URTICARIA AND/OR ANGIOEDEMA MANAGEMENT PATHWAY (ADULTS)

Please use algorithms below to assess and manage patients with either urticaria +/- angioedema or angioedema in isolation
Refer to photographs on Dermnet NZ for photographs of urticaria and urticarial vasculitis.

**What to tell patients**

**Most episodes of urticaria are not allergic.** It is important to reassure patients with history not suggestive of allergy that this is the case to prevent them from needlessly trying to identify an allergic trigger.

Most cases of urticaria resolve spontaneously over time; how long is not predictable. Antihistamines mask symptoms but do not alter the natural history e.g. how long it will take before resolution.

Inducible (physical urticaria) may be life-long particularly dermographism and cholinergic urticaria.

More information and patient leaflets on urticaria and angioedema can be found on the British Association of Dermatologists and Allergy UK websites.

**Prescribing**

NICE and the British Society of Allergy and Clinical Immunology (BSACI) guidelines recommend higher than licensed doses of antihistamines.

Titrate up according to sedative side effects (which may occur at these doses in patients who tolerate licensed doses) and patient tolerance.

<table>
<thead>
<tr>
<th>Medication</th>
<th>License</th>
<th>Recommended dose</th>
<th>Doses used in urticaria/angioedema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cetirizine</td>
<td>The relief of nasal and ocular symptoms of seasonal and perennial allergic rhinitis. The relief of symptoms of chronic idiopathic urticaria.</td>
<td>Adults: 10mg once daily (1 tablet)</td>
<td>Up to 20mg twice a day.</td>
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<tr>
<td>Fexofenadine</td>
<td>The relief of symptoms associated with chronic idiopathic urticaria.</td>
<td>Adults: 120mg or 180mg once daily taken before a meal.</td>
<td>Up to 540mg daily as 360mg in the morning and 180mg in the evening.</td>
</tr>
<tr>
<td>Tranexamic acid</td>
<td>Hereditary angioneurotic oedema.</td>
<td>Some patients are aware of the onset of illness; suitable treatment for these patients is intermittently 1g-1.5g two to three times daily for some days. Other patients are treated continuously at this dosage.</td>
<td>1g three times daily increased to 1.5g three times daily.</td>
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<tr>
<td>Montelukast</td>
<td>The treatment of asthma as add-on therapy. In those asthmatic patients in whom montelukast is indicated in asthma, it can also provide symptomatic relief of seasonal allergic rhinitis.</td>
<td>The dosage for adults is one 10 mg tablet daily to be taken in the evening.</td>
<td>10mg at night.</td>
</tr>
</tbody>
</table>

**Avoid** sedating antihistamines.

Oral corticosteroids are effective but should be used for short courses only as tachyphylaxis (diminishing efficacy for the same dose) may occur and morbidity due to the side effects can be significant. There is no role for topical corticosteroids.

Patients who have had anaphylaxis (a life-threatening generalised allergic reaction that in 80% cases includes urticaria) should have adrenaline auto-injectors (AAI) prescribed unless there is a clear history that the reaction is due to drugs. Patients require training in how and when to use. This should not be deferred until specialist review.
For diagnostic purposes urticaria is divided into two: **acute urticaria** includes any urticarial symptoms which are of less than 6 weeks duration whilst **chronic urticaria** is more or less daily urticaria for 6 weeks or more.

**Acute urticaria** will include urticaria happening in the context of an allergic reaction (in which case there will be a typical history of symptoms following shortly after exposure and often with other allergic symptoms), spontaneous (isolated) urticaria and urticaria associated with infections. Acute urticaria may evolve into chronic urticaria.

**Chronic urticaria** includes inducible (physical urticaria) and chronic spontaneous urticaria (the majority of which is thought to be autoimmune in aetiology). Inducible urticaria may co-exist with chronic spontaneous urticaria (particularly pressure urticaria).

**Angioedema** can co-exist with both acute and chronic urticaria or can occur in isolation. When it occurs with urticaria it is likely mast cell driven and should respond to antihistamines. **Isolated angioedema** can be mast cell driven or due to bradykinins; if the latter, it will not improve with antihistamines.
**DIAGNOSIS OF TYPE OF URTICARIA**

1. **Single episodes of urticaria** (+/- angioedema lasting) <24 hours?
   - Yes: Consider **allergy** particular if occurs within 90 minutes of eating, medication use, insect stings or exercise. If so, **refer to allergy service** particularly if features of **anaphylaxis** (difficulty in breathing, symptoms of hypotension). If future risk of anaphylaxis prescribe two adrenaline auto-injectors (AAI).
   - No

2. **Atypical rash: episodes lasting >24 hours with residual bruising and systemic unwell (fever, myalgia)?**
   - Yes: Consider **urticarial vasculitis. Refer to Dermatology.** Review medication use. Check FBC, CRP, C3 and C4, ANA, U&E, diptest urine.
   - No

