FDA Pregnancy Categories

FDA Pregnancy Risk Information: An Update

In 2015 the FDA replaced the former pregnancy risk letter categories (**see below**) on prescription and biological drug labeling **with new information to make them more meaningful** to both patients and healthcare providers. The FDA received comments that the old five-letter system left patients and providers ill-informed and resulted in false assumptions about the actual meaning of the letters.

The new labeling system allows better patient-specific counseling and informed decision making for pregnant women seeking medication therapies. While the new labeling improves the old format, it still does not provide a definitive "yes" or "no" answer in most cases. Clinical interpretation is still required on a case-by-case basis.

The **Pregnancy and Lactation Labeling Final Rule (PLLR)** went into effect on June 30, 2015; however, the timelines for implementing this new information on drug labels (also known as the package insert) is variable.

Prescription drugs submitted for FDA approval after June 30, 2015 will use the new format immediately, while labeling for prescription drugs approved on or after June 30, 2001 will be phased in gradually. Medications approved prior to June 29, 2001 are not subject to the PLLR rule; however, the pregnancy letter category must be removed by June 29, 2018. For generic drugs, if the labeling of a reference listed drug is updated as a result of the final rule, the abbreviated new drug application (ANDA) labeling must also be revised. Labeling for over-the-counter (OTC) medicines will not change, as OTC drug products are not affected by the new FDA pregnancy labeling.

The A, B, C, D and X risk categories, in use since 1979, are now replaced with narrative sections and subsections to include:

Pregnancy (includes Labor and Delivery):

- Pregnancy Exposure Registry
- Risk Summary
- Clinical Considerations
- Data

Lactation (includes Nursing Mothers)

- Risk Summary
- Clinical Considerations
- Data

Females and Males of Reproductive Potential

- Pregnancy Testing
- Contraception
- Infertility

The **Pregnancy** subsection will provide information about dosing and potential risks to the developing fetus and registry information that collects and maintains data on how pregnant women are affected when they use the drug or biological product. Information in drug labeling about the existence of any pregnancy registries has been previously recommended but not required until now. Contact information for the registries will also be included, and pregnant women are encouraged to enroll to help provide data on the effects of drug use or biologics in pregnancy.

If information for the subsections of Pregnancy Exposure Registry, Clinical Considerations, and Data is not available, these subsections will be excluded. The Risk Summary subheadings are always required, even if no data is available.

The **Lactation** subsection will replace the "Nursing Mothers" subsection of the old label. Information will include drugs that should not be used during breastfeeding, known human or animal data regarding active metabolites in milk, as well as clinical effects on the infant. Other information may include pharmacokinetic data like metabolism or

excretion, a risk and benefit section, as well as timing of breastfeeding to minimize infant exposure.

In the subsection entitled **Females and Males of Reproductive Potential**, relevant information on pregnancy testing or birth control before, during or after drug therapy, and a medication's effect on fertility or pregnancy loss will be provided when available.

Why Did the FDA Make This Change?

Clinically, many women require drug treatment during pregnancy due to chronic conditions such as epilepsy, diabetes, hypertension (high blood pressure), or asthma. To withhold drug treatment would be dangerous for both mother and baby. In addition, women are having babies at a later age, which can boost the number of women with chronic conditions. Accessible and understandable **pregnancy and lactation information** is important for women and their health care provider's to assess risk versus benefit.

The FDA has received requests to improve the decades-old content and format of pregnancy prescription drug labeling since 1992. According to the Drug Information Division at the FDA, they obtained input from many affected groups and held public hearings, advisory committee meetings, and focus groups to assess the changes. In 2008, the FDA issued the proposed rule and then opened a docket for public comments.

Clinicians and patients were often confused by the meaning of the pregnancy risk categories because, according to the FDA, it was overly simplistic, led to misinformation, and did not adequately address the available information.