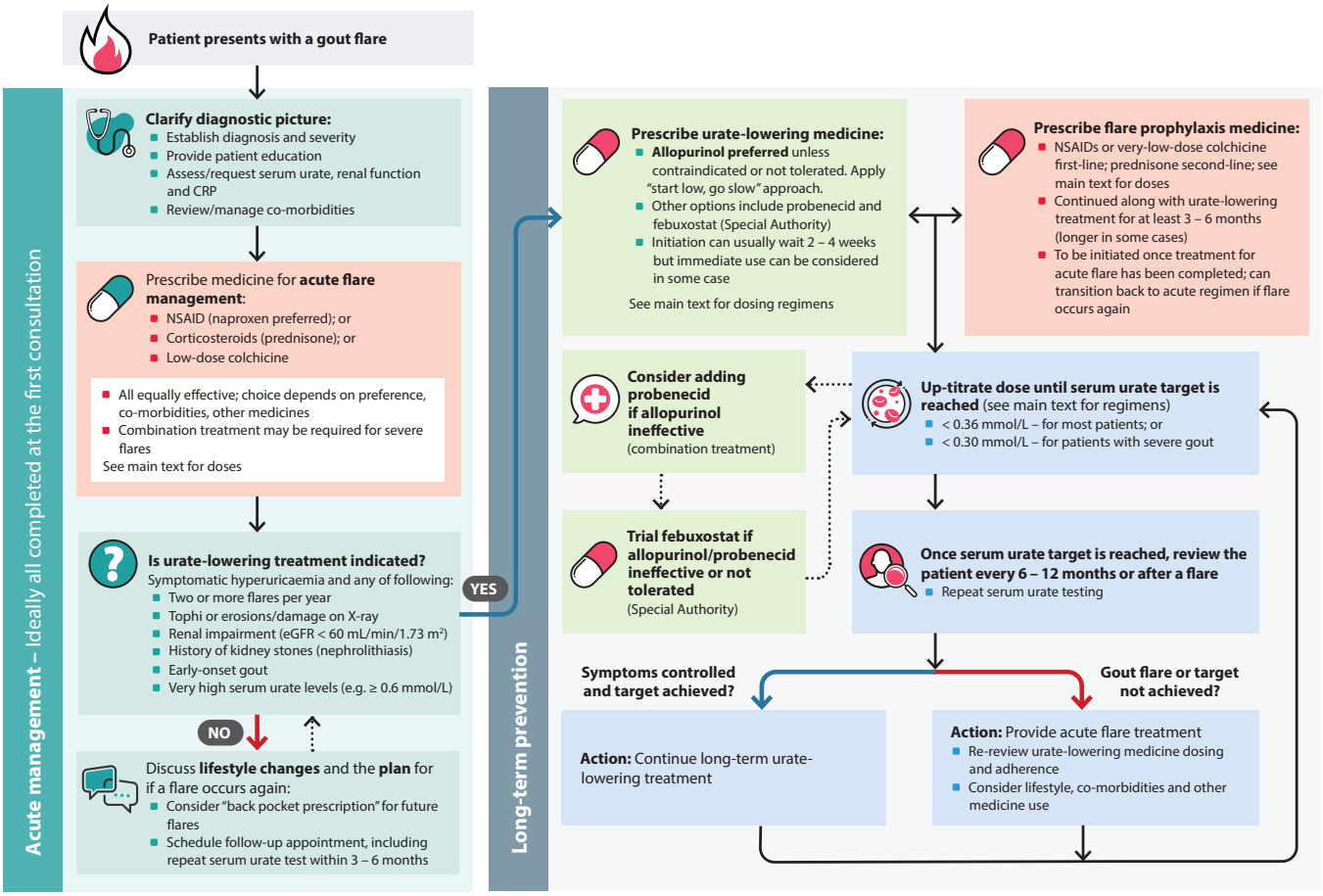
B-QuiCK: Gout

Diagnosis

- Gout can be diagnosed based on:
  - Clinical presentation, e.g. joint involvement with characteristic pain/swelling/erythema, presence of tophi or systemic symptoms
  - History, e.g. onset, previous potential flares or elevated serum urate
  - Elevated serum urate levels
    - Levels during a flare are within the normal range in up to 40% of cases. If levels are normal, repeat testing once the flare has subsided.
    - Hyperuricaemia in an asymptomatic person is not diagnostic of gout, but may inform lifestyle changes and subsequent monitoring
- Differential diagnoses to consider include septic arthritis and calcium pyrophosphate deposition (CPPD) disease (formerly known as pseudogout)
- In addition to **serum urate**, request **CRP** to detect inflammation and assist in interpreting the validity of the urate level and a **renal function test** to allow for prompt urate-lowering treatment initiation, if gout is confirmed
- Assess for relevant co-morbidities as this may influence medicine selection and the approach to long-term management

An overview of gout management in primary care



Acute management of gout flares

- NSAIDs, corticosteroids or colchicine are equally effective at treating gout flares, so choice is based on individual factors
- Encourage rest and elevation of the affected joint (an ice pack may provide relief), and adequate hydration
- Discuss urate-lowering treatment with all patients at their first presentation (even if it is not prescribed)

Community pharmacists: be alert for persistent over-the-counter NSAID use. Refer patients to their primary care clinician for a discussion regarding urate-lowering treatments.

