

MHRA

Drug Safety Update

May 2023



Febuxostat: updated advice for the treatment of patients with a history of major cardiovascular disease

The advice in this article relates to treatment of chronic hyperuricaemia (gout).

In July 2019, the MHRA advised healthcare professionals to avoid febuxostat treatment in patients with pre-existing major cardiovascular disease (for example, myocardial infarction, stroke, or unstable angina), unless no other therapy options were appropriate. This followed a review of the findings from a phase 4 clinical trial (the CARES study).

A further trial has now been concluded on the cardiovascular safety of febuxostat, the FAST study. The FAST study concluded that febuxostat was non-inferior to allopurinol therapy with respect to the primary cardiovascular endpoint, and, unlike the CARES study results, that long-term use was not associated with an increased risk of death or cardiovascular death compared to allopurinol.

Following a review of the FAST study findings and advice from the Pharmacovigilance Expert Advisory Group of the Commission on Human Medicines, the product information for febuxostat has been updated to include the results. The product information retains the warning for cardiovascular disorders and now advises that treatment of patients with pre-existing major cardiovascular diseases with febuxostat should be exercised cautiously. In particular, treatment should be exercised cautiously in patients with pre-existing major cardiovascular diseases with evidence of high urate crystal and tophi burden or those initiating urate lowering therapy. Prescribing clinicians should titrate febuxostat appropriately to minimise gout flares following initiation, thus minimising additional inflammation.

It is also noted that clinical guidelines for gout (for example, [NICE guideline 219 – Gout: diagnosis and management](#) which has been updated since the time of the FAST study publication), state that allopurinol should be offered as first-line treatment to people with gout who have major cardiovascular disease (for example, previous myocardial infarction or stroke, or unstable angina).

Advice for healthcare professionals:

- in patients with pre-existing major cardiovascular diseases, febuxostat therapy should be used cautiously, particularly in those with evidence of high urate crystal and tophi burden or those initiating urate-lowering therapy
- following initiation of febuxostat, prescribers should titrate the febuxostat dose to minimise gout flares and inflammation
- note that clinical guidelines for gout (see, for example, [NICE guideline 219 – Gout: diagnosis and management](#)) recommend that allopurinol should be offered as first line treatment for people with gout who have major cardiovascular disease
- report suspected adverse drug reactions associated with febuxostat to the [Yellow Card scheme](#)

Advice for healthcare professionals to give to patients and caregivers:

- febuxostat is used to treat gout by reducing an excess of a chemical called uric acid (urate) in the body, which prevents attacks of gout in the long term; it can also be used to treat and prevent high blood levels of uric acid that may occur when you start to receive chemotherapy for blood cancer
- there are new recommendations to healthcare professionals about use of febuxostat in patients with previous heart problems
- if you currently have or have previously had heart failure, heart problems or stroke, it is recommended to talk to your doctor before taking febuxostat
- no action is needed from patients already on febuxostat, but talk to a healthcare professional if you are concerned