

## New Prescription Labeling Requirements for the Use of Medications in Pregnancy and Lactation

Cortney M. Mospan, PharmD, BCACP, Assistant Professor of Pharmacy Practice, East Tennessee State University Bill Gatton College of Pharmacy, Johnson City, TN

Dr. Cortney Mospan has no relevant financial relationships to disclose.

**Goal.** The goal of this lesson is to provide an overview of changes to the U.S. Food and Drug Administration (FDA) labeling requirements for medications used in pregnancy and lactation, and strategies for application.

**Objectives.** At the completion of this activity, the participant will be able to:

1. recognize labeling requirements of the previous pregnancy letter categories for medications, and associated limitations;
2. describe requirements of the FDA update in pregnancy and lactation labeling and support for revision;
3. identify the role of pregnancy and lactation labeling for medications in provision of patient care for these populations; and
4. demonstrate an understanding of additional patient considerations in evaluating medication effects during pregnancy and lactation.

### Background

Prevalence of chronic conditions is increasing among women in the United States, with an estimated 39 percent of women of childbearing age (19 to 45 years of age) having a diagnosis. There has been an increased population of pregnant women who have pre-existing conditions due to the increasing

age of the childbearing population and new and improved treatments for these conditions. Further, nearly half of all pregnancies in the United States are unplanned. Nine out of 10 women in the United States take an over-the-counter (OTC) or prescription medication during pregnancy; approximately 64 percent of women are prescribed these medications during pregnancy. This results in 5.4 million pregnancies exposed to medications each year. With the increasing age at which women are becoming pregnant today and the subsequent likelihood of medication use due to chronic disease, it is critical that pharmacists adequately understand pregnancy and lactation labeling to appropriately counsel about safe use of medications by women of childbearing potential, pregnant women, and breastfeeding women. Lack of treatment of a maternal condition such as diabetes or hypertension may present greater risk than medication exposure.

The possibility that medications may cause birth defects during pregnancy became more widely understood with the thalidomide tragedy in the early 1960s. Thalidomide was first submitted to FDA for approval in 1960 as a treatment of nausea and vomiting in pregnancy. Due to concerns over a lack of safety data by pharmacologist Frances Kelley, the drug was never approved in the United States. Teratogenesis phocomelia,

the congenital absence or underdevelopment of extremities, was less impactful in the United States than in Europe as a result.

In the 1970s, clinicians were presented with increasing information regarding medication use in pregnancy and lactation that they did not fully understand due to complex research designs and clinical evidence of varying quality and utility. In response to this, FDA developed the 1979 *Labeling for Prescription Drugs Used in Man* to help guide practitioners. The pregnancy letter category system was designed to help assess risk versus benefit of medications used during pregnancy and lactation. However, this system quickly saw limitations to its use due to a lack of data and incorrect interpretation. Since 1980, fewer than 10 percent of the medications approved by FDA have had enough information within their new drug application to determine risk of birth defects. With incorrect interpretation of risk categories, wanted pregnancies may unwarrantingly be terminated due to fear rather than actual risk of teratogenic potential, necessitating a change in the system.

Although new labeling recommendations were made official in the December 4, 2014 edition of the *Federal Register* (Volume 79, Number 233), the pregnancy letter category system will slowly be phased out. The Pregnancy and Lactation Labeling Final Rule (PLLR) went into effect on June 30,

**Table 1**  
**FDA pregnancy letter categories**

FDA Pregnancy Category	FDA Definition
A	Adequate and well-controlled studies (AWC) in humans have failed to demonstrate risk to the fetus during the first trimester with no evidence of harm; no evidence of harm in second or third trimester
B	(1) No AWC in humans <b>AND</b> animal studies have failed to demonstrate a risk to the fetus <i>OR</i> (2) AWC in humans fail to demonstrate a risk to the fetus during the first trimester; no evidence of harm in second or third semester <b>AND</b> animal studies demonstrate an adverse effect
C	(1) No AWC in humans <b>AND</b> animal studies have shown an adverse effect on the fetus <b>AND</b> benefits from the use of the medication may be acceptable despite potential risks <i>OR</i> (2) there are no animal studies or AWC in humans
D	Positive evidence of human fetal risk based on human data; potential benefits from use of the medication may be acceptable despite its potential risks
X	Studies in humans or animals have demonstrated fetal abnormalities or there is positive evidence of fetal risk; risk of use of the medication clearly outweighs any possible benefit

