Myopathy and rhabdomyolysis have been reported in patients taking colchicine with a statin or fibrate.

Corticosteroids – Short courses of systemic corticosteroids such as prednisone or methylprednisolone given orally or parenterally are effective for treatment of acute flares. Intra-articular injection of methylprednisolone or triamcinolone is also considered effective, but randomized controlled trials are lacking.6

Interleukin-1 (IL-1) Inhibitors – Canakinumab (Ilaris),7 which is FDA-approved for treatment of systemic juvenile idiopathic arthritis and is extraordinarily expensive, has also been reported to be effective in relieving gout pain and inflammation.8 Anakinra (Kineret), which is approved for use in rheumatoid arthritis, has also reduced the pain and inflammation of gout and is widely used off-label.8 These drugs may be options for patients with gout who cannot tolerate or have contraindications to NSAIDs, colchicine, and corticosteroids.

PREVENTION OF FLARES — Prophylaxis with colchicine or an NSAID can prevent flares of acute gout associated with initiation of urate-lowering therapy. In
older patients or in those with comorbidities such as renal disease or peptic ulcer disease, colchicine is preferred.

**URATE-LOWERING AGENTS** — The goal of therapy with urate-lowering drugs is to reduce the serum urate level to <6.0 mg/dL and preferably to <5.0 mg/dL, but asymptomatic, incidental hyperuricemia should not be treated with urate-lowering drugs. Initial treatment of hyperuricemia should be with a xanthine oxidase inhibitor.

**Xanthine Oxidase Inhibitors — Allopurinol** lowers serum urate levels by inhibiting xanthine oxidase, the enzyme that converts xanthine into uric acid. It is effective in preventing recurrences of acute gout arthritis and in reducing the size of tophi, and may prevent urate nephrolithiasis. The dosage of allopurinol should be started at 100 mg/day and gradually increased until the target urate level (<6 mg/dL) is reached. Doses as high as 900 mg daily may be required; 300 mg daily is widely used, but often fails to normalize serum urate levels. The starting dose should be lowered in patients with moderate to severe renal impairment, but still should be titrated up to a maintenance dose that may be higher than 300 mg.

Adverse effects can include a variety of cutaneous reactions (including Stevens-Johnson syndrome), liver enzyme abnormalities, leukopenia, and generalized vasculitis. Severe cutaneous reactions are associated with the HLA-B*5801 allele, which is especially common in some Asians (e.g., Han Chinese, Thai); such patients should be screened for this allele before receiving the drug.

**Febuxostat** is a newer xanthine oxidase inhibitor that can be used as an alternative to allopurinol. Febuxostat is effective in preventing acute gout recurrences and in reducing the size of tophi. Its effectiveness in preventing urate nephrolithiasis remains to be established. The dose of febuxostat does not need to be reduced in patients with moderate renal insufficiency. (Data are insufficient to make recommendations for patients with severe renal insufficiency.) Stevens-Johnson syndrome and hypersensitivity reactions have also been reported with febuxostat.

**Uricosuric Agents** — When a xanthine oxidase inhibitor fails to lower serum urate to target levels, addition of probenecid or another uricosuric agent may be effective. Probenecid can also be used as the initial urate-lowering drug in patients who cannot tolerate xanthine oxidase inhibitors. Probenecid can lower serum urate levels to <6.0 mg/dL, but patients must have adequate renal function for an optimal response. Uricosuric agents increase the risk of urate nephrolithiasis and are contraindicated in patients with kidney stones. Patients with high urinary uric acid excretion (>800 mg/24 h) are at high risk for nephrolithiasis and should not be treated with uricosuric agents. Probenecid may decrease the renal clearance of methotrexate. Salicylates can antagonize the uricosuric effect of probenecid.

The antihypertensive drug losartan and the triglyceride-lowering drug fenofibrate, which both have uricosuric effects, have also been used (off-label) to treat hyperuricemia.

**Pegloticase** — Pegloticase is an intravenous pegylated urate oxidase enzyme that converts uric acid to allantoin, an inert water-soluble purine metabolite, which is cleared by the kidney. The drug rapidly lowers serum urate levels in patients with gout, but it is very expensive and development of anti-pegloticase antibodies can interfere with its continued effectiveness. Infusion reactions occur frequently, and anaphylaxis has been reported. Pegloticase should be reserved for use in highly symptomatic patients with severe tophaceous gout who have not responded to both a xanthine oxidase inhibitor and a uricosuric agent.

**CONCLUSION** — Acute flares of gout can be treated with an NSAID, colchicine, or a corticosteroid. Colchicine and NSAIDs can be used prophylactically to prevent flares associated with urate-lowering therapy. Allopurinol, febuxostat, or probenecid can prevent gout attacks by lowering serum urate levels. Pegloticase can be used in patients with severe disease when other urate-lowering drugs fail to achieve target serum urate levels.

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