OMALIZUMAB Therapy in Children and Young People

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Key Amendments

Date	Amendment	Approved by
19th November 2020	Document extended for 1 year	Dr J West/Paediatric QIM
17th March 2021	Nursing assessment forms added to document	Paediatric QIM
26th March 2021	No further changes required-approved for further 3 years	Paediatric QIM
22nd December 2022	New appendix 'Omalizumab injections' added to document	MSC

Omalizumab (Xolair) is a biological monoclonal antibody used in the management of severe, persistent asthma in adults and children aged 6 years and above as recommended by NICE (2013).

It is an add-on treatment option for selected individuals aged 6 years and above with difficult-to-control asthma and a strong allergic component, whose symptoms are inadequately controlled on Step 5 of the BTS Guidelines (high dose inhaled corticosteroid, under paediatric respiratory team **and** continuous or frequent (more than 4 courses in previous 12 months) oral corticosteroids) (BTS 2014).

Omalizumab is also used in the management of severe, chronic spontaneous urticaria in adults and children aged 12 years and above as recommended by NICE (2015). It is an add-on therapy used in those young people who have not responded to standard treatment

Omalizumab specifically binds to circulating IgE in the blood and interstitial fluid, and primarily prevents the binding of IgE to high-affinity FceRI receptors on mast cells and basophils or the low-affinity FceRII (CD23) receptors on B cells resulting in down-regulation of these receptors

Omalizumab for Allergic Asthma

Inclusion criteria:

- A positive skin prick or specific IgE test to a perennial aeroallergen (e.g. dust mites, cats, dogs, and mould)
- Serum total IgE concentration between 30-1500 IU/mL (Patients with IgE <76 IU/ml are unlikely to experience benefit. If >12 years and IgE<76 IU/ml or 6-12 years and IgE <200 IU/ml should have positive IgE to perennial aeroallergen)
- Body weight between 20-150kg, although the weight limit may be lower depending on total IgE level (see dosing table)
- Reduced lung function (FEV1 <80% in adolescents >12 years and adults)

- Frequent day-time symptoms *or* nocturnal awakenings *despite* full trial of high-dose inhaled corticosteroids with good compliance and adequate inhaler technique, LABA medications, leukotriene receptor antagonists, theophyllines and oral corticosteroids and smoking cessation if appropriate
- Multiple documented severe exacerbations
- Continuous or frequent oral prednisolone courses (>4 courses per year)
- Smoking cessation measures if appropriate

The primary benefits to patients who respond to therapy are reduced disease exacerbations requiring fewer unplanned medical visits and fewer hospitalisations with resulting improvement in quality of life. Lung function may also improve, while some patients are able to reduce or discontinue systemic corticosteroids. Approximately 1 in 5 eligible patients fail to respond to a 16 week trial of therapy.

Assessments:
A formal assessment should occur before therapy is initiated (baseline assessment).
This assessment includes confirmation of diagnosis via reversibility and exclusion of overlapping diagnosis, compliance with asthma treatment and correct use of inhalers, co-morbidities optimally treated and optimal control to exposure of sensitizing and non-sensitizing substances).

Then after 16 weeks of treatment (decision point) a Physician Global Evaluation of Treatment Effectiveness (GETE) will take place. This will include a patient interview, review of patient's notes, diary cards, key response indicator assessments and supportive assessments.

Key Response Indicator Assessments will include the completion of the Asthma Control Test (ACT) at each appointment

Supportive Assessment will include

- the recording of number of unscheduled healthcare episodes including GP visits and telephone calls, unplanned escalation of therapy, ED visits and admissions
- a PEF diary additionally documenting use of reliever therapy
- lung function at each appointment

(See the omalizumab assessment document)

To continue with the treatment after the baseline treatment, individuals must achieve improvement in the Key Response Indicators at 16 weeks and an Excellent or Good GETE score. A moderate response could be considered by the respiratory paediatrician for an extended trial period. Patients who have a poor or worsening evaluations should be reported as adverse events and reported in line with the Trust medicine policy.

