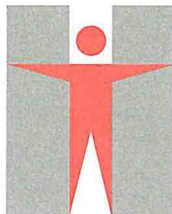


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(IN REPLY PLEASE QUOTE THIS FILE REF.)

Dear Healthcare Professionals,

**FDA adds Boxed Warning for increased risk of death with gout medicine Uloric (febuxostat)**

Your attention is drawn to the US Food and Drug Administration's (FDA) announcement that it has concluded there is an increased risk of death with Uloric (febuxostat) compared to another gout medicine, allopurinol. This conclusion is based on FDA in-depth review of results from a safety clinical trial that found an increased risk of heart-related death and death from all causes with Uloric.

As a result, FDA is updating the Uloric prescribing information to require a Boxed Warning, FDA most prominent warning, and a new patient Medication Guide. FDA is also limiting the approved use of Uloric to certain patients who are not treated effectively or experience severe side effects with allopurinol.

Patients should tell their health care professional if they have a history of heart problems or stroke and discuss the benefits and risks of using Uloric to treat their gout. Seek emergency medical attention right away if they experience the following symptoms while taking Uloric: chest pain, shortness of breath, rapid or irregular heartbeat, numbness or weakness on one side of their body, dizziness, trouble talking, sudden severe headache. Do not stop taking Uloric without first talking to their health care professional, as doing so can worsen their gout.

Health care professionals should reserve Uloric for use only in patients who have failed or do not tolerate allopurinol. Counsel patients about the cardiovascular risk with Uloric and advise them to seek medical attention immediately if they experience the symptoms listed above.

When FDA approved Uloric in 2009, FDA included a Warning and Precaution regarding possible cardiovascular events in patients treated with Uloric in the current prescribing information and required the drug manufacturer, Takeda Pharmaceuticals, to conduct a large postmarket safety clinical trial.

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aspire to be an internationally renowned public health authority*

The trial was conducted in more than 6,000 patients with gout treated with either Uloric or allopurinol. The primary outcome was a combination of heart-related death, non-deadly heart attack, non-deadly stroke, and a condition of inadequate blood supply to the heart requiring intervention, called unstable angina. The results showed that overall, Uloric did not increase the risk of these combined events compared to allopurinol. However, when the outcomes were evaluated separately, Uloric showed an increased risk of heart-related deaths and death from all causes. In patients treated with Uloric, 15 deaths from heart-related causes were observed for every 1,000 patients treated for a year compared to 11 deaths from heart-related causes per 1,000 patients treated with allopurinol for a year. In addition, there were 26 deaths from any cause per 1,000 patients treated for a year with Uloric compared to 22 deaths per 1,000 patients treated for a year with allopurinol. This safety trial was also discussed at a public Advisory Committee meeting of outside experts on 11 Jan 2019.

Please refer to the following website in FDA for details:

<https://www.fda.gov/Drugs/DrugSafety/ucm631182.htm>

In Hong Kong, there are 2 registered pharmaceutical products containing febuxostat, namely Feburic Tablets 80mg (HK-61185) and Feburic Tablets 120mg (HK-61186) registered by Astellas Pharma Hong Kong Company Limited. Both products are prescription-only medicines. So far, the Department of Health (DH) has received one case of adverse drug reaction related to febuxostat, but this case is not related to death. Related news was previously issued by FDA, and was posted on the Drug Office website on 16 Nov 2017. In light of the above FDA's updated safety information and recommendations, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: [adr@dh.gov.hk](mailto:adr@dh.gov.hk)). For details, please refer to the website at Drug Office under "ADR Reporting": <http://www.drugoffice.gov.hk/adr.html>. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,



(Joseph LEE)

for Assistant Director (Drug)