Xolair® Omalizumab
FOR SUBCUTANEOUS USE 75 mg • 150 mg • 300 mg

BIO ADVO KIT

BIOLOGIC COORDINATOR ADVOCACY KIT

GUIDEBOOK

Your resource for helpful **access and reimbursement** support

INDICATIONS

XOLAIR® (omalizumab) is indicated for:

- Adults and pediatric patients 6 years of age and older 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.

  Limitations of Use: XOLAIR is not indicated for the relief of acute bronchospasm or status asthmaticus.
- Add-on maintenance treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids.
- The 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 is to be used in conjunction with food allergen avoidance.

  Limitations of Use: XOLAIR is not indicated for the emergency treatment of allergic reactions, including anaphylaxis.
- 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.

Please see front cover, pages 21-23, and accompanying full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.

For more information about these programs and services, visit Genentech-Access.com/XOLAIR or call the **Genentech Patient Resource Center** at **(877) GENENTECH/** (877) 436-3683

What Is the Bio-ADVO Kit Guidebook?

This guidebook was developed to help you identify appropriate **XOLAIR patient support services**. You'll find information outlining the steps and processes needed to effectively utilize the resources available.

For people who need help understanding health insurance coverage and costs related to XOLAIR*:

XOLAIR ACCESS SOLUTIONS

For people who have health insurance and can't afford XOLAIR:

AFFORDABILITY OPTIONS

For people who do not have health insurance coverage or who have concerns about the cost of XOLAIR and meet eligibility criteria†:

GENENTECH PATIENT FOUNDATION

For people who want information and resources about a diagnosis and treatment with XOLAIR:

SUPPORT FOR YOU

*Genentech and Novartis Pharmaceuticals Corporation provide coverage and reimbursement services to patients to help them understand benefits, coverage and reimbursement. Genentech and Novartis Pharmaceuticals Corporation provide these services to patients only after a healthcare provider has prescribed a Genentech product.

†To be eligible for free Genentech medicine from the Genentech Patient Foundation, insured patients who have coverage for their medicine should try to pursue other forms of financial assistance, if available, and meet certain income requirements. Uninsured patients and insured patients without coverage for their medicine must meet a different set of income requirements.

Please see front cover, pages 21-23, and accompanying full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.

TABLE OF CONTENTS

*Independent co-pay assistance foundations have their own rules for eligibility. Genentech and Novartis Pharmaceuticals Corporation have no involvement or influence in independent foundation decision-making or eligibility criteria and does not know if a foundation will be able to help your patient. We can only refer your patient to a foundation that supports their disease state. Genentech and Novartis Pharmaceuticals Corporation do not endorse or show preference for any particular foundation. The foundations to which we refer your patient may not be the only ones that might be able to help.

Xolair® Omalizumab
FOR SUBCUTANEOUS USE 75 mg • 150 mg • 300 mg

Please see front cover, pages 21-23, and accompanying full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.

IMPORTANT SAFETY INFORMATION (cont)

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 with asthma, 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.

SECTION 01

ENROLLMENT

ENROLLING IN XOLAIR PATIENT SUPPORT SERVICES

PRESCRIBERS CHOOSE A FORM BASED ON SPECIFIC PATIENT NEEDS

PATIENTS always complete the Patient Consent Form and
PRESCRIBERS always complete the Prescriber Service Form

ALL PATIENT SITUATIONS

XOLAIR patient support services

If the patient needs:

- Help understanding coverage
- Financial assistance to help pay for their co-pays
- Educational support

Complete the **Prescriber SERVICE Form**

SERVICE

PATIENTS ELIGIBLE FOR FREE MEDICINE

Genentech Patient Foundation

If the patient meets income requirements and has:

- No insurance
- Insurance but no coverage
- Insurance with coverage but is struggling with high out-of-pocket costs and meets eligibility criteria

Complete the **Prescriber FOUNDATION Form**

FOUNDATION

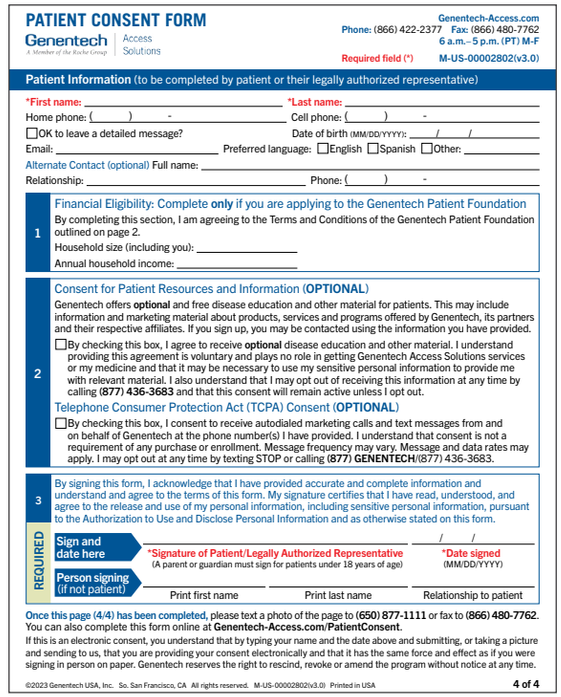
Only the information requested on these forms is required. Providing unrequested documents or information will delay processing.

Please see front cover, pages 21-23, and accompanying full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.

Xolair® Omalizumab
FOR SUBCUTANEOUS USE 75 mg • 150 mg • 300 mg

SUBMITTING THE PATIENT CONSENT FORM

The **PATIENT CONSENT FORM** is filled out by the patient and gives permission for Genentech to work with your practice and the patient's health insurance plan.



