Urticaria and Angioedema Primary Care 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. Patients should be advised not to drive if they do feel drowsy (drowsiness can occur at higher doses even if licensed doses were tolerated). Titrate up according to sedative side effects (which may occur at these doses in patients who tolerate licensed doses) and patient tolerance.

Medication	License	Recommended dose	Doses used in urticaria/angioedema
Cetirizine	The relief of nasal and ocular symptoms of seasonal and perennial allergic rhinitis. The relief of symptoms of chronic idiopathic urticaria.	Adults: 10mg once daily (1 tablet)	Up to 20mg twice a day (off-label).
Fexofenadine	The relief of symptoms associated with chronic idiopathic urticaria.	Adults: 120mg or 180mg once daily taken before a meal.	Up to 540mg daily as 360mg in the morning and 180mg in the evening (off-label).
Tranexamic acid	Hereditary angioneurotic oedema.	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.	1g three times daily increased to 1.5g three times daily. Dose and dose interval reduced if eGFR <50ml/min (Table 1) or if serum creatinine is ≥120micromol according to the SPC. **GFR (ml/min)** / **Tranexamic acid oral dose** / **Dose frequency** 20 -50 / 25 mg/kg / 12 hourly 10 -20 / 25 mg/kg / 12 to 24 hourly <10 / 12.5 mg/kg / 24 hourly Table 1- The Renal Drug Database
Montelukast	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.	The dosage for adults is one 10 mg tablet daily to be taken in the evening.	10mg at night.

Avoid sedating antihistamines.

Pregnancy: Medication should be reviewed if planning, or in the event of pregnancy. Please refer to advice on oral anti-histamines in the following link: Hayfever or allergic rhinitis: treatment during pregnancy – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice

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 medications. Patients require training in how and when to use an AAI. Supporting information can be found on the manufacturer's website for the devices and Anaphylaxis UK website 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.

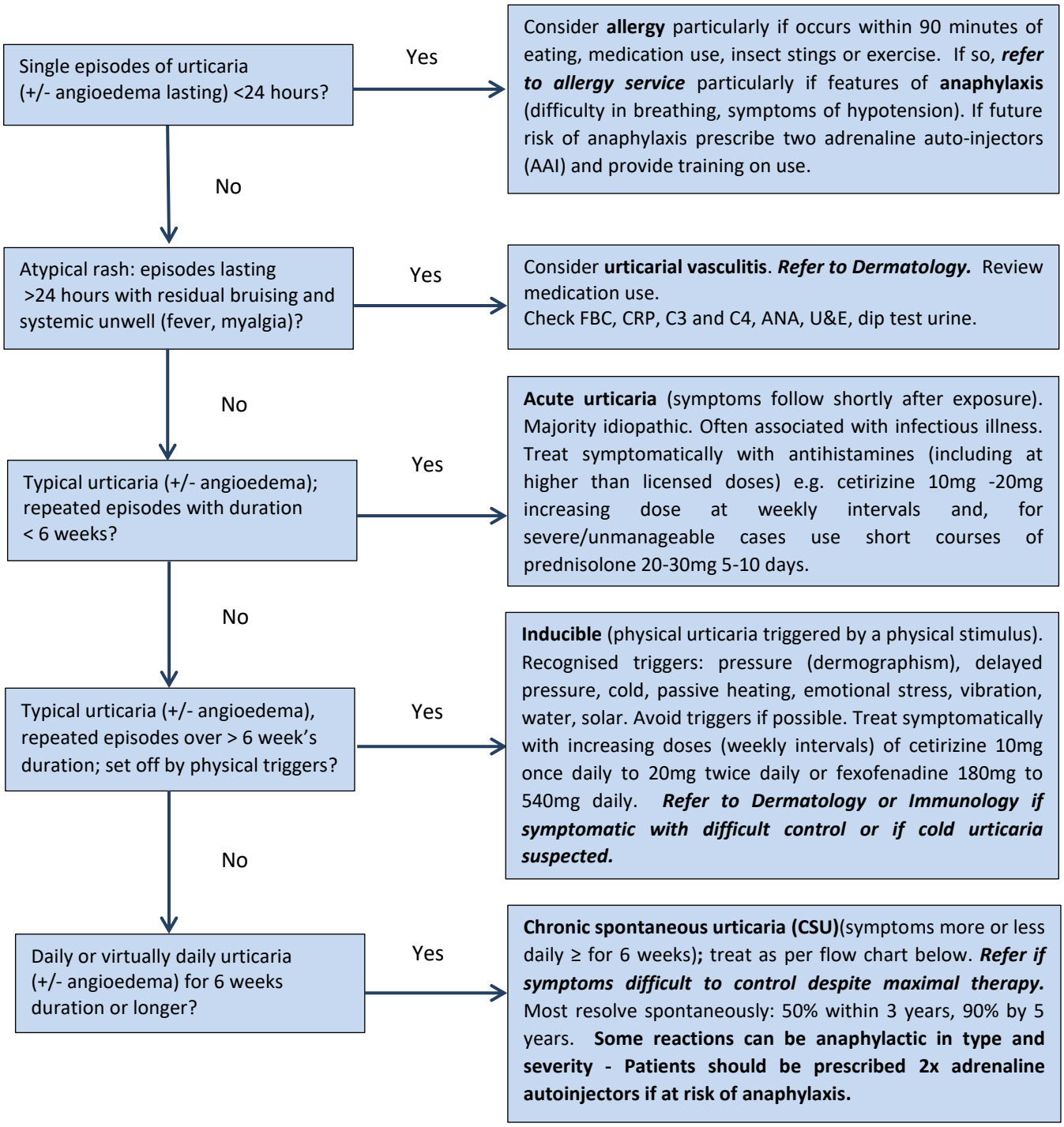
Acute urticaria will include urticaria happening in the context of an allergic reaction (in which case there will be a typical history of symptoms following shortly after exposure and often with other allergic symptoms), spontaneous (isolated) urticaria and urticaria associated with infections. Acute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

