

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Febuxostat for the management of hyperuricaemia in patients with gout

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost-effectiveness of febuxostat for the management of hyperuricaemia in patients 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. Hyperuricemia is generally divided into 3 pathophysiologic categories; uric acid underexcretion, uric acid overproduction, and combined causes. Urate crystals are more likely to form in people with hyperuricaemia (with a serum uric acid concentration of 7 mg/100ml in men and postmenopausal women and 6 mg/100ml in premenopausal women). 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.

Between 1990-1999 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.

Recent guidelines from the European League Against Rheumatism (EULAR), recommend that for an acute attack of gout, first-line treatment should be oral colchicine and/or a non-steroidal anti-inflammatory drug (NSAID) to alleviate pain and inflammation. Intra-articular aspiration, and an injection of a long

acting steroid maybe useful in those in whom an NSAID and colchicine are contraindicated. Patient education and appropriate lifestyle advice are also recommended 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.

The EULAR guidelines recommend urate-lowering therapy 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. The aim is to reduce the plasma urate level to the normal range (less than or equal to 6mg/dl). Allopurinol (a xanthine oxidase inhibitor) is used as a long term urate lowering therapy, and uricosuric agents such as probenecid and sulfinpyrazone can be used in patients with normal renal function. Benzbromarone can also be used on a named patient basis. The guidelines also recommend anti-inflammatory medication (low-dose colchicine or NSAID) as prophylaxis against an acute flare-up of gout.

The technology

Febuxostat (TMX 67, TEI 6720; Ipsen) is an oral non-purine, selective xanthine oxidase inhibitor. Its ability to decrease and maintain serum uric acid levels (<6mg/dl) has been studied in patients with symptomatic hyperuricaemia. There is currently no marketing authorisation for the use of febuxostat for hyperuricaemia in patients with gout.

Intervention(s)	Febuxostat
Population(s)	People with hyperuricaemia in whom urate deposition has already occurred (including a history or presence of tophus, gouty arthritis and/or nephrolithiasis).
Standard comparators	Allopurinol or sulfinpyrazone or probenecid (with co-prescribed NSAID or colchicine).
Outcomes	The outcome measures to be considered include: <ul style="list-style-type: none"> • serum urate levels • gout flares • reduction in tophus area • pain • adverse effects of treatment • health-related quality of life.

<p>Economic analysis</p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The time horizon for the economic evaluation should be sufficiently long so as to incorporate all the important costs and benefits.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>
<p>Other considerations</p>	<p>Where evidence permits, the appraisal of febuxostat should identify patient subgroups for whom the technology is particularly appropriate.</p> <p>Guidance will only be issued in accordance with the marketing authorisation.</p>
<p>Related NICE recommendations</p>	<p>None.</p>