

Local Omalizumab Treatment Protocol – Adults and Adolescents (12years +)

1.	New medicine name: Omalizumab 150mg powder and solvent for injection (Xolair [®])
2.	Licensed indication(s): Omalizumab is indicated as add-on therapy to improve asthma control in patients with severe persistent allergic asthma who have a positive skin test or <i>in vitro</i> reactivity to a perennial aeroallergen and who have reduced lung function (FEV ₁ <80%) as well as frequent daytime symptoms or night-time awakenings and who have had multiple documented severe asthma exacerbations despite daily high-dose inhaled corticosteroids (ICS), plus a long-acting inhaled beta ₂ -agonist (LABA). Omalizumab treatment should only be considered for patients with convincing immunoglobulin E (IgE) mediated asthma.
3.	<p>Scottish Medicines Consortium advice: omalizumab (Xolair[®]) is accepted for restricted use within NHS Scotland as add-on therapy to improve asthma control in adult and adolescent patients (12 years of age and above) with severe persistent allergic asthma.</p> <p>It is restricted to initiation and monitoring by hospital physicians experienced in the diagnosis and treatment of severe persistent asthma. It is restricted to patients who are prescribed chronic systemic steroids and in whom all other treatments have failed. The response to omalizumab treatment should be assessed in all patients at 16 weeks and treatment should be discontinued in patients who have not shown a marked improvement in overall asthma control.</p> <p>Medicines Advisory Group advice: HOSPITAL ONLY (Chest or Rhinology Clinic)</p>
4.*	<p>Prescriber details: Consultant respiratory physicians</p> <p>(Contact Arlene Shaw, Specialist Clinical Pharmacist, Respiratory Medicine to check eligibility and arrange registration of patient in the Outcomes-Based Reimbursement scheme)</p>
5.*	<p>Criteria for patient selection: Patients with objective evidence of refractory persistent severe allergic asthma not controlled on optimised BTS step 5 therapy – who have adequately implemented allergen avoidance measures and where other relevant trigger factors have been addressed such as concomitant allergic rhinosinusitis, smoking, occupation, GERD.</p> <p>See Summary of Product Characteristics for baseline IgE / weight specific criteria.</p>
6.	<p>Administration details: The injections are administered subcutaneously in the deltoid region of the arm. Alternatively, the injections can be administered in the thigh if there is any reason precluding administration in the deltoid region.</p> <p>There is limited experience with self administration, therefore treatment is intended to be administered by a healthcare professional only.</p>
7.	<p>Contra-indications: Hypersensitivity to the active substance or to any of the excipients.</p>
8.	<p>Side-effects/cautions: During clinical trials the most commonly reported adverse reactions were injection site reactions, including injection site pain, swelling, erythema and pruritus, and headaches. Other side effects reported include idiopathic severe thrombocytopenia, parasitic infection, anaphylactic reaction and other allergic conditions, dizziness, somnolence, paraesthesia, syncope, postural hypotension, flushing, pharyngitis, coughing, allergic bronchospasm, allergic granulomatosis vasculitis, nausea, diarrhoea, dyspepsia, arthralgia, myalgia, joint swelling, rash, pruritis, photosensitivity, angiodema, alopecia, increase in weight, fatigue, swelling arms, influenza like illness laryngodema, abdominal pain, pyrexia and serum sickness.</p>

Not indicated for the treatment of acute asthma exacerbations, acute bronchospasm or status asthmaticus.

Omalizumab has not been studied in patients with hyperimmunoglobulin E syndrome or allergic bronchopulmonary aspergillosis or for the prevention of anaphylactic reactions, including those provoked by food allergy, atopic dermatitis and allergic rhinitis.

Therapy has not been studied in patients with autoimmune diseases, immune complex-mediated conditions, or pre-existing renal or hepatic impairment. Caution should be exercised in these patient populations.

Abrupt discontinuation of systemic or inhaled corticosteroids after initiation of omalizumab therapy is not recommended. Decreases in corticosteroids should be performed under the direct supervision of a physician and may need to be performed gradually.

Patients with diabetes mellitus, the glucose-galactose malabsorption syndrome, fructose intolerance or sucrase-isomaltase deficiency should be warned that one 150 mg dose contains 108 mg of sucrose.

See [Summary of Product Characteristics](#) for more information.

9.* Monitoring - response to treatment:

Refer to 'Algorithm for assessment of response to treatment with omalizumab in Tayside' (below). After 16 weeks, only patients achieving excellent/good evaluation should continue with omalizumab.

Total IgE levels are elevated during treatment and remain elevated for up to one year after the discontinuation of treatment. Therefore, re-testing of IgE levels during treatment cannot be used as a guide for dose determination.