Angioedema can be caused by medication such as nonsteroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), antiplatelets, factor Xa inhibitors and statins. Clinicians should consider stopping or changing the medication, however this may require specialist advice prior to making any amendments to a patient's regimen.

DIAGNOSIS OF TYPE OF URTICARIA



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

Check FBC, TFTs and ferritin and manage accordingly

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

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.

SIGNIFICANT ANGIOEDEMA?

No

IF INADEQUATE RESPONSE

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

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. Dose and dose interval reduced if eGFR <50ml/min (Table 1) or if serum creatinine is ≥120micromol according to the SPC . Allow 4 weeks to assess response. Patients should be warned to report visual symptoms especially halos around the eyes which would warrant ophthalmology referral. *Patients taking tranexamic acid long-term require FBC, U+Es, eGFR and LFTs to be monitored 6 monthly.

IF INADEQUATE RESPONSE

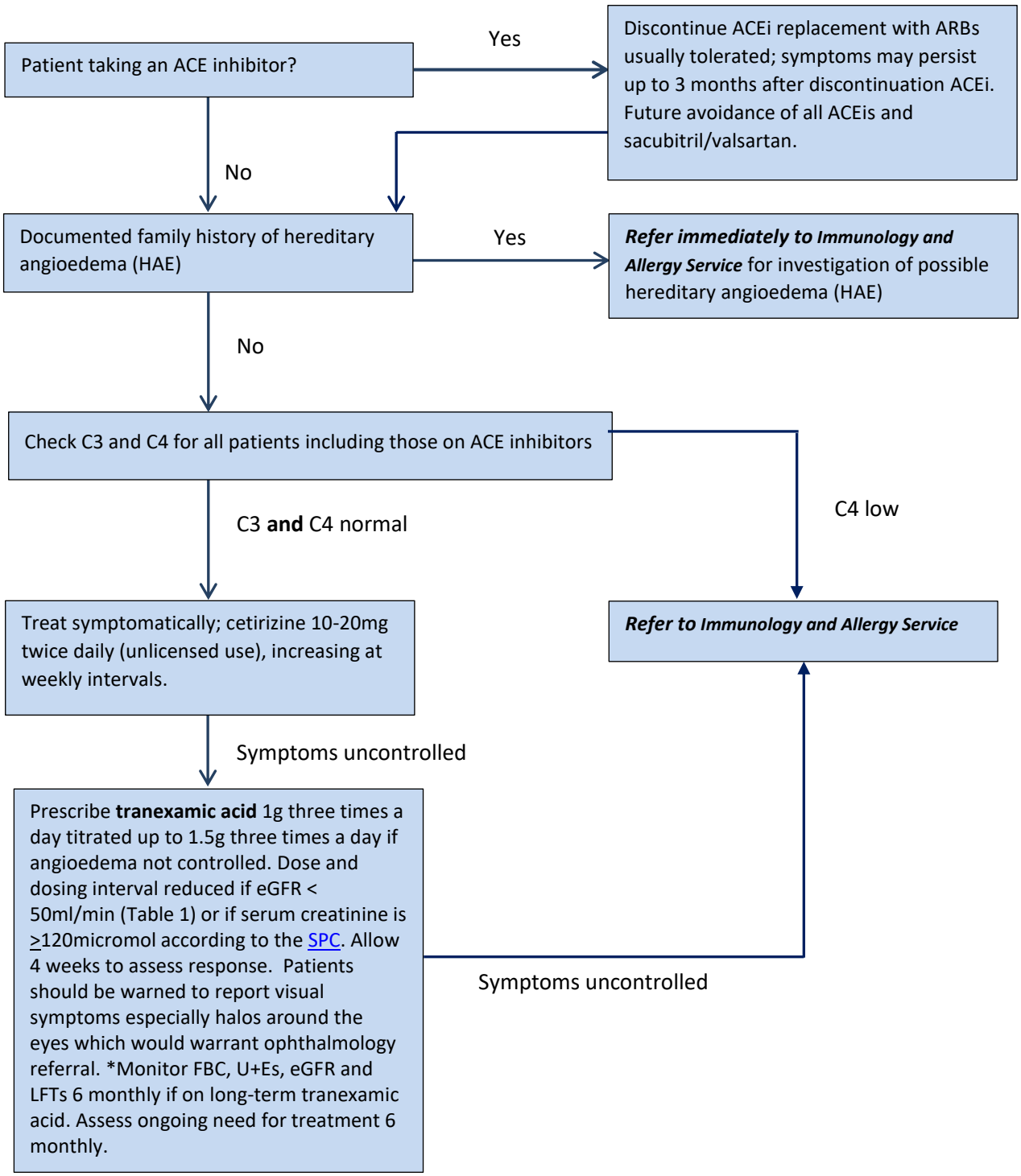
Step 5 -
Refer to Immunology and Allergy Service or to **Dermatology** for consideration of **omalizumab** treatment.
Omalizumab is to be prescribed in secondary care.

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.

MANAGEMENT OF ISOLATED ANGIOEDEMA



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.

Version Control - **Urticaria and/or Angioedema Management Pathway (Adults)**			
Version	Author(s)	Date	Changes
1.0	Irina Varlan, Medicines Optimisation Interface Pharmacist	June 2019	
2.0	Bhavika Lad, Medicines Optimisation Pharmacist, Nottingham and Nottinghamshire ICB	January 2023	• Guideline title changed from Urticaria Primary Care Pathway to Urticaria and Angioedema Primary Care Pathway (Adults). • Advice on drowsiness at tolerated doses and clarity around unlicensed doses. • Guidance on antihistamine use in pregnancy. • Supply of Adrenaline Autoinjectors to those at risk of anaphylaxis and signposting for instructions of use. • Potential causes of angioedema updated • C3 and C4 to be checked for all patient's angioedema pathway. Dose change for the treatment of isolated angioedema when C3 and C4 are normal • Tranexamic acid – ophthalmology counselling included dose reduction in eGFR<50ml/min and monitoring guidance for long term use