When H1 antihistamines are not enough, help patients aged ≥12 years with CSU

MOVE FORWARD WITH PROVEN RELIEF FROM ITCH AND HIVES[1,2]*

THE ONLY ONCE-MONTHLY CSU TREATMENT[1,3]

*Reductions from baseline in mean weekly itch severity score (Study 1: XOLAIR 150 mg, -6.66; XOLAIR 300 mg, -9.40) and mean weekly hive count score (Study 1: XOLAIR 150 mg, -7.78; XOLAIR 300 mg, -11.35) were observed in 2 placebo-controlled, multiple-dose efficacy and safety studies at Week 12 (Study 1: 24 weeks, N=319; Study 2: 12 weeks, N=322).[1]

Models are for illustrative purposes only. Individual results may vary.

CSU=chronic spontaneous urticaria.

INDICATION

XOLAIR® (omalizumab) is indicated for the treatment of chronic spontaneous urticaria (CSU) in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment.

Limitations of Use: XOLAIR is not indicated for treatment of other forms of urticaria.

IMPORTANT SAFETY INFORMATION

WARNING: Anaphylaxis

Anaphylaxis presenting as bronchospasm, hypotension, syncope, urticaria, and/or angioedema of the throat or tongue, has been reported to occur after administration of XOLAIR. Anaphylaxis has occurred as early as after the first dose of XOLAIR, but also has occurred beyond 1 year after beginning regularly administered treatment. Because of the risk of anaphylaxis, initiate XOLAIR therapy in a healthcare setting and closely observe patients for an appropriate period of time after XOLAIR administration. Health care providers administering XOLAIR should be prepared to manage anaphylaxis which can be life-threatening. Inform patients of the signs and symptoms of anaphylaxis and instruct them to seek immediate medical care should symptoms occur. Selection of patients for self-administration of XOLAIR should be based on criteria to mitigate risk from anaphylaxis.

Xolair® Omalizumab

FOR SUBCUTANEOUS USE 150 mg ▪ 300 mg

Please see full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.

Primary efficacy analysis: Relief by

12 WEEKS[4]

Placebo	XOLAIR 150 mg	XOLAIR 300 mg
26%	48%	67%

Post hoc analysis*:

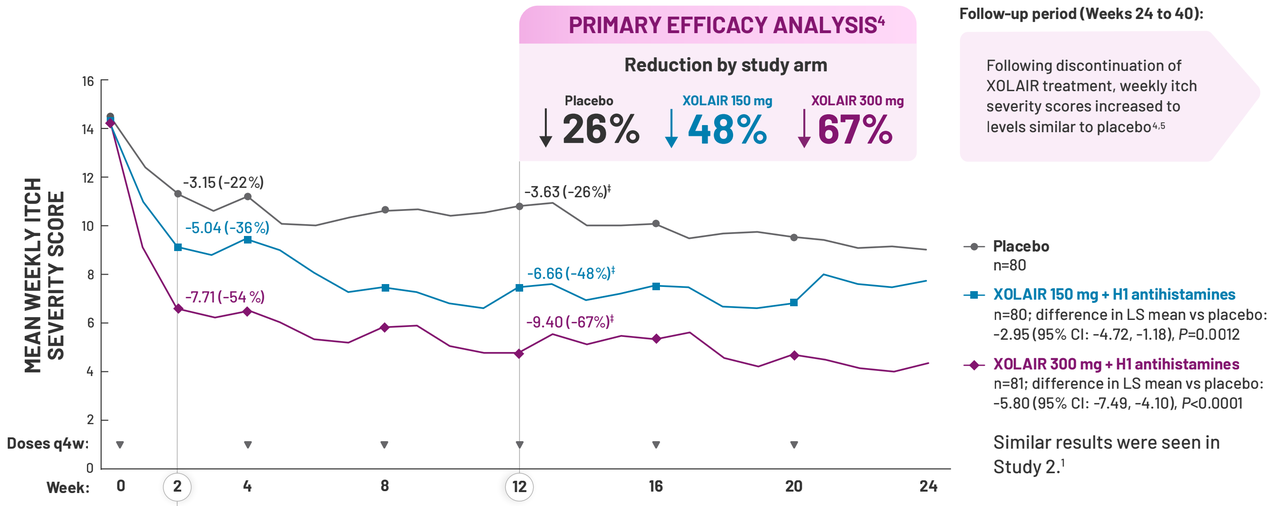
OBSERVED AS EARLY AS 2 WEEKS[4]