PATIENT CONSENT FORM
Genentech | Access Solutions
A Member of the Roche Group

Genentech-Access.com
Phone: (866) 422-2377 Fax: (866) 480-7762
6 a.m.–5 p.m. (PT) M-F
Required field (*) M-US-00002802(v3.0)

Patient Information (to be completed by patient or their legally authorized representative)

*First name: _____ *Last name: _____
Home phone: (___) ___-____ Cell phone: (___) ___-____
☐OK to leave a detailed message? Date of birth (MM/DD/YYYY): __/__/____
Email: _____ Preferred language: ☐English ☐Spanish ☐Other: _____
Alternate Contact (optional) Full name: _____
Relationship: _____ Phone: (___) ___-____

1 Financial Eligibility: Complete **only** if you are applying to the Genentech Patient Foundation
By completing this section, I am agreeing to the Terms and Conditions of the Genentech Patient Foundation outlined on page 2.
Household size (including you): _____
Annual household income: _____

2 Consent for Patient Resources and Information (**OPTIONAL**)
Genentech offers **optional** and free disease education and other material for patients. This may include information and marketing material about products, services and programs offered by Genentech, its partners and their respective affiliates. If you sign up, you may be contacted using the information you have provided.
☐By checking this box, I agree to receive **optional** disease education and other material. I understand providing this agreement is voluntary and plays no role in getting Genentech Access Solutions services or my medicine and that it may be necessary to use my sensitive personal information to provide me with relevant material. I also understand that I may opt out of receiving this information at any time by calling **(877) 436-3683** and that this consent will remain active unless I opt out.
Telephone Consumer Protection Act (TCPA) Consent (**OPTIONAL**)
☐By checking this box, I consent to receive autodialed marketing calls and text messages from and on behalf of Genentech at the phone number(s) I have provided. I understand that consent is not a requirement of any purchase or enrollment. Message frequency may vary. Message and data rates may apply. I may opt out at any time by texting STOP or calling **(877) GENENTECH**/(877) 436-3683.

3 By signing this form, I acknowledge that I have provided accurate and complete information and understand and agree to the terms of this form. My signature certifies that I have read, understood, and agree to the release and use of my personal information, including sensitive personal information, pursuant to the Authorization to Use and Disclose Personal Information and as otherwise stated on this form.

REQUIRED
Sign and date here _____ *Signature of Patient/Legally Authorized Representative (A parent or guardian must sign for patients under 18 years of age) __/__/____ *Date signed (MM/DD/YYYY)
Person signing (if not patient) _____ Print first name _____ Print last name _____ Relationship to patient

Once this page (4/4) has been completed, please text a photo of the page to **(650) 877-1111** or fax to **(866) 480-7762**. You can also complete this form online at **Genentech-Access.com/PatientConsent**.
If this is an electronic consent, you understand that by typing your name and the date above and submitting, or taking a picture and sending to us, that you are providing your consent electronically and that it has the same force and effect as if you were signing in person on paper. Genentech reserves the right to rescind, revoke or amend the program without notice at any time.

 4 of 4

WHERE TO FIND

This form is included in this kit and available at **Genentech-Access.com/PatientConsent**

FOUR WAYS TO SUBMIT THE COMPLETED FORM

1. Patients can eSubmit at **Genentech-Access.com/PatientConsent**
2. Practices can upload a scanned copy to My Patient Solutions® for Health Care Practices
3. Text a photo of the form to **(650) 877-1111**
4. Fax to **(866) 480-7762**

TIP **Patients should consider completing all sections of the Patient Consent Form** to receive additional support from these programs if they are eligible. **Form must be signed and dated.**

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

Anaphylaxis (cont): 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.

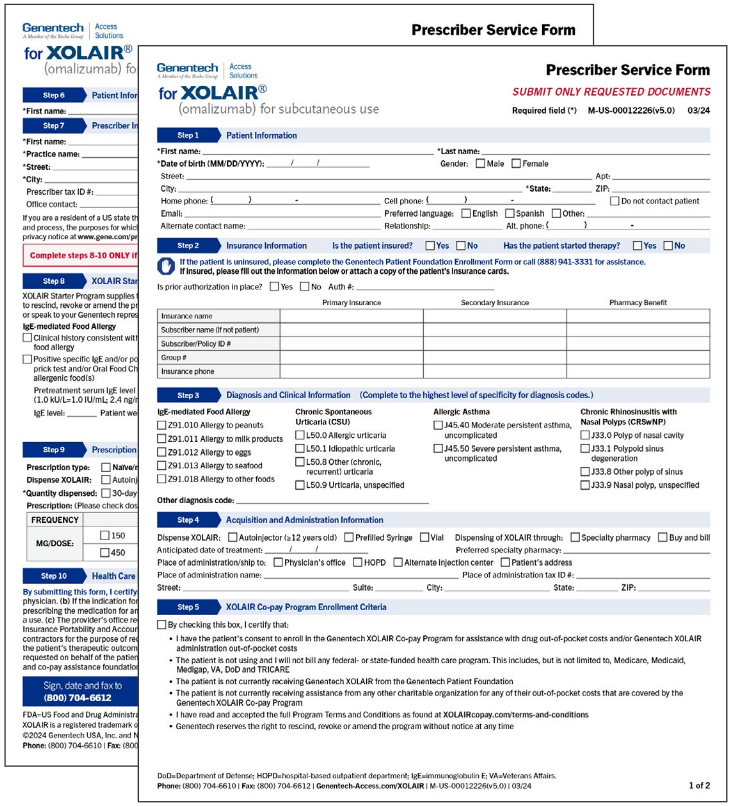
In postmarketing spontaneous reports, the frequency of anaphylaxis attributed to XOLAIR use was estimated to be at least 0.2% of patients based on an estimated exposure of about 57,300 patients from June 2003 through December 2006. Approximately 60% to 70% of anaphylaxis cases have been reported to occur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

ENROLLING IN XOLAIR PATIENT SUPPORT SERVICES

SERVICE

SUBMITTING THE PRESCRIBER SERVICE FORM

The Prescriber Service Form is **filled out by the healthcare provider** and is used to collect the patient's health insurance and treatment information.



