

COLCHICINE- SAFE PRESCRIBING - TOE THE LINE!

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- ▶ ASSESS IF COLCHICINE IS APPROPRIATE AS A FIRST-LINE TREATMENT
- ▶ CONSIDER RENAL FUNCTION AND DRUG INTERACTIONS WITH OTHER MEDICINES
- ▶ ENSURE PATIENTS UNDERSTAND THE RISKS ASSOCIATED WITH COLCHICINE

Colchicine is indicated for the treatment and prevention of gout flares. It is best initiated within 24 hours of a gout flare because early treatment leads to better patient-reported outcomes.¹ If the response to colchicine is considered inadequate, try other options such as NSAIDs (non-steroidal anti-inflammatory drugs) or corticosteroids.¹

Colchicine inhibits the inflammatory response to urate crystals that cause pain and inflammation during a flare of gout. Colchicine also helps to prevent flares and relieve residual pain following a flare.² This is especially useful while urate-lowering medicines such as allopurinol are being initiated.^{3,4} Colchicine alone will not prevent the progression of gout to chronic gouty arthritis or tophaceous gout.

Make sure patients understand that they should continue their established urate lowering medicines (eg allopurinol, probenecid, benzbromarone or febuxostat) without interruption during a gout flare.

ASSESS IF COLCHICINE IS APPROPRIATE AS A FIRST-LINE TREATMENT

The most appropriate therapy for a gout flare should be based upon patient preference, prior response to therapy and associated comorbidities.¹ For some patients NSAIDs or oral corticosteroids will be most appropriate.⁵ Colchicine is useful if patients have an increased risk of toxicity with NSAIDs or prednisone, eg diabetes, or peptic ulcer disease.⁶ Doses of colchicine need to be adjusted if renal function is compromised, or if there are interactions with other medicines that delay colchicine metabolism.¹ (See table).

Note: Co-administration of NSAIDs or prednisone with colchicine may be considered when gout flares are characterised by severe pain, particularly in an acute polyarticular flare, or a flare involving 1-2 large joints.¹ Please note, both colchicine and NSAIDs are renally excreted, and NSAIDs are associated with decreased renal blood flow which may increase the likelihood of colchicine toxicity.

CONSIDER RENAL FUNCTION AND DRUG INTERACTIONS WITH OTHER MEDICINES

Lower doses of colchicine are recommended for the elderly, for patients with hepatic or renal impairment, and for patients who weigh less than 50kg.

Colchicine is contraindicated in severe renal or hepatic disease.⁷

The elderly are particularly sensitive to cumulative toxicity with colchicine due to age-related renal impairment. If colchicine is required, prescribe half the recommended dose (see Table 1) and ensure they are aware of the signs of toxicity. Acute renal failure has occurred in elderly patients taking colchicine who become dehydrated following episodes of diarrhoea and vomiting.⁸

| Renal function (eGFR) | Initial dose | Continuing dose* | Maximum dose* |
|---|------------------|-------------------------------|--|
| Over 50mL/min/1.73m ² | 1mg (2 tablets) | 0.5mg (1 tablet) 1 hour later | 1.5mg per course 6mg over 4 days |
| 10-50 mL/min/1.73m ² Or elderly | 0.5mg (1 tablet) | 0.5mg (1 tablet) every 12-24h | 1mg (2 tablets) in first 24 hours 3mg (6 tablets) over 4 days |
| Under 10mL/min/1.73m ² | Avoid | Avoid | Avoid |

Table 1: Colchicine dose recommendations for gout flares⁹

*Stop when relief obtained or at the first sign of toxicity.

All patients should be encouraged to use the lowest effective dose of colchicine because toxicity is dose-related.¹⁰ Low-dose colchicine (2 tablets initially, followed by 1 tablet an hour later) compared with high-dose colchicine (2 tablets initially, followed by 1 tablet every

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▶ COLCHICINE

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hour for 6 hours) in the first 24 hours of acute gout, provides no loss of efficacy but a significant reduction in adverse effects.^{1,11}

The total dose of colchicine should not exceed 6 mg over 4 days.⁹ In high-risk groups (elderly patients and those with renal impairment), the maximum dose in the first 24 hours should not exceed 1 mg and the total dose of colchicine should not exceed 3 mg over four days.⁹

It is important that there is a gap of at least **3 days** between courses of acute treatment to avoid toxicity from colchicine accumulation.²

Colchicine prophylaxis

Colchicine prophylaxis therapy (0.5 mg daily or twice daily, or on alternate days)^{5,12} may be commenced the day following treatment for a gout flare.

At this dose, colchicine is effective at preventing flares of gout when patients start urate-lowering medicines (eg allopurinol or febuxostat). It is important that patients are aware of this, and continue to take colchicine prophylaxis for 3-6 months after they achieve target serum urate with their urate-lowering medicines.^{5,12}

Notable interactions

Colchicine is **contraindicated** if patients have renal or hepatic impairment **and** they are taking other medicines that increase the risk of colchicine toxicity. These medicines include macrolides (eg erythromycin, clarithromycin), imidazoles (eg fluconazole, ketoconazole, itraconazole), protease inhibitors (eg ritonavir), diltiazem, verapamil and ciclosporin.²

Patients who are taking these medicines without renal or hepatic impairment may take colchicine at a reduced dose. See the New Zealand Formulary www.nzf.org.nz for a comprehensive list.⁹

Patients who are taking statins or fibrates in combination with colchicine, should be advised to promptly report any unexplained muscle pain or weakness; there have been some case reports of rhabdomyolysis and myopathy with this combination.⁹

ENSURE PATIENTS UNDERSTAND THE RISKS ASSOCIATED WITH COLCHICINE

During a gout flare, patients are likely to start treatment with colchicine by themselves at home.¹⁰ *Appropriate patient education is important given the narrow therapeutic range of colchicine.* Patients are particularly at risk of toxicity if they have a poor understanding of how to take colchicine, possible side-

effects and consequences of overdose.¹¹

A report of nine cases of colchicine overdose in the Auckland region showed that 3 of the 4 accidental poisonings occurred in Pacific Island men. Even allowing for increased prevalence of gout in these groups, this suggests that a special effort is needed when colchicine is prescribed for these patients, especially if English is not their first language.¹¹

Patients should be informed to stop colchicine, and see their doctor if they develop:

- abdominal pain
- diarrhoea, nausea, vomiting⁹
- burning sensation of the throat, stomach or skin²

Ask the patient to take note of the dose taken so they know to use lower doses during subsequent flare of gout.

In some circumstances toxic effects may not appear until 24 hours after ingestion of an acute dose.² If toxicity is suspected, prompt admission to a hospital with intensive care facilities is essential. There is no antidote; charcoal may be considered but treatment is generally supportive.^{2,10}

Remind patients to keep all medicines well out of reach and out of sight of children and grandchildren. Children are very vulnerable to colchicine poisoning; **Doses as small as 1 or 2 tablets can cause serious toxicity.**¹³

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