Urticaria Treatment Pathway

Guideline Summary
This clinical guideline outlines the treatment pathway for adult patients with urticaria

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1. Scope

This treatment pathway applies to adult patients with a diagnosis of urticaria and is primarily to set out the different treatment options available in secondary care

2. Rationale

This treatment pathway provides an evidence-based approach for the treatment of urticaria whilst maximising cost effectiveness and clinical outcome for use by all healthcare professionals involved in patient care.

3. Background

Chronic urticaria (CU) is a disease characterised by pruritic weals, angio-oedema or both occurring for at least 6 weeks. Around half of patients present with weals alone, 40% with weals and angio-oedema and 10% with angio-oedema only. It encompasses chronic spontaneous urticaria (CSU) and chronic inducible urticarias.

For information and guidance on management of urticaria in primary care please refer to the NICE Clinical Knowledge Summary (CKS) on urticaria

Patients can have an inducible element to their urticaria which is triggered by heat, cold, pressure, vibration, water, ultraviolet light (UV), etc. These urticarias are induced reproducibly after a specific physical stimulus is applied, however there can be a certain degree of overlap between spontaneous and inducible urticarias.

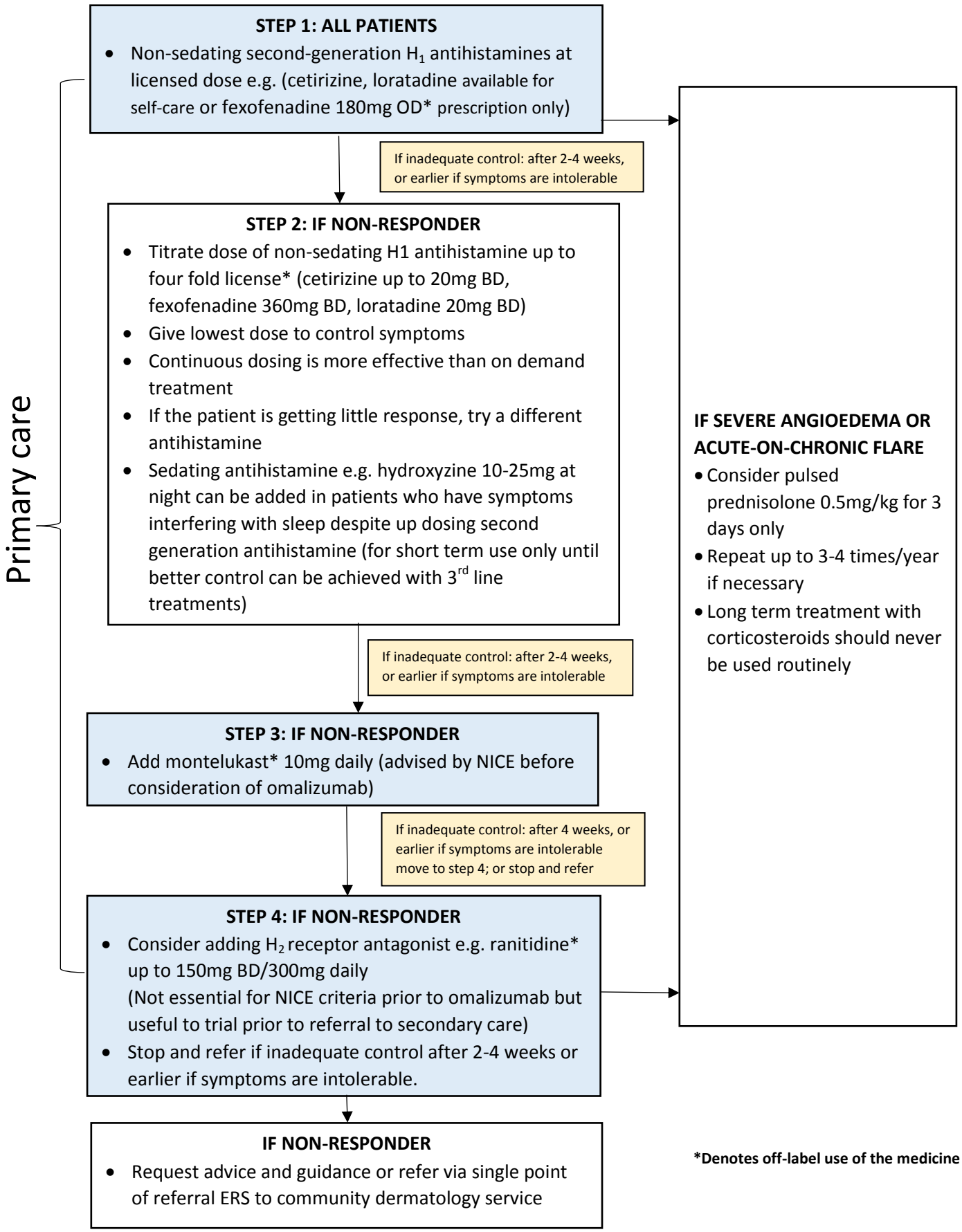
Unlicensed use of medicines: a number of medications recommended within the pathway are not licensed for use in urticaria and so are being used 'off-label'. These have been highlighted with an asterisk * throughout the document for information. Patients should be informed and consent to receive such treatments.