WHERE TO FIND

This form is included in this kit and available at **Genentech-Access.com/XOLAIR**

THREE WAYS TO SUBMIT THE COMPLETED FORM

1. eSubmit using Quick Enroll at **Genentech-Access.com/XOLAIR**
2. Complete online using My Patient Solutions® for Health Care Practices
3. Fax to **(800) 704-6612**

Page 1 may be submitted alone to request a benefits investigation (BI) or support for prior authorizations (PAs), appeals, co-pay assistance or specialty pharmacies (SPs).

Page 2 is only to request assistance from the XOLAIR Starter Program. See section 05.

TIP **Only the information requested on these forms is required. Providing additional documents or information will delay processing.** Common mistakes such as incomplete and incorrect information, missing signatures and illegible forms can cause delays in processing.

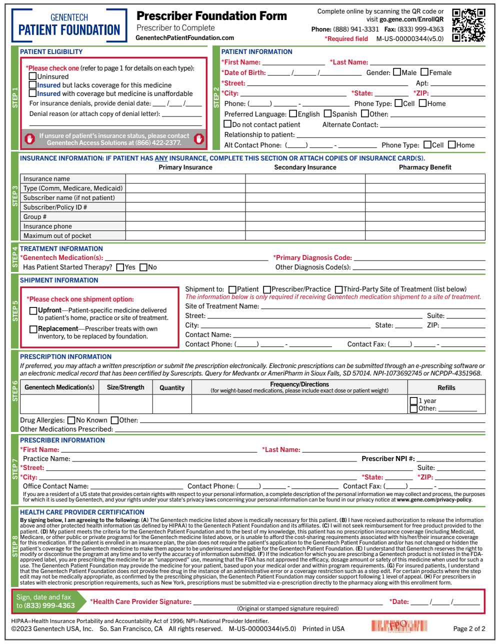
FOUNDATION

SUBMITTING THE PRESCRIBER FOUNDATION FORM

The Prescriber Foundation Form is **filled out by the healthcare provider** and is used to collect the patient's treatment information and determine eligibility for **free XOLAIR** from the Genentech Patient Foundation.

The Genentech Patient Foundation gives free Genentech medicine to people who meet income guidelines and:

- Who don't have health insurance
- Whose treatment is not covered by health insurance
- Whose treatment is covered by health insurance and have an out-of-pocket maximum that is more than 7.5% of their household income



WHERE TO FIND

This form is included in this kit and available at **Genentech-Access.com**

THREE WAYS TO SUBMIT THE COMPLETED FORM

1. eSubmit using Quick Enroll
2. Complete online using My Patient Solutions for Health Care Practices
3. Fax to **(888) 249-4919**

To be eligible for free Genentech medicine from the Genentech Patient Foundation, insured patients who have coverage for their medicine should try to pursue other forms of financial assistance, if available, and meet certain income requirements. Uninsured patients and insured patients without coverage for their medicine must meet a different set of income requirements. Genentech reserves the right to modify or discontinue the program at any time and to verify the accuracy of information submitted.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

Anaphylaxis (cont): 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.

Xolair Omalizumab FOR SUBCUTANEOUS USE 75 mg • 150 mg • 300 mg

SECTION 02

XOLAIR ACCESS SOLUTIONS

WHAT IS XOLAIR ACCESS SOLUTIONS?

XOLAIR ACCESS SOLUTIONS

is your resource for helpful access and reimbursement support. We can help your patients and practice by providing:

- Benefits investigations (BIs)
- Prior authorization (PA) resources
- Resources for denials and appeals
- The XOLAIR Recertification Reminder Program
- Information about authorized specialty pharmacies (SPs) and specialty distributors
- Sample coding and billing information
- Financial assistance options

TIP Visit **Genentech-Access.com/XOLAIR** to find the resources appropriate for your patients.

Genentech and Novartis Pharmaceuticals Corporation provide coverage and reimbursement services to patients to help them understand benefits, coverage and reimbursement. Genentech and Novartis Pharmaceuticals Corporation provide these services to patients only after a health care provider has prescribed XOLAIR.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

Anaphylaxis (cont): 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) with asthma 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.

Xolair® Omalizumab
FOR SUBCUTANEOUS USE 75 mg • 150 mg • 300 mg

Please see front cover, pages 21-23, and accompanying full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.

MY PATIENT SOLUTIONS® FOR HEALTH CARE PRACTICES

MY PATIENT SOLUTIONS

is an online tool to help you enroll patients in XOLAIR Access Solutions or the Genentech Patient Foundation and manage your service requests.

With My Patient Solutions, you can:

- Message a XOLAIR Access Solutions or Genentech Patient Foundation Specialist
- View BI Reports
- See which service requests require action
- Follow up on PAs or appeals and download PA forms (if available)
- View Genentech Patient Foundation eligibility and coordinate shipments
- Enroll and re-enroll eligible patients in XOLAIR Access Solutions or the Genentech Patient Foundation

To register for My Patient Solutions

1. Visit **Genentech-Access.com/XOLAIR** and select the My Patients Solutions Login button in the top right corner
2. Select **REGISTER YOUR ACCOUNT** in the top right corner
3. Answer a series of questions to help you determine if My Patient Solutions for Health Care Practices is right for you
4. Enter your information
   - **a.** Scroll all the way to the bottom of the screen to read and agree to the practice agreement
   - **b.** Add users, locations and prescribers as needed

TIP **Each user must activate his or her account** and create an individual login after the practice has been registered.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

Malignancy (cont): A subsequent 5-year observational study of 5007 XOLAIR-treated and 2829 non-XOLAIR-treated adolescent and adult patients with moderate to severe persistent asthma and a positive skin test reaction or in vitro reactivity to a perennial aeroallergen 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.