Adapted from *Pharmacotherapy*. 2014;34(4):389-395; *US Pharm*. 2014;39(10):40-43; *Pharmacy Times*. 2010. <http://www.pharmacytimes.com/publications/issue/2010/june2010/pregnancylabeling-0610>

2015. Any medications whose new drug application was submitted after that date must automatically follow PLLR requirements. Medications that were approved prior to June 29, 2001 are not subject to the PLLR; however, they must remove any pregnancy letter category designations within three years of the PLLR effective date (June 29, 2018). Prescription medications have three to five years to follow the PLLR, based on year of approval. This includes new drug applications submitted to FDA prior to June 30, 2015 that had yet to be reviewed. The PLLR does not apply to OTC medications. OTC medications are still subject to the pregnancy letter categories approved by FDA.

### Previous Labeling Requirements

Within the original FDA regula-

tions developed in 1979, prescribing information for use in pregnancy, labor and delivery, and lactation labeling for prescription drugs must include a risk evaluation regarding use during pregnancy. This can be located under the “Use in Specific Populations” within the medication’s monograph or drug product label. Medications excluded from this requirement include those that are not systemically absorbed, or those with insignificant data to demonstrate risk to the fetus. As part of this system, a pregnancy letter category system was developed with A, B, C, D, and X designations described in Table 1. These categories were originally touted by the *FDA Consumer* as “mak[ing] it easier for the doctor to determine the safety of a prescription drug for the use intended.” A standardized risk summary was provided in conjunction with the

letter category.

The pregnancy letter category system was not designed as a grades of risk system, but rather was an assessment of risk to the fetus, as well as a balance of risk versus benefit for both the fetus and the mother.

This system saw limited celebration as an effective tool for evaluation of medication use during pregnancy; limitations were quickly identified starting in 1992 by the Teratology Society. The Public Affairs Committee of the Teratology Society further published a position paper titled, “FDA Classification of Drugs for Teratogenic Risk” in 1994, which recommended elimination of the letter categories and insertion of narrative statements that summarized and interpreted available data to provide an estimation of teratogenic risk. As a result of the Teratology Society’s efforts, FDA held a public hearing in 1997 to initiate evaluation of the labeling regulation.

**Limitations.** The biggest fault of this system is the misinterpretation by care providers, due to the impression that a letter-based system gives. Approximately 65 to 70 percent of medications currently approved fall into category C, most frequently due to lack of information. The teratogenic risk was “undetermined” for 97.7 percent of the medications approved between 2000 and 2010. The amount of data available for assessing safety in pregnancy was rated as “none” for 73.3 percent of these medications as well. Information is infrequently updated due to lack of required updates by FDA in the current system, as well as a general lack of availability. Medications are infrequently studied in pregnancy, so we must rely on case reports and industry-sponsored pregnancy registry reporting databases (i.e., anticonvulsants and antiretroviral agents), of which many patients are unaware. For medications approved from 1980 to 2000, only 5 percent had changed a full risk category or more in the previous 10 years. Only 30 medica-

tions have clearly demonstrated teratogenic effects.

Many healthcare providers interpret a “C” as safer than a “D,” but that may not be the case. Medications in category D may have situations in which benefit is greater than risk, but medications in category C are frequently those that we have no data regarding their risk or lack thereof. Providers frequently assume that drugs within the same category share the same extent of risk, but the risk and potential fetal effects of medications vary greatly based on clinical presentation, degree of severity, rate of occurrence, and level of support. The pregnancy letter categories are also falsely interpreted to be an interpretation of teratogenic risk, when they are simply a tool to evaluate risk versus benefit of medication use in pregnancy.

