

FDA Implements New Labeling for Medications Used During Pregnancy and Lactation

JOHN WHYTE, MD, MPH, *U.S. Food and Drug Administration, Silver Spring, Maryland*

With more than 6 million pregnancies in the United States every year, and with pregnant women taking an average of three to five prescription drugs during pregnancy, physicians and their patients depend on proper safeguards to make informed decisions about medication choices. The U.S. Food and Drug Administration (FDA) has recently implemented the Pregnancy Lactation Labeling Rule (PLLR), which amends the previously issued Physician Labeling Rule. The PLLR provides a set framework for drug manufacturers to provide information about the risks and benefits of using prescription drugs and biologic products during pregnancy and lactation.¹

The PLLR,² implemented on June 30, 2015, requires changes to the content and format of prescription drug labeling to help clinicians assess benefit vs. risk and counsel pregnant women and breastfeeding mothers who need to take medications, allowing them to make more informed and educated decisions. The PLLR replaces the pregnancy letter categories (i.e., A, B, C, D, and X) previously printed on drug labels with a summary of information about the product. It also requires manufacturers to update the label when information becomes outdated.

The new labeling rule provides updated information, when it is available, to help clinicians explain the potential benefits and risks for the mother, fetus, and breastfeeding child. The FDA decided to replace the letter categories with a summary paragraph after consulting with many experts and stakeholders. The main concern was that the letter categories were often misinterpreted as a grading system for the risks of a drug, resulting in prescribing decisions based on the category rather than on an understanding of the underlying information. To provide

clear, evidence-based explanations of the risks and benefits of a medication that clinicians can easily share with their patients, prescribing information for clinicians has been updated in the labeling subsections: Pregnancy, Lactation, and Females and Males of Reproductive Potential. Specific changes include the following:

- The **Pregnancy** subsection includes a narrative risk summary of the maternal and fetal risks based on available human, animal, and pharmacologic data. A clinical considerations heading is included when there is information important to consider when deciding on use during pregnancy. An example would be information on dosing adjustments in pregnancy and the postpartum period. This subsection also includes information about a pregnancy exposure registry for the drug when one is available. Pregnancy exposure registries are observational studies that collect health information from women who take prescription drugs or vaccines when they are pregnant. The FDA does not maintain these registries, but may recommend or require that a drug manufacturer implement one based on certain criteria. Information about the existence of pregnancy registries in drug labeling has been recommended but not required until now. Information formerly found in the Labor and Delivery subsection is now included in the Pregnancy subsection.
- The Nursing Mothers subsection is now called **Lactation** and provides information about using the drug while breastfeeding, such as the amount of drug in breast milk and potential effects on the breastfed infant. The new format is similar to the Pregnancy subsection and organizes the information into risk summary, clinical considerations, and data headings.
- The **Females and Males of Reproductive Potential** subsection is new and, when necessary, includes information about the need for pregnancy testing, contraception recommendations, and information about infertility as it relates to the drug. ▶

So, when will prescribers see these changes? Prescribers will begin to see new labeling now. Prescription drugs and biologic products submitted for approval after June 30, 2015, will use the new format immediately. For products approved after June 30, 2001, labeling changes will be phased in over the next two to four years. Products approved before June 30, 2001, are not required to reformat their labeling but are required to remove the letter category by June 30, 2018. Labeling for over-the-counter medications will not change. The FDA is continually reviewing the safety of these products, including impacts on pregnancy, lactation, and reproductive potential. When new information arises that causes the labeling to be inaccurate, false, or misleading, drug manufacturers are required by regulation to update labeling for all medications. All labeling changes, including the changes required by the PLLR, must be submitted to the FDA for review and approval.

At the time the PLLR was published, the FDA also issued draft guidance to make it easier for drug manufacturers to understand and comply with the new labeling requirements. This guidance will be finalized after the FDA completes its review and integration of input that was submitted during an open comment period earlier this year,³ a further step to help keep prescribers informed and protect pregnant women and breastfed children from adverse reactions to medications. See related video at <http://www.aafp.org/patient-care/public-health/breastfeeding/pllr.html>.

Deciding which medications to take during pregnancy and lactation can be a complex and individualized decision that should be discussed with a physician, but the new PLLR can help remove some of the uncertainty clinicians and patients face by replacing the potentially confusing letter categories with a narrative structure that can convey the potential risks of drug exposure based on available, evidence-based data.

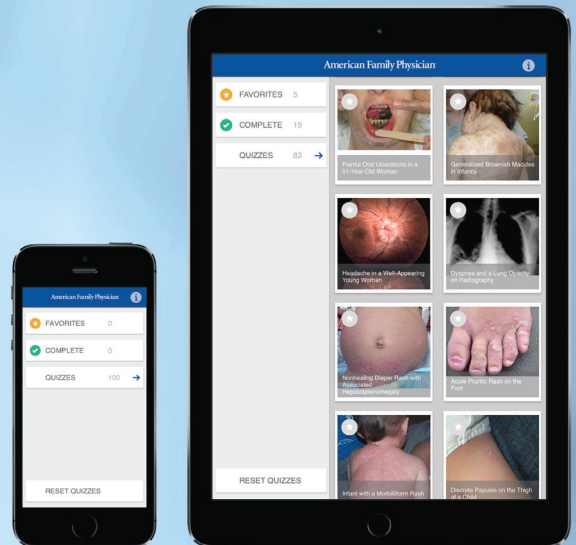
Address correspondence to John Whyte, MD, MPH, at John.Whyte@fda.hhs.gov. Reprints are not available from the author.

Author disclosure: No relevant financial affiliations.

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