BENEFITS INVESTIGATIONS (BIs)

XOLAIR Access Solutions can conduct BIs on behalf of your patients so you can understand their coverage.

Request a BI by submitting the Prescriber Service Form and the Patient Consent Form to XOLAIR Access Solutions.

The results of your BI are provided to you in a BI Report, which can be viewed online via My Patient Solutions® Health Care Practices, our online patient management tool or faxed to your office.

The completion and submission of coverage- or reimbursement-related documentation are the responsibility of the patient and healthcare provider. Genentech and Novartis Pharmaceuticals Corporation make no representation or guarantee concerning coverage or reimbursement for any service or item.

TIP **Please check the Recertification Date** for a reminder when authorization is needed to avoid interruption in patient therapy.

PRIOR AUTHORIZATIONS (PAs)

Submitting PAs

The Specialists at XOLAIR Access Solutions can help you identify if a PA is necessary and offer resources as you request it for your patient.

Considerations for requesting a PA

- **Understand** payer guidelines
- **Submit** all required supporting documents with the PA request
- **Keep** complete records, including a copy of everything you send and a log of every phone call you make to the patient's health insurance plan
- **Check** with the payer to determine the length of the authorization, as this can vary

Commonly Requested Information for PAs

Payers typically require the following documentation

- Payer's PA form
- Patient history and physical findings (e.g. treatment history and response)
- Physician's chart notes
- Labs and other test results

TIP **Consider keeping a copy of these documents for your records.**

DENIALS AND APPEALS

After submitting a claim, you may find that the claim was denied. The denial letter identifies the reason why the patient's coverage has been denied and is critical in supporting the basis for an appeal.

Coverage can be denied for various reasons, such as:

- Simple errors on the forms, including coding errors
- Failure to request or document necessary PAs
- Payer determines the treatment is not covered

XOLAIR Access Solutions can provide resources as you prepare an appeal submission, per your patient's plan requirements. **Contact your Field Reimbursement Manager (FRM) or XOLAIR Access Solutions Specialist** if the appeal is denied and learn about possible next steps.

TIP **Visit Genentech-Access.com/XOLAIR** for considerations for composing an appeal letter and a sample appeal letter.

Appeals cannot be completed or submitted by XOLAIR Access Solutions on your behalf.

XOLAIR RECERTIFICATION REMINDER PROGRAM

This program can help patients avoid potential gaps in their XOLAIR therapy due to healthcare recertification requirements. Once enrolled, if one or more patients are within 45 to 60 days of health plan certification expiration, XOLAIR Access Solutions will automatically send a Recertification Reminder Report to your practice.

GETTING STARTED

- A representative can provide you with the Recertification Reminder Program Enrollment Form or it can be downloaded at **Genentech-Access.com/XOLAIR**
- Complete the form and fax it to **(800) 704-6612**

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

Acute Asthma Symptoms and Deteriorating Disease: XOLAIR has not been shown to alleviate asthma exacerbations acutely. Do not use XOLAIR to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with XOLAIR.

Corticosteroid Reduction: Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of XOLAIR therapy for asthma or CRSwNP. Decrease corticosteroids gradually under the direct supervision of a physician. In CSU patients, the use of XOLAIR in combination with corticosteroids has not been evaluated.

Eosinophilic Conditions: In rare cases, patients with asthma on therapy with XOLAIR may present with serious systemic eosinophilia, sometimes presenting with clinical features of vasculitis consistent with Churg-Strauss syndrome. These events usually, but not always, have been associated with the reduction of oral corticosteroid therapy. Physicians should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients. A causal association between XOLAIR and these underlying conditions has not been established.

BUY AND BILL

The decision to use buy and bill is up to the individual practice and the patient's health insurance plan. XOLAIR Access Solutions can help you determine if a patient's health insurance plan requires use of buy and bill or specialty pharmacy (SP).

The process of obtaining XOLAIR through buy and bill

1 ORDERING

- Practice orders drug from authorized specialty distributor of its choice
- A list of authorized specialty distributors is available at **Genentech-Access.com/XOLAIR**

2 ADMINISTRATION

Practice administers medication.

3 CO-PAY AND CLAIMS

Follow the health insurance plan's policies for determining co-pay and billing

- Practice collects patient co-pay (if applicable)
- Practice bills health insurance plan for both drug and administration procedure

SPECIALTY PHARMACY (SP)

Based on the outcome of the benefits investigation (BI), XOLAIR Access Solutions can identify an appropriate SP based on the patient's health insurance plan.

You can follow these potential steps for using SPs

1 ORDERING

- Practice sends prescription to SP
- SP coordinates payment with the patient for drug only
- SP coordinates shipment of the drug to the practice, alternate injection center (AIC) or the patient

2 ADMINISTRATION

- Practice administers medication (if administering in-office)
- Patient administers medication (if they self-inject)

3 CO-PAY AND CLAIMS

Practice coordinates payment and claims for administration only (if applicable). If the injection is administered in the office, the practice may bill for the administration of XOLAIR only.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

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. Do not use serum total IgE levels obtained less than 1 year following discontinuation to reassess the dosing regimen for asthma, CRSwNP, or IgE-mediated food allergy patients, because these levels may not reflect steady state free IgE levels.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

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

Asthma: In patients ≥12 years of age, the most common adverse reactions (≥1% more frequent in XOLAIR-treated patients) were: arthralgia (8%), pain (general) (7%), leg pain (4%), fatigue (3%), dizziness (3%), fracture (2%), arm pain (2%), pruritus (2%), dermatitis (2%), and earache (2%). In pediatric patients 6 to <12 years of age, the most commonly observed adverse reactions (≥3% more frequent in XOLAIR-treated pediatric patients) were: nasopharyngitis, headache, pyrexia, upper abdominal pain, pharyngitis streptococcal, otitis media, viral gastroenteritis, arthropod bite, and epistaxis.

