NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Febuxostat for the management of hyperuricaemia in patients with gout

Final scope

Remit/appraisal objective

To appraise the clinical and cost-effectiveness of febuxostat for the management of hyperuricaemia in adults with gout.

Background

Gout is a metabolic disorder that causes acute, intermittent and painful attacks of arthritis in the joints of the foot (especially the big toe), knee, hand and wrist. Gout occurs when there is a sudden onset of inflammation as a result of excess uric acid (crystals of monosodium urate) in the blood (hyperuricaemia) and tissues. With persistent saturation of the serum with urate crystals, gout may progress from acute episodic attacks to a disabling chronic deforming arthropathy, with destructive deposits of urate crystals (tophi) in bones, joints, subcutaneous tissue and other organs. Renal damage may occur due to urate crystal deposition and urinary tract stones composed entirely or partly of uric acid crystals.

Hyperuricaemia is associated with the development of gout, however not all patients with hyperuricaemia develop the disorder. Hyperuricaemia is generally divided into three pathophysiologic categories; uric acid underexcretion, uric acid overproduction, and combined causes. Serum uric acid concentration increases with age and is higher in men than women. Other factors that tend to raise serum uric acid concentration, and are related to gout, include obesity; high alcohol consumption; hypertension; a diet rich in purines (red meat and offal, game, seafood and legumes); severe psoriasis; and drugs such as aspirin, diuretics and immunosuppressants such as ciclosporin. Hyperuricaemia is associated with increased cardiovascular risk.

Between1990-1999 the annual incidence in the UK of gout ranged from 11.9-18.0 cases per 10,000 patient years. The ratio of men to women with gout was 3.6 to 1. In 1999, the prevalence of gout in the UK was 1.4% (approximately 742,600 people) with the highest prevalence estimates among elderly men. It is estimated that approximately 247,500 patients with gout are receiving active treatment with urate lowering drugs.

Current management of an acute attack of gout includes oral colchicine and/or a non-steroidal anti-inflammatory drug (NSAID) to alleviate pain and inflammation. Patient education and appropriate lifestyle advice are seen as core aspects of the management of this disease (e.g. reduction in intake of alcohol, calories and/or purines). Associated comorbidity and risk factors, such as hyperlipidaemia, hypertension, hyperglycaemia and obesity should also be addressed as an important part of the management of gout.

If recurrent attacks of gouty arthritis occur despite attempts to reduce risk factors, or if the patient has one or more tophi, or clinical or radiological signs of chronic gouty arthritis or recurrent uric acid renal stones urate-lowering therapy is used. Allopurinol (a xanthine oxidase inhibitor) is generally used as a first-line long term urate lowering therapy. Concomitantly, in the first months of urate-lowering therapy, anti-inflammatory medication (low-dose colchicine or NSAID) can be administered as prophylaxis against an acute flare-up of gout. When patients are unresponsive or present with hypersensitivity to allopurinol, alternative uricosuric agents such as probenecid, sulfinpyrazone or benzbromarone can be used alone or in combination. Patients with renal impairment require a dose adjustment of allopurinol according to the Glomerular Filtration Rate (GFR) and, when they are unresponsive to allopurinol, benzbromarone alone or in combination with allopurinol in low doses can be used. This is in line with the British Society for Rheumatology and British Health Professionals in Rheumatology guidelines and the European League Against Rheumatism guidelines.

The technology

Febuxostat (Adenuric, Ipsen) is an oral non-purine, selective xanthine oxidase inhibitor. Its ability to decrease and maintain serum uric acid levels (<0.36 mmol/l) has been studied in patients with symptomatic hyperuricaemia. Febuxostat is therefore expected to have a place in the treatment pathway along with the other urate-lowering therapies, both when allopurinol is indicated and when allopurinol is considered not to be appropriate. There is currently no marketing authorisation for the use of febuxostat for hyperuricaemia in patients with gout.

Intervention(s)	Febuxostat.
Population(s)	Adults with hyperuricaemia in whom urate deposition has already occurred (including a history or presence of tophus, gouty arthritis and/or nephrolithiasis).
Standard comparators	The standard comparators to be considered include: • allopurinol • alternative standard care (including sulphinpyrazone, benzbromarone, probenecid or a combination of those) for adults unresponsive or with hypersensitivity to allopurinol • allopurinol (dose adjusted according to GFR), benzbromarone or a combination of those for adults with renal impairment.

Outcomes	The outcome measures to be considered include: • gout flares • serum urate levels • reduction in tophus area • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The time horizon for the economic evaluation should be sufficiently long so as to incorporate all the important costs and benefits related to long-term therapy in this chronic condition. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	If the evidence allows, the appraisal will consider: • subgroups of patients for whom the technology is particularly appropriate due to greater clinical effectiveness or higher baseline risk (for example subgroups related to risk factors, co-morbidities or clinical features). • patients intolerant of, or contraindicated to, allopurinol • patients whose gout is unresponsive to allopurinol Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	None.