The use of Omalizumab within secondary care for the inducible urticarias listed in section 2 of the treatment pathway requires the submission of a category B* notification form to the relevant CCG.

See appendix 1 for prescribing responsibilities and RAG rating as per the South East London Joint Formulary.

4. Treatment Pathway

For ALL types of urticaria



***Denotes off-label use of the medicine**

Specialist Care
The decision on the choice of medication will be made by the specialist based on individual patient factors. The specialist will initiate these treatments.

1) CHRONIC SPONTANEOUS URTICARIA

Chronic Spontaneous Urticaria

Trial of omalizumab if CSU severe despite optimal anti-mediator treatments in line with NICE TA339
See dosing schedule below

ANGIOEDEMA WITHOUT WEALS
Consider tranexamic acid* 500mg BD– 1.5gram TDS

IF AUTOIMMUNE URTICARIA suspected (e.g. positive basophil histamine release assay)
Consider ciclosporin* 4mg/kg/day starting dose reducing to 2mg/kg if possible (treatment duration generally ≤ 1 year).
Other immunosuppressive agents for CSU and omalizumab failures are:
- Methotrexate* up to 30mg weekly ≥ 3/12
- Mycophenolate mofetil* up to 1500mg BD or hydroxychloroquine* up to 200mg BD would be last line options
- Azathioprine* 2mg/kg/day up to 2.5mg/kg/day in steroid dependent patients

Consider doxepin* 25-50mg at night in the appropriate context (CSU often coexists with anxiety and depression)

If non-responder, reassess in a specialist urticaria clinic

Omalizumab in CSU

1. **Eligibility**
   - ≥ 12 years of age
   - Severity of condition is assessed objectively e.g. using a weekly urticaria activity score (UAS) of ≥ 28 or angioedema activity score (AAS) ≥ 28/week
   - Not responded to standard treatment with H_1-antihistamines and leukotriene receptor antagonists
2. **Dosing**
   - 300mg every 4 weeks for 4 doses and review
   - Omalizumab is stopped at or before the fourth dose if the condition has not responded
   - Omalizumab is stopped at the end of a course of treatment (6 doses) if the condition has responded, to establish whether the condition has gone into spontaneous remission, and is restarted only if the condition relapses
3. **Administration**
   - Omalizumab is administered as an outpatient in a secondary care specialist centre in dermatology, immunology or allergy clinic due to a very small risk of anaphylaxis

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2) INDUCIBLE URTICARIAS

a) SYMPTOMATIC DERMOGRAPHISM

1. Consider narrow band UVB phototherapy for at least 6 weeks
2. If DLQI ≥15 consider omalizumab* (150mg monthly increasing to 300mg monthly if necessary)

Omalizumab stopping criteria

Stop at or before the fourth dose if condition has not responded/DLQI does not reduce below 10 ₸

No increase in objective wealing threshold from 36g/mm^2 using a calibrated dermographometer

b) CHOLINERGIC URTICARIA

1. Consider danazol* 200-600mg daily (in divided doses) in men, propranolol* up to 40mg BD, or oxybutynin* 5mg 2-3 times a day increased to 5mg QDS if necessary. If failure of these consider propantheline* up to 30mg QDS or hyoscine butylbromide* 10mg TDS increased up to 20mg QDS. All of the above should be stopped if no response after 6 weeks at the maximum dose.
2. If DLQI ≥15 consider omalizumab* (150mg monthly increasing to 300mg monthly if necessary)

