FDA Pregnancy Categories

Appropriate prescribing and use of medications requires a risk-versus-benefit assessment of the medication for a specific patient. There are many risk factors that must be evaluated, including pregnancy. In 1979, the United States FDA introduced a classification of fetal risks due to pharmaceuticals. This was based on a similar system that was introduced in Sweden just 1 year earlier.

The FDA has established five categories that can be used to estimate the potential of a systemically absorbed drug for causing birth defects. The reliability of the documentation is the key differentiation factor among the categories for determining the risk-versus-benefit ratio. The Pregnancy Category "X" is the strongest and states that if any data exist that a drug may be implicated as a teratogen and the risk-versus-benefit ratio does not support the use of the drug, then the drug is contraindicated during pregnancy.

The FDA-assigned pregnancy categories are as follows:

- Category A: Adequate and well-controlled studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters).
- Category B: Animal reproduction studies have failed to demonstrate a risk to the fetus, and there are no adequate and well-controlled studies in pregnant women.
- Category C: Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
- Category D: There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
- Category X: Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

Medication Exposures During Pregnancy and Lactation

Every woman in the general population has a 3% to 5% risk of having a child with a birth defect or mental retardation. Birth defects are the leading cause of infant mortality in the United States. Two important factors to consider when assessing the teratogenic potential of a medication are the stage of pregnancy at which the exposure occurred and the amount of medication taken. It is critical to evaluate each exposure on a case-by-case basis in order to give an accurate risk assessment. Some of the known, possible, and unlikely human teratogens are listed in Table 1.1. In a pregnant or breast-feeding patient who is currently taking, or considering taking, a medication, the patient needs to be counseled about potential adverse effects the medication could have on her fetus or infant (11). This counseling needs to be documented.

Black Box Warnings

A *black box warning* in prescription drug labeling is used to call attention to one of the following situations: (*a*) there is an adverse reaction so serious in proportion to the potential benefit that it be considered in assessing the risks and benefits of using the drug, (*b*) the risk of a serious adverse reaction can be prevented or reduced in severity by careful use of the drug (e.g., patient selection, special monitoring, certain concomitant therapy), or (*c*) the FDA has approved the drug *with restrictions* to prescribing/distribution to ensure its safe use (12).

Drug Listing Act of 1972

The Drug Listing Act was enacted to provide the FDA with the legislative authority to compile a list of marketed drugs to assist in the enforcement of federal laws requiring that drugs be safe and effective and not