SAFER® HEALTHY PRESCRIBING

Waitemata District Health Board
Best Care for Everyone

ALLOPURINOL- SAFE PRESCRIBING - DOSE UP

- PRESCRIBE EARLY BEFORE THE DEVELOPMENT OF TOPHI OR FREQUENT GOUT FLARES
- MONITOR SERUM URATE
- START AT A LOW DOSE AND GRADUALLY INCREASE UNTIL THE SERUM URATE TARGET IS ACHIEVED
- REPORT ANY SIGNS OF RASH

Gout is a major cause of arthritis in New Zealand and causes significant disability.[1] Gout is estimated to affect over 5% of adult New Zealanders and is 2 to 3 times more prevalent in Māori and Pacific people.[2] In the Northern Region DHB areas alone, over 75,000 people were identified as suffering from gout in 2016.[2]

Allopurinol inhibits the enzyme that is responsible for the production of urate[3] and is considered to be the first-line urate-lowering medicine, unless there is a history of allergy or intolerance.[4]

PRESCRIBE EARLY, BEFORE THE DEVELOPMENT OF TOPHI OR FREQUENT GOUT FLARES

It is generally recommended to use a urate-lowering medicine, before tophi or frequent gout flares occur.[5] Non -steroidal anti-inflammatory drugs (NSAIDs) and other 'over-the-counter' analgesics will not stop urate crystal deposition or joint damage. People using anti-inflammatory drugs alone, rather than preventative medicines, will eventually experience an increase in urate crystal deposition and the frequency of gout flares, 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 gout flare per year[6]
- tophaceous gout
- clinical or radiographic changes consistent with erosive gout[3]
- early onset of gout and family history
- recurrent nephrolithiasis

The severity of a gout flare and the presence of comorbidities may also influence the decision about when to begin treatment.[3]

Data has shown that in areas where more people are taking allopurinol regularly, there are lower rates of gout-related hospital admissions, and fewer people take other medicines such as anti-inflammatory drugs, to treat gout.[7] Long-term urate lowering is required for the effective management of gout.[8]

MONITOR SERUM URATE .

It has been suggested that people with gout should think about their urate level in the same way that people with diabetes relate to their HbA1c.[4]

Aim for target serum urate consistently less than 0.36mmol/L

This will reduce the risk of gout flares occurring and prevent the development of tophi.[3,8] Lower serum urate targets (less than 0.30mmol/L) may be required for people with tophi.[5,6,8]

Monitor serum urate monthly until the target has been reached, and then check 3 to 6 monthly[8] together with renal function tests.

Explain the importance of reaching target urate and the need for close monthly 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 recommended for the *asymptomatic* treatment of hyperuricaemia.[9] Although serum urate should be monitored in suspected cases of gout, people with hyperuricaemia will not necessarily develop gout. Serum levels alone do not confirm or exclude gout; they may be normal during a gout flare.[3] Routine urate screening of people considered 'high-risk' is not recommended.[8]

Note: It is not advisable to test serum urate during a gout flare due to the possibility of false negative results.

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

There is a wide variation in the allopurinol dose required for each person with gout. The daily dose should be individualised depending on tolerance and target serum urate level.

'Start low and go slow'. The recommended starting dose is 100mg daily, or lower (50mg daily) in stage 3 or worse chronic kidney disease.[6] If allopurinol is well tolerated, the dose may be increased until the target serum urate is reached.[3] The maximum recommended dose is 900mg daily;[9] 300mg per day is not usually sufficient to manage most people with gout.[6]

Sudden changes in serum urate levels are likely to precipitate a gout flare.[4] To reduce the risk of triggering a flare, increase the dose gradually (by 50-100mg)[10] at monthly intervals[11] and prescribe in combination with a prophylactic dose of either 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 allopurinol at 50-100mg daily
Increase daily dose by 50-100mg each month
until serum urate is reached
Maximum dose 900mg daily

Explain the reason for gradual dose increases and close monitoring in the initial stages. Gout flares during this time may contribute to non-adherence with long-term gout treatment.[6] It is more important to achieve long-term adherence to therapy than to achieve the target in the shortest time.[11] Patient resources are available here

Once allopurinol is established, **it should not be stopped at the time of a gout flare.**

Remind people prescribed allopurinol that it is a long-term therapy and ongoing adherence is important for symptom control.[3] **Allopurinol should be continued indefinitely unless a rash appears.[4]**

Consult a rheumatologist if the patient has persistent hyperuricaemia or recurrent episodes of inflammatory arthritis despite taking their maximum tolerated allopurinol dose,[4] or if there is doubt about the diagnosis, or progressive bone and joint damage on X-ray.

Auckland Regional Clinical Pathways has decision support tools for gout prevention and acute gout which are available for primary care providers in the Auckland region here.

REPORT ANY SIGNS OF RASH

Hypersensitivity syndromes are rare but can be fatal. People taking allopurinol 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 people taking allopurinol; this may precede the more serious hypersensitivity syndrome which is estimated to occur in 0.1-0.4% of people.[10]

Allopurinol hypersensitivity syndrome (AHS) is characterised by a rash (Stevens-Johnson syndrome, toxic epidermal necrolysis), eosinophilia, leukocytosis, fever, hepatitis and renal failure.[11] Slow titration will help to reduce the risk of AHS.[8] The risk is greatest during the first few months of therapy,[6] so remind people 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.[13] 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 there is 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.[3] There is also an increased risk of rash when allopurinol is given together with amoxicillin.[9]

People of Chinese, Thai and Korean ancestry are at higher risk of AHS, due to high rates of a genetic marker, *HLA-B*5801*. Testing of this marker, and avoidance of allopurinol for *HLA-B*5801* carriers can reduce the incidence of AHS.[14]

If allopurinol is not tolerated, alternative urate-lowering medicines (eg probenecid, benzbromarone, or febuxostat) should be considered.

There are many precautions surrounding concomitant prescribing of allopurinol with azathioprine;[9,15] refer to the specialist team for appropriate management of gout for these people.

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