

FDA Drug Safety Warning: Potential Risk for Liver Injury among Samsca® (tolvaptan) users (28 Jan 2013)

Pharmacy, Patient Safety, Internal Medicine, Family Practice, and Gastroenterology communities: Please share with pharmacists and providers at your MTFs and regions.

ISSUE: Otsuka and FDA notified healthcare professionals of significant liver injury associated with the use of Samsca® (tolvaptan). In a double-blind, 3-year, placebo-controlled trial in about 1400 patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD) and its open-label extension trial, 3 patients treated with the drug developed significant increases in serum alanine aminotransferase (ALT) with concomitant, clinically significant increases in serum total bilirubin. In the trials the maximum daily dose of Samsca® administered (90 mg in the morning and 30 mg in the afternoon) was higher than the maximum 60 mg daily dose approved for the treatment of hyponatremia.

Most of the liver enzyme abnormalities were observed during the first 18 months of therapy. Following discontinuation of treatment, all 3 patients improved. An external panel of liver experts assessed these 3 cases as being either probably or highly likely to be caused by tolvaptan. These findings indicate that Samsca® (tolvaptan) has the potential to cause irreversible and potentially fatal liver injury. These data are not adequate to exclude the possibility that patients receiving Samsca® for its indicated use of clinically significant hypervolemic and euvolemic hyponatremia are at a potential increased risk for irreversible and potentially fatal liver injury.

BACKGROUND: Samsca® is a selective vasopressin V2-receptor antagonist indicated for the treatment of clinically significant hypervolemic and euvolemic hyponatremia. Samsca® is not approved for the treatment of ADPKD.

TOLVAPTAN USE IN THE DoD: A Pharmacovigilance Center (PVC) analysis of DoD data conducted in response to this FDA message found approximately 271 individuals and 1,272 (total) prescriptions for Samsca® (tolvaptan) since market inception (May 2009).

RECOMMENDATIONS: Healthcare providers should perform liver tests promptly in patients who report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine or jaundice. If hepatic injury is suspected, Samsca® should be promptly discontinued, appropriate treatment should be instituted, and investigations should be performed to determine probable cause. Samsca® should not be re-initiated in patients unless the cause for the observed liver injury is definitively established to be unrelated to treatment with Samsca®.

Additional information is contained in the attached Dear Healthcare Provider letter from Otsuka, the manufacturer of Samsca®, also available at:

<http://www.fda.gov/downloads/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/UCM336675.pdf>

Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program at: www.fda.gov/MedWatch/report.htm

QUESTIONS OR ADDITIONAL INFORMATION: Send requests for additional information regarding this alert or the analysis conducted by the Pharmacovigilance Center (PVC) to: mark.s.maneval2.mil@mail.mil