. Accessed March 16, 2023.
9. Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA^{2}LEN/EDF/WAO guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy.* 2018;73(7):1393-1414. doi: 10.1111/all.13397.
10. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Systemic Mastocytosis. Version 2.2022. https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf. Accessed March 16, 2023.
11. Bachert C, Han JK, Wagenmann M, et al, EUFOREA expert board meeting on uncontrolled severe chronic rhinosinusitis with nasal polyps (CRSwNP) and biologics: Definitions and management. *J Allergy Clin Immunol.* 2021;147(1):29-36.
12. WJ Fokkens, VJ Lund, C Hopkins, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. *Rhinology.* 2020;58(Suppl S29):1-464.
13. Hopkins C. Chronic Rhinosinusitis with Nasal Polyps. *N Engl J Med.* 2019;381(1):55-63.
14. Nayak A, Casale T, Miller SD, et al: Tolerability of retreatment with omalizumab, a recombinant humanized monoclonal anti-IgE antibody, during a second ragweed pollen season in patients with seasonal allergic rhinitis. Allergy Asthma Proc 2003; 24(5):323-329.
15. Chervinsky P, Casale T, Townley R, et al: Omalizumab, an anti-IgE antibody, in the treatment of adults and adolescents with perennial allergic rhinitis. Ann Allergy Asthma Immunol 2003; 91(2):160-167.
16. Leung DYM, Sampson HA, Yunginger JW, et al: Effect of anti-IgE therapy in patients with peanut allergy. N Engl J Med 2003; 348:986-993.
17. Casale TB, Busse WW, Kline JN, et al: Omalizumab pretreatment decreases acute reactions after rush immunotherapy for ragweed-induced seasonal allergic rhinitis. J Allergy Clin Immunol 2006; 117(1):134-140.
18. Leynadier F, Doudou O, Gaouar H, et al: Effect of omalizumab in health care workers with occupational latex allergy. J Allergy Clin Immunol 2004; 113(2):360-361.