Category X medications are generally viewed as teratogenic medications, when many of these medications have lack of benefit for use in pregnancy. Oral contraceptives carry a Category X rating, which is more related to the absence of efficacy for their FDA indication of prevention of pregnancy in women who are already pregnant than evidence of congenital disorders in animals. Statins provide a similar illustration. This class of medications is also Category X, which is due to the lack of benefit of treating hypercholesterolemia in pregnancy, versus the limited evidence of congenital abnormalities, which is stronger in animal studies than human studies.

For many medications, there are infrequent updates to their pregnancy letter category, if any. Concerns have also been raised with this system, due to inconsistency in teratogenicity risk between animal and human studies. Thalidomide was shown to be safe in animal studies, but resulted in severe congenital abnormalities in humans. With the pregnancy letter category system, the simplification of data into letter categories allows false assumptions of what

that letter’s risk profile means, and utilizes data (i.e., animal) that may not accurately transfer to humans.

## **Pregnancy and Lactation Labeling Final Rule (PLLR)**

The PLLR revises how information will be presented to healthcare providers, and creates a consistent format for discussion of risk and benefit of a prescription medication and biologic product. As previously mentioned, OTC medications are not subject to this rule.

Based on feedback from public meetings, focus groups, advisory committees, and the 2008 Proposed Rule, FDA developed its Final Rule published within the *Federal Register* in December 2014. These regulations eliminate the pregnancy letter categories, and have significantly revised the format of the *Use in Specific Populations* section (Sections 8.1-8.3) of the Prescription Drug Label. Information previously included in Section 8.2 (*Labor and Delivery*) has been moved to Section 8.1 (*Pregnancy*). Section 8.3 (*Nursing Mothers*) has been revised to a new Section 8.2 (*Lactation*). A completely new section was created, *Females and Males of Reproductive Potential* (Section 8.3). The goal of this rule is to provide a format that is conducive to effective patient counseling to facilitate a transfer of clinical information that allows the patient to make an informed decision. This format was designed to help the provider with the provision of patient-specific information to improve the standard of care.

**Pregnancy.** Information in the *Pregnancy* (Section 8.1) subsection will include “Pregnancy Exposure Registry,” “Risk Summary,” “Clinical Considerations,” and “Data” subsections. Preceding these subsections is an introduction with a concise statement regarding risk in all pregnancies. If there is a pregnancy exposure registry for a medication, the registry must be provided along with contact information (toll-free telephone number, website to enroll or

gain information). The labeling will direct women to the registry in efforts to enhance patient awareness of previous use of the medication during pregnancy, and to hopefully increase reporting if there are adverse outcomes. If there is not a registry, this section can be omitted. Registries do not make medication interventions, they simply record data about pregnant women who already took a medication with the goal of detecting any effects from the medication on the fetus.

The “risk summary” subheading is always required on the label due to requirements on generalized risk statements, even when there are no data available. Unlike previous labeling requirements, this is required for medications with limited evidence of risk and those that are not systemically absorbed. If a medication is contraindicated in pregnancy, this must be listed first in the risk summary. Risk statements must be provided for all relevant sources including human data, animal data, and the medication’s pharmacology. Data should be placed in order of clinical importance within an integrated summary. When human data are available, the risk statement must summarize the specific developmental outcome as well as incidence, effect of dose, effect of duration of exposure, and gestational age. This should be quantitatively compared to the risk for the same outcome in infants born to women who were not exposed. If no human data are available or the data do not establish the presence of risk, it must be stated in the risk summary.

When animal data are available, the risk summary must describe the potential adverse developmental outcomes, along with the number and types of species affected, timing of exposure, animal doses (expressed in human dose/exposure equivalents), and outcomes for the pregnant animals and offspring. The risk summary must state when there are no animal data, or when the data do not meet standards for non-clinical developmental toxicity studies.

If the medication has a well-defined mechanism of action for fetal effects, the risk summary must explain the pharmacologic mechanism of action along with potential associated risk. The risk summary should further explain the pharmacologic mechanism of action that may result in drug class-associated adverse developmental outcomes, if known. This should be cross-referenced, to the clinical pharmacology section of the label where pharmacologic data will be more fully described.

