

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Febuxostat for acute gout

Gout is a syndrome caused by deposition of urate crystals in the joints, leading to inflammation. The first attack of gout is usually in a single joint, most often in the foot or big toe, and the joint is typically painful, red and swollen. Hyperuricaemia (serum uric acid concentration > 0.46 mmol/l) is an important risk factor for developing gout, but many people with hyperuricaemia never develop gout. Conversely, up to 40 % of people experiencing an attack of gout have normal serum urate levels. The management of gout involves pain relief, prevention of further attacks, prevention of formation of tophi and destructive arthritis, and reducing risk factors. These include hypertension, obesity, use of loop and thiazide diuretics, alcoholism, insulin resistance and hyperlipidemia. For those who experience more than two attacks of gout per year, uric acid lowering treatment with allopurinol is recommended.

Febuxostat is a new uric acid lowering treatment for the long term control of chronic gout. It is not as yet marketed in Australia but is available only under the Special Access Scheme. Febuxostat is a non-purine selective inhibitor of xanthine oxidase. This agent works by non-competitively blocking the channel leading to the active site on xanthine oxidase. Xanthine oxidase is needed to successively oxidate both hypoxanthine and xanthine to uric acid. Febuxostat inhibits xanthine oxidase, therefore reducing production of uric acid.

A randomized controlled trial (The FACT trial) compared febuxostat with allopurinol in 762 patients. Patients were randomized to receive febuxostat 80 mg or 120 mg or allopurinol 300 mg daily for 52 weeks. The primary efficacy end point was a serum urate concentration of less than 6 mg per deciliter at the last three measurements, and was reached by 53% of patients taking 80 mg and 62% of patients taking 120 mg febuxostat, compared to the allopurinol-treated patients (21%); $p < 0.001$. During weeks 9-52 of the trial period the number of patients in each group requiring treatment for a gout flare was similar, 64% receiving febuxostat 80 mg, 70% febuxostat 120 mg and 64% receiving allopurinol.

The incidence of side effects was similar in the three groups. Reported side effects include abnormal liver function, diarrhea, headaches, joint related signs and symptoms and musculoskeletal and connective tissue symptoms. Rash was reported by four subjects receiving febuxostat 80 mg, four patients receiving 120 mg febuxostat and one patient receiving allopurinol.

In patients with a creatinine clearance between 30-89mls/min the manufacturer states no dose adjustment is necessary. There is insufficient data to provide guidance for patients with severe renal impairment. A higher rate of cardiovascular thromboembolic events was observed amongst patients treated with febuxostat. The manufacturer also recommends monitoring of liver function periodically.

Febuxostat is already available in the US and Europe but is currently only available in Australia under the Special Access Scheme

This E-Bulletin is based on work by Margie Harlow, Drug Distribution Coordinator, RGH

FOR FURTHER INFORMATION CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@health.sa.gov.au
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