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# NATIONAL PBM BULLETIN

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DEPARTMENT OF VETERANS AFFAIRS VETERANS HEALTH ADMINISTRATION (VHA)  
PHARMACY BENEFITS MANAGEMENT SERVICES (PBM), MEDICAL ADVISORY PANEL (MAP),  
AND CENTER FOR MEDICATION SAFETY (VA MEDSAFE)

## SAXAGLIPTIN AND CARDIOVASCULAR SAFETY

### I. ISSUE

A recent study published in the New England Journal of Medicine identified a possible association of heart failure with saxagliptin use.

### II. BACKGROUND

Saxagliptin, marketed under the names Onglyza and Kombiglyze XR, is a selective dipeptidyl peptidase-4 (DPP-4) inhibitor that gained FDA approval in July 2009. One randomized, placebo-controlled, phase 4 trial (the Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus [SAVOR] – Thrombolysis in Myocardial Infarction [TIMI] 53) that investigated the efficacy and safety of saxagliptin in diabetic patients at risk for cardiovascular events suggested an increase in the rate of hospitalization for heart failure, but did not show an increase or decrease in the rate of ischemic events among users of the agent. FDA considers these results as preliminary and will investigate further as well as request clinical trial data from the manufacturer.

### III. DISCUSSION

Results from the SAVOR trial show no increase or decrease in the primary endpoint (composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal ischemic stroke) with saxagliptin use. Among the secondary endpoints, saxagliptin was associated with an increase in hospitalizations for heart failure compared to the placebo group (3.5% vs. 2.8%; HR 1.27 [95% CI 1.07 to 1.51]). Authors state that: “The observation of a higher incidence of hospitalization for heart failure among patients treated with saxagliptin was unexpected and should be considered within the context of multiple testing that may have resulted in a false positive result.” Further, the absence of long-term data with sitagliptin or linagliptin makes it difficult to determine the potential for a class effect.

### IV. PROVIDER RECOMMENDATIONS

FDA recommends that:

- Providers should consider whether the benefits of saxagliptin treatment will outweigh the potential risks.
- Providers should comply with the prescribing information in the product labelling.
- Patients should not discontinue their saxagliptin treatment without prior discussion with their health care providers.

Providers should continue to report any adverse reactions with the use of saxagliptin by entering the information into CPRS’ Allergies/ Adverse Reactions field and/or via local reporting mechanisms. Adverse events should also be reported, as appropriate, to the VA ADERS program and FDA MedWatch (1-800-FDA-1088, fax 1-800-FDA-0178, online at <https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm>, or by mail).

### V. REFERENCES

1. FDA Drug Safety Communication: FDA to review heart failure risk with diabetes drug saxagliptin (marketed as Onglyza and Kombiglyze XR). <http://www.fda.gov/Drugs/DrugSafety/ucm385287.htm> . Accessed 02-11-14.
2. Scirica B et al. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. New Engl J Med 2013 Oct 3; 369 (14): 1317-26.

#### ACTIONS

- **Facility Director** (or physician designee): Forward this document to the Facility Chief of Staff (COS).
- **Facility COS and Chief Nurse Executives:** Forward this document to all appropriate providers who prescribe these medications (e.g., **primary care providers, endocrinology, cardiology, including contract providers, etc.**). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.
- **ACOS for R&D:** Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).