Background/Purpose: Urate-lowering therapy (ULT) is considered key to the optimal management of hyperuricemia in gout. We systematically reviewed the published data on the pharmacological ULT agents in gout.

Method: PubMed and CENTRAL databases were searched to find published English language articles on gout up to March 2011. A total of 21 manuscripts were selected for this systematic review. A meta-analysis was carried out to assess the average effect size for the proportion achieving target SUA <6.0 mg/dl across studies between allopurinol (ALLO ≤ 300mg/day) and the comparator drugs (benzbromarone [100- 200 mg/day] or febuxostat [40-120mg/day]). Mantel-Haenszel method of weighting was employed using a random-effects model. The average effect size is reported as an odds ratio (OR).

Result: The pooled mean (SD) age in the trials was 52.6 (12.0), 93.7% were males, and the disease duration 11.5 (9.2) years. ALLO at dose of 300 mg/day is largely ineffective in reaching the target goal of SUA< 6 mg/dl (24% to 53% achieved SUA< 6 mg/dl). The meta-analysis showed that the odds of achieving SUA < 6.0 mg/dl with ALLO (≤300mg/day) is 76% lower than with comparator drugs OR 0.23 [95%0.11-0.46; Figure]. Upwards dose titration every 4 weeks of ALLO, starting from 50-100 mg/day (to higher than 300 mg/day) is associated with achieving SUA < 6 mg/dl in 63% -100%. ALLO AEs in large RCTs included 2% with AST and ALT elevation> 3 ULN and 1.6% with rash. Renal impairment is associated with a significantly higher risk of severe cutaneous drug reaction with ALLO. Febuxostat (FEB) 80mg and 120 mg daily (not approved in USA) is more effective than ALLO 300 mg/day in achieving SUA< 6 mg/dl. There is lack of robust data in patients with CKD stage 4 or worse, including patients on dialysis. Rare skin hypersensitivity events also have been reported with FEB. Combination of 200-300 mg ALLO daily and probenecid 500 mg to 1 gram bid is effective in those with CrCl> 50 ml/min, at achieving SUA of <5 mg/dl. Fenofibrate and losartan also have been shown, in investigator-initiated trials, to be effective “add-on” uricosuric therapy for patients who have not achieved the target on ALLO that is not titrated above 300 mg daily.

Conclusion: Our systematic review established that ALLO ≤300mg/day fails to achieve a target SUA <6.0 mg/dl in the majority (>50%) of subjects with gout. The meta-analysis showed odds of achieving target SUA with ALLO (≤300mg/day) is 76% lower than with the comparator drugs benzbromarone and FEB. FEB at 80 and 120 mg/day is more effective than ALLO ≤300mg/day at achieving target SUA. Addition to ALLO of probenecid, or other weaker uricosurics (fenofibrate, losartan) with ALLO and probenecid is effective in patients with adequate renal function.
### Keywords: gout and meta-analysis

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