Placebo	XOLAIR 150 mg	XOLAIR 300 mg
22%	36%	54%

*See limitations language. →

RELIEF BY WEEK 12, OBSERVED AS EARLY AS 2 WEEKS AFTER THE FIRST DOSE[1,4,5]

Demonstrated reductions in mean weekly itch severity score at Week 12 in Study 1 (N=241)†



Follow-up period (Weeks 24 to 40):

Following discontinuation of XOLAIR treatment, weekly itch severity scores increased to levels similar to placebo[4,5]

- **Placebo** n=80
- **XOLAIR 150 mg + H1 antihistamines** n=80; difference in LS mean vs placebo: -2.95 (95% CI: -4.72, -1.18), *P*=0.0012
- **XOLAIR 300 mg + H1 antihistamines** n=81; difference in LS mean vs placebo: -5.80 (95% CI: -7.49, -4.10), *P*<0.0001

Similar results were seen in Study 2.[1]

Week 2: Based on post hoc analysis, reductions by study arm were observed as follows[4]:

Placebo: 22% | **XOLAIR 150 mg: 36%** | **XOLAIR 300 mg: 54%**

Limitations: Itch severity score at Week 2 was not a prespecified endpoint. Limitations of the Week 2 percent reduction from baseline analysis include that it is a post hoc analysis, and should therefore be interpreted with caution.[4]

1 INJECTION once a month[1§]

- **Once-a-month dosing:** Administer XOLAIR 150 mg or 300 mg by subcutaneous injection every 4 weeks
- Dosing of XOLAIR in CSU patients is **not dependent on serum IgE level** (free or total) or body weight
- **Duration of therapy:** The appropriate duration of therapy for CSU has not been evaluated. Periodically reassess the need for continued therapy

According to the **2021 International EAACI/GA²LEN/EuroGuiDerm/APAAACI Guideline for Urticaria,‖** XOLAIR is the next step in the CSU treatment algorithm after H1 antihistamine failure[3]

IMPORTANT SAFETY INFORMATION (cont'd)

CONTRAINDICATIONS

XOLAIR is contraindicated in patients with a severe hypersensitivity reaction to XOLAIR or to any ingredient of XOLAIR.

WARNINGS AND PRECAUTIONS

Anaphylaxis

Anaphylaxis has been reported to occur after administration of XOLAIR in premarketing clinical trials and in postmarketing spontaneous reports. In premarketing clinical trials in patients for a different indication, anaphylaxis was reported in 3 of 3507 (0.1%) patients. Anaphylaxis occurred with the first dose of XOLAIR in two patients and with the fourth dose in one patient. The time to onset of anaphylaxis was 90 minutes after administration in two patients and 2 hours after administration in one patient.

A case-control study in asthma patients showed that, among XOLAIR users, patients with a history of anaphylaxis to foods, medications, or other causes were at increased risk of anaphylaxis associated with XOLAIR, compared to those with no prior history of anaphylaxis.

Please see full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.

CLINICAL TRIAL DESIGN: STUDIES 1 AND 2

The safety and efficacy of XOLAIR for the treatment of CSU was assessed in 2 placebo-controlled, multiple-dose clinical studies of 24 weeks' duration (CSU Study 1; N=319) and 12 weeks' duration (CSU Study 2; N=322). Patients received XOLAIR 300 mg, 150 mg, 75 mg, or placebo in addition to their baseline level of H1 antihistamine therapy.[1] The 75-mg dose is not approved for use. Concomitant CSU treatments other than H1 antihistamines were not allowed during the study.[1,2,5]

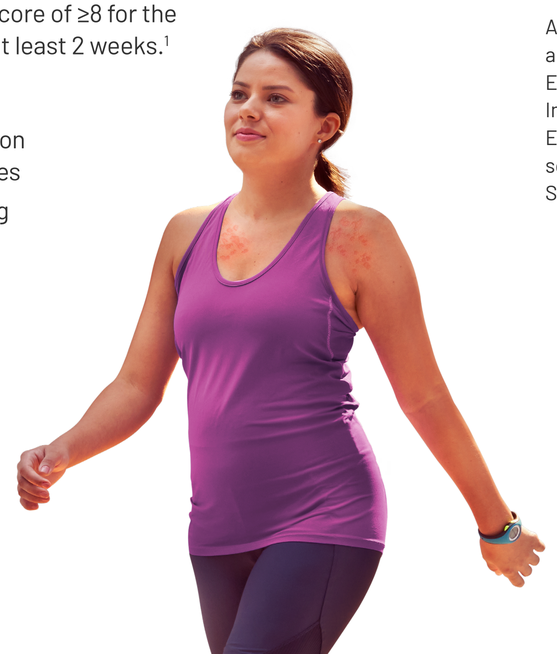
All patients were required to have a UAS7 of ≥16 and a weekly itch severity score of ≥8 for the 7 days prior to randomization, despite having used an H1 antihistamine for at least 2 weeks.[1]