GETE scoring:

Excellent: complete control of asthma
Good: marked improvement of asthma
Moderate: discernible, but limited improvement in asthma
Poor: no appreciable change in asthma
Worsening: overall deterioration in asthma control

Omalizumab for Chronic Spontaneous Urticaria (CSU)

Chronic spontaneous urticaria is characterised by persistent itching, which can interfere with activities of daily living and sleep and, in severe cases, can be unbearable, disabling and considerably affects quality of life.

There is no licensed treatment option for patients whose disease does not respond to H1‑antihistamines but, in practice, clinicians offer patients H2‑antihistamines and leukotriene receptor antagonists (LTRAs).

Patients with severe chronic spontaneous urticaria whose disease does not respond to the initial treatments are often offered immunosuppressants such as ciclosporin.

Guidelines for urticaria recommend omalizumab at the same point in the pathway as immunosuppressants such as ciclosporin.

Inclusion Criteria

- The young person aged 12 years or more is diagnosed with chronic spontaneous urticaria.
- The severity of the condition is monitored objectively using a weekly urticarial score of > or = 28 on more than one occasion in the preceeding six weeks.
- The condition has not responded to standard treatment with H1 –antihistamines (up to 4x approved dose) and either H2 –antihistamines or leukotriene receptor antagonists (LTRAs)

Dosing and risks

Recognised side effects include headache and upper respiratory tract infections in treatment for urticaria. The risk of anaphylaxis is quoted as 0.09% for allergic asthma. In urticarial the standard dose is 300mg (given in two 150mg subcutaneous doses) every 4 weeks. If there is no response at the fourth dose the treatment should be discontinued. The treatment should be stopped after 6 doses (24 weeks) and is only restarted if the condition returns.

Omalizumab Safety:

Ensure that written information and informed consent has been given from the patient (or parent). Before commencing the treatment the Respiratory Specialist Nurse, allergy nurse or consultant will spend time with the patient and the family educating them about the treatment using appropriate literature such as the “Starting your new Xolair treatment book”.

The nurse will encourage the patient and the family to complete the weekly diary card and document any symptoms that are experienced during the treatment.

The dose of omalizumab **for asthma** should have determined and prescribed by the respiratory paediatrician using a recently measured serum total IgE concentration and patient weight. **The dose of omalizumab for urticaria is (300mg) every 4 weeks should be prescribed by the allergy consultant / nurse.**

The medication will be checked in accordance with the Trust medicine policy Omalizumab should be initiated and monitored in a paediatric day case unit or on the paediatric ward.

For asthma: Omalizumab is administered subcutaneously via prefilled syringe every 2-4 weeks. In asthma the dose is dependent upon the individual’s weight and total serum IgE concentration. IgE concentrations cannot be re-measured during omalizumab therapy because the drug “holds” IgE in the circulation, although dose changes can be made to accommodate significant changes in body weight (assuming that the serum IgE concentration at the commencement of therapy is unchanged). The maximum recommended dose is 600mg every 2 weeks.

Dosing Table: (for asthma)

Total Serum IgE IU/ml	Body weight (kg)									
	20-25	>25-30	>30-40	>40-50	>50-60	>60-70	>70-80	>80-90	>90-125	>125-150
29-100	75	75	75	150	150	150	150	150	300	300
>100-200	150	150	150	300	300	300	300	300	450	600
>200-300	150	150	225	300	300	450	450	450	600	375
>300-400	225	225	300	450	450	450	600	600	450	525
>400-500	225	300	450	450	600	600	375	375	525	600
>500-600	300	300	450	600	600	375	450	450	600	
>600-700	300	225	450	600	375	450	450	525		
>700-800	225	225	300	375	450	450	525	600		
>800-900	225	225	300	375	450	525	600			
>900-1000	225	300	375	450	525	600				
>1000-1100	225	300	375	450	600					
>1100-1200	300	300	450	525	600					
>1200-1300	300	375	450	525						
>1300-1500	300	375	525	600						

xxx	**4 Weekly dosing schedule**
xxx	**2 Weekly dosing schedule**
	Do not administer

For Chronic Spontaneous Urticaria: 300mg Omalizumab is administered subcutaneously via two prefilled 150mg syringes every 4 weeks**.**

How to administer Omalizumab therapy:

Always wash hands before administering subcutaneous injections and prepare injection materials according to Trust policy.

