Treatment Plan for subcutaneous use of XOLAIR® (omalizumab) for Chronic Spontaneous Urticaria (CSU)

This guidance document has been produced by Novartis Pharmaceuticals Australia Pty Ltd with an expert advisory panel comprising:
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To be completed by treating specialist (clinical immunologist, allergist, dermatologist or general physician with expertise in the management of CSU)

Details:

Date:

Patient name: Date of birth:

Referring specialist name: Contact phone number:

Xolair® for CSU Indication:[1]

Xolair® is indicated for adults and adolescents (12 years of age and above) with CSU who remain symptomatic despite H1 antihistamine treatment.

Dosing schedule:[1]

Recommended: 300mg by subcutaneous injection every 4 weeks

Other:

Requirements for administering Xolair® for CSU:[1]

As with any protein, local or systemic allergic or Type I hypersensitivity events, can occur.

In post-marketing experience, anaphylaxis has been reported following the first and subsequent administrations of Xolair®. Although most of these reactions occurred within 2 hours after Xolair® administration, some occurred beyond 2 hours and even beyond 24 hours after injections.

The rate of anaphylaxis for Xolair® is uncommon (i.e. ≥1/1000 to <1/100) and is estimated to be 0.2% based on a total number of anaphylactic reactions observed from an estimated exposure of over 500,000 patient years from post-marketing reports (including allergic asthma and CSU)

EXPERT ADVISORY PANEL RECOMMENDATIONS:

- Treatment is to be administered by a healthcare professional only, in a setting where a medical professional is available
- Adrenaline and other medications for the treatment of anaphylactic reactions should always be available for immediate use following administration of Xolair®
- Patients should be fully informed that such reactions are possible and that prompt medical attention should be sought if allergic reactions occur

Signs and symptoms of anaphylaxis that patients should be aware of are:[2]

- Difficult / noisy breathing
- Swelling of tongue
- Swelling / tightness in throat
- Wheeze or persistent cough
- Difficulty talking +/- hoarse voice
- Persistent dizziness or collapse
- Rapidly developing urticaria or rash

Patient checklist at time of administration of Xolair® for CSU:

EXPERT ADVISORY PANEL RECOMMENDATIONS:

- Check patient and determine whether they had any reaction following the last injection
- Defer injection if systemically unwell and/or febrile (>38°C) and/or unstable asthma
- Do not give injection and contact specialist if:
  - Patient now pregnant
  - Anaphylaxis with most recent omalizumab injection

Management of anaphylaxis:

EXPERT ADVISORY PANEL RECOMMENDATIONS:

If *any one* of the below signs or symptoms of anaphylaxis[2] are present:

- Difficult / noisy breathing
- Swelling of tongue
- Swelling / tightness in throat
- Wheeze or persistent cough
- Difficulty talking +/- hoarse voice
- Persistent dizziness or collapse
- Rapidly developing urticaria or rash

1. Lay patient flat (if unconscious, place in recovery position, if breathing is difficult allow them to sit)
2. Administer adrenaline 0.3 to 0.5mg IMI as initial dose and repeat as necessary
3. Consider ancillary treatment such as corticosteroids, non-sedating antihistamines or salbutamol
4. Call ambulance if outside hospital

Additional considerations regarding anaphylaxis when administering Xolair® for CSU:[3]

In 2017, Lieberman *et al*, reported that in 96 cases adjudicated to be anaphylaxis related to Xolair®:

- In 80% of patients it was prescribed for asthma
- 43% (n = 37) of patients, who provided an anaphylaxis history, documented a prior anaphylactic event unrelated to Xolair®
- 72% of anaphylactic reactions were observed during the first 3 doses of Xolair®
- 64% of reactions occurred within 60 minutes of Xolair® administration (in the 81 cases that reported time to onset of reaction)
- No case of anaphylaxis resulted in death

EXPERT ADVISORY PANEL RECOMMENDATIONS:

1. **Observation periods of:**
   - 60 minutes after each of the first 3 doses
   - 30 minutes, or length recommended by specialist, for dose 4 and onwards

   Specialist recommendation re observation period for dose 4 and onwards: *Please indicate*

   ☐ mins
2. **Requirement for EpiPen® prescription to be based on specialist assessment**

