Long-Term Management of Gout
Nonpharmacologic and Pharmacologic Therapies

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KEYWORDS

• Gout • Hyperuricemia • Risk reduction • Urate-lowering therapy • Allopurinol
• Febuxostat • Uricosuric agents • Pegloticase

KEY POINTS

- Management of hyperuricemic individuals, whether asymptomatic or with gout, aims primarily at maintaining serum urate concentrations in a subsaturating range (usually <6 mg/dL), thus preventing or reversing the clinical consequences of urate crystal formation and deposition.
- Although nonpharmacologic (lifestyle) adjustments may lessen the risk for incident gout in hyperuricemic individuals and ameliorate the course of patients with established gout, pharmacologic urate-lowering therapy to achieve goal-range serum urate is, in most instances, required.
- Inhibition of xanthine oxidase (XO) activity with allopurinol at doses titrated to achieve goal-range serum urate levels remains the first-line urate-lowering pharmacotherapy in the US; febuxostat, an alternative XO inhibitor, or benzbromarone (where available) are suitable alternative first-line options, especially for patients at high-risk for allopurinol toxicity.
- Nonadherence to long-term medication use and inadequate monitoring/titration of urate-lowering therapies are important factors contributing to the suboptimal outcomes for patients with gout documented in many countries.
- For patients who have progressed to severe gout with impaired physical function or quality of life (because of either refractoriness to or intolerance of oral urate-lowering agents or inadequate previous therapy), the modified recombinant uricase, pegloticase, is a biological therapeutic option warranting consideration.

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INTRODUCTION

The clinical signs and symptoms of gout reflect inflammatory responses to monosodium urate crystals deposited in tissues from extracellular fluids saturated for urate.[1] Hyperuricemia (defined as serum or plasma urate concentrations exceeding 6.8 mg/dL, the limit of urate solubility) is a necessary but not sufficient pathogenetic factor in gout, as shown by recent estimates of 8.3 million and 40 million persons for the respective prevalences of gout and asymptomatic hyperuricemia (hyperuricemia without clinical gout) in the American population.[2] Persons with gout or with asymptomatic hyperuricemia alone have considerably increased prevalences of significant chronic comorbidities (discussed later), which can affect the safety and efficacy of treatment of hyperuricemia and can, in turn, be affected by it.[3,4]

Treatment of acute gouty arthritis typically involves brief courses of antiinflammatory medication aimed at reducing the pain, duration, and disability of flares with acceptable benefit/risk ratios (see later discussion). However, antiinflammatory agents do not lower urate concentrations and are thus not appropriate for long-term management of established gout or prevention of incident gout. Instead, accomplishment of the latter aims center on nonpharmacologic and pharmacologic means to achieve and maintain serum urate levels in a subsaturating range, because persistent goal-range decrease of urate levels is accompanied over time by resolution and even reversal of the signs and symptoms of established gout.[5–9]

NONPHARMACOLOGIC APPROACHES TO CHRONIC GOUT: RISK REDUCTION

Among risk factors for the development of gout (**Table 1**), some such as age, gender, race, and ethnicity are not modifiable, whereas others are. Advanced age is strongly associated with increases in both the incidence and prevalence of gout.[10–13] The risk of gout is also higher in men than women at all ages, although this gap narrows after the female menopause.[11,13] Racial and ethnic disparities in gout risk have also been observed.[14–16]

Nonpharmacologic management of gout relies on lifestyle adjustments aimed at reducing the roles of modifiable risk factors in the expression or severity of gout. In addition to institution of appropriate pharmacologic or nonpharmacologic treatment of comorbid disorders, lifestyle adjustments should be considered and appropriately recommended to patients with gout (or asymptomatic hyperuricemia). It is thought that these initiatives promote overall health and may lead to sustained goal-range decrease in urate levels and/or lessen the burden of pharmacologic urate-lowering therapy (ULT). Lifestyle measures directly decrease urate levels by reducing the availability of uric acid

Table 1
Nonmodifiable and modifiable risk factors for gout

Nonmodifiable Risk Factors	Modifiable Risk Factors
Age	Hyperuricemia
Gender	Obesity
Race	Hypertension
Ethnicity	Hyperlipidemia
	Ischemic cardiovascular disease
	Diabetes mellitus
	Chronic kidney disease
	Dietary factors
	Medications that alter urate balance