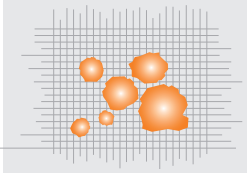
Allopurinol—dose according to effect, not renal function



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Gout is not a benign or minor condition. Hyperuricaemia with gout results in:

- reduced exercise and activity levels
- lost productivity
- hospital admissions
- joint damage
- renal damage

...and is associated with cardiovascular disease—particularly raised blood pressure.

It is a chronic disease and we may have been doing a disservice to many people by under-treating it because of strict adherence to some 'dosing in renal impairment' guidelines.

Previous concerns were that oxypurinol, a renally excreted metabolite of allopurinol, accumulated in renal impairment and was associated with allopurinol hypersensitivity syndrome. More recent information indicates that allopurinol hypersensitivity reactions are not necessarily dose dependent and do not always correlate to serum oxypurinol concentrations.[1,2]

STARTING ALLOPURINOL: Start allopurinol as soon as can be negotiated with the patient after the first episode. This is particularly important for Maori and Pacific people in whom there is a strong genetic basis for gout, and gout will be frequent and lifelong. The traditional 'wait for two episodes per year' no longer holds true. Each episode of gout damages the joints—and the kidneys.

Initial dose: To help avoid confusion for the patient with multiple dosage changes, start allopurinol at 150 mg [1/2 x 300 mg] daily and double the dose to 300 mg after four weeks. Titrate according to serum uric acid concentrations.

Prophylactic cover: Use colchicine, usually 0.5 mg daily, for three to six months. Remember to stop the colchicine after this time.

ADVERSE EFFECTS: General skin reactions may occur in 4–10% of people. Allopurinol must be discontinued at the appearance of a skin rash or other signs (fever, arthralgia, lymphadenopathy) which could indicate an allergic reaction (hypersensitivity syndrome).

MINI-NUGGETS:

- Gout affects 10–14% of Maori and Pacific people compared to 3–5% of Europeans.
- Men in their 20s and 30s are getting gout resulting in lost time at work and stopping sports and other activities.
- Exercise may precipitate gout, so don't assume that sudden severe joint pain is a 'sports injury' in high-risk populations. It may be gout.
- Some people may be more inclined to take allopurinol earlier, and regularly, if they realise that it could allow them to eat small amounts of gout-inducing food, e.g. shellfish.
- Fructose containing soft drinks and fruit juices may precipitate gout.
- When serologic human leukocyte antigen (HLA) typing becomes more readily available (near future) you may be able to test for HLA-B*5801, which is a strong marker for allopurinol-induced severe cutaneous adverse reactions.[5]

References

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3. Stamp l, O'Donnell J, Zhang M et al. Using allopurinol above the dose based on creatinine clearance is effective and safe in chronic gout, including those with renal impairment. Arthritis Rheum. 2010; Oct 27th [published ahead of print].
4. Vazquez-Mellado J, Morales E, Pacheco-Tena C, Burgos-Vargas R. Relation between adverse events associated with allopurinol and renal function in patients with gout. Ann Rheum Dis. 2001;60:981–3.
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KEY POINTS

- Treat to target serum uric acid concentrations (< 0.36 mmol/L) rather than according to renal function. This has been shown to be safe and effective.[3,4]
- Doses of allopurinol may need to be titrated up to 600 mg.

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NUGGETS *of* KNOWLEDGE provides succinct summaries of pharmaceutical evidence about treatment of common conditions presenting in primary care and possible adverse drug reactions.