“Clinical considerations” is designed to provide healthcare providers with information to aid care decisions and counseling in response to unexpected drug exposure, in prescribing decisions, and use in labor and delivery. This heading should be omitted if there is no information available or if it is not informative. The first information provided should be focused on any serious risk of untreated conditions in pregnancy for both the mother and the fetus. Dose adjustments based on pharmacokinetic data during pregnancy and the postpartum period should also be provided. Maternal adverse reactions, as well as fetal/neonatal adverse reactions, are also a part of this section. Adverse reactions that are unique to pregnancy or that occur with an increased frequency or severity during pregnancy should be discussed with interventions to monitor or mitigate these adverse reactions. If known, the effect of the dose, timing, and duration of exposure on the maternal risk should be discussed. For fetal/neonatal adverse reactions, the potential severity and reversibility of the adverse reaction and available interventions must be discussed. The final piece of this section is the labor and delivery section, discussing the medication’s effects on the mother, fetus/neonate, and the impact on duration of labor and delivery.

Within the “data” section, both human and animal data should be presented if available, and in that order. For human data, both posi-

tive and negative findings must be presented. This portion of labeling must describe data regarding adverse developmental outcomes and adverse reactions with the following elements: (1) data source (controlled clinical trial, surveillance study); (2) number of subjects; (3) duration of study; (4) exposure information (timing, duration, and dose); and (5) limitations of the data (potential biases and confounders if known). Individual case reports should generally not be included. Under the animal data section, the following should be provided: (1) types of studies; (2) animal species (if available, correlation to humans); (3) animal doses or exposures expressed in human dose equivalents; (4) duration and timing of exposure; (5) study findings; (6) presence or absence of maternal toxicity; and (7) limitations of the data.

**Lactation.** This section replaces the nursing mothers subsection of the old label, and is formatted similarly to the pregnancy subsection. The PLLR uses lactation to refer to the biological state in which a woman is producing and excreting milk. Breastfeeding is used to refer to all *human milk feeding* situations in which an infant or child is fed with human milk. Information in this section will include the subheadings “risk summary,” “clinical considerations,” and “data.”

The “risk summary” subsection is always required because certain statements must be included, even when no data are available. If a medication is contraindicated during breastfeeding (i.e., radioactive iodine-containing products), this must be stated first with a brief explanation. If human data are available, only human data should be provided, unless it is known that the animal model is known to be predictive for humans. This subheading should summarize information on the presence of a medication or its active metabolite in human milk, including concentration or the actual or estimated infant daily dose. The effects of the

drug or metabolite on the breastfed infant should also be provided; if a medication is not expected to be systemically bioavailable to the breastfed infant (drug is degraded in infant’s gastrointestinal tract), the summary must describe the disposition of the medication.

Data regarding the pharmacological action of a medication or its metabolite on milk production and excretion should be provided, including if the effect is temporary or permanent. If there are no data available for these considerations, it must be specifically stated. This section should conclude with a risk and benefit statement. If only animal data are available, the species should be specified.

Under “clinical considerations,” strategies to minimize infant exposure should be discussed, including timing medication administration around feedings or pumping sessions, as well as “pump and dump” for medications utilized for short courses with adverse effects. Monitoring for adverse effects should also be described within this section with strategies for mitigating effects (i.e., dosage adjustment). If there are no data to fulfill this subheading, it should be omitted.

Within the “data” subsection, data on which the “risk summary” and “clinical considerations” are based must be provided. This must be updated as new data become available. This subsection should be omitted if no data are available.

**Males and Females of Reproductive Potential.** This section should have the subheadings “pregnancy testing,” “contraception,” and “infertility” as applicable in this order. Manufacturers are required to provide information for these populations when there are recommendations or requirements for pregnancy testing and/or contraception before, during, or after drug therapy. Recommendations or requirements may be based on potential or demonstrated adverse developmental outcomes associated with drug exposure during pregnancy. There must also be provision of any human or animal

data suggesting drug-associated effects on fertility and/or pre-implantation pregnancy loss effects. If there are no suggested adverse effects on fertility, this should be presented under “infertility.” If animal data raise concerns about impairment of human fertility in males or females, the summary and implications must be provided in this section with a cross-reference to nonclinical toxicology. If none of the subheadings are applicable, this section should be omitted.

