Local Omalizumab Treatment Protocol (For children 6 to <12 years of age)

Significant prescribing issues are highlighted but the protocol should be used in conjunction with the ABPI summary of product characteristics where available: http://www.medicines.org.uk/

1.	**New medicine name:** Omalizumab 150mg powder and solvent for injection (Xolair®)
2.	**Licensed indication under review:** Xolair is indicated as add-on therapy to improve asthma control in children (6 to <12 years of age) with severe persistent allergic asthma who have a positive skin test or *in vitro* reactivity to a perennial aeroallergen and frequent daytime symptoms or night-time awakenings and who have had multiple documented severe asthma exacerbations despite daily high-dose inhaled corticosteroids, plus a long-acting inhaled beta2-agonist. Omalizumab treatment should only be considered for patients with convincing IgE (immunoglobulin E) mediated asthma.
3.	**Scottish Medicines Consortium advice:** Omalizumab (Xolair®) is accepted for restricted use within NHS Scotland as add-on therapy to improve asthma control in children (6 to < 12 years of age) with severe persistent allergic asthma. 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. **Medicines Advisory Group advice:** HOSPITAL ONLY (paediatrics**)**
4.*	**Prescriber details:** Consultant in paediatric respiratory medicine or consultant with expertise in paediatric respiratory medicine.
5.*	**Criteria for patient selection:** Patients with objective evidence of refractory persistent severe allergic asthma (baseline IgE <700units/mL) not controlled on optimised BTS step 5 therapy including regular pulses of oral steroids. Patients should have adequately implemented allergen avoidance measures. They should also have addressed other relevant trigger factors such as GORD, allergic rhinitis, parental/carer cigarette smoke exposure or patient smoking and environmental factors including pets.
6.	**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.
7.	**Contra-indications:** Hypersensitivity to the active substance or to any of the excipients.
8.	**Side-effects/cautions:** In clinical trials in patients 6 to <12 years of age, the most commonly reported adverse reactions suspected of being related to the medicinal product were headache, pyrexia and upper abdominal pain. Most of the reactions were mild or moderate in severity. Other side effects reported include idiopathic severe thrombocytopenia, parasitic infection, anaphylactic reaction and other allergic conditions, dizziness, somnolence, parasthesia, 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 and influenza like illness.

Omalizumab is not indicated for the treatment of acute asthma exacerbations, acute bronchospasm or status asthmaticus.

Xolair 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. Xolair is not indicated for the treatment of these conditions.

Xolair 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 when administering Xolair in these patient populations.

Abrupt discontinuation of systemic or inhaled corticosteroids after initiation of Xolair 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 Xolair dose contains 108 mg of sucrose.

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 (and parent/carer) 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).