Treatment options for an acute gout flare:

Medicine	Dose	Notes
NSAIDs – Naproxen preferred	■ 750 mg initially, followed by 500 mg eight hours later, then 250 mg every eight hours until the flare has settled	■ Avoid if eGFR < 30 mL/min/1.73 m^2 ■ Consider adding a proton pump inhibitor ■ Consider celecoxib if intolerant to naproxen (unapproved indication)
Prednisone	■ 20 – 40 mg, once daily, for five days or until the flare has settled	■ Tapering the dose over 10 – 14 days can reduce the likelihood of a rebound flare, but is not always necessary with a short course
Colchicine	■ **Low-dose regimen***: 1 mg immediately, followed by 500 micrograms after one hour; maximum dose 1.5 mg per course ■ If eGFR 10 – 50 mL/min/1.73 m^2, reduce the initial dose by half (i.e. 500 micrograms); do not exceed 1.5 mg over three days	■ Do not repeat acute course within three days ■ Do not commence prophylaxis (very-low-dose colchicine) until 12 hours or more after the acute dose is taken ■ Ideally avoid, or use with caution, in frail patients, those who weigh < 50 kg, or patients with hepatic or renal impairment (eGFR 10 – 50 mL/min/1.73 m^2) ■ Contraindicated in patients with an eGFR < 10 mL/min/1.73 m^2
Corticosteroid (triamcinolone acetonide)	■ Intra-articular injection, 2.5 – 40 mg	■ May be considered in patients where the oral route is problematic and if only one or two joints are affected ■ Dose determined by the size of the affected joint

* This regimen is based on a trial in which patients received treatment within 12 hours of onset of the flare; efficacy may therefore be reduced if started later

Long-term management with urate-lowering treatment

Start urate-lowering treatment in patients with symptomatic hyperuricaemia and any of the following**:**

- Two or more flares per year (including if self-managed)
- Tophi or erosions/damage on X-ray
- Renal impairment (eGFR < 60 mL/min/1.73 m^2)
- History of kidney stones (nephrolithiasis)
- Early-onset gout, e.g. aged < 40 years (higher risk in Māori and Pacific peoples)
- Very high serum urate levels, e.g. ≥ 0.6 mmol/L

Test serum urate levels:

- Prior to dose adjustment while up-titrating urate-lowering treatment, e.g. initially every four weeks
- Every 6 – 12 months for monitoring once targets have been achieved
- Avoid testing serum urate levels during a flare

Recommended target:

- < 0.36 mmol/L – for most patients; or
- < 0.30 mmol/L – for patients with severe gout, e.g. those with tophi, chronic gouty arthritis or frequent flares

Prescribe flare prophylaxis for the first 3 – 6 months of urate-lowering treatment (doses are lower than acute treatment; Table 3)

- Can be stopped at three-month review if symptom-free and there is a substantial drop in serum urate levels
- May be required for longer than six months if frequent ongoing flares or tophi; weigh the risks (i.e. adverse effects of NSAIDs or colchicine) against the potential benefits

Table 3. Treatment options for gout flare prophylaxis.

Medicine	Dose	Additional notes
Naproxen	250 mg, twice daily	■ Consider adding a proton pump inhibitor ■ Avoid if eGFR < 30 mL/min/1.73 m^2
Colchicine (unapproved indication)	**Very-low-dose regimen**: 500 micrograms, twice daily Reduce dose if required (see notes)	■ Reduce dose to 500 micrograms, once daily, or on alternate days, if not tolerated, e.g. diarrhoea develops, chronic kidney disease or concurrent use of CYP3A4/P-glycoprotein inhibitors (such as erythromycin, verapamil) ■ Ideally avoid, or use with caution, in frail patients, those who weigh < 50 kg, or patients with hepatic or renal impairment (eGFR 10 – 50 mL/min/1.73 m^2) ■ Contraindicated in patients with an eGFR < 10 mL/min/1.73 m^2
Prednisone	5 mg, once daily	■ Second-line option if contraindications to NSAIDs or colchicine ■ Taper slowly on withdrawal ■ Monitor for corticosteroid-related adverse effects

Allopurinol (fully funded) – first line

- Start at a low dose (renal function dependent) and slowly up-titrate until target serum urate level is reached (Table 4)
  - Dose reductions are not routinely required in patients with declining renal function already established on allopurinol
- Discuss possible adverse effects, most commonly gastrointestinal symptoms, and very rarely, hypersensitivity reactions (see NZF)
- Consider checking patients of Han Chinese, Korean or Thai ancestry for the *HLA-B*5801* allele before prescribing allopurinol

Before modifying the medicines regimen, assess adherence to treatment if the patient cannot meet the serum urate target

Table 4. Allopurinol starting doses and dose titration determined by renal function.

