NATIONAL PBM COMMUNICATION · July 2, 2009

Varenicline (Chantix®) and Bupropion (Zyban®, Wellbutrin®, and generics) and Neuropsychiatric Events

- The Food and Drug Administration (FDA) has continued to receive post-marketing reports of mood and behavioral changes temporally associated with the use of varenicline (Chantix) and bupropion (Zyban and generics) for smoking cessation. [1,2]
- FDA has required the manufacturers of these medications to add new *Boxed Warnings* and develop patient Medication Guides that delineate the risk of the above neuropsychiatric symptoms.
- These warnings with varenicline have been known to VA, and are consistent with current VA prescribing criteria. (For further guidance on varenicline, please refer to the PBM-MAP Criteria for Use for Varenicline at http://www.pbm.va.gov/default.aspx.)
- The warning with bupropion is not new and holds true for all antidepressants as well.
- Neuropsychiatric events reported to the FDA in patients taking varenicline (Chantix) and bupropion (Zyban and generics) include[1,2]:
    - Changes in behavior
    - Hostility
    - Agitation
    - Depressed mood
    - Suicidal thinking and behavior
    - Attempted suicide
- FDA recommends[1,2]:
    - *Healthcare professionals should advise patients to stop taking varenicline or bupropion and contact a healthcare provider immediately if they experience agitation, depressed mood, and any changes in behavior that are not typical of nicotine withdrawal, or if they experience suicidal thoughts or behavior.*
    - *If varenicline or bupropion is stopped due to neuropsychiatric symptoms, patients should be monitored until the symptoms resolve.*
    - *Family members and caregivers should also be alerted to the potential for changes in mood or behavior and contact the health care provider if they observe these changes in the person taking varenicline or buporpion.*
- VA Center for Medication Safety (VAMedSAFE) has been monitoring and analyzing reports of adverse events with varenicline (Chantix) and bupropion (Zyban and generics) since 2007 to better characterize the adverse event profile in the veteran population.
- Providers should document/report all possible adverse events related to varenicline and bupropion as per the usual protocols used at their VA and continue to use these medications according to VA criteria.
- Providers interested in additional information please see the APPENDIX posted on the PBM Intranet website under the *"VAMedSAFE Project Results (Select)"* link on the Quick Launch bar.

REFERENCES:

1. FDA Public Health Advisory. http://www.fda.gov/Drugs/DrugSafety/PublicHealthAdvisories/ucm169988.htm (Accessed July 1, 2009).
2. FDA Information for Healthcare Professionals. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm169986.htm (Accessed July 1, 2009).

ACTIONS

- ***Facility Director (or physician designee):*** *Report completion of actions to the VISN Director.*
- ***Facility COS and Chief Nurse Executives:*** *Forward this document to all appropriate providers who prescribe/use/handle this agent (e.g.,* ***primary care providers, mental health providers, psychiatrists, and smoking cessation specialists,*** *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. Report completion of actions to the Facility Director.*
- ***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).*
- ***VISN Directors:*** *Within 10 business days of receipt (due 07/17/2009), communicate to PBM/VAMedSAFE that all actions have been completed via the Feedback tool: http://vaww.national.cmop.va.gov/PBM/visn_drug_recalls_alerts/default.aspx.*