FDA Warning: CV Deaths, Risks With Obstetric Terbutaline

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The Food and Drug Administration has issued a warning advising against the use of injectable terbutaline for preterm labor and prolonged treatment of preterm labor and against any use of oral terbutaline in this setting, prompted by postmarketing reports of deaths and other serious cardiovascular events associated with the use of the drug in this setting.

“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,” according to an FDA statement.

Based on these reports and a review of the medical literature, FDA revised the obstetric-related risks of terbutaline, an FDA-approved treatment for bronchospasm that has been used off label to treat and prevent preterm labor and to treat uterine hyperstimulation. In 1997, the agency notified health care professionals in a letter about concerns over the safety of long-term administration of subcutaneous terbutaline and revised the drug’s labeling about the risk of serious cardiovascular adverse events associated with this use. But despite studies reporting a lack of safety and efficacy of terbutaline for the treatment of recurrent preterm labor and professional association recommendations, “prolonged use of terbutaline continues, with serious and sometimes fatal consequences,” the FDA statement said.

Between 1976, when terbutaline was first marketed, and 2009, 16 maternal deaths associated with the obstetric use of terbutaline were reported to the FDA’s Adverse Event Reporting System (AERS). Between January 1998, soon after the FDA issued the warning letter, and July 2009, 12 maternal cases of serious cardiovascular events associated with the use of terbutaline were reported.

While there are “certain obstetrical conditions” in which health care professionals “may decide that the benefit of terbutaline injection for an individual patient in a hospital setting clearly outweighs the risk,” the FDA statement said that terbutaline administered by injection or continuous infusion pump should not be used for more than 48-72 hours, and injectable terbutaline should not be used in outpatient settings. These warnings are being added to a new boxed warning in terbutaline labels.

In an interview, Dr. Washington Hill of Sarasota (Fla.) Memorial Hospital, welcomed the FDA warnings. Still, he cautioned that subcutaneous terbutaline should not be entirely abandoned because there are some obstetric situations where its use is beneficial, when used in the hospital setting and not in a pump. These include reducing contractions in a woman with tachysystole of the uterus due to pitocin or for intrauterine resuscitation, adjunct to external cephalic version, relaxing an inverted uterus or as an adjunct to managing inversion of the uterus, transporting a patient with contractions from one location to another, and rarely when delivering a second twin when the uterus needs to be relaxed.

Dr. Hill had no relevant financial disclosures. ■