Targeting Exacerbations in Moderate to Severe Persistent Allergic Asthma
A Modular Speaker Program

You are invited to attend a speaker program to learn more about allergic asthma and XOLAIR® (omalizumab), the only IgE-targeting immunomodulator for use in appropriate moderate to severe persistent allergic asthma patients.

The module XOLAIR® (omalizumab): Overview of Efficacy, Safety, and Clinical Experience will be presented; additional modules may also be presented including but not limited to:

- The Impact of Moderate to Severe Persistent Allergic Asthma
- Targeting IgE in the Treatment of Moderate to Severe Persistent Allergic Asthma
- Case Study 1
- Case Study 2

Please join us for a presentation by:

Hosted by:
Genentech USA, Inc.
Novartis Pharmaceuticals Corporation

Kevin Murphy, MD
Boys Town National Research Hospital
Boys Town, Nebraska

Friday, June 24, 2016
1:00 PM
Blue Mountain Room
The Hershey Hotel
Hershey, Pennsylvania

**INDICATION**

XOLAIR® (omalizumab) is indicated for adults and adolescents (12 years of age and above) 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. XOLAIR has been shown to decrease the incidence of asthma exacerbations in these patients.

**LIMITATIONS OF USE**

- XOLAIR is not indicated for treatment of other allergic conditions.
- XOLAIR is not indicated for the relief of acute bronchospasm or status asthmaticus.

**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, observe patients closely for an appropriate period of time after XOLAIR administration. Healthcare providers administering XOLAIR should be prepared to manage anaphylaxis that can be life-threatening. Inform patients of the signs and symptoms of anaphylaxis and instruct them to seek immediate medical care should symptoms occur.

**CONTRAINDICATIONS**

The use of 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 asthma premarketing clinical trials and in postmarketing spontaneous reports. The frequency of anaphylaxis attributed to XOLAIR use was estimated to be 0.1% and at least 0.2% (based on an estimated exposure of about 57,300 patients from June 2003 through December 2006), respectively.

A case-control study 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.

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. Anaphylaxis occurred with the first dose of XOLAIR in 2 patients and with the fourth dose in 1 patient; the time to onset of anaphylaxis was 90 minutes after administration in 2 patients and 2 hours after administration in 1 patient. 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 and older) 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 (eg, elderly, current smokers) is not known.

A subsequent 5-year observational study of 5007 XOLAIR-treated and 2829 non-XOLAIR-treated 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 page 2 and accompanying full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information.
IMPORTANT SAFETY INFORMATION (cont’d)

Acute Asthma Symptoms
XOLAIR has not been shown to alleviate asthma exacerbations acutely. Do not use XOLAIR to treat acute bronchospasm or status asthmaticus.

Corticosteroid Reduction
Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of XOLAIR therapy for asthma. Decrease corticosteroids gradually under the direct supervision of a physician.

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 postapproval use, some patients have experienced a constellation of signs and symptoms, including arthralgia/arthritis, 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 patients, because these levels may not reflect steady state free IgE levels.

ADVERSE REACTIONS
In patients ≥12 years of age, the most commonly observed adverse reactions (≥1% more frequent in XOLAIR-treated patients) from 4 placebo-controlled asthma studies 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%).

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

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 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.

USE IN SPECIFIC POPULATIONS
Pregnancy (Category B)
There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to XOLAIR during pregnancy. Encourage patients to call 1-866-4xolair (1-866-496-5247) or visit www.xolairpregnancyregistry.com for information about the pregnancy exposure registry and the enrollment procedure. Adequate and well-controlled studies with XOLAIR have not been conducted in pregnant women. XOLAIR should be used during pregnancy only if clearly needed.

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 page 1 and accompanying full Prescribing Information, including Boxed WARNING and Medication Guide, for additional Important Safety Information located at the registration table.

Genentech and Novartis Pharmaceuticals Corporation act in accordance with the PhRMA Code on Interactions with Healthcare Professionals. The PhRMA Code states that inclusion of a healthcare professional’s spouse or guest at an educational program is not appropriate. Your support of these ethical guidelines will help to ensure a high-quality learning environment for all participating healthcare professionals.

Minnesota, Vermont, the Department of Defense, and the Department of Veterans Affairs have restrictions on receiving in-kind benefits (e.g., meals, paid parking) at company-sponsored events. You are accountable for understanding such restrictions and complying with them. If you are licensed in or affiliated with any of these states or federal agencies, Genentech policies may restrict you from consuming any portion of the Genentech-sponsored meal at this program or from receiving any other in-kind benefit from Genentech (e.g., paid parking) in connection with the program.

When you RSVP please indicate whether you will accept or opt out of Genentech’s in-kind benefits (e.g., meals, paid parking) at the program. If you choose to opt out you may either pay for the meal and parking fees on your own, or not consume anything at the program.

For all program attendees who receive Genentech’s in-kind benefits at this program, Genentech will report the attendee’s name and the value received as required by federal and state disclosure laws (for more information on the federal law please visit http://sunshine.gene.com).

The cost may vary by event location and be up to $125 per person, including meal costs and parking fees (exceptions may apply).

This is a non-CME event and does not qualify for continuing medical education credit.

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