Estimated glomerular filtration rate (eGFR) mL/min/1.73 m^2	Initial dose of allopurinol	Dose increase
> 60	100 mg, daily	Increase by 100 mg, every four weeks*, if tolerated, until the serum urate target is reached, or to a maximum of 900 mg, daily. Usual maintenance dose is 100 – 600 mg/day.
30 – 60	50 mg, daily	Increase by 50 mg, every four weeks, if tolerated, until the serum urate target is reached, or to a maximum of 900 mg, daily†
< 30	50 mg, every second day	

* Some prescribers prefer a more rapid titration (e.g. every two weeks), but this needs to be balanced against the increased risk of adverse effects

† Many patients with renal dysfunction will be unable to tolerate the maximum dose of allopurinol; consider referral to, or discussion with, a rheumatologist if serum urate targets are unable to be achieved and an increase in dose is not tolerated, e.g. over 300 mg allopurinol daily

Probenecid (fully funded)

- Add if serum urate target not achieved with relatively high dose of allopurinol, e.g. 600 mg, daily
  - Or monotherapy if intolerance or resistance to allopurinol
- Titrate dose according to serum urate level
  - Initially, 250 mg, twice daily, for one week, then 500 mg, twice daily, increased by 500 mg every four weeks, to 1 g, twice daily (i.e. 2 g total per day), if required
- Efficacy reduces with declining renal function; avoid if eGFR < 30 mL/min/1.73 m^2 or nephrolithiasis
- Advise patients to drink adequate fluids (e.g. ≥2 L per day) to prevent uric acid stones and to take the medicine with, or just after, a meal
- For adverse effects, see NZF

Febuxostat (Special Authority required)

- Alternative if allopurinol and/or probenecid are ineffective or not tolerated
- Can be prescribed in combination with probenecid if target serum urate level is not achieved with febuxostat alone
  - Results in a more rapid decline in serum urate which can trigger flares
  - Prescribe prophylactic NSAIDs or colchicine for at least the first six months of combination treatment
- Arrange baseline liver function testing; repeat periodically thereafter based on clinical judgement
- Recommended dose is 80 mg, once daily, increased to 120 mg, once daily, after two to four weeks if the serum urate is > 0.36 mmol/L
  - Maximum daily dose 80 mg if mild hepatic impairment (no dose information available for moderate to severe impairment)
- Use with caution in patients with renal dysfunction or a history of CVD (particularly heart failure and coronary artery disease)
- For adverse effects, see NZF

Supporting patients in the long term

- Acknowledge challenges and discuss concerns or barriers to regularly taking medicines; suggest strategies to make it easier, e.g. blister packaging, reminders on their phone
- Explain the importance of continuing urate-lowering treatment; urate levels return to previous levels within one week of stopping a urate-lowering medicine
- Reiterate that although biological factors (e.g. CKD, genetics) are the main causes of gout, other modifiable factors such as diet can still trigger flares. Discussion points include:
  - Eat regular meals – periods of fasting/starvation may trigger flares
  - Avoid/limit foods if they trigger flares, e.g. red meat, seafood (kaimoana); some purine-rich foods may be more likely to trigger flares
  - Increase vegetable intake and switch to low-fat dairy products
  - Limit alcohol and high fructose/sucrose drinks
  - Keep hydrated
  - Be aware that continuous, vigorous exercise can trigger flares
  - Vitamin C supplementation is unnecessary (no evidence it reduces serum urate)

Prescribing cardiovascular medicines to people with gout

- Losartan is the preferred choice for patients with gout and hypertension
- If possible, avoid diuretics, especially high-dose thiazides (increases risk of DRESS)
- If indicated, the benefits of low-dose aspirin outweigh the risks

When to consider rheumatology referral

Discussion with, or referral to, a rheumatologist is recommended for patients who despite optimal pharmacological treatment and lifestyle management, have:

- A serum urate level consistently ≥ 0.36 mmol/L and the presence of tophi; in patients without tophi, a higher threshold for referral may be considered, e.g. > 0.42 mmol/L
- Persistent flares or progressive joint damage despite a serum urate level that is consistently < 0.36 mmol/L
- Significant renal dysfunction and concerns about increasing the dose of urate-lowering treatment