NATIONAL PBM COMMUNICATION
ISMP Quarterly Report of Increase in Reported Serious ADEs with Varenicline
October 28, 2008

The most recent Quarter Watch report from the Institute for Safe Medication Practices (ISMP) detailed a sharp increase in the number of serious adverse events reported to the FDA for which varenicline was the suspected drug. In the first quarter of 2008, the FDA received 1001 case reports of serious injury, confined to the United States. The events with varenicline accounted for more serious adverse events than any other drug. In the report, 15 case reports were linked to road traffic accidents describing possible effects of varenicline including seizure, disturbance of vision, panic attack, and impaired judgment. There were also 52 cases indicating various kinds of blackouts or loss of consciousness with a potential for accidents. Additional events included 52 cases of angioedema and 226 cases classified as suicide/self injury. The full report may be found here: http://www.ismp.org/QuarterWatch/2008Q1.pdf.

Data from spontaneous reporting has limitations as noted by the ISMP. First, the submission of a report does not prove the drug caused the adverse event, only that someone suspected a connection; second, since this is a voluntary system, only a fraction of adverse events are reported and the true number of those who were harmed and the total number of those exposed is unknown, making it impossible to calculate the risk of an adverse drug event. Reporting may also increase following public warnings about new risks as was the case with varenicline in February of 2008.

There are no new recommendations by the FDA at this time. However, the ISMP has recommended additional actions including:

- **Making patients aware of the potential accident risks;**
- **Recommending to the FDA the addition of a prominent warning about accident risks to the Patient Medication Guide and prescribing information;**
- **Suggesting that providers consider alternative therapies for smoking cessation (see below).**

VA EFFORTS

Varenicline Criteria for Prescribing (located at: http://vaww.national.cmop.va.gov/PBM/Clinical%20Guidance/Criteria%20For%20Use/Varenicline%20Criteria%20for%20Prescribing.doc) reminds providers to communicate warnings to patients about driving and operating heavy machinery due to the potential for loss of consciousness, seizures, muscle spasms, visual disturbances, or hallucinations. The VA Center for Medication Safety continues to monitor and analyze reports of adverse events with varenicline to better characterize the adverse event profile in the veteran population.

ALTERNATIVE TREATMENTS FOR CONSIDERATION

The 2008 update to the US Department of Health and Human Services Public Health Service Clinical Practice Guideline on Treating Tobacco Use and Dependence reviewed effectiveness and abstinence rates for various medications and combinations compared to placebo and used meta-analysis methods to develop estimated odds ratios and abstinence rates. The following table presents some alternatives to consider.

MEDICATION	ODDS RATIO (95%CI)	ABSTINENCE RATE (95%CI)
Varenicline	3.1 (2.5-3.8)	33.2 (28.9-37.8)
Patch (> 14 weeks) + *ad lib* gum or spray	3.6 (2.5-5.2)	36.5 (28.6-45.3)
Patch + bupropion SR	2.5 (1.9-3.4)	28.9 (23.5-35.1)

http://www.surgeongeneral.gov/tobacco/treating_tobacco_use08.pdf.