Procedure	Rationale
Omalizumab should be given in a controlled healthcare setting with access to emergency medications	There is a risk of anaphylaxis
Check patient's current weight with the prescribed dose. Check total IgE before 1st dose only	To ensure that an effective dose will be administered
Assess current health status, record PEF, lung function, Blood Pressure, Pulse, Respirations and SaO2	To reduce the risk of respiratory compromise in the event of an anaphylactic reaction
Ensure female patients are aware of the need for effective contraception	The safety profile of Omalizumab in pregnancy has not yet been established
The box containing the syringe of medication should be stored in the fridge. 20 minutes before the injection the box should be removed from the fridge to allow it to reach room temperature, but should never be placed in direct sunlight. The syringe must not be kept out of the fridge for more than 4 hours Check expiry date and ensure the liquid in each prefilled syringe is clear and not discoloured	To ensure that the drug is safe to use
Dose should be limited to 150mg per injection site. Several sites may be needed. Ensure skin is clear, unbroken and without bruising. Confirm the preferred site with the patient. Rotate sites where possible.	Due to the large volume of fluid
Topical anaesthesia may be used to numb the area as per manufacturer's guidelines	To numb the area and reduce discomfort
Prepare the injection as per the manufacturer's instructions (appendix 3) Administer subcutaneously. Pinch the skin together.	To facilitate deep subcutaneous injection
Remove needle and ask patient to press with gauze or cotton wool for 30 seconds. Apply plaster	To prevent drug leakage
Dispose of sharp safely	As per local infection control policy

Maintain accurate documentation. Sign prescription chart and record dose, route, time, batch, expiry date and time of administration.	To maintain accurate documentation
Observe the patient following drug administration: a) For 2 hours following the first three injections b) For 1 hour after subsequent injections	Due to the risk of anaphylaxis
Prior to discharge check injection site. Repeat Peak Flow measurement	To ensure patient is well
Advise patient not to discontinue regular medications without medical advice	Omalizumab is an add-on therapy rather than replacement for usual preventative medications
Ensure patient has an appointment for the next dose and a point of contact for any queries. All patients receiving omalizumab will have open access to the children's ward.	For assistance with any concerns or queries
For treatment of chronic spontaneous urticarial please ensure discharge with UAS7 for 4 weeks monitoring. (see appendix 1)	To monitor response to treatment

Appendix 1

Weekly Urticaria
Activity Score (UAS7)

Complete this questionnaire over 7 consecutive days. Your responses will help your doctor assess how active your chronic idiopathic urticaria (CIU) is. Please circle the score that corresponds to the number of wheals you have and the score that represents the intensity of your pruritus (itching) on a daily basis (see description in chart below). Remember to bring your completed questionnaire to your next visit.

Date	Daily number of wheals	+	Daily intensity of pruritus	=	Daily UAS score*
Example	0 (1) 2 3	+	0 1 (2) 3	=	0 1 2 (3) 4 5 6
Day 1	0 1 2 3	+	0 1 2 3	=	0 1 2 3 4 5 6
Day 2	0 1 2 3	+	0 1 2 3	=	0 1 2 3 4 5 6
Day 3	0 1 2 3	+	0 1 2 3	=	0 1 2 3 4 5 6
Day 4	0 1 2 3	+	0 1 2 3	=	0 1 2 3 4 5 6
Day 5	0 1 2 3	+	0 1 2 3	=	0 1 2 3 4 5 6
Day 6	0 1 2 3	+	0 1 2 3	=	0 1 2 3 4 5 6
Day 7	0 1 2 3	+	0 1 2 3	=	0 1 2 3 4 5 6
					UAS7 score†

Adapted from Zuberbier *et al.*

*The sum of the daily number of wheals and daily intensity of pruritus.
†The sum of the daily UAS scores over 7 consecutive days.