Xolair® Omalizumab
FOR SUBCUTANEOUS USE 75 mg • 150 mg • 300 mg

Please see front cover, pages 21-23, and accompanying full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.

SECTION 03

FINANCIAL ASSISTANCE OPTIONS

FINANCIAL ASSISTANCE OPTIONS

are available to help your eligible patients obtain XOLAIR, regardless of their ability to pay. We can accommodate a wide range of insurance situations to help with out-of-pocket costs.

ASSISTANCE AVAILABLE INCLUDES

THE XOLAIR CO-PAY PROGRAM

If eligible commercially insured patients need assistance with their out-of-pocket costs, the XOLAIR Co-pay Program may help.

The final amount owed by a patient may be as little as $0 for XOLAIR.*

REFERRALS TO INDEPENDENT CO-PAY ASSISTANCE FOUNDATIONS

If eligible publicly or commercially insured patients have difficulty paying for their co-pay, co-insurance or other out-of-pocket costs, XOLAIR Access Solutions can refer them to an independent co-pay assistance foundation supporting their diagnosis.†

GENENTECH PATIENT FOUNDATION

If patients don't have health insurance coverage or have financial concerns and meet eligibility criteria, they may be able to get free medicine from the Genentech Patient Foundation.‡

XOLAIR CO-PAY PROGRAM

FOR ELIGIBLE COMMERCIALLY INSURED PATIENTS, the XOLAIR Co-pay Program may help them with:

Drug out-of-pocket costs

Pay as little as $0 per XOLAIR drug out-of-pocket costs, up to $15,000 per a 12-month calendar year

Injection out-of-pocket costs

Pay as little as $0 per XOLAIR injection out-of-pocket costs, up to $1,500 per a 12-month calendar year

*The final amount owed by patients may be as little as $0, but may vary depending on the patient's health insurance plan. Eligible commercially insured patients who are prescribed XOLAIR for an FDA-approved use can receive up to $15,000 in assistance annually for drug costs and/or up to $1,500 in assistance annually for injection costs. For more information, see full program Terms and Conditions.

†Independent co-pay assistance foundations have their own rules for eligibility. Genentech has no involvement or influence in independent foundation decision-making or eligibility criteria and does not know if a foundation will be able to help your patient. We can only refer your patient to a foundation that supports their disease state. Genentech does not endorse or show preference for any particular foundation. The foundations to which we refer your patient may not be the only ones that might be able to help.

‡To be eligible for free Genentech medicine from the Genentech Patient Foundation, insured patients who have coverage for their medicine should try to pursue other forms of financial assistance, if available, and meet certain income requirements. Uninsured patients and insured patients without coverage for their medicine must meet a different set of income requirements. Genentech reserves the right to modify or discontinue the program at any time and to verify the accuracy of information submitted.

Xolair® Omalizumab
FOR SUBCUTANEOUS USE 75 mg • 150 mg • 300 mg

TIP For more information, call **(855) 965-2472** or visit **XOLAIRcopay.com**

XOLAIR Co-pay Program Terms and Conditions

The Product and Administration Co-pay Programs ("Programs") are valid ONLY for patients with commercial (private or non-governmental) insurance who have a valid prescription for a Food and Drug Administration (FDA)-approved indication of a Genentech medicine. Patients using Medicare, Medicaid or any other federal or state government program (collectively, "Government Programs") to pay for their Genentech medicine and/or administration services are not eligible.

Under the Programs, the patient may be required to pay a co-pay for drug costs and a co-pay for administration costs. The final amount owed by a patient may be as little as $0 for the Genentech medicine or administration of the Genentech medicine (see Program specific details available at the Program website). The total patient out-of-pocket cost is dependent on the patient's health insurance plan. The Programs assist with the cost of the Genentech medicine and the Genentech medicine administration only. It does not assist with the cost of other administrations, medicines, procedures or office visit fees. After reaching the maximum Programs' benefit amounts, the patient will be responsible for all remaining out-of-pocket expenses. The amount of the Programs' benefits cannot exceed the patient's out-of-pocket expenses for the cost of the Genentech medicine or administration fees for the Genentech medicine.

All participants are responsible for reporting the receipt of all Programs' benefits as required by any insurer or by law. The Programs are only valid in the United States and U.S. Territories and are void where prohibited by law. The Drug Co-pay Program shall follow state restrictions in relation to AB-rated generic equivalents (e.g., MA, CA) where applicable. The Administration Co-pay Program is not valid for Massachusetts or Rhode Island residents. No party may seek reimbursement for all or any part of the benefit received through the Programs. The value of the Programs is intended exclusively for the benefit of the patient. The funds made available through the Programs may only be used to reduce the out-of-pocket costs for the patient enrolled in the Programs. The Programs are not intended for the benefit of third parties, including without limitation third party payers, pharmacy benefit managers, or their agents. If Genentech determines that a third party has implemented programs that adjust patient cost-sharing obligations based on the availability of support under the Programs and/or excludes the assistance provided under the Programs from counting towards the patient's deductible or out-of-pocket cost limitations, Genentech may impose a per fill cap on the cost-sharing assistance available under the Programs. Submission of true and accurate information is a requirement for eligibility and Genentech reserves the right to disqualify patients who do not comply from Genentech programs. Genentech reserves the right to rescind, revoke or amend the Programs without notice at any time.

Additional terms and conditions apply. Please visit the co-pay Program website for the full list of Terms and Conditions.

Genentech reserves the right to modify or discontinue the program at any time and to verify the accuracy of information submitted.

IMPORTANT SAFETY INFORMATION (cont)

ADVERSE REACTIONS (cont)

Chronic Rhinosinusitis with Nasal Polyps: The most common adverse reactions (≥3% in XOLAIR-treated patients) included: headache (8.1%), injection site reactions (5.2%), arthralgia (3.0%), upper abdominal pain (3.0%), and dizziness (3.0%).

