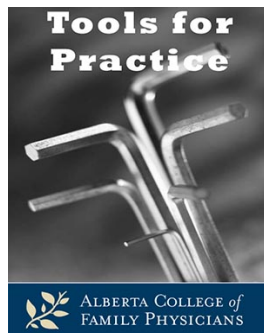


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Evidence Updated: Updated
Bottom Line: No change
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Febuxostat: Precipitating Crystals of Evidence About Gout Prevention

Clinical Question: Does febuxostat (Uloric®) offer any advantages over allopurinol in preventing gout?

Bottom Line: Febuxostat is not better than allopurinol for preventing gout and has a higher rate of gout flares. It should only be considered in patients who have experienced a serious adverse event with allopurinol.

Evidence:

- Meta-analysis¹ of five Randomized Controlled Trials (RCT) conducted in Canada,¹ US²⁻⁴ and Japan^{5,6} including 4250 mostly-male patients with gout.
 - Three RCTs gave colchicine or naproxen (eight or 24 weeks²⁻⁴), whereas the other two trials did not provide any prophylaxis against gout flares.^{5,6}
 - Febuxostat 40-240 mg compared to allopurinol 200-300 mg daily x8-52 weeks.
 - Gout episodes: Significant increase with febuxostat.
 - 43.6% versus 38.1% with allopurinol (Number Needed to Harm [NNH]=19).
 - Tophi number and size: No difference.^{2,3}
 - Achieved serum uric acid <360 µmol/L: Febuxostat 66.4% versus 43.2% with allopurinol.
- Two RCTs conducted in China.^{7,8}
 - 516⁷ and 504⁸ mostly-male patients, given colchicine or NSAID x8 weeks⁷ or NSAID for trial duration,⁸ randomized to febuxostat 40 or 80 mg, or allopurinol 300 mg daily for ~six months.
 - No difference in gout episodes between groups.
 - No difference in number of tophi.⁷
 - Serum uric acid <360 µmol/L more likely with febuxostat 80 mg versus both febuxostat 40 mg and allopurinol.

Studies' methodological weaknesses: Selective reporting of clinical outcomes, emphasizing surrogate outcomes, and under-dosing allopurinol.

Context:

- Start urate-lowering therapy at low dose and titrate up every two-six weeks, and use colchicine or NSAIDs for ~six months to prevent initial flares.⁹⁻¹¹
- Though it lowers serum uric acid, allopurinol has never been shown in RCTs to reduce gout flares.¹²
- Allopurinol adverse events: Mild rash, pruritus (~2%); allopurinol hypersensitivity syndrome (severe rash, fever, hepatitis and renal toxicity) [$\leq 1/1000$].^{13,14}
- Yearly costs: Febuxostat 80 mg ~\$680 (approved Canadian dose), allopurinol 300 mg ~\$100.¹⁵
- Febuxostat cardiovascular safety has been questioned¹⁶ and is being studied (NCT01101035).

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