Assessment of disease activity in patients with CIU (UAS scale)

Score	Wheals	Pruritus
0	**None**	**None**
1	**Mild** (less than 20 wheals/24 hours)	**Mild** (present but not annoying or troublesome)
2	**Moderate** (20-50 wheals/24 hours)	**Moderate** (troublesome but does not interfere with normal daily activity or sleep)
3	**Intense** (more than 50 wheals/24 hours or large confluent areas of wheals)	**Intense** (severe pruritus, which is sufficiently troublesome to interfere with normal daily activity or sleep)

Appendix 2

Pathway for patients considered for Omalizumab injections.

Omalizumab is used for the management of persistent, severe Chronic Spontaneous Urticaria (CSU). This is a treatment pathway to ensure patients, considered treatment with Omalizumab, have the appropriate assessments completed.

Name:

NHS no/Hospital number:

Date of Birth:

1) Paediatric Consultant considers Omalizumab for treatment of persistent, severe Chronic Spontaneous Urticaria (CSU) following inclusion criteria outlined in Omalizumab guideline 'Investigation, Diagnosis and Management of Chronic Urticaria in Childhood' and 'Omalizumab therapy in children and Young People'
   Link: http://whitsweb/KeyDocs/KeyDocs/Sub_Webpage/1178?persist=True
   Date and sign:_____

2) Patient to complete 4-6 weeks of UAS 7 scores (printed sheets or UAS7 booklets from Novatis kept with allergy CNS team and allergy secretaries)
   Link: M:\Acute\Paediatrics\Dr Dawson Clinics\Allergy Patient Info\Urticaria.
   Date and sign:_____

3) Provides family with Patient Information on Omalizumab
   Link: http://whitsweb/KeyDocs/KeyDocs/Sub_Webpage/1179?persist=True
   Date and sign:_____

4) Assesses any asthma medication, compliance and asthma control. If necessary, performs Peak Flow, FeNo or Spirometry if necessary. Date and sign:_____

5) Considers and discusses with young person and family, social arrangements, potential concordance issues and patient concerns. Date and sign:_____

6) Discusses patient in MDT and documents in minutes. Date and sign:_____

7) Discusses treatment with family and decides plan of action - ***proceed*** or ***withhold treatment*** with appropriate follow up (delete as necessary) Date and sign:_____

8) Completes BlueTeq pharmacy request. Date and sign:_____

9) In patient bed is confirmed. Date and sign:_____

10) BRIT registry patient information sheet given to family with explanation.
    Date and sign:_____

11) In patient prescription chart is completed approximately 2 weeks before admission date to allow pharmacy to order drug. Date and sign:_____

File pathway and UAS7 scores in electronic filing system under 'Investigations/results' when complete.

Additional information to be documented in clinic appointment paperwork and clinic letter.

Only for use by Paediatric Allergy Team

References

NICE technology appraisal guidance [TA278] (Apr 2013) Omalizumab for treating severe persistent allergic asthma.

NICE technology appraisal guidance [TA339] (June 2015) Omalizumab for previously treated chronic spontaneous urticarial.