   Specialist recommendation re EpiPen®: *Please check appropriate box below*

   YES ☐ NO ☐

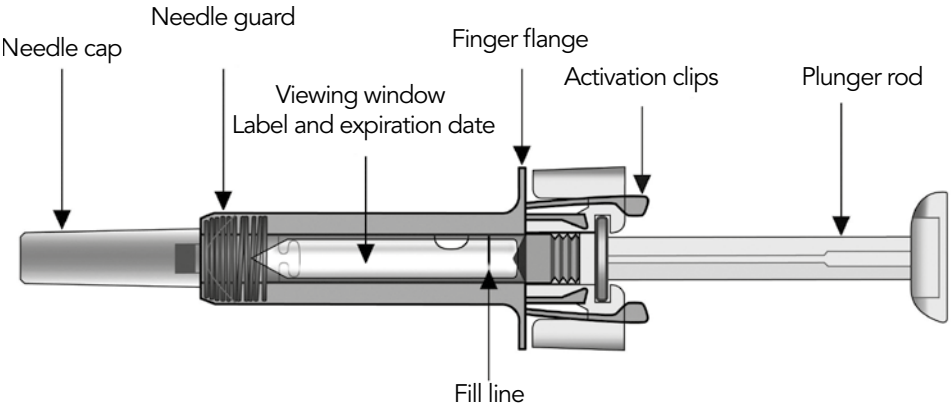
Preparation and subcutaneous use of the Xolair® pre-filled syringe for CSU:[1]

A single use pre-filled syringe contains 150mg of Xolair® and is for subcutaneous administration by a healthcare professional only, in a setting where a medical professional is available.

PREPARATION:

1. Take box containing syringe out of refrigerator and leave unopened for about 20 minutes to reach room temperature
2. When ready to use syringe, wash hands thoroughly with soap and water
3. Clean injection site - Xolair® can be injected in upper outer thigh, upper outer arm or abdomen. If more than one injection at a time, repeat injection in another location
4. Remove plastic tray from box, peel back paper cover, remove and inspect syringe. DO NOT USE if broken or if liquid looks cloudy or contains particles and return entire product pack to pharmacy

Parts of the syringe:



Note: Prior to completion of injection, avoid contact with device activation clips to keep from prematurely covering needle with needle guard

5. Hold syringe horizontally and look into viewing window to check dose (150 mg) of medicine and expiration date printed on label. DO NOT USE if product has expired or if dose is incorrect and return entire product pack to the pharmacy
6. Hold syringe vertically with plunger uppermost and tap side of syringe to allow air bubble to rise. Check to see if liquid level is at or above minimum fill line. If liquid is below fill line DO NOT USE and return entire product pack to pharmacy

USE:

1. Holding syringe with needle pointing up, pull off needle cap and discard. Do not touch exposed needle. Gently tap syringe until air bubble rises to top. Slowly push plunger up to force air bubble out of syringe without inadvertently expelling solution
2. Gently pinch skin at injection site. Insert needle into skin fold
3. Holding onto finger flange, slowly press plunger all the way down until all the solution is injected
4. After complete dose is given, remove needle from skin while holding plunger down
5. Slowly release plunger and allow needle guard to automatically cover exposed needle. If needle guard does not extend automatically, firmly push on plunger, then release and allow guard to cover needle
6. Dispose of used syringe immediately in a sharps container

PBS Information: Section 100 Public and Private Hospital Authority Required for the treatment of severe chronic spontaneous urticaria.
Refer to PBS Schedule for full authority information.

See Approved Product Information before prescribing. TGA Approved Product Information available on request. For the most up-to-date Product Information, go to: https://www.novartis.com.au/products/healthcare-professionals

XOLAIR omalizumab (rch)

