Evidence-Based Urate-lowering Therapy (ULT)

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Gout is an inflammatory condition characterized by the deposition of monosodium urate crystals in the joints or soft tissue. The worldwide incidence and prevalence of gout appear to be increasing substantially for a variety of reasons, such as longevity, diet trends, diuretics use and even organ transplant with cyclosporin use. The associations of hyperuricemia with cardiovascular disease, hypertension, chronic kidney disease and metabolic syndrome are being examined intensively in epidemiologic, experimental, and clinical interventional studies.

Xanthine oxidase inhibitor therapy with either allopurinol or febuxostat is recommended as the first-line pharmacologic ULT approach. Serum urate level should be lowered with the target < 6 mg/dl at a minimum, and often < 5 mg/dl. Starting dosage of allopurinol should be no greater than 100 mg/day for any patient, and start at 50 mg/day in stage 4 or worse CKD (evidence B). Gradually titrate maintenance dose upward every 2–5 weeks to appropriate maximum dose in order to treat to target (evidence C). Dose can be raised above 300 mg daily, even with renal impairment as long as it is accompanied by adequate patient education and monitoring for drug toxicity (evidence B). Prior to initiation, consider HLA–B*5801 in selected patients, specifically in subpopulations at higher risk for severe allopurinol hypersensitivity reaction (evidence A). Probenecid is the first choice among uricosuric agents for ULT monotherapy (evidence B). In gout patients with a creatinine clearance < 50 ml/ minute, probenecid is not recommended as first-line ULT monotherapy (evidence C). Use of agents other than probenecid with clinically significant uricosuric effects, such as fenofibrate and losartan, can be therapeutically useful as components of a comprehensive ULT strategy (evidence B). History of urolithiasis contraindicates first-line uricosuric urate-lowering monotherapy (evidence C). Urinary uric acid should be measured before initiation of uricosuric ULT (evidence C). Elevated urine uric acid indicative of uric acid overproduction contraindicates uricosuric ULT (evidence C). Continue to monitor urinary uric acid during uricosuric ULT (evidence C). Consider urine alkalinization (e.g., with potassium citrate) with monitoring of urine pH, in addition to increased fluid intake, as a risk management strategy for urolithiasis (evidence C).