Itch severity‡ and hive count scores[1,4]

- Itch severity and hive count scores were measured twice a day (am and pm) on a scale of 0 (none) to 3 (severe) for itch and 0 (no hives) to 3 (>12 hives) for hives
- Daily itch severity and hive count scores were the average of the morning and evening scores
- Weekly itch severity score (0-21) and hive count score (0-21) were the sum of these daily scores over 7 days

Primary endpoint for Studies 1 and 2

Change from baseline in mean weekly itch severity score at Week 12. Secondary efficacy endpoints across all studies included change from baseline in UAS7 at Week 12 and change from baseline in weekly hive count score at Week 12[2,5]



Model is for illustrative purposes only. Individual results may vary.

†Change from baseline in the weekly itch severity score at Week 12 was the primary endpoint.[4]

‡The weekly itch severity score was calculated for each patient at each week. The mean change from baseline and the mean percentage change in weekly itch severity score were calculated for each treatment group for comparison vs placebo at Week 12.[2,4]

§XOLAIR 300 mg may be administered as one subcutaneous injection of 300 mg/2 mL or as two subcutaneous injections of 150 mg/mL.[1]

‖2021 EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline (Zuberbier T, et al. *Allergy*. 2022).

APAAACI=Asia Pacific Association of Allergy, Asthma and Clinical Immunology; CI=confidence interval; EAACI=European Academy of Allergology and Clinical Immunology; GA²LEN=Global Allergy and Asthma European Network; IgE=immunoglobulin E; LS=least squares; q4w=every 4 weeks; UAS7=Urticaria Activity Score over 7 days.

Xolair® Omalizumab
FOR SUBCUTANEOUS USE 150 mg • 300 mg

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Anaphylaxis (cont'd)

In postmarketing spontaneous reports, the frequency of anaphylaxis attributed to XOLAIR use was estimated to be at least 0.2% of patients based on an estimated exposure of about 57,300 patients from June 2003 through December 2006. Approximately 60% to 70% of anaphylaxis cases have been reported to occur within the first three doses of XOLAIR, with additional cases occurring sporadically beyond the third dose.

Initiate XOLAIR only in a healthcare setting equipped to manage anaphylaxis which can be life-threatening. Observe patients closely for an appropriate period of time after administration of XOLAIR, taking into account the time to onset of anaphylaxis seen in premarketing clinical trials and postmarketing spontaneous reports. Inform patients of the signs and symptoms of anaphylaxis, and instruct them to seek immediate medical care should signs or symptoms occur.

Once XOLAIR therapy has been established, administration of XOLAIR prefilled syringe or autoinjector outside of a healthcare setting by a patient or a caregiver may be appropriate for selected patients. Patient selection, determined by the healthcare provider in consultation with the patient, should take into account the pattern of anaphylaxis events seen in premarketing clinical trials and postmarketing spontaneous reports, as well as individual patient risk factors (e.g. prior history of anaphylaxis), ability to recognize signs and symptoms of anaphylaxis, and ability to perform subcutaneous injections with XOLAIR prefilled syringe or autoinjector with proper technique according to the prescribed dosing regimen and Instructions for Use.

Discontinue XOLAIR in patients who experience a severe hypersensitivity reaction.

Malignancy

Malignant neoplasms were observed in 20 of 4127 (0.5%) XOLAIR-treated patients compared with 5 of 2236 (0.2%) control patients in clinical studies of adults and adolescents (≥12 years of age) for a different indication and other allergic disorders. The observed malignancies in XOLAIR-treated patients were a variety of types, with breast, non-melanoma skin, prostate, melanoma, and parotid occurring more than once, and five other types occurring once each. The majority of patients were observed for less than 1 year. The impact of longer exposure to XOLAIR or use in patients at higher risk for malignancy (e.g., elderly, current smokers) is not known.

A subsequent 5-year observational study of 5007 XOLAIR-treated and 2829 non-XOLAIR-treated adolescent and adult patients for a different indication found that the incidence rates of primary malignancies (per 1000 patient years) were similar in both groups (12.3 vs 13.0, respectively). Study limitations which include the observational study design, the bias introduced by allowing enrollment of patients previously exposed to XOLAIR (88%), enrollment of patients (56%) while a history of cancer or a premalignant condition were study exclusion criteria, and the high study discontinuation rate (44%) preclude definitively ruling out a malignancy risk with XOLAIR.