3. **Typical urticaria (+/- angioedema); repeated episodes with duration < 6 weeks?**
   - Yes: **Acute urticaria.** Majority idiopathic. Often associated with infectious illness. Treat symptomatically with antihistamines (including at higher than licensed doses) e.g. cetirizine 10mg -20mg increasing dose at weekly intervals and, for severe/unmanageable cases use short courses of prednisolone 20-30mg 5-10 days.
   - No

4. **Typical urticaria (+/- angioedema), repeated episodes over > 6 week’s duration; set off by physical triggers?**
   - Yes: **Inducible (physical urticaria).** Recognised triggers: pressure (dermographism), delayed pressure, cold, passive heating, emotional stress, vibration, water, solar. Avoid triggers if possible. Treat symptomatically with increasing doses (weekly intervals) of cetirizine 10mg once daily to 20mg twice daily or fexofenadine 180mg to 540mg daily. **Refer to Dermatology or Immunology if symptomatic control difficult or cold urticaria.**
   - No

5. **Daily or virtually daily urticaria (+/- angioedema) for 6 weeks duration or longer?**
   - Yes: **Chronic spontaneous urticaria (CSU);** treat as per flow chart below. **Refer if symptoms difficult to control despite maximal therapy.** Most resolve spontaneously: 50% within 3 years, 90% by 5 years. Some reactions can be anaphylactic in type and severity - Patients should be prescribed 2x adrenaline autoinjectors.
FOR PATIENTS WITH CHRONIC SPONTANEOUS URTICARIA (CSU)

+/- ANGIOEDEMA SYMPTOMS REQUIRING TREATMENT:

**Step 1 – Self management and oral antihistamine**
Advise purchase of over the counter oral antihistamine:
**Cetirizine** 10mg once daily

**Cetirizine and fexofenadine** are not normally sedating but advise caution with driving/operating machinery if patient feels sleepy.

**IF SYMPTOMS IMPROVE**
If it is likely that symptoms will be persistent or recurrent recommend daily antihistamine treatment for 3–6 months, then review; if asymptomatic gradually withdraw treatment and see if symptoms have resolved. If urticaria recurs prescribe antihistamines again and repeat process every 3-6 months

If symptoms were short lived and frequent recurrence thought unlikely, recommend treatment to be taken as required or prophylactically.

**IF INADEQUATE RESPONSE**
**Step 2**
Increase cetirizine dose to 10mg twice daily; increasing the dose at weekly intervals to up to 20mg twice a day (off-label use).
Loratadine is not superior in efficacy but can be sometimes better tolerated. It can also be trialled at doses of up to 4 times the licensed dose.

**IF INADEQUATE RESPONSE**
**Step 3**
Change antihistamine to **fexofenadine** and titrate up to a max of 540mg/day (off-label use) usually dosed as 360mg in the morning and 180mg in the evening.

For severe, unmanageable episodes consider an emergency pack of **prednisolone** 20-30 mg once daily for 5-10 days duration. The background medication should also be escalated and if maximal background medication is reached and patient is still symptomatic, referral should be considered. Long term use of corticosteroid (more than 10 days) should be avoided.

**IF INADEQUATE RESPONSE**
**Step 4**
Prescribe **montelukast** 10mg at night (off-label use) as per **BSAC** and **NICE** guidance.

**IF INADEQUATE RESPONSE**
**Step 5**
*Refer to Immunology and Allergy Service* or *to Dermatology* for consideration of **omalizumab** treatment.

Omalizumab is to be prescribed in secondary care.

**SIGNIFICANT ANGIOEDEMA?**

No

Yes

If significant angioedema despite maximum doses of antihistamines prescribe **tranexamic acid** 1g three times a day (off-label use) titrated up to 1.5g three times a day if angioedema not controlled.
**MANAGEMENT OF ISOLATED ANGIOEDEMA**

Documented family history of hereditary angioedema (HAE)

- Yes → Refer immediately to Immunology and Allergy Service for investigation of possible hereditary angioedema (HAE)
- No → Patient taking an ACE inhibitor?

Patient taking an ACE inhibitor?

- Yes → Discontinue ACEi replacement with ARBs usually tolerated; symptoms may persist up to 3 months after discontinuation ACEi. Future avoidance of all ACEis and sacubitril/valsartan.
- No → Check C4

Check C4

- C4 normal → Treat symptomatically; cetirizine 10-40mg daily (unlicensed use), increasing at weekly intervals.
- C4 low → Refer to Immunology and Allergy Service

Symptoms persist after 3 months

- Yes → C4 low
- No → Symptoms uncontrolled

Symptoms uncontrolled

- Yes → Prescribe tranexamic acid 1g three times a day titrated up to 1.5g three times a day if angioedema not controlled.
- No → Symptoms persist after 3 months

Patients who are asymptomatic on therapy should gradually reduce treatment to see whether there has been resolution (as is often the case). When symptoms are infrequent it is suggested that a period twice the longest interval between previous episodes should pass before assuming resolution.

Frequency and severity of episodes may influence whether treatment is given prophylactically and discussion with patients who have infrequent symptoms should include the use of treatment on an as required basis versus treating for very many asymptomatic days to prevent symptoms on one day.