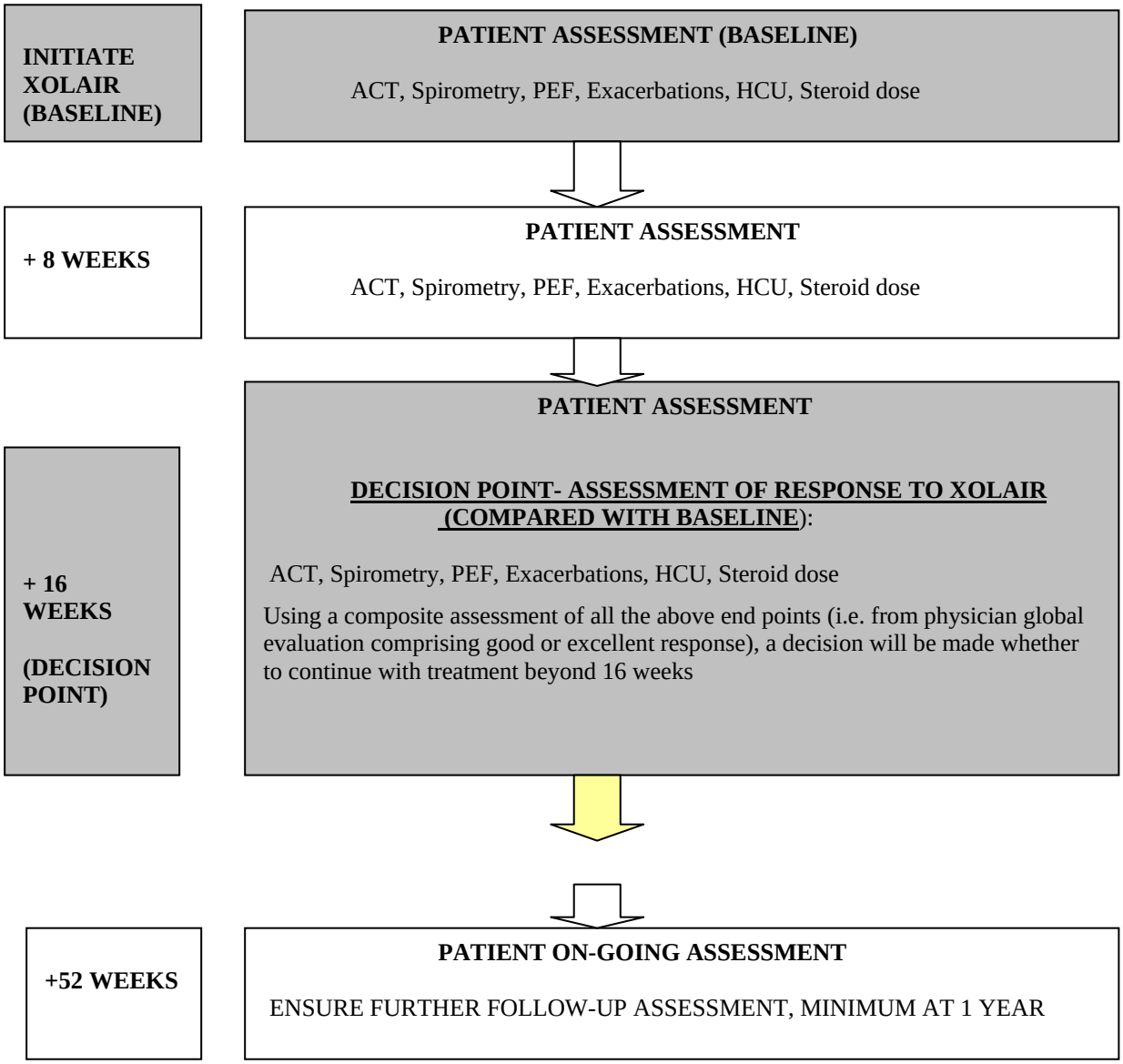
During clinical trials, there was a numerical imbalance in cancers arising in the omalizumab treatment group compared to the control group (0.5% of patients in the omalizumab group versus 0.18% in the control group). The overall observed incidence rate of malignancy in the omalizumab clinical trial programme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

IgE may be involved in the immunological response to some helminth infections. In patients at chronic high risk of helminth infection, a placebo-controlled trial showed a slight increase in infection rate with omalizumab, although the course, severity, and response to treatment of infection were unaltered. The helminth infection rate in the overall clinical programme, which was not designed to detect such infections, was less than 1 in 1,000 patients. However, 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 Xolair should be considered.

	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. 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. Serum sickness and serum sickness-like reactions, which are delayed allergic type III reactions, have rarely been seen in patients treated with humanized monoclonal antibodies including omalizumab. The suggested pathophysiologic mechanism includes immune-complex formation and deposition due to development of antibodies against omalizumab. The onset has typically been 1 – 5 days after administration of the first or subsequent injections, also after long duration of treatment. Symptoms suggestive of serum sickness include arthritis/arthralgias, rash (urticaria or other forms), fever and lymphadenopathy. Antihistamines and corticosteroids may be useful for preventing or treating this disorder, and patients should be advised to report any suspected symptoms.
11.*	**Written by:** Iain Hewitt**,** Specialist pharmacist, Women and Child Health **Date:** 20/07/2010 **Approved by:** Jonathan McCormick,Consultant ,Paediatrics **Date:** 20/07/2010
12.*	**Review date:** 20/07/2012

- **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 – i.e. 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 (e.g. nasal steroids, cromoglycate, antihistamine), allergen avoidance , and other relevant triggers – e.g. GORD, parental/carer cigarette smoke exposure or patient smoking and environmental factors including pets.

- **ASTHMA CONTROL TEST (ACT)**
  An age appropriate ACT should be carried out. See www.asthmacontrol.com/child.html for further information.

- **SPIROMETRY**

- **MORNING PEAK EXPIRATORY FLOW RATE (PEF)**
  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 a patient is classified as a responder to omalizumab.
  AFTER 16 WEEKS TREATMENT, ONLY PATIENTS ACHIEVING EXCELLENT/GOOD EVALUATION SHOULD CONTINUE WITH OMALIZUMAB