Febuxostat Prescribing Guidelines

Prescribing Guidance

- **Allopurinol remains the first line choice in patients with gout**, unless contraindicated or not tolerated or renal impairment prevents sufficient dose escalation. Intolerance to allopurinol occurs in approximately 10% of patients. *(Intolerance to allopurinol is defined as adverse effects that are sufficiently severe to warrant its discontinuation, or to prevent full dose escalation for optimal effectiveness as appropriate within its marketing authorisation).* The risk of intolerance to Allopurinol can be reduced by starting therapy at a dose of 100mg/day and building in increments of 50-100mg every four weeks until urate levels are within the target range of 200-300micromol/Litre.
- Febuxostat has been given a green traffic light status, as a **second line option**, for the treatment of **symptomatic gout**. It **should be reserved for patients in whom allopurinol is contraindicated or not tolerated.**
- The dose of allopurinol should be titrated up to the maximum tolerated dose (900mg per day dependent on renal function) in patients who are still experiencing symptoms of gout or have a urate level above the target range. Doses above 300mg/day should be administered in divided doses.
- Although clinical symptoms should be treated rather than the uric acid level, patients with gout should aim to have a urate level of <300micromol/L. This can be relaxed to between 300-360micromol/L in patients who have remained below 300micromol/L and have been asymptomatic for a number of years.
- Febuxostat is not a treatment for acute gout, but should be continued if an attack develops when already receiving Febuxostat. The acute attack should be treated separately.
- The British Society for Rheumatology guidelines[6] do not recommend that asymptomatic hyperuricaemia is treated.

Dosage

- **Treatment of chronic hyperuricaemia in gout**
  Initially 80 mg once daily, if after 4 weeks of initial dose, serum uric acid greater than 300 micromol/Litre then increase dose; increased if necessary to 120 mg once daily.

Contra-indications

- Hypersensitivity to the active substance or to any of the excipients (see SmPC for full list)
- Pregnancy and breastfeeding

Special Warnings and Precautions for Use

1. **Cardio-vascular disorders** - Treatment with febuxostat in patients with ischaemic heart disease or congestive heart failure is not recommended. Please see MHRA alert 2019 here for more information

2. **Medicinal product allergy / hypersensitivity** - Rare reports of serious allergic/hypersensitivity reactions, including life-threatening Stevens-Johnson Syndrome, Toxic epidermal necrolysis and acute anaphylactic reaction/shock, have been collected in the post-marketing experience. In most cases, these reactions occurred during the first month of therapy with febuxostat. Some, but not all of these patients reported renal impairment and/or previous hypersensitivity to allopurinol. Severe hypersensitivity reactions, including Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) were associated with fever, haematological, renal or hepatic involvement in some cases.

Updated By: Lauren Clarke, Senior Pharmacist – Interface, BHNFT, July 2020
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3. **Acute gouty attacks (gout flare)** – If possible, Febuxostat treatment should not be started until an acute attack of gout has completely subsided. Gout flares may occur during initiation of treatment. At treatment initiation with febuxostat flare prophylaxis for up to 6 months with an NSAID or colchicine is recommended. If an acute attack occurs during febuxostat treatment, it should not be discontinued. Continuous treatment with febuxostat decreases frequency and intensity of acute attacks

4. **Liver Disorders** - During the combined phase 3 clinical studies, mild liver function test abnormalities were observed in patients treated with febuxostat (5.0%). Liver function test is recommended prior to the initiation of therapy with febuxostat and periodically thereafter based on clinical judgment.

5. **Lactose** - Febuxostat tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Cautions

- Congestive heart failure
- Ischaemic heart disease
- Thyroid disorders
- Transplant recipients

Administer prophylactic NSAID (*not* aspirin or salicylates) or colchicine for up to 6 months after starting febuxostat to avoid precipitating an acute attack.

Hepatic Impairment

The maximum dose of febuxostat in mild liver impairment is 80mg once a day. There is no dose information available about the use of febuxostat in moderate to severe hepatic impairment. Liver function tests are recommended prior to the start of treatment and periodically thereafter based on clinical judgement.

