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FEBUXOSTAT - SAFE PRESCRIBING - SORTING OUT GOUT

- PROVIDE PROPHYLACTIC COLCHICINE OR NSAIDS FOR AT LEAST 6 MONTHS WHEN STARTING FEBUXOSTAT
- GRADUALLY TITRATE DOSE UPWARDS TO ACHIEVE TARGET SERUM URATE
- ADVISE PATIENTS TO CONTINUE WITH FEBUXOSTAT DURING ACUTE FLARES OF GOUT
- INFORM PATIENTS TO REPORT ANY RASH OR SIGNS OF ALLERGIC REACTIONS

Febuxostat is indicated for the treatment of chronic hyperuricaemia in patients with gout[1] where urate deposition has already occurred.[2] It is a useful alternative for patients who are intolerant of allopurinol, or if serum urate remains greater than their target level despite optimal doses of allopurinol,[2] and probenecid.[3]

Note: The target serum urate level is usually 0.36mmol/L, however a lower target (0.30mmol/L) may be required for patients with gouty tophi.[4]

PROVIDE PROPHYLACTIC COLCHICINE OR NSAIDS FOR AT LEAST 6 MONTHS WHEN STARTING FEBUXOSTAT

When a patient is being initiated on febuxostat, it is essential that prophylactic doses of a NSAID (eg naproxen 250mg twice daily) or colchicine (0.5mg once or twice daily) are continued for at least the first 6 months.[2,3,5] This is because there is a very high risk of acute gout attacks when serum urate changes rapidly.

- When urate-lowering therapies are started there is a rapid **decrease** of serum urate
- When urate-lowering therapies are suddenly stopped, there is a rapid **increase** of serum urate.

GRADUALLY TITRATE DOSE UPWARDS TO ACHIEVE TARGET SERUM URATE

The usual starting dose of febuxostat is 80mg once daily, this dose may be adequate to achieve target serum urate. If serum urate is still above target after 2-4 weeks, the dose may be gradually increased to a maximum dose of 120mg once daily.[2] If the patient has mild hepatic impairment, it is advisable not to exceed a febuxostat dose of 80mg daily.[2] There is no dosing information available for patients with moderate-to-severe hepatic impairment.[2]

Liver function abnormalities have been associated with febuxostat use. These appear to be more frequent when patients are concomitantly treated with colchicine.[1]

It is advisable to check liver function prior to the initiation of febuxostat, after 1 and 3 months of treatment, and periodically thereafter based on clinical judgment. Inform patients that blood testing will be required during treatment to monitor their liver function, and explain that they need to report any symptoms of potential hepatic impairment such as nausea, fatigue, jaundice and dark urine.[3]

There is no dose adjustment necessary for patients with mild-to-moderate renal impairment,[6] however, the efficacy and safety have not been fully evaluated in patients with severe renal impairment (eGFR < 30mL/min/1.73m^2).[1]

RECOMMENDED DOSING[1]

CONDITION	STARTING DOSE	MAXIMUM DAILY DOSE
No hepatic impairment Adequate renal function (eGFR>30mL/min/1.73m^2)	80mg	120mg
Mild hepatic impairment	80mg	80mg

Note: Treatment with febuxostat in patients with ischaemic heart disease or congestive heart failure is not recommended.[1]

ADVISE PATIENTS TO CONTINUE WITH FEBUXOSTAT DURING ACUTE FLARES OF GOUT

As with other urate-lowering therapies, it is important that patients are aware that they need to take febuxostat continuously, even during acute flares of gout when they may also be taking colchicine or NSAIDs.

Explain to patients that good compliance with febuxostat is essential to prevent acute flares. If febuxostat is stopped suddenly, rapid increases in serum urate will increase the risk of an acute flare of gout.[5]

It is important that patients understand that they continue to take febuxostat, even if they have not experienced an acute attack for a long time. Gout is a long-term condition that requires long-term treatment to prevent acute flares and reduce the risk of joint erosion and permanent disability.[7]

Hyperuricaemia is also associated with other risks including hypertension, renal damage, diabetes, hyperlipidaemia and cardiovascular disease.[7]

➥ continued

INFORM PATIENTS TO REPORT ANY RASH OR SIGNS OF ALLERGIC REACTIONS

Febuxostat has a similar safety profile to allopurinol,[6,8] and like allopurinol there is a risk of hypersensitivity. These reactions are considered to be rare, and are more likely to occur during the first month of treatment. Reactions range from a mild rash to Stevens-Johnson Syndrome, toxic epidermal necrolysis and anaphylaxis.[1] It is important that patients know they should stop taking febuxostat as soon as they notice a progressive rash, swelling, or any other signs of allergic reaction, and to seek medical attention immediately. Early withdrawal is associated with a better prognosis.[2]

There appears to be greater risk of hypersensitivity with patients who have experienced a reaction with allopurinol, or if they have renal impairment. If hypersensitivity reactions do occur with febuxostat, re-challenge is not recommended.[2]

Some patients may experience dizziness or blurred vision with febuxostat.[2] Advise patients not to drive or to use dangerous machinery until they are certain that they will not be affected.[2]

As with allopurinol, febuxostat is not recommended in patients concomitantly treated with azathioprine.[1]

Note: Febuxostat is not recommended during pregnancy or breastfeeding due to lack of data in such patients.[1]

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REFERENCES

1. Te Arai BioFarma Ltd. Febuxostat (Adenuric) data sheet 19-04-14 www.medsafe.govt.nz/profs/datasheet/a/adenurictab.pdf (Accessed 26-06-14)
2. New Zealand Formulary, febuxostat http://www.nzf.org.nz/nzf_5685 (Accessed 26-06-14)
3. Stamp L, Dalbeth N. Febuxostat now subsidised on Special Authority. Best Practice Journal 2014;62:38-44. www.bpac.org.nz/BPJ/2014/July/febuxostat.aspx (Accessed 02-09-14)
4. Khanna D, Fitzgerald JD, Khanna PP et al. 2012 American College of Rheumatology guidelines for management of gout. Part 1: Systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia. Arthritis Care & Research 2012;64(10):1431-46 http://onlinelibrary.wiley.com/doi/10.1002/acr.21772/pdf (Accessed 10-03-15)
5. Edwards NL. Febuxostat: a new treatment for hyperuricaemia in gout. Rheumatology 2009;48:ii15-19 http://rheumatology.oxfordjournals.org/content/48/suppl_2/ii15.full (Accessed 26-06-14)
6. Jackson RL, Hunt B, MacDonald PA. The efficacy and safety of febuxostat for urate lowering in gout patients >65 years of age. BioMed Central Geriatrics 2012;12:11 www.biomedcentral.com/content/pdf/1471-2318-12-11.pdf (Accessed 27-06-14)
7. Te Karu L. A conversation about gout. Best Practice Journal 2014;60:27-33. www.bpac.org.nz/BPJ/2014/April/gout.aspx (Accessed 27-06-14)
8. Becker M, Espinoza L, Lademacher C, et al. The urate-lowering efficacy and safety of febuxostat in the treatment of hyperuricemia and gout: the CONFIRMS trial. Arthritis Research and Therapy 2010;12:R63. www.ncbi.nlm.nih.gov/pmc/articles/PMC2888216/pdf/ar2978.pdf (Accessed 27-06-14)

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