10.* Monitoring – treatment safety:

Local or systemic allergic reactions, including anaphylaxis and anaphylactic shock, may occur when taking omalizumab, also with onset after a long duration of treatment. Most of these reactions occurred within 2 hours after the first and subsequent injections but some started beyond 2 hours and even beyond 24 hours after the injection. Therefore medications for the treatment of anaphylactic reactions should always be available for immediate use following administration. Patients should be informed that such reactions are possible and prompt medical attention should be sought if allergic reactions occur. Anaphylactic reactions were rare in clinical trials (<1/1000).

Serum sickness and serum sickness like reactions have been seen in patients treated with humanised monoclonal antibodies including omalizumab. Onset is typically 1-5 days after injection or after long duration of treatment. Suggestive symptoms of serum sickness include arthritis / arthralgias, rash, fever and lymphadenopathy. Antihistamine and corticosteroids are useful to treat / prevent this disorder, and patients should be advised to report suspected symptoms.

During clinical trials, there was a numerical imbalance in cancers arising in the omalizumab treatment group compared with the control group ie 0.5% of patients treated with omalizumab compared with 0.18% control patients. The overall observed incidence rate of malignancy in the omalizumab clinical trial programme was comparable to that reported in the general population.

IgE may be involved in the immunological response to some helminth infections. Caution may be warranted in patients at high risk of helminth infection, in particular when travelling to areas where helminthic infections are endemic. If patients do not respond to recommended anti-helminth treatment, discontinuation of omalizumab should be considered.

Patients with severe asthma may rarely present with 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.

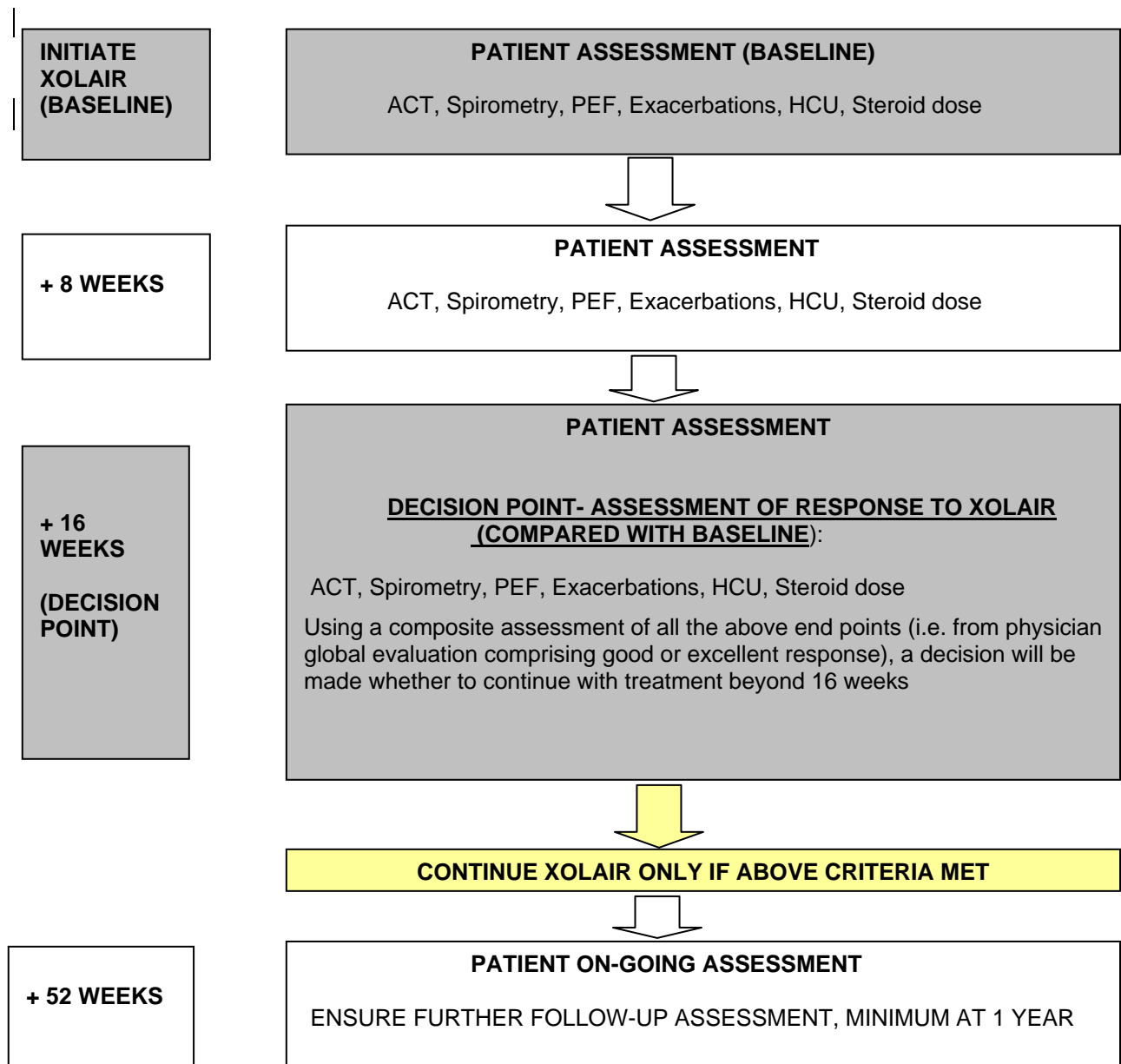
These events are commonly associated with the reduction of oral corticosteroid therapy. In these patients, physicians should be alert to the development of marked eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy.