Renal Impairment

Use with caution if eGFR less than 30ml/minute/1.73m^2

Drug interactions

The manufacturer of febuxostat advises to avoid concomitant use with:

- Azathioprine
- Mercaptopurine

Please note: The above summary is not exhaustive, please see Summary of Product Characteristics for further information.[1]

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Febuxostat (Adenuric®) is a non-purine selective xanthine oxidase inhibitor for the treatment of chronic hyperuricaemia in gout. It has been shown to be more effective than placebo and allopurinol at lowering uric acid levels in studies of up to 40 months duration. However, it has not been shown to reduce the incidence of episodes of acute gout.[3]

A recent meta-analysis of randomised controlled trials identified that febuxostat was superior to allopurinol and well tolerated for urate reduction. Dose increases showed more patients achieve the target urate levels .[4] However it concluded that both allopurinol and febuxostat were effective in achieving target urate levels at 6 months compared with placebo. [4]

Allopurinol remains the first line choice in patients with gout. Febuxostat has significant side effects and there is currently no long term data available on its safety. It is also significantly more expensive than current treatment options (see chart below).

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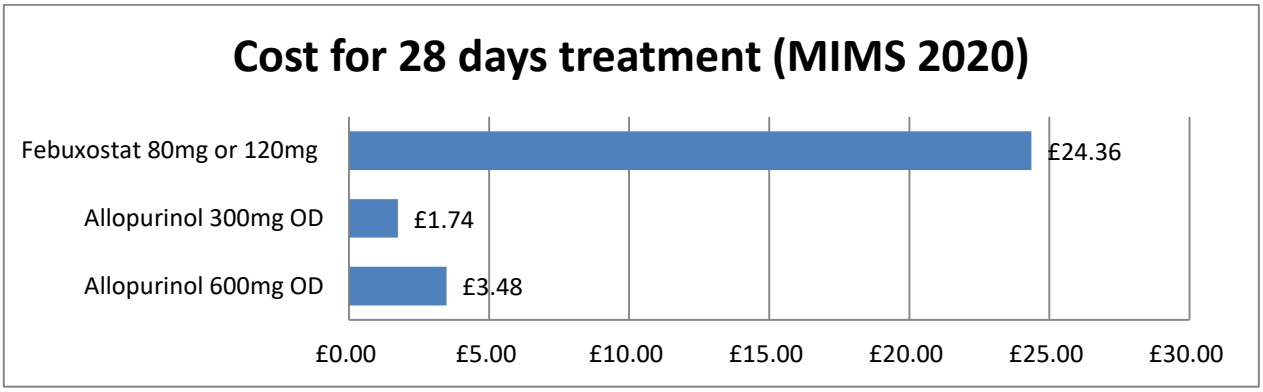
Cost[5]

Febuxostat 80mg Tablets, 28 pack = £24.36.
Febuxostat 120mg Tablets, 28 pack = £24.36



References

1. Summary of product characteristics. Adenuric® 80mg Film-Coated Tablets. April 2018. https://www.medicines.org.uk/emc/product/487/smpc Accessed <17/07/20>

2. NICE technology appraisal No.164. Febuxostat for the management of hyperuricaemia in people with gout. Dec 2008. Available at: www.nice.org.uk/Guidance/TA164 Accessed <17/07/20>

3. New Drug Evaluation – Febuxostat. NYRDTC. Available at: http://www.nyrdtc.nhs.uk/docs/nde/NDE_101_Febuxostat.pdf Accessed <18.1.12>

4. Fan M, Liu J, Zhao B et al. Comparison of efficacy and safety of urate-lowering therapies for hyperuricemic patients with gout: a meta-analysis of randomised , controlled trials. Clinical rheumatology (2020) https://doi.org/10.1007/s10067-020-05272-4 Accessed <17/07/20>

5. Mims. Adenuric®. https://www.mims.co.uk/drugs/musculoskeletal-disorders/gout/adenuric <17/07/20>

6. British Society for Rheumatology. Gout Guidelines 2017. Available at: https://academic.oup.com/rheumatology/article/56/7/e1/3855179 Accessed <17/07/20>

This prescribing guideline was ratified by the Area Prescribing Committee on 14th October 2020.