

19 April, 2019

**KINGDOM OF SAUDI ARABIA**

**SAUDI FOOD AND DRUG AUTHORITY**

**DRUG SECTOR**

**Febuxostat, Adenuric ®: Higher rate of cardiovascular death in gout patients with established cardiovascular disease.**

Dear Healthcare professional,

"Algorithm SAL, the Marketing Authorization Holder of Adenuric, in agreement with the Saudi Food and Drug Authority, would like to inform you of the following":

We would like to update you on the results obtained from CARES, a clinical study conducted to compare CV outcomes associated with Febuxostat and allopurinol in patients with gout and established cardiovascular (CV) disease. As a result, the rates of major cardiovascular events (MACE) were similar with Febuxostat and Allopurinol groups and a higher all-cause mortality, resulting from an imbalance in CV death was observed with Febuxostat group than with Allopurinol.

The prescriber is thus requested to counsel patients currently on Adenuric or those who will be prescribed for the first time about the risks and benefits of Adenuric including:

- The higher rate of CV death in patients treated with Febuxostat compared to allopurinol in a CV outcome study.
- The Febuxostat is prescribed for the treatment of chronic hyperuricaemia in conditions where urate deposition has already occurred (including a history, or presence of, tophus and/or gouty arthritis).
- The symptoms of heart attack or stroke, including instructions to contact a healthcare provider or get medical help right away if they have any of these symptoms.
- That effective serum urate lowering and maintaining urate levels to target is important in treatment of gout and hyperuricemia.

Algorithm is the trusted partner for the medical community and patient safety is a priority, therefore the Adenuric® SmPC had, since its release, indicated under "*special warnings and precautions for use*" that "*treatment with Febuxostat in patients with ischemic heart disease or congestive heart failure is not recommended*"

Further information on the safety concerns and the recommendations

*The Cardiovascular Safety of Febuxostat and Allopurinol in Patients with Gout and Cardiovascular Comorbidities (CARES)" was a multicenter, double-blind, randomized, active-control, Phase 3B study*

that was conducted to evaluate the cardiovascular safety of Febuxostat and Allopurinol in subjects with gout and existing major cardiovascular disease including:

- Myocardial infarction (MI)
- Hospitalized unstable angina,
- Cardiac or cerebrovascular revascularization procedure (ex: coronary artery bypass surgery, extracranial bypass surgery)
- Stroke
- Hospitalized transient ischemic attack (TIA) - brief episode of neurologic dysfunction caused by ischemia
- Peripheral vascular disease (PVD)- narrowing of the vessels that carry blood to the legs, arms stomach or kidneys
- History of diabetes mellitus with evidence of micro- or macrovascular disease (retinopathy, neuropathy, nephropathy, small vessel vascular diseases)

There was a higher rate of CV death in patients treated with Adenuric<sup>®</sup> compared to allopurinol (4.3% vs 3.2%) ; in the same study, Adenuric<sup>®</sup> was non-inferior to allopurinol for the primary endpoint of major adverse cardiovascular events (MACE). Consider the risks and benefits of Adenuric<sup>®</sup> when deciding to prescribe or continue patients.

Since Approval, Adenuric<sup>®</sup> SmPC indicates under "special warnings and precautions for use" that "treatment with Febuxostat in patients with ischemic heart disease or congestive heart failure is not recommended".

#### Call for reporting

In case of any adverse event occurrence with the use of Adenuric<sup>®</sup>, we kindly ask you to report it as soon as possible to the following email address: Pharmacovigilance-KSA@blgx.net

The National Pharmacovigilance Centre (NPC)  
Saudi Food and Drug Authority (SFDA)

SFDA call center: 19999  
Toll free phone: 8002490000  
Fax: +966-11-2057662  
E-mail: npc.drug@sfd.a.gov.sa  
Website: <http://ade.sfda.gov.sa/>

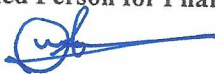
For extra copies please contact (00966 11 4646 955)

#### References:

Cardiovascular Safety of Febuxostat or Allopurinol in Patients with Gout (CARES trial)  
Summary of product characteristics Adenuric<sup>®</sup>

Sincerely yours,  
ALGORITHM S.A.L

Omar Ali Al-Faifi  
Qualified Person for Pharmacovigilance



  
Paula Hayek  
Medical Affairs Lead