In controlled clinical trials and an ongoing observational study, a numerical imbalance of arterial thromboembolic events (ATEs) was observed between omalizumab treated patients and control patients. ATE included stroke, transient ischaemic attack, myocardial infarction, unstable angina, and cardiovascular death (including death from unknown cause). In a multivariate analysis controlling for baseline cardiovascular risk factors, omalizumab was not associated with ATE risk.

11.*	Written by: Professor Brian Lipworth Mrs Arlene Shaw	Date: 8/11/07
	Reviewed by: Professor Brian Lipworth Mrs Arlene Shaw	Date: Nov 2010
12.*	Review date: November 2012	

*** essential fields**

ALGORITHM FOR THE ASSESSMENT OF RESPONSE TO TREATMENT WITH OMALIZUMAB IN TAYSIDE



ESSENTIAL ASSESSMENTS

- Patients must have allergic asthma ,already be taking and compliant on step 5 BTS therapy, with evidence of uncontrolled disease –ie taking high dose ICS/LABA and maintenance oral steroids [or frequent oral steroid pulses with low dose macrolide] +/- anti-histamine/anti-leukotriene, and having addressed treatment for concomitant allergic rhinosinusitis [eg nasal steroids, cromoglycate, antihistamine] ,and allergen avoidance , and other relevant triggers – eg smoking cessation ,GERD
- **ASTHMA CONTROL TEST (ACT)**
The ACT, is a five-item, self-administered survey that can be done in the clinic or at home. (see Appendix A)
- **SPIROMETRY**
- **Am PEF**
Peak Expiratory Flow Rate (PEF) should be measured within 30 minutes of waking in the morning, on alternate weekdays (i.e. Mon, Wed and Fri).
- Dose of oral steroid requirement –if possible to step down while taking omalizumab
- **EXACERBATIONS**
Defined as an asthma worsening episode requiring use of additional oral corticosteroid. Patients should have *at least* a 4-week period free from exacerbations before entering the assessment period at baseline. The absolute number of exacerbations over the assessment period will be recorded. The Physician Global Evaluation (see below) will put this into context of the number and frequency of exacerbations that were occurring in an undefined period prior to the assessment period.
- **UNSCHEDULED HEALTHCARE UTILISATION (HCU)**
Defined as unscheduled hospital admission for asthma, unscheduled A&E attendance or unscheduled GP visit, since the last assessment. Order of clinical relevance: hospitalization > A&E visit > GP visit. Again, the Physician Global Evaluation (see below) will put this into context of the number of episodes of unscheduled care that were occurring in an undefined period prior to the assessment period.
- **PHYSICIAN GLOBAL EVALUATION OF TREATMENT EFFECTIVENESS**
The treating physician should make an overall clinical evaluation as to how much improvement in asthma control the patient has experienced compared to baseline (week 0). Physician overall evaluation should be a clinical judgement, at 16 weeks, based on all available information

Physician overall evaluation of treatment effectiveness should be graded using the following descriptors:

Excellent	(complete control of asthma)
Good	(marked improvement of asthma)
Moderate	(discernible, but limited improvement in asthma)
Poor	(no appreciable change in asthma)
Worsening	(of asthma)

Score of Excellent/Good indicates patient is classified as a responder to omalizumab.

AFTER 16 WEEKS TREATMENT, ONLY PATIENTS ACHIEVING EXCELLENT/GOOD EVALUATION SHOULD CONTINUE WITH OMALIZUMAB

Appendix A -Asthma Control Test™

This survey is designed to help you describe your asthma and how your asthma affects how you feel and what you are able to do. To complete it, please circle the answer for each question.

In the **past 4 weeks**, how much of the time did your asthma keep you from getting as much done at work, school, or at home?

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

During the **past 4 weeks**, how often have you had shortness of breath?

1. More than once a day
2. Once a day
3. 3 to 6 times a week
4. Once or twice a week
5. Not at all

During the **past 4 weeks**, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?

1. 4 or more nights a week
2. 2 or 3 nights a week
3. Once a week
4. Once or twice
5. Not at all

During **the past 4 weeks**, how often have you used your rescue inhaler or nebulizer medication?

1. 3 or more times per day
2. 1 or 2 times per day
3. 2 or 3 times per week
4. Once a week or less
5. Not at all

How would you rate your asthma control during the **past 4 weeks**?

1. Not controlled at all
2. Poorly controlled
3. Somewhat controlled
4. Well controlled
5. Completely controlled

Total Score =