

A word of caution regarding FebuxostatRohan Kumar Ochani,¹ Farah Yasmin,² Simran Batra,³ Ameema Asad⁴

Madam, Hyperuricaemia (HU), characterized by raised serum uric acid levels (SUA), is a cause of substantial morbidity affecting 1-2% of the population globally with a prevalence of 39% in Pakistan of which 9.2% of the cases are reported to be asymptomatic.¹ According to a pooled analysis, HU was shown to be associated with ischaemic heart disease and higher SUA levels are a risk factor for dyslipidaemia and hypertension resulting in adverse cardiovascular events.¹

Febuxostat — a non-competitive xanthine oxidase inhibitor has been increasingly prescribed for the potential management of hyperuricaemia with gout, after being approved by U.S. Food and Drug Administration (FDA) in 2009,² with a better efficacy as compared to other hyperuricaemic medications such as allopurinol. It has proved to significantly lower SUA levels with a success rate of 64% as compared to allopurinol (32%).³ Mechanically, it works by blocking the molybdenum pterin center- the active site on xanthine oxidase and thereby reduces the oxidation of xanthine to uric acid.³

However recently in February 2019, FDA released a warning alert on a possible link between febuxostat and adverse cardiovascular events.^{4,5} This boxed warning is based on the outcomes of a multicenter, randomized control study (CARES trial) comprising a cohort of 6000 gout patients, assigned to receive either febuxostat or allopurinol.⁵ This non-inferiority trial was carried out to measure cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or unstable angina with urgent revascularization as the primary outcome while death from all-causes and heart-related deaths were considered as secondary end points.^{4,5} The primary endpoint was observed at similar rates in both febuxostat and allopurinol group, while all-cause mortality and cardiovascular mortality were observed to be higher in

febuxostat group, sudden cardiac death being the most prevalent reported in 83 (2.7%) patients in the febuxostat group and 56 (1.8%) patients in the allopurinol group.^{4,5}

Despite this warning issued by the FDA to limit the use of febuxostat, this drug is still being prescribed in many countries, including Pakistan. It is imperative that the physicians restrict the use of the drug only to patients for whom allopurinol has proved to be ineffective. Furthermore, physicians should prescribe this drug with caution among patients with gout and cardiovascular disease, and should inform patients of any possible cardiovascular-related adverse effects associated with febuxostat. They should be advised to immediately consult a physician, in case they experience any signs and symptoms associated with heart diseases such as chest pain, shortness of breath, rapid heartbeats. These and many more efforts are the need of the hour to reduce the modifiable causes of increasing burden of deaths due to cardiovascular events.

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