### **Additional Counseling Considerations**

While the PLLR should help to improve utilization of available data regarding use of medications during pregnancy and lactation in an appropriate manner, there are still limitations with the revised labeling. The most frequent limitation being lack of information and data. Further, these pregnancy and lactation categories do not provide pharmacists a definitive *yes* or *no* answer for determining if use of a medication is appropriate, but rather a guide to determine safety of using medications during pregnancy and lactation.

**Pregnancy.** When considering the impact of a medication on a developing fetus, the first factor to consider is timing of gestation. Many medications are limited to having impact during a small window within the pregnancy. Many medications have limited impact on development when a particular organ is developing. For example, tetracycline is labeled as a Pregnancy Category D medication due to its potential to cause tooth discoloration and disruption of bone formation. Week 15 of gestation is approximately when a baby’s skeleton is developing. Thus, while tetracyclines should be avoided if possible, if there is no acceptable alternative, it may be tolerable if used before development of teeth and cartilage (around week 15). Avoidance is most critical during the second and third trimesters; however, effective treatment of infections during pregnancy is

critical for both mother and baby. Additional consideration should be given to the duration of exposure as well.

Several physiologic changes occur during pregnancy that can impact the pharmacokinetics of medications, which may necessitate dosage adjustments to maintain therapeutic drug levels. Volume of distribution for hydrophilic medications increases dramatically due to a 40 to 50 percent increase in blood volume, potentially leading to subtherapeutic levels in pregnant women given standard doses. Pregnancy also causes an increase in CYP3A4 activity, increasing clearance of its substrates. Some affected medications include carbamazepine, loratadine, and amlodipine. Elimination rate of renally-cleared medications also increases due to glomerular filtration rates increasing by 50 percent during pregnancy. Medications that are heavily renally excreted, such as digoxin and piperacillin, are eliminated from the body quicker, thus decreasing the half-life of the medication. Changes in absorption, distribution, metabolism, and elimination must be carefully evaluated to ensure safe and therapeutic doses of medications in pregnant women.

There are two classifications of adverse events that can occur to a fetus when exposed to a medication during pregnancy. The first being a *teratogenic effect*, when there is alteration of tissue development or organ formation, which occurs early in pregnancy. When counseling pregnant patients about the risk of medication exposure during pregnancy, one should keep in mind that the teratogenic period is generally two to eight weeks after conception, often with an all or nothing effect during the first two weeks of pregnancy. This is not to say that teratogenic effects cannot occur after the eighth week of pregnancy, it is simply less likely. There is also a dose-response curve for teratogenic medications. This means that there is a dose below which no effects occur. Once the dose reaches threshold, the mag-

nitude of the teratogenic effect increases.

The second type of adverse event is referred to as an *adverse fetal effect*, which is the dysfunction of an organ or tissue after the organ or tissue has formed. Most medications can cross the placenta, exposing the developing fetus to the medication. When evaluating the safety of medication exposure to a fetus during pregnancy, pharmacists should evaluate the FDA-required pregnancy labeling, but should also try to ascertain how much of the medication that fetus will actually be exposed to. Fetal exposure will be higher when medications are lipophilic, unionized, weakly basic, and have low molecular size. Weakly basic and unionized medications then become trapped within the placenta. Placental transporters have also been identified which pump medications (i.e., doxorubicin, vinblastine) out of fetal tissue back into maternal circulation. Highly protein-bound medications will result in lower fetal exposure.