Please see front cover, pages 21-23, and accompanying full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.

REFERRALS TO INDEPENDENT CO-PAY ASSISTANCE FOUNDATIONS*

AN INDEPENDENT CO-PAY ASSISTANCE FOUNDATION

is a charitable organization providing financial assistance to patients with specific disease states. We offer referrals to independent co-pay assistance foundations for eligible patients who are commercially or publicly insured, including those covered by Medicare or Medicaid.

These organizations may be able to help your patients. Please check their websites for up-to-date information on the assistance they provide.

Allergy

- Patient Access Network Foundation (PANF)
- Patient Advocate Foundation (PAF)
- The Assistance Fund, Inc.
- The HealthWell Foundation

Dermatology

- The HealthWell Foundation

TIP For more information, visit **Genentech-Access.com**

*Independent co-pay assistance foundations have their own rules for eligibility. Genentech and Novartis Pharmaceuticals Corporation have no involvement or influence in independent foundation decision-making or eligibility criteria and do not know if a foundation will be able to help your patient. We can only refer your patient to a foundation that supports their disease state. This information is provided as a resource for you. Genentech and Novartis Pharmaceuticals Corporation do not endorse or show preference for any particular foundation. The foundations in this list may not be the only ones that might be able to help your patient.

Xolair® Omalizumab
FOR SUBCUTANEOUS USE 75 mg • 150 mg • 300 mg

Please see front cover, pages 21-23, and accompanying full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.

GENENTECH PATIENT FOUNDATION

THE GENENTECH PATIENT FOUNDATION

gives free Genentech medicine to people who don't have health insurance coverage or who have financial concerns and meet eligibility criteria.

Genentech Patient Foundation

Is My Patient Eligible?

Genentech Patient Foundation eligibility depends on your patients' health insurance and financial situation. They may qualify if they are in 1 of the 3 groups below.

1. "I **have no insurance**."

For a household of 1 to 4 people, total yearly income is under $150,000.

- For households with more than 4 people, add $25,000 to the yearly income limit for each additional person

2. "I **have insurance**, but it doesn't cover my Genentech medicine."

3. "I **have insurance** that covers my Genentech medicine, but the out-of-pocket maximum set by my health insurance plan is more than 7.5% of my yearly income."

Household size	Yearly income
1 person	Under $75,000
2 people	Under $100,000
3 people	Under $125,000
4 people	Under $150,000

For households with more than 4 people, add $25,000 to the yearly income limit for each additional person.

Not sure if you're eligible?

- Call **(888) 941-3331** to speak with a live Foundation Specialist
  - We offer support in many different languages
- You can also visit **GenentechPatientFoundation.com** for more information

Genentech reserves the right to modify or discontinue the program at any time and to verify the accuracy of information submitted.

Genentech A Member of the Roche Group | Patient Foundation

TIP To learn more and apply, visit **GenentechPatientFoundation.com**

IMPORTANT SAFETY INFORMATION (cont)

ADVERSE REACTIONS (cont)

IgE-Mediated Food Allergy: The most common adverse reactions (≥3% in XOLAIR-treated pediatric patients 1 year of age and older) included: injection site reactions (15.5%) and pyrexia (6.4%). Safety data obtained from adults (n=3) in this trial was limited.

Chronic Spontaneous Urticaria : The most common adverse reactions (≥2% in XOLAIR-treated patients) 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%).

SECTION 04

THE SUPPORT FOR YOU PROGRAM

SUPPORT FOR YOU PROGRAM

With Support For You, patients can get tools and resources to help them stay motivated and informed about what to expect along their XOLAIR treatment journey. **SIGNING UP IS FREE.**

The Support For You program is only available for XOLAIR patients with allergic asthma, chronic spontaneous urticaria or IgE-mediated food allergy.

YOUR PATIENT WILL GET A SUPPORT KIT THAT INCLUDES:

- Information to get started on XOLAIR, including full Prescribing Information and Medication Guide
- Information about financial resources

Your patient will also receive periodic emails with information related to treatment with XOLAIR.

PATIENTS WILL ALSO HAVE THE ABILITY TO SCHEDULE A 1:1 SESSION WITH A CLINICAL EDUCATION MANAGER TO:

- Discuss questions about XOLAIR
- Provide a path to additional product support
- Help your patient get started with treatment
- Guide your patient to additional resources

GETTING STARTED

Call us at **(877) GENENTECH/**(877) 436-3683,
Monday through Friday, 9 AM to 8 PM ET
or go to **XOLAIR.com/SupportForYou**

IMPORTANT SAFETY INFORMATION (cont)

ADVERSE REACTIONS (cont)

Injection Site Reactions

Asthma: In adults and adolescents with asthma, injection site reactions of any severity occurred at a rate of 45% in XOLAIR-treated patients compared with 43% in placebo-treated patients. Severe injection site reactions occurred more frequently in XOLAIR-treated patients compared with patients in the placebo group (12% vs 9%, respectively). The types of injection site reactions in asthma studies included: bruising, redness, warmth, burning, stinging, itching, hive formation, pain, indurations, mass, and inflammation.

Chronic Rhinosinusitis with Nasal Polyps: Injection site reactions occurred at a rate of 5.2% in XOLAIR-treated patients compared with 1.5% in placebo-treated patients. Injection site reactions were mild to moderate severity and none resulted in study discontinuation.

IgE-Mediated Food Allergy: Injection site reactions occurred at a rate of 15.5% in XOLAIR-treated patients compared with 10.9% in placebo-treated patients. The types of injection site reactions included: urticaria, discomfort, erythema, pain, and rash. All injection site reactions were mild to moderate severity and none resulted in study discontinuation.