Omalizumab stopping criteria

Stop at or before the fourth dose if condition has not responded/DLQI does not reduce below 10 ₸

No subjective increase in exercise or heat tolerance

c) DELAYED PRESSURE URTICARIA

1. Consider dapsone* 50mg/day up to max. 150mg/day or sulfasalazine* 0.5-4g/day (if not aspirin sensitive). Stop after 6 weeks if no response at the maximum dose.
2. If DLQI ≥15 consider omalizumab* (150mg monthly increasing to 300mg monthly if necessary)

Omalizumab stopping criteria

Stop at or before the fourth dose if condition has not responded/DLQI does not reduce below 10 ₸

d) COLD URTICARIA

1. If DLQI ≥15 consider omalizumab* (150mg monthly increasing to 300mg monthly if necessary)
2. Consider ciclosporin* (4mg/kg for 4 weeks reducing by 1mg/kg every 6 weeks to zero for omalizumab non-responder. Longer treatment is an option)

Omalizumab stopping criteria

Stop at or before the fourth dose if condition has not responded/DLQI does not reduce below 10 ₸

No fall in temperature threshold using Temp Test

e) SOLAR URTICARIA

1. Consider ciclosporin* (4mg/kg for 4 weeks reducing by 1mg/kg every 6 weeks to zero. Longer treatment is an option)
2. If DLQI ≥15 consider omalizumab* (150mg monthly increasing to 300mg monthly if necessary)

Omalizumab stopping criteria

Stop at or before the fourth dose if condition has not responded/DLQI does not reduce below 10 ₸

No objective improvement in monochromator phototest thresholds

₸ In line with licensed use, omalizumab should be stopped at 6 months if the condition has responded, and restarted only if the condition relapses.

- As part of the local commissioning arrangements for omalizumab in inducible urticarias, a category B* notification form will need to be submitted to commissioners for patients initiated on this treatment.

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3) OTHER URTICARIAS

a) IDIOPATHIC PRURITIS

- Consider amitriptyline* (up to 75mg ON), pregabalin* (up to 75mg BD), or gabapentin* (up to 600mg TDS) can be used for symptoms of dysesthesia/pruritus.
- Naltrexone* (initially 25mg daily increased to 50mg per day. Total weekly dose may be divided and given on 3 days of the week – max. 350mg per week) may rarely be used for idiopathic pruritus that has not responded to amitriptyline* (up to 75mg ON), pregabalin* (up to 75mg BD) or gabapentin* (up to 600mg TDS), reviewed every 3 months. Stop if no clinical response

b) URTICARIAL VASCULITIS OR AUTOINFLAMMATORY SYNDROMES

- Consider colchicine* 0.5mg BD up to 2.5mg daily (in divided doses)
- Hydroxychloroquine*, azathioprine*, methotrexate* or corticosteroids may also be considered

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Appendix 1

Traffic Light Status Information

- **Red** – Specialist / hospital prescribing only.
- **Amber 1** – treatment can be initiated in primary care after a recommendation from an appropriate specialist
- **Amber 2** – Specialist initiation and supply followed by maintenance prescribing in primary care
- **Amber 3** – specialist initiation with ongoing monitoring required. Transfer of prescribing to the GP using either the approved APC GP Information sheets where applicable or full shared care (under development for drugs indicated with **),
- **Green** – specialist and non-specialist initiation

Green	Amber 1	Amber 2	Amber 3	Red
• Non-sedating second generation H1 antihistamines at licensed dose • Non-sedating antihistamines up to four fold license • Ranitidine • Montelukast • Prednisolone		• Tranexamic acid • Colchicine • Amitriptyline • Oxybutynin • Propantheline • Hyoscine butylbromide • Pregabalin • Gabapentin	GP Information sheets: • Doxepin • Danazol • Naltrexone	Omalizumab Dapsone • *Ciclosporin*** • *Mycophenolate*** • *Methotrexate* ** • *Hydroxychloroquine*** • *Sulfasalazine*** • *Azathioprine***

**Note, these immunomodulatory drugs are currently RED listed, however will move to AMBER 3 upon completion of the SE London immunomodulatory shared care guideline.

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