URATE-LOWERING THERAPY

Ultimate control of gout requires correction of the underlying chronic hyperuricemia, the central cause for gout. Attempts to normalize serum urate to a subsaturation point (typically, <300–360 μmol/L [5.0–6.0 mg/dL]) to prevent recurrent gout flares and eliminate tophi are critical and entail a commitment to urate-lowering regimens that are required usually for life (Fig. 372-1). Urate-lowering drug therapy should be considered when, as in most patients, the hyperuricemia cannot be corrected by risk factor interventions (control of body weight, healthy diet, limitation of alcohol use, decreased consumption of fructose-rich foods and beverages, and avoidance of thiazide and loop diuretics). The decision to initiate urate-lowering drug therapy usually is made considering the number of gout flares (urate lowering may be cost-effective with more than two attacks yearly), severity and duration of flares, quality of life, or the patient's willingness to commit to lifelong therapy. Urate-lowering therapy should be initiated in any patient who already has subcutaneous tophi or chronic gouty arthritis or known uric acid stones.

Allopurinol, a xanthine oxidase inhibitor, is the first-line urate-lowering drug among gout patients. Allopurinol can be given in a single morning dose, starting at 100 mg daily or less and titrating up (to 800 mg daily) to achieve a target serum urate level <5–6 mg/dL (i.e., a subsaturation point of MSU crystals). In patients with chronic kidney disease (CKD), the starting allopurinol dose should be lowered depending on the CKD levels; for example, with an estimated glomerular filtration rate of 30–45 mL/min, one would start at 50 mg daily and titrate up slowly. Starting at a low dose and titrating up reduces the risk of severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome and toxic epidermal necrolysis, as well as the risk of gout flares associated with rapid serum urate reduction due to introduction of urate-lowering therapy (Fig. 372-1). Allopurinol is generally well tolerated, but mild cutaneous reactions can develop in ~2% of users. SCARs to allopurinol are rare but can be life-threatening, and thus, appropriate precaution is advised. Presence of CKD, higher allopurinol initial dosing (e.g., >100 mg daily in CKD patients), and