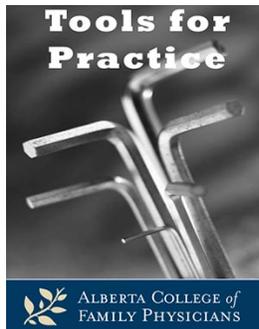


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## **Febuxostat: Precipitating crystals of evidence about gout prevention**

**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 initial flares. It should only be considered in patients who have experienced a serious adverse event with allopurinol.**

**Evidence:** Three industry sponsored randomized controlled trials<sup>1-3</sup> comparing febuxostat to allopurinol in primarily men with gout for ~10 years. All given colchicine or naproxen for 8<sup>1,2</sup> to 24<sup>3</sup> weeks.

1. 762 patients: Febuxostat 80mg or 120mg, or allopurinol 300mg daily x 52 weeks.<sup>1</sup>
  - o Initial flares (first 8 weeks): statistically significant increase with febuxostat 120mg (36%) > allopurinol (21%) or febuxostat 80mg (22%)
  - o Gout episodes weeks 9-52: all 64%-70% (no statistical difference)
  - o Significantly more discontinued febuxostat (39% for 120mg) versus allopurinol (26%)
2. 1072 patients: Febuxostat 80, 120 or 240 mg; allopurinol 300mg (100 mg for renal impairment) or placebo x28 weeks.<sup>2</sup> Found the same thing.
  - o Initial flares: significant increase with febuxostat
  - o Gout episodes weeks 9-28: no differences
  - o More discontinued in febuxostat arms
3. 2269 patients: Febuxostat 40 or 80mg or allopurinol 300mg (200mg if moderate renal impairment) x24 weeks.<sup>3</sup> 65% mild or moderate renal insufficiency.
  - o Initial flares: febuxostat > allopurinol (numbers not reported)
  - o Gout episodes weeks 9-24: similar (numbers not reported)

Studies' methodological weaknesses: selective reporting of clinical outcomes,<sup>2,3</sup> emphasizing surrogate outcomes,<sup>1,2,3</sup> and under-dosing allopurinol<sup>2</sup>.

### **Context:**

- Delay starting uric acid lowering therapy for 2-4 weeks after acute gout attack<sup>4</sup> and use colchicine or NSAIDs to prevent initial flares.<sup>4,5,6</sup>

- Allopurinol adverse events: mild rash, puritis (~2%); allopurinol hypersensitivity syndrome (severe rash, fever, hepatitis and renal toxicity) [~1/1000].<sup>7,8</sup>
- Yearly costs: Febuxostat 80mg (approved Canadian dose) =\$730, Allopurinol 300mg =\$135.
- Febuxostat cardiovascular safety has been questioned<sup>9</sup> and is being studied (NCT01101035).

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