IMPORTANT SAFETY INFORMATION (cont)

ADVERSE REACTIONS (cont)

Injection Site Reactions (cont)

Chronic Spontaneous Urticaria: 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.

Xolair® Omalizumab
FOR SUBCUTANEOUS USE 75 mg • 150 mg • 300 mg

Please see front cover, pages 21-23, and accompanying full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.

SECTION 05

XOLAIR STARTER PROGRAM

XOLAIR STARTER PROGRAM

WHILE AWAITING AN INSURANCE COVERAGE DETERMINATION,
eligible patients may receive free medicine through the XOLAIR Starter Program.

If you think your patient qualifies, submit the completed **PRESCRIBER SERVICE FORM** and the **PATIENT CONSENT FORM** to XOLAIR Access Solutions.

VISIT GENENTECH-ACCESS.COM/XOLAIR TO LEARN MORE

The Genentech Starter Program ("Program") provides eligible patients who have experienced an insurance coverage delay of 5 days minimum with up to a 30-day supply of Genentech Starter medicine. If a coverage delay persists, a patient may be eligible for one refill, up to 30-days of Genentech Starter medicine. There is no obligation to purchase any future product and receipt of free product is not contingent on any future purchase. Requests for the Genentech Starter medicine cannot be processed without a completed and signed 1) Product Prescriber Service Form and 2) Patient Consent Form. Patients must be prescribed the Genentech medicine for a valid FDA-approved indication. Neither the prescriber, the pharmacy, nor any patient receiving free Genentech medicine via the Genentech Starter Program may seek reimbursement or credit for any part of the benefit received by the patient through this offer from any insurer, health plan, or government program.

The Genentech Starter Program cannot be counted towards any out-of-pocket costs under any plan (such as true out-of-pocket cost under a Medicare Part D prescription drug plan). The Genentech Starter Program enrollment team may notify the patient's insurer that the patient is receiving a free supply of product from the Program. Prescribers may not advertise or otherwise use the Program as a means of promoting their services or Genentech's medicines to patients. This Program is void where prohibited by law and may not be used in or by residents of restricted states, where applicable. The free supply may not be sold, purchased or traded or offered for sale. This Program is not a benefit plan. Submission of true and accurate information is a requirement for eligibility and Genentech reserves the right to disqualify patients who do not comply from Genentech programs. Genentech reserves the right to rescind, revoke or amend the program without notice at any time.

WHO MAY BE ELIGIBLE?

- **Insured patients who have not received their initial benefits investigation (BI)/prior authorization (PA) decision for XOLAIR within 7 days**
- **New XOLAIR patients or patients who have not been on XOLAIR within the last 12 months**

IMPORTANT SAFETY INFORMATION (cont)

ADVERSE REACTIONS (cont)

Injection Site Reactions (cont)

Cardiovascular and Cerebrovascular Events from Clinical Studies in Patients with Asthma: A 5-year observational study was conducted in 5007 XOLAIR-treated and 2829 non-XOLAIR-treated patients ≥12 years of age with moderate to severe persistent asthma and a positive skin test reaction to a perennial aeroallergen to evaluate the long term safety of XOLAIR, including the risk of malignancy. Similar percentages of patients in both cohorts were current (5%) or former smokers (29%). Patients had a mean age of 45 years and were followed for a mean of 3.7 years. More XOLAIR-treated patients were diagnosed with severe asthma (50%) compared to the non-XOLAIR-treated patients (23%). A higher incidence rate (per 1000 patient-years) of overall cardiovascular and cerebrovascular serious adverse events (SAEs) was observed in XOLAIR-treated patients (13.4) compared to non-XOLAIR-treated patients (8.1). Increases in rates were observed for transient ischemic attack (0.7 vs 0.1), myocardial infarction (2.1 vs 0.8), pulmonary hypertension (0.5 vs 0), pulmonary embolism/venous thrombosis (3.2 vs 1.5), and unstable angina (2.2 vs 1.4), while the rates observed for ischemic stroke and cardiovascular death were similar among both study cohorts. 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.

Xolair® Omalizumab
FOR SUBCUTANEOUS USE 75 mg • 150 mg • 300 mg

Please see front cover, pages 21-23, and accompanying full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.

SECTION 06

FREQUENTLY ASKED QUESTIONS

FREQUENTLY ASKED QUESTIONS

1 HOW CAN I FIND FINANCIAL ASSISTANCE AND OFFICE SUPPORT RESOURCES?

Determine which financial assistance option is right for your patient with the Patient Assistance Tool available at **Genentech-Access.com/XOLAIR**.

2 ONCE ENROLLED IN A PROGRAM, HOW LONG WILL MY PATIENT KEEP RECEIVING ASSISTANCE?

Each program has its own time period in which your eligible patients will receive assistance.

Call XOLAIR Access Solutions at **(800) 704-6610** for more information.

3 MY PATIENT'S CO-PAYS ARE TOO HIGH. HOW CAN I HELP THEM?

There may be options to help your patients get their XOLAIR prescription. XOLAIR Access Solutions can refer your patients to financial assistance options.

Visit **Genentech-Access.com/XOLAIR** or call XOLAIR Access Solutions at **(800) 704-6610** to learn more.

4 HOW LONG WILL IT TAKE MY PATIENTS TO GET MEDICINE?

Your patients might not be able to get XOLAIR right away as the time for patients to receive XOLAIR may vary. Once a benefits investigation to determine their coverage is performed, the next step is a prior authorization. After both of these steps, then your patients will be able to get their XOLAIR prescription. Patients may also qualify for the XOLAIR Starter Program described on page 33.

Call Genentech Patient Resource Center at **(877) 436-3683** with any questions you might have.

5 WHAT IF I HAVE QUESTIONS ABOUT YOUR PROGRAMS?

To learn more about our programs and services, contact your XOLAIR Specialist.

