Te Awakairangi Health NETWORK

Medicines Update September 2014

Febuxostat (Adenuric®)

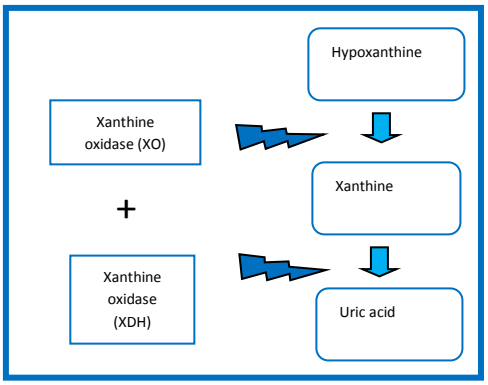
Febuxostat (pronounced fe-buks-O-stat) is a relatively new medicine - a non-purine xanthine oxidase inhibitor - available as a ***third-line preventative*** for the treatment of gout (after allopurinol and probenecid). For most patients with chronic gout, allopurinol should remain first-line in preference to febuxostat.

Key Messages: Registered, now fully funded under Special Authority

- **Restrict prescribing of febuxostat** - to treating patients with gout who are *intolerant* of allopurinol or for who allopurinol is *contraindicated or ineffective* when optimally administered.
- **Start febuxostat at 80mg once daily** - increase to 120mg daily if the serum uric acid (sUA) remains above 0.36mmol/L after 2-4 weeks. Following oral administration febuxostat is rapidly and well absorbed, it may be taken with or without food
- **Co-prescribe prophylaxis -** *low dose colchicine and/or NSAIDs for at least 6 months of* febuxostat therapy, as with other urate-lowering therapies
- **Monitor liver function tests (LFTs) -** Febuxostat can be safely used in patients with mild hepatic impairment and possibly in moderate impairment, although the data is more limited. Check base-line LFTs prior to initiation, early in treatment (one to three months), then intermittently based on clinical judgement.
- **Stop treatment -** if patient develops signs or symptoms of *serious hypersensitivity reactions.* Most cases occur in the first month of therapy

How is febuxostat different to allopurinol?

- **Similar but potentially enhanced mode of action -** Unlike allopurinol, febuxostat inhibits *both* the oxidised (XO) and reduced (XDH) forms of enzyme xanthine oxidase required for the formation of uric acid
- **No dose adjustment with mild to moderate renal impairment -** Unlike allopurinol, febuxostat is eliminated by both hepatic and renal pathways and requires no dosage adjustment in patients with mild or moderate impairment of renal function (creatinine clearance >30ml/min).



How effective is febuxostat at lowering sUA?

Efficacy and safety of febuxostat compared to optimal dosing of allopurinol is unknown. Clinical trials (FACT, APEX & CONFIRMS) have shown that febuxostat 80mg or 120mg daily is more effective than allopurinol 300mg in lowering the serum uric acid concentration 9sUA) below 0.36mmol/L (target set by guidelines from European League Against Rheumatism (ULAR). However, no published studies have compared febuxostat with allopurinol in doses titrated up to a maximum of 900mg daily to reach this therapeutic target.

What are the Risks & Benefits

The main safety issue is risk of *hepatotoxicity*. Treatment should be stopped with abnormal LFTs if the ALT is three times the upper limit of normal. There is some evidence febuxostat may *increase cardiovascular risk*. It should be used with *caution in patients with ischaemic heart disease and congestive heart failure*. Hypersensitivity reactions have been reported in post-marketing surveillance. Other reported common adverse effects are nausea, diarrhoea, skin rashes, and gout flares. Long term safety in patients with severe renal impairment (creatinine clearance below 30ml/min) is unknown.

Special Authority criteria for febuxostat

Febuxostat is available as 80 mg and 120 mg tablets. The Special Authority criteria for initial approval for six months are as follows (application from any relevant practitioner):

Any of the following:

1. The patient has a serum urate level greater than 0.36 mmol/L despite treatment with allopurinol at doses of at least 600 mg/day and appropriate doses of probenecid;

OR

2. The patient has experienced intolerable side effects from allopurinol such that treatment discontinuation is required and serum urate remains greater than 0.36 mmol/L despite appropriate doses of probenecid;

OR

3. ***Both*:**

    3.1 The patient has renal impairment and serum urate remains greater than 0.36 mmol/L despite optimal treatment with allopurinol (see note);

    AND

    3.2 The patient has a rate of creatinine clearance greater than or equal to 30 mL/min.

Renewal of the Special Authority (from any relevant practitioner), for two years, is possible where the treatment remains appropriate and the patient is benefitting from treatment.

References

1. Gout Update Febuxostat now subsidised on Special Authority. Best Practice Journal (BPJ) July 2014 Issue 26:38-44
2. Febuxostat for gout. Drugs & Therapeutics Bulletin (DTB) July 2010 48:7;78-82
3. Febuxostat stop treatment if signs or symptoms of serious hypersensitivity. Drug Safety Update June 2012 5:11 A3
4. Febuxostat for treating chronic gout (Review). The Cochrane Collaboration http://www.thecochranelibrary.com

For further prescribing information go to The New Zealand National Formulary www.nzf.org.nz