Indication: Asthma: Adult and adolescents ≥12 years of age: for the management of adult and adolescent patients with moderate to severe allergic asthma, who are already being treated with inhaled steroids, and who have serum immunoglobulin E levels corresponding to the recommended dose range. ♦ **Children 6 to <12 years of age:** In children aged 6 to <12 years, Xolair is indicated as add-on therapy to improve asthma control in patients with severe allergic asthma who have documented exacerbations despite daily high dose inhaled corticosteroids, and who have immunoglobulin E levels corresponding to the recommended dose range (see Table 10 under "Dosage and Administration"). ♦ **Chronic Spontaneous Urticaria:** for adults and adolescents ≥ 12 years of age who remain symptomatic despite H1 antihistamine treatment. **Contraindications:** hypersensitivity to omalizumab or any other component of the formulation. **Precautions:** Local or systemic allergic reactions, including anaphylaxis, may occur. Anaphylaxis and anaphylactoid reactions have been reported following the first and subsequent administrations. Although most of these reactions occurred within 2 hours after administration, some occurred beyond 2 hours and even beyond 24 hours after injections. Medications for the treatment of anaphylactic reactions should always be available for immediate use. Patients should be informed that such reactions are possible and prompt medical attention should be sought if allergic reactions occur. - Serum sickness and serum sickness-like reactions have rarely been seen in patients treated with humanised monoclonal antibodies including omalizumab, typically 1-5 days after administration of the first or subsequent injections. Patients should be advised to report any symptoms suggestive of serum sickness such as arthritis/arthralgia, rash (urticaria or other forms), fever and lymphadenopathy. - Patients with severe asthma may rarely present systemic hypereosinophilic syndrome or allergic eosinophilic granulomatous vasculitis (Churg-Strauss syndrome), both of which are usually treated with systemic corticosteroids. In rare cases, patients on therapy with anti-asthma agents, including omalizumab, may present or develop systemic eosinophilia and vasculitis. A causal association has not been established. These events are commonly associated with the reduction of oral corticosteroid therapy. In these patients, physicians should be alert to the development of marked eosinophilia, vasculitic rash, worsening pulmonary symptoms, paranasal sinus abnormalities, cardiac complications, and/or neuropathy. Discontinuation of omalizumab should be considered in all severe cases with the above mentioned immune system disorders. - Patients treated have a rapid reduction in free IgE in the serum but an overall increase in the total serum IgE, which reflects free IgE and IgE bound. IgE measured following treatment cannot be used to guide treatment or dosing decisions. Because Xolair reduces free IgE in the serum and tissues, results of skin prick testing, patch testing, and RAST testing for hypersensitivity to potential allergens may be affected. A positive test to a potential allergen in a patient receiving Xolair can be correctly interpreted as representing hypersensitivity to that allergen; however, a negative test may not be interpretable. Physicians are urged to use caution in interpreting such tests in patients receiving Xolair.- In controlled clinical trials, interim and final analyses of an observational study, a numerical imbalance of ATE was observed. - Patients may potentially develop antibodies to the protein. - Parasitic infestation may also result in elevation of serum IgE concentrations, although there is no evidence to suggest that parasitic infections are predisposed to by omalizumab. - Should be used with caution in patients with thrombocytopenia and patients with a history of thrombocytopenia. Patients should have a platelet count before commencing therapy and then periodically during treatment. - Should be used with caution in patients with renal or hepatic impairment. - Patients should be informed that if they experience dizziness, fatigue, faintness or somnolence they should not drive or use machines. - The safe use of the pre-filled syringe in latex-sensitive individuals has not been studied: a derivative of natural rubber latex is present in the removable needle cap. - Caution should be exercised when prescribing to pregnant women or when administered to breast-feeding women (Category B1). - No formal drug interaction studies have been performed. **Dosage and administration: Asthma:** *Xolair is administered subcutaneously every two or four weeks according to the dose determination chart.* Doses (mg) and dosing frequency are determined by baseline serum total IgE level (IU/mL), measured before the start of treatment, and bodyweight (kg). See full PI for dose determination chart. ♦ **Chronic Spontaneous Urticaria:** 300 mg s.c. every 4 weeks. Some patients may achieve control of their symptoms with a dose of 150 mg s.c. every 4 weeks. Prescribers are advised to periodically reassess the need for continued therapy. Clinical trial experience of long-term treatment beyond 6 months in this indication is limited. Xolair should be used as add-on therapy to H1 antihistamine treatment. **Side effects:** pyrexia, injection site reactions including pain, abdominal pain upper, swelling, itching, and redness, pruritus, headaches; nasopharyngitis, upper respiratory tract infection and viral upper respiratory tract infections, sinusitis and sinus headache, arthralgia, myalgia, pain in extremity, musculoskeletal pain, dizziness, somnolence, postural hypotension, weight increase, urticaria, fatigue, swelling arms, nausea, pharyngitis, skin rashes, post-injection phenomena, syncope and vasovagal syncope, diarrhoea, dyspeptic signs and symptoms, flushing, moniliasis, paresthesia, coughing, laryngoedema, angioedema, photosensitivity, asymptomatic platelet decreases, parasitic infections. Serious AEs reported in clinical trials include were appendicitis and fractures. Other serious, but rare, AEs include anti-therapeutic antibody development, anaphylactic reactions (a history of anaphylaxis may be a risk factor) and other allergic conditions such as anaphylactic reactions, allergic bronchospasm and serum sickness. **Sponsor:** Novartis Pharmaceuticals Australia Pty. Limited, ABN 18 004 244 160, 54 Waterloo Road, Macquarie Park, NSW 2113. *(xol240717m).*

**Please note changes to Product Information in italics.*

References: 1. XOLAIR®. TGA-Approved Product Information. Novartis Pharmaceuticals Australia Pty Ltd. 30 March 2017; **2.** ASCIA Action Plans for Anaphylaxis available from https://www.allergy.org.au/health-professionals/anaphylaxis-resources/ascia-action-plan-for-anaphylaxis. Accessed 23 October 2017; **3.** Lieberman PL et al. JACI 2017 In Press (http://dx.doi.org/10.1016/j.jaci.2017.07.013). EpiPen® is a registered trademark of Mylan, Inc. XOLAIR® is a registered trademark of Novartis Pharmaceuticals. Novartis Pharmaceuticals Australia Pty Limited. ABN 18 004 244 160. 54 Waterloo Road, Macquarie Park, NSW 2113. Telephone:(02) 9805 3555. AU-4032. November 2017. CRD2843.

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Xolair® omalizumab