Visit **Genentech-Access.com/XOLAIR** or call XOLAIR Access Solutions at **(800) 704-6610.**

Xolair® Omalizumab
FOR SUBCUTANEOUS USE 75 mg • 150 mg • 300 mg

SECTION 07

INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS

XOLAIR® (omalizumab) is indicated for:

- Adults and pediatric patients 6 years of age and older 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.

  Limitations of Use: XOLAIR is not indicated for the relief of acute bronchospasm or status asthmaticus.
- Add-on maintenance treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids.
- The 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 is to be used in conjunction with food allergen avoidance.

  Limitations of Use: XOLAIR is not indicated for the emergency treatment of allergic reactions, including anaphylaxis.
- 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.

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 with asthma, 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.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

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.

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) with asthma 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 with moderate to severe persistent asthma and a positive skin test reaction or in vitro reactivity to a perennial aeroallergen 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.

Please see front cover, pages 22-23, and accompanying full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

Acute Asthma Symptoms and Deteriorating Disease: XOLAIR has not been shown to alleviate asthma exacerbations acutely. Do not use XOLAIR to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with XOLAIR.

Corticosteroid Reduction: Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of XOLAIR therapy for asthma or CRSwNP. Decrease corticosteroids gradually under the direct supervision of a physician. In CSU patients, the use of XOLAIR in combination with corticosteroids has not been evaluated.

Eosinophilic Conditions: In rare cases, patients with asthma on therapy with XOLAIR may present with serious systemic eosinophilia, sometimes presenting with clinical features of vasculitis consistent with Churg-Strauss syndrome. These events usually, but not always, have been associated with the reduction of oral corticosteroid therapy. Physicians should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients. A causal association between XOLAIR and these underlying conditions has not been established.

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. Do not use serum total IgE levels obtained less than 1 year following discontinuation to reassess the dosing regimen for asthma, CRSwNP, or IgE-mediated food allergy patients, because these levels may not reflect steady state free IgE levels.

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

Asthma: In patients ≥12 years of age, the most common adverse reactions (≥1% more frequent in XOLAIR-treated patients) were: arthralgia (8%), pain (general) (7%), leg pain (4%), fatigue (3%), dizziness (3%), fracture (2%), arm pain (2%), pruritus (2%), dermatitis (2%), and earache (2%). In pediatric patients 6 to <12 years of age, the most commonly observed adverse reactions (≥3% more frequent in XOLAIR-treated pediatric patients) were: nasopharyngitis, headache, pyrexia, upper abdominal pain, pharyngitis streptococcal, otitis media, viral gastroenteritis, arthropod bite, and epistaxis.

IMPORTANT SAFETY INFORMATION (cont)

ADVERSE REACTIONS (cont)

Chronic Rhinosinusitis with Nasal Polyps: The most common adverse reactions (≥3% in XOLAIR-treated patients) included: headache (8.1%), injection site reactions (5.2%), arthralgia (3.0%), upper abdominal pain (3.0%), and dizziness (3.0%).

IgE-Mediated Food Allergy: The most common adverse reactions (≥3% in XOLAIR-treated pediatric patients 1 year of age and older) included: injection site reactions (15.5%) and pyrexia (6.4%). Safety data obtained from adults (n=3) in this trial was limited.

Chronic Spontaneous Urticaria : The most common adverse reactions (≥2% in XOLAIR-treated patients) 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

Asthma: In adults and adolescents with asthma, injection site reactions of any severity occurred at a rate of 45% in XOLAIR-treated patients compared with 43% in placebo-treated patients. Severe injection site reactions occurred more frequently in XOLAIR-treated patients compared with patients in the placebo group (12% vs 9%, respectively). The types of injection site reactions in asthma studies included: bruising, redness, warmth, burning, stinging, itching, hive formation, pain, indurations, mass, and inflammation.

Chronic Rhinosinusitis with Nasal Polyps: Injection site reactions occurred at a rate of 5.2% in XOLAIR-treated patients compared with 1.5% in placebo-treated patients. Injection site reactions were mild to moderate severity and none resulted in study discontinuation.

IgE-Mediated Food Allergy: Injection site reactions occurred at a rate of 15.5% in XOLAIR-treated patients compared with 10.9% in placebo-treated patients. The types of injection site reactions included: urticaria, discomfort, erythema, pain, and rash. All injection site reactions were mild to moderate severity and none resulted in study discontinuation.

Chronic Spontaneous Urticaria: 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.

Please see front cover, pages 21 and 23, and accompanying full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.

IMPORTANT SAFETY INFORMATION (cont)

ADVERSE REACTIONS (cont)

Injection Site Reactions (cont)

Cardiovascular and Cerebrovascular Events from Clinical Studies in Patients with Asthma: A 5-year observational study was conducted in 5007 XOLAIR-treated and 2829 non-XOLAIR-treated patients ≥12 years of age with moderate to severe persistent asthma and a positive skin test reaction to a perennial aeroallergen to evaluate the long term safety of XOLAIR, including the risk of malignancy. Similar percentages of patients in both cohorts were current (5%) or former smokers (29%). Patients had a mean age of 45 years and were followed for a mean of 3.7 years. More XOLAIR-treated patients were diagnosed with severe asthma (50%) compared to the non-XOLAIR-treated patients (23%). A higher incidence rate (per 1000 patient-years) of overall cardiovascular and cerebrovascular serious adverse events (SAEs) was observed in XOLAIR-treated patients (13.4) compared to non-XOLAIR-treated patients (8.1). Increases in rates were observed for transient ischemic attack (0.7 vs 0.1), myocardial infarction (2.1 vs 0.8), pulmonary hypertension (0.5 vs 0), pulmonary embolism/venous thrombosis (3.2 vs 1.5), and unstable angina (2.2 vs 1.4), while the rates observed for ischemic stroke and cardiovascular death were similar among both study cohorts. 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.

Genentech
A Member of the Roche Group

NOVARTIS