Monitoring Tool

Key control:	Checks to be carried out to confirm compliance with the policy:	How often the check will be carried out:	Responsible for carrying out the check:	Results of check reported to: *(Responsible for also ensuring actions are developed to address any areas of non-compliance)*	Frequency of reporting:
WHAT?	**HOW?**	**WHEN?**	**WHO?**	**WHERE?**	**WHEN?**
These are the 'key' parts of the process that we are relying on to manage risk. We may not be able to monitor every part of the process, but we MUST monitor the key elements, otherwise we won't know whether we are keeping patients, visitors and/or staff safe.	What are we going to do to make sure the key parts of the process we have identified are being followed? (Some techniques to consider are; audits, spot-checks, analysis of incident trends, monitoring of attendance at training.)	Be realistic. Set achievable frequencies. Use terms such as '10 times a year' instead of 'monthly'.	Who is responsible for the check? Is it listed in the 'duties' section of the policy? Is it in the job description?	Who will receive the monitoring results? Where this is a committee the committee's specific responsibility for monitoring the process must be described within its terms of reference.	Use terms such as '10 times a year' instead of 'monthly'.
Inclusion criteria followed	Audit eligibility criteria completed on omalizumab assessment document	Once a year	Respiratory paediatric consultant and respiratory specialist nurse	Any exceptions reported via incident reporting. Audit presented to paediatric audit meeting	Once a year
Dose calculated correctly	Audit dosage calculated from dosing table	Once a year	Respiratory paediatric consultant and respiratory specialist nurse	Any exceptions reported via incident reporting. Audit presented to paediatric audit meeting	Once a year
A Physician Global Evaluation of Treatment Effectiveness (GETE) and decision to continue or discontinue made at 16 weeks	Omalizumab assessment form completed	Once a year	Respiratory paediatric consultant and respiratory specialist nurse	Any exceptions reported via incident reporting. Audit presented to paediatric audit meeting	Once a year

Omalizumab Assessment For asthma:

Please attach patient sticker here or record:

Name:……

NHS No:……

Unit No:……

D.O.B: ……....Male/ Female

Eligibility: Do not continue unless Y documented for each question

Age 6 or above: **Y / N**
Diagnosis of severe persistent asthma: **Y / N**
4 or more courses of OCS or maintenance OCS: **Y / N**
Positive skin prick or specific IgE to perennial aeroallergen: **Y / N**
Total IgE 76-1500 IU: **Y / N** IgE: _____
Body weight between 20-150kg: **Y / N** _____
Dosage checked on dosage table **Y / N**
Discussed pregnancy **Y / N**

Start Date: _____
Assessment Date: _____

Dose: _____ 2 / 4 weekly

Advice leaflet given **Y/N**
Informed consent documented **Y/N**
Do not continue unless Y documented for each question

	BASELINE	Week 2	Week 4	Week 6	Week 8	Week 10	Week12	Week14	Week 16
Date of visit									
Weight									
ACT									
FEV_1 / FVC (%)									
PEF									
In previous 2/4 weeks:									
Number of exacerbations?									
No. of courses of oral prednisolone?									
No. of days off school / work?									
GP Visits?									
A&E / Out of Hours?									
Hospital admissions?									
Global Assessment	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	
Any adverse events reported?									
Injection site used									
Observed for number of hours post injection (write time in box)									
Anaphylaxis advice?									
Comments									
16 week review:	**Continue**		**Discontinue**						

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Omalizumab For Chronic Urticaria Assessment:

Please attach patient sticker here or record:

Name:……

NHS No:……..

Unit No:……

D.O.B: ……Male/ Female

Eligibility: Do not continue unless Y documented for each question

age 12 or above: **Y / N**
Diagnosis of chronic urticaria: **Y / N**
UAS score >28 once in last 6 weeks: **Y / N**
Not responded to 4x dose of antihistamine and monteleukast: **Y / N**
Verbal confirmation that weekly UAS documented **Y / N**
Discussed pregnancy: **Y / N**
Comments

Start Date: _____
Assessment Date:
_____

Dose: 300mg 4 weekly
Advice leaflet given **Y/N**
Informed consent documented **Y/N**
Do not continue unless Y documented for each question

	BASELINE	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32
Date of visit									
Weight									
UAS									
PEF (if asthmatic)									
In previous 4 weeks:									
Number of UAS scores > 28?									
No. of days off school?									
GP Visits?									
A&E / Out of Hours?									
Hospital admissions?									
Global Assessment									
Any adverse events reported? (if Y document in history sheet)									
Injection site used									
Observed for number of hours post injection (write time in box)									
Anaphylaxis advice?									
Comments									
Sign & date									

16 week review: Continue Discontinue **32 week review: Continue Discontinue**