**Lactation.** When evaluating the use of medications in lactation, many of the same factors discussed within pregnancy must be considered. Most medications will passively diffuse into breast milk; transfer will be higher with low molecular weight, lipid soluble, and unionized medications. Weakly acidic medications cannot easily cross into the breast milk. While lipophilic medications will cross more readily, both water-soluble and lipid-soluble medications can cross since there are both water and lipid components within breast milk. Milk-to-plasma (M/P) ratio may be discussed in medication resources. Generally, medications with a higher M/P ratio will have a relatively greater concentration in breast milk; however, there are several limitations to use of this tool. M/P is a helpful description of how much of a medication passes into breast milk. It does not account for multiple daily doses, timing of breastfeeding in relation to medication dose time, maternal

**Table 2**  
**Additional resources for medication use in pregnancy and lactation**

Reference	Details
<i>Drugs in Pregnancy and Lactation</i> by Briggs, Freeman, Yaffe	Pregnancy and lactation; published every three years; limited lactation data
LactMed <a href="http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT">http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT</a>	Lactation only; free access; updated regularly; supported by NIH
Lexi-Drugs	Provides in-depth pregnancy and lactation information, in addition to standard information; updated regularly
<i>Medications and Mother's Milk</i> by Thomas W. Hale	Lactation only, published every two years; classified medication based on risk, L1 (safest) – L5 (contraindicated); provides suggested alternatives within medication class
Micromedex	Pregnancy and lactation; updated regularly, contains TERIS and <i>Shepard's Catalog of Teratogenic Agents</i> ; provides U.S. and Australian pregnancy classification (with detailed information when available); provides AAP (American Academy of Pediatrics) and Hale Lactation classification
REPROTOX	Provides summaries of effects of medications, chemicals, infections, and physical agents on pregnancy, reproduction, and development (includes fertility and lactation); updated regularly; will research searched items not in database
TERIS (Teratogen Information System) part of <i>Clinical Teratology Web</i>	Online version of <i>Shepard's Catalog of Teratogenic Agents</i> ; assessing risk of possible teratogenic exposures in women (none, unlikely, minimal, small, moderate, high, undetermined)

disease, time postpartum, or differences in milk production throughout the day. If the M/P is less than one, there is poor transfer into breast milk; M/P of one to five may be sequestered into the milk. This does not reflect absolute concentration, which is affected by total daily dose, frequency of dosing, frequency of feeding, and other physiologic factors. Another consideration for pharmacists is the bioavailability of a medication for the infant. Most medications have 1 to 2 percent of a maternally-administered dose in breast milk; low doses like this may not be absorbed within the infant's gastrointestinal tract

if the medication has poor bioavailability.

Thousands of women who must take medication do not breastfeed due to a misperception of the risk of exposure for their infants. It is critical to remember that formula feeding is associated with higher morbidity and mortality in all socioeconomic groups. Unless there is significant risk associated with medication exposure for an infant, efforts should be made to continue breastfeeding due to the nutritional, immunologic, and psychological benefits. Most medications are excreted in amounts too small to have an adverse effect on the

infant's health.

To minimize medication exposure or risk, the following strategies should be employed. Medications should be taken 30 to 60 minutes after nursing and, optimally, there should be a three- to four-hour window before the next feeding. However, medications with long half-lives that extend beyond three to four hours will not be effectively managed by this approach. If the mother is taking a short-term therapy with potential adverse effects such as tetracycline, she should be counseled to "pump and dump" during that course of therapy to maintain adequate oxytocin levels to preserve milk production. Medications without data on safety during lactation should generally be avoided or breastfeeding should be discontinued while they are given.

Additional resources to assist in patient counseling for medication use in pregnancy and lactation are listed in Table 2. Recommendations from each of these references are not always the same, thus, it is prudent to refer to more than one reference in making a determination of safety.

## Conclusion

With pregnancy becoming more common later in life and the increased likelihood of pregnant females having chronic conditions that require medications, knowledge of safety data in pregnancy and lactation has become more relevant in today's society than when the original pregnancy letter categories were created by FDA in 1979. The PLLR format will enhance the ability of healthcare providers and their patients to evaluate what risks may be associated with medication use during pregnancy and lactation.

Implementation of the rule will take three to five years, and while the labeling is a step in the right direction, there are still many limitations. Much of the data that healthcare providers are looking for regarding use in pregnancy and lactation simply are not

there, limiting value of the new format. The PLLR will minimize the misinterpretation of risk that has plagued the pregnancy letter category system; however, OTC medications will still be subject to the old system.

