DEPARTMENT OF VETERANS AFFAIRS VETERAN HEALTH ADMINISTRATION (VHA)
PHARMACY BENEFITS MANAGEMENT SERVICES (PBM) & MEDICAL ADVISORY PANEL (MAP)
VA CENTER FOR MEDICATION SAFETY (VAMedSAFE)

NATIONAL PBM COMMUNICATION · March 9, 2011

Maternal and Newborn Risks with Certain Medications Used During Pregnancy

ANTIPSYCHOTIC MEDICATION USE DURING PREGNANCY AND RISKS TO NEWBORNS

- The Food and Drug Administration (FDA) updated the *Pregnancy* section of drug labels for the entire class of antipsychotic drugs with information about possible abnormal muscle movements (i.e., extrapyramidal signs or EPS) and withdrawal symptoms in newborns whose mothers received antipsychotic medications during the third trimester of pregnancy.
- FDA recommends for healthcare professionals to:
  - *Know that antipsychotic medications cross the placenta.*
  - *Be aware that neonates exposed to antipsychotic medications during the third trimester of pregnancy are at risk for EPS and/or withdrawal symptoms following delivery.*
  - *Counsel patients about the benefits and risks of taking antipsychotic drugs during pregnancy.*
  - *Monitor neonates exhibiting EPS or withdrawal symptoms. Some neonates recover within hours or days without specific treatment; others may require prolonged hospitalization.*
  - *Inform patients that they should not stop taking these medications if they become pregnant without talking to their healthcare professional, as abruptly stopping antipsychotic medications can cause significant complications for treatment.*

TERBUTALINE OFF-LABEL USE IN PRETERM LABOR: MATERNAL CARDIOVASCULAR EVENTS AND DEATH

- FDA is requiring the addition of a *Boxed Warning* and *Contraindication* to the terbutaline injection label, as well as the terbutaline oral tablet label, stating that:
  - *injectable terbutaline should not be used in pregnant women for prevention or prolonged treatment (beyond 48-72 hours) of preterm labor in either the hospital or outpatient setting because of the potential for serious maternal heart problems and death; and*
  - *oral terbutaline should not be used for prevention or any treatment of preterm labor because it has not been shown to be effective and has similar safety concerns.*
- FDA is recommending that healthcare professionals:
  - *Be aware that death and serious adverse reactions, including increased heart rate, transient hyperglycemia, hypokalemia, cardiac arrhythmias, pulmonary edema, and myocardial ischemia have been reported after prolonged administration of oral or injectable terbutaline to pregnant women.*
  - *Recognize that treatment with terbutaline administered by injection or by continuous infusion pump should not be used beyond 48 to 72 hours. In particular, injectable terbutaline should not be used in the outpatient or home setting.*
  - *Acknowledge that there are certain obstetrical conditions where the healthcare professional may decide that the benefit of terbutaline injection for an individual patient in a hospital setting clearly outweighs the risk.*
  - *Know that oral terbutaline is contraindicated for the treatment or prevention of preterm labor.*

TOPIRAMATE AND ORAL CLEFTS

- Topiramate changed classifications from Pregnancy Category C to Pregnancy Category D due to new human data that show an increased risk for oral clefts in infants born to women treated with topiramate (Topamax and generic products) during pregnancy.
- FDA is recommending that healthcare professionals should:
  - *Inform women of childbearing age of the increased risk for oral clefts when topiramate is used in the first trimester of pregnancy.*
  - *Weigh the benefits and risks of topiramate when prescribing this drug to women of childbearing age, particularly when treating a condition not usually associated with permanent injury or death. Alternative medications that have a lower risk of oral clefts and other adverse birth outcomes should be considered. Healthcare professionals should discuss the relative risks and benefits of appropriate alternative therapies.*
  - *Recommend use of effective contraception for women who are not planning a pregnancy if the decision is made to prescribe topiramate to women of childbearing age. Keep in mind the potential for a decrease in hormonal exposure and a possible decrease in contraceptive efficacy when using estrogen-containing birth control with topiramate.*
  - *Inform patients of the North American Antiepileptic Drug (NAEED) Pregnancy Registry and encourage patients who become pregnant to enroll by calling 1-888-233-2334.*

- Providers should continue to report any adverse events with antipsychotic agents, terbutaline, and/or topiramate by entering the information into CPRS' Allergies/Adverse Reactions field and/or via local reporting mechanisms. Facilities should continue to report adverse events into VA ADERS and to the FDA (as appropriate).

REFERENCES

1. FDA Drug Safety Communication: FDA Drug Safety Communication: Antipsychotic drug labels updated on use during pregnancy and risk of abnormal muscle movements and withdrawal symptoms in newborns. http://www.fda.gov/Drugs/DrugSafety/ucm243903.htm . (Accessed March 3, 2011)
2. FDA Drug Safety Communication: New warnings against use of terbutaline to treat preterm labor. http://www.fda.gov/Drugs/DrugSafety/ucm243539.htm. (Accessed March 4, 2011)
3. FDA Drug Safety Communication: Risk of oral clefts in children born to mothers taking Topamax (topiramate). http://www.fda.gov/Drugs/DrugSafety/ucm245085.htm (Accessed March 4, 2011)

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, Women's Health, Mental and Behavioral Health,and Neurologists,*** *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).*