

ALLOPURINOL – SAFE PRESCRIBING - DOSE UP

- ▶ PRESCRIBE EARLY BEFORE THE DEVELOPMENT OF TOPHI
- ▶ MONITOR SERUM URATE
- ▶ START AT A LOW DOSE AND GRADUALLY INCREASE UNTIL THE SERUM URATE TARGET IS ACHIEVED
- ▶ TELL PATIENTS TO REPORT ANY SIGNS OF RASH

Gout is a major cause of arthritis in New Zealand and causes significant disability, especially in Maori and Pacific men.¹ Gout is estimated to affect 3.75% of adult New Zealanders and up to one third of Maori and Pacific men over 65 years of age.² In the Northern Region DHB area alone, over 47,000 people suffer from gout.³

Allopurinol inhibits the enzyme that is responsible for the production of urate⁴ and is considered to be the first-line urate-lowering medicine, unless there is a history of allergy or intolerance.⁵

PRESCRIBE EARLY, BEFORE THE DEVELOPMENT OF TOPHI

It is generally recommended to use a urate-lowering medicine before the onset of tophi or erosive disease occurs.⁶ Non-steroidal anti-inflammatory drugs (NSAIDs) and other 'over-the-counter' analgesics will not stop urate crystal deposition or joint damage. Patients using analgesics alone, rather than preventative medicines, will eventually experience an increase in urate crystal deposition and the frequency of attacks, and will be at high risk for joint damage.

Indications for long-term urate-lowering treatment in patients with a history of gout are:

- more than 1 acute attack per year⁷
- tophaceous gout
- clinical or radiographic changes consistent with erosive gout⁴
- early onset of gout and family history
- recurrent nephrolithiasis

The severity of an acute attack and the presence of comorbidities may also influence the decision about when to begin treatment.⁴

Data has shown that in areas where more patients are taking allopurinol regularly, there are lower rates of gout-related hospital admissions, and fewer patients taking other medicines (eg analgesics) to treat gout.⁸

MONITOR SERUM URATE

It has been suggested that patients with gout should think about their urate level in the same way that patients with diabetes relate to their HbA1c.⁵

Aim for target serum urate of less than 0.36mmol/L.

This will reduce the risk of gout attacks occurring and prevent the development of tophi.⁴ Lower serum urate targets (less than 0.30mmol/L) may be required for patients with gouty tophi.^{6,7}

Monitor serum urate monthly until the target has been reached, and then check 3 – 6 monthly together with renal function tests.

Explain the importance of reaching target urate and the need for close monitoring in the initial stages to ensure the appropriate dose is prescribed.

Liver function tests, serum creatinine and full blood count should also be monitored periodically when commencing allopurinol.

Note: Allopurinol is not indicated for the *asymptomatic* treatment of hyperuricaemia.⁹ Although serum urate should be monitored in suspected cases of gout, not all patients with hyperuricaemia will develop gout. Serum levels alone do not confirm or exclude gout; they may be normal during acute attacks.⁴

START AT A LOW DOSE AND GRADUALLY INCREASE UNTIL THE SERUM URATE TARGET IS ACHIEVED

There is a wide variation in the optimal dose required for patients with gout. The daily dose should be individualised depending on patient tolerance and their target serum urate level.

'Start low and go slow'. The recommended starting dose is 100mg daily, or lower (50mg daily) in stage 4 or worse chronic kidney disease.⁷ If allopurinol is well tolerated, the dose may

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be increased until the target serum urate is reached.⁴ The maximum recommended dose is 900mg daily;⁹ 300mg per day is not usually sufficient.⁷

Sudden changes in serum urate levels are likely to precipitate gout attacks.⁵ To reduce the risk of triggering an acute attack, increase the daily dose **gradually** (by 50-100mg)¹⁰ at monthly intervals¹¹ **and** prescribe in combination with a prophylactic dose of colchicine* (eg 0.5mg daily or twice daily), or low-dose NSAID (eg naproxen 250mg twice daily), for 3-6 months after achieving target serum urate.¹²

*please refer to the SafeRx[®] bulletin about colchicine for more details

Start at 50-100mg daily
Increase monthly by 50-100mg daily
until target serum urate is reached
Maximum dose 900mg daily

Explain the reason for gradual dose increases and close monitoring in the initial stages. Acute gout attacks during this time may contribute to non-adherence of long-term gout treatment.⁷ It is more important to achieve long-term adherence to therapy than to achieve the target in the shortest time.¹¹

Remind patients that allopurinol is a long-term therapy and ongoing adherence is important for symptom control.⁴

Allopurinol should be continued indefinitely unless a rash appears.⁵

Consult a rheumatologist if the patient has persistent hyperuricaemia or gout attacks despite taking their maximum tolerated allopurinol dose,⁵ if there is doubt about the diagnosis, or if there is progressive bone and joint damage on x-ray.

For more information, Auckland Regional Clinical Pathways¹³ has provided decision support tools for gout prevention and acute gout which are available on:

www.healthpointpathways.co.nz

TELL PATIENTS TO REPORT ANY SIGNS OF RASH

Hypersensitivity syndromes are rare but can be fatal. Patients should be advised to inform their doctor immediately if they develop any type of skin reaction while being treated with allopurinol. Rash is thought to occur in 2% of patients; this may precede the more serious hypersensitivity syndrome which is estimated to occur in 0.1-0.4% of patients.¹⁰

Allopurinol hypersensitivity syndrome (AHS) is characterised by a rash (Stevens-Johnson syndrome, toxic epidermal necrolysis), eosinophilia, leukocytosis, fever, hepatitis and renal failure.¹¹ The risk of AHS is greatest during the first few months of therapy,⁷ so remind patients particularly in the initial stages when up-titrating the dose, to be aware of, and to report any skin reactions immediately. Prompt recognition and discontinuation of allopurinol will help to minimise morbidity and mortality.¹⁴ Mortality associated with AHS is reported to be as high as 27%.¹¹

There is an increased risk of AHS when allopurinol is given together with diuretics, especially if the patient has impaired renal function. Thiazide diuretics in particular are associated with increased serum urate levels and an elevated risk of gout; consider alternative medicines if possible.⁴ There is also an increased risk of rash if allopurinol is given together with amoxicillin.⁹

For those patients who do not tolerate allopurinol, alternative urate-lowering medicines (eg probenecid, febuxostat and benzbromarone) should be considered for gout prevention.

Note: There are many precautions surrounding concomitant prescribing of allopurinol with azathioprine;^{9,15} refer to the patient's specialist team for appropriate management of gout or hyperuricaemia for these patients.

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For further information on other high-risk medicines visit our website at: www.saferx.co.nz

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