Corticosteroid Reduction

In CSU patients, the use of XOLAIR in combination with corticosteroids has not been evaluated.

Fever, Arthralgia, and Rash

In post-approval use, some patients have experienced a constellation of signs and symptoms, including arthritis/arthralgia, rash, fever, and lymphadenopathy with an onset 1 to 5 days after the first or subsequent injections of XOLAIR. These signs and symptoms have recurred after additional doses in some patients. Physicians should stop XOLAIR if a patient develops this constellation of signs and symptoms.

Parasitic (Helminth) Infection

Monitor patients at high risk of geohelminth infection while on XOLAIR therapy. Insufficient data are available to determine the length of monitoring required for geohelminth infections after stopping XOLAIR treatment.

Laboratory Tests

Due to formation of XOLAIR:IgE complexes, serum total IgE levels increase following administration of XOLAIR and may remain elevated for up to 1 year following discontinuation of XOLAIR.

Potential Medication Error Related to Emergency Treatment of Anaphylaxis

XOLAIR should not be used for the emergency treatment of allergic reactions, including anaphylaxis. In studies to simulate use, some patients and caregivers did not understand that XOLAIR is not intended for the emergency treatment of allergic reactions, including anaphylaxis. The safety and effectiveness of XOLAIR for emergency treatment of allergic reactions, including anaphylaxis, have not been established. Instruct patients that XOLAIR is for maintenance use to reduce allergic reactions, including anaphylaxis, while avoiding food allergens.

ADVERSE REACTIONS

Chronic Spontaneous Urticaria

The most common adverse reactions (≥2% incidence in XOLAIR-treated patients and more frequent than in placebo) for XOLAIR 150 mg and 300 mg, respectively, included: headache (12%, 6%), nasopharyngitis (9%, 7%), arthralgia (3%, 3%), viral upper respiratory infection (2%, 1%), nausea (1%, 3%), sinusitis (1%, 5%), upper respiratory tract infection (1%, 3%), and cough (1%, 2%).

Injection Site Reactions

Injection site reactions of any severity occurred in more XOLAIR-treated patients (11 patients [2.7%] at 300 mg, 1 patient [0.6%] at 150 mg) compared with 2 placebo-treated patients (0.8%). The types of injection site reactions included: swelling, erythema, pain, bruising, itching, bleeding, and urticaria. None of the events resulted in study discontinuation or treatment interruption.

Injection Site Reactions in Healthy Adults

In an open label trial in healthy adults, in which the 300 mg/2 mL autoinjector was compared to the 300 mg/2 mL prefilled syringe, injection site reactions (e.g., induration, pain, erythema, hemorrhage, swelling, discomfort, bruising, hypoesthesia, edema, pruritus) were observed in 24% (16/66) of subjects treated with the autoinjector compared with 14% (9/64) of subjects treated with the prefilled syringe.

Cardiovascular and Cerebrovascular Events from Clinical Studies in Patients for a Different Indication

A 5-year observational study was conducted in 5007 XOLAIR-treated and 2829 non-XOLAIR-treated patients ≥12 years of age for a different indication to evaluate the long term safety of XOLAIR, including the risk of malignancy. The results suggest a potential increased risk of serious cardiovascular and cerebrovascular events in patients treated with XOLAIR, however the observational study design, the inclusion of patients previously exposed to XOLAIR (88% for a mean of 8 months), baseline imbalances in cardiovascular risk factors between the treatment groups, an inability to adjust for unmeasured risk factors, and the high study discontinuation rate (44%) limit the ability to quantify the magnitude of the risk.

Pregnancy

Data with XOLAIR use in pregnant women are insufficient to inform on drug associated risk.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555 or Novartis Pharmaceuticals Corporation at (888) 669-6682.

Please see full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.

References: 1. XOLAIR. Prescribing information. Genentech USA, Inc. and Novartis Pharmaceuticals Corporation. **2.** Maurer M, Rosén K, Hsieh H-J, et al. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. *N Engl J Med*. 2013;368(10):924-935. **3.** Zuberbier T, Abdul Latiff AH, Abuzakouk M, et al. The international EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy*. 2022;77(3):734-766. **4.** Data on file. Genentech USA, Inc. South San Francisco, CA. **5.** Saini SS, Bindslev-Jensen C, Maurer M, et al. Efficacy and safety of omalizumab in patients with chronic idiopathic/spontaneous urticaria who remain symptomatic on H1 antihistamines: a randomized, placebo-controlled study. *J Invest Dermatol*. 2015;135(1):67-75.

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NOVARTIS

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