



PIC QUESTION OF THE WEEK: 08/15/05

Q: What is the basis for contraindicating the use of Macrochantin® in a woman who is nine months pregnant?

A: Nitrofurantoin is designated as a Pregnancy Category B drug by the Food and Drug Administration. Animal reproductive studies at doses twenty-five times the usual human dose have not revealed any increase or specific pattern of congenital anomalies. A large number of registries and retrospective studies such as the Michigan Medicaid Program and Collaborative Perinatal Drug Project have not identified any association between use of nitrofurantoin and congenital malformations. The product information does, however, include a contraindication to use of nitrofurantoin *in pregnant women at term (38-42 weeks gestation), including during labor and delivery or when the onset of labor is imminent, because of the possibility of hemolytic anemia in the neonate secondary to immature enzyme systems*. This warning is based on a small number of cases of hemolytic anemia in mothers who received the drug in late stages of pregnancy. These post-marketing reports provided few of the specific details necessary to truly evaluate this potential problem. It is not known whether the mothers and/or children were glucose-6 phosphate dehydrogenase (G6PD) deficient. A case report in 2000 describes hemolytic anemia in a newborn whose mother had taken the drug during the last month of pregnancy. G6PD is an essential enzyme for maintaining optimal levels of reduced glutathione within the red blood cell (RBC). It protects the RBC against oxidative stress that can result in structural changes in hemoglobin and subsequent hemolysis. Drugs such as nitrofurantoin, primaquine, large doses of ascorbic acid, dapsone, sulfonamides, etc. are oxidative compounds and can induce hemolysis in susceptible patients with G6PD deficiency. The concern for possible newborn hemolysis is the primary reason for the existing contraindication to use of nitrofurantoin near term. Occurrence of this complication appears to be rare, but the warning should be considered.

References:

- Briggs GG, Freeman RK, Yaffe SJ. Drugs in pregnancy and lactation. 7th edition. Philadelphia (PA): Lippincott Williams Wilkins; 2005.
- Nitrofurantoin (TERIS Document). In:Klasco RK (Ed): REPRORISK® System. Thomson Micromedex, Greenwood Village, Colorado (Edition expires September, 2005).

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