Updated content requirements of the PLLR can be found on each medication's individual Prescription Drug Label, in accordance with the timeline specified, based on the date of medication approval. These can be accessed at the U.S. National Library of Medicine's website, the Daily Med (<http://dailymed.nlm.nih.gov>).

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*The author, the Ohio Pharmacists Foundation and the Ohio Pharmacists Association disclaim any liability to you or your patients resulting from reliance solely upon the information contained herein. Bibliography for additional reading and inquiry is available upon request.*

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## New Prescription Labeling Requirements for the Use of Medications in Pregnancy and Lactation

1. Which medication heightened awareness of the possibility that medications used during pregnancy may cause birth defects?

- a. Tetracycline
- b. Warfarin
- c. Doxorubicin
- d. Thalidomide

2. The Pregnancy and Lactation Labeling Final Rule (PLLR) applies to both prescription and OTC medications.

- a. True
- b. False

3. The pregnancy letter category labeling required:

- a. provision of pregnancy registry information.
- b. standardized risk summary.
- c. separation of human and animal data.

4. What was the intended purpose of the pregnancy letter category system?

- a. Grades of risk
- b. Estimate of teratogenicity
- c. Balance of risk vs. benefit for both mother and fetus

5. Which pregnancy letter category represents a medication that has evidence of fetal risk in human studies, but potential benefits from use may be acceptable in spite of risks?

- a. B
- b. C
- c. D
- d. X

6. Under the PLLR, which subheading under section 8.1 (*Pregnancy*) is always required within the drug label?

- a. Pregnancy Exposure Registry
- b. Clinical Considerations
- c. Risk Summary
- d. Data

7. Under the PLLR, in which subheading of *Pregnancy* would adverse reactions unique to pregnancy be provided?

- a. Risk Summary
- b. Clinical Considerations
- c. Data

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Completely fill in the lettered box corresponding to your answer.

- |                    |                     |                     |
|--------------------|---------------------|---------------------|
| 1. [a] [b] [c] [d] | 6. [a] [b] [c] [d]  | 11. [a] [b]         |
| 2. [a] [b]         | 7. [a] [b] [c]      | 12. [a] [b] [c] [d] |
| 3. [a] [b] [c]     | 8. [a] [b] [c]      | 13. [a] [b]         |
| 4. [a] [b] [c]     | 9. [a] [b] [c]      | 14. [a] [b] [c]     |
| 5. [a] [b] [c] [d] | 10. [a] [b] [c] [d] | 15. [a] [b] [c] [d] |

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If no, list any unmet \_\_\_\_\_
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4. Did the program meet your educational/practice needs?  yes  no
5. How long did it take you to read this lesson and complete the quiz? \_\_\_\_\_
6. Comments/future topics welcome.

8. Under the PLLR, in which subheading of *Lactation* would an estimated infant daily dose be provided?

- a. Risk Summary
- b. Clinical Considerations
- c. Data

9. Under the PLLR, information regarding recommendations/requirements for contraception use before, during or after drug therapy is found in which section?

- a. Pregnancy
- b. Lactation
- c. Males and Females of Reproductive Potential

10. When considering the impact of a medication on a developing fetus, what is the first factor to consider?

- a. Mother's age
- b. Mother's health status
- c. Weeks gestation
- d. Family history

11. What type of medication has an increased volume of distribution in pregnancy?

- a. Hydrophilic
- b. Lipophilic

12. All of the following medication characteristics will result in increased fetal exposure EXCEPT:

- a. hydrophilic.
- b. unionized.
- c. weakly basic.
- d. low protein binding.

13. An M/P ratio of 4 means:

- a. high concentration in breast milk.
- b. low concentration in breast milk.

14. To minimize medication exposure or risk to an infant, breastfeeding mothers should be counseled to do all of the following EXCEPT:

- a. take the medications 30-60 minutes after nursing.
- b. allow 1-2 hour window before feeding.
- c. pump and dump.

15. Which reference provides an estimation of risk of neonatal exposure during lactation using L categories?

- a. Briggs
- b. LactMed
- c. *Medications and Mother's Milk*
- d. Micromedex

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