處方集附錄二　懷孕哺乳用藥安全評估

FDA[1] Pregnancy Risk Categories Prior to 2015

1979 年，美國 FDA 設立了風險類別 - A、B、C、D、X - 來顯示藥物在懷孕期間使用的安全性。這些類別是透過評估研究文獻的可靠性和風險效益比決定的。這些類別沒有考慮母乳中藥物或其代謝物的任何風險。以前的懷孕分級（仍然可以在某些包裝說明書中找到）如下：

Table 1. FDA Pregnancy Risk Categories Prior to 2015

Risk category	FDA statement
A	Adequate and well-controlled (AWC) studies in pregnant women have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of a risk in later trimesters)
B	Animal reproduction studies have failed to demonstrate a risk to the fetus, and there are no AWC studies in pregnant women or animal studies that demonstrate an adverse effect, but AWC studies in pregnant women fail to demonstrate a risk to the fetus during the first trimester of pregnancy (and there is no evidence of risk in later trimesters)
C	Animal reproduction studies have shown an adverse effect on the fetus, there are no AWC studies in humans, and the benefits from the use of the drug in pregnant women may be acceptable despite its potential risks; or animal studies have not been conducted andthere are no AWC studies in humans
D	There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks
X	Studies in animals or humans have demonstrated fetal abnormalities or there is positive evidence of fetal risk based on adverse reaction reports from investigational or marketing experience, or both, and the risk of the use of the drug in a pregnant woman clearly outweighs any possible benefit

FDA's Pregnancy and Lactation Labeling Final Rule (PLLR) Since June 30, 2015

2015 年 6 月 30 日之後提交美國 FDA 核准的處方藥需使用新規定的格式刊載懷孕、哺乳相關

[1] FDA = Food and Drug Administration

風險資訊。非處方 (OTC[2]) 藥物的標籤不會改變，因為非處方藥產品不受新規定的影響。

自 1979 年以來使用的 A、B、C、D、X 風險類別現已替換為以下敘述格式：

Pregnancy

- Pregnancy exposure registry
- Risk summary
- Clinical considerations
- Data

Lactation

- Risk summary
- Clinical considerations
- Data

Females and Males of Reproductive Potential

- Pregnancy testing
- Contraception
- Infertility

Definitions of Pregnancy Recommendations in *Briggs Drugs in Pregnancy and Lactation*

Compatible

The human pregnancy experience, either for the drug itself or drugs in the same class or with similar mechanisms of action, is adequate to demonstrate that the embryo–fetal risk is very low or nonexistent. Animal reproduction data are not relevant.

No (Limited) Human Data—Probably Compatible

There may or may not be human pregnancy experience, but the characteristics of the drug suggest that it does not represent a significant risk to the embryo–fetus. For example, other drugs in the same class or with similar mechanisms are compatible or the drug does not obtain significant systemic concentrations. Any animal reproduction data are not relevant.

Compatible—Maternal Benefit >> Embryo–Fetal Risk

There may or may not be human pregnancy experience, but the potential maternal benefit far outweighs the known or unknown embryo–fetal risk. Animal reproduction data are not relevant.

Human Data Suggest Low Risk

There is limited human pregnancy experience, either for the drug itself or drugs in the same class or

[2] OTC = Over-the-Counter

with similar mechanisms of action, including the 1st trimester, suggesting that the drug does not represent a significant risk of developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death) at any time in pregnancy. The limited human pregnancy data outweigh any animal reproduction data.

No (Limited) Human Data—Animal Data Suggest Low Risk

Either there is no human pregnancy experience or the few pregnancy exposures have not been associated with developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death). The drug does not cause developmental toxicity (at doses that did not cause maternal toxicity) in all animal species studied at doses ≤10 times the human dose based on body surface area (BSA) or AUC[3].

No (Limited) Human Data—Animal Data Suggest Moderate Risk

Either there is no human pregnancy experience or the few pregnancy exposures have not been associated with developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death). The drug causes developmental toxicity (at doses that did not cause maternal toxicity) in one animal species at doses ≤10 times the human dose based on body surface area (BSA) or AUC.

No (Limited) Human Data—Animal Data Suggest Risk

Either there is no human pregnancy experience or the few pregnancy exposures have not been associated with developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death). The drug causes developmental toxicity (at doses that did not cause maternal toxicity) in two animal species at doses ≤10 times the human dose based on body surface area (BSA) or AUC.

No (Limited) Human Data—Animal Data Suggest High Risk

Either there is no human pregnancy experience or the few pregnancy exposures have not been associated with developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death). The drug causes developmental toxicity (at doses that did not cause maternal toxicity) in three or more animal species at doses ≤10 times the human dose based on body surface area (BSA) or AUC.

Contraindicated—1st Trimester

Human exposures in the 1st trimester, either to the drug itself or to drugs in the same class or with similar mechanisms of action, have been associated with developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death). The drug should not be used in the 1st trimester.

Contraindicated—2nd And 3rd Trimesters

Human exposures in the 2nd and 3rd trimesters, either to the drug itself or to drugs in the same class or with similar mechanisms of action, have been associated with developmental toxicity (growth restriction, structural anomalies, functional/behavior deficits, or death). The drug should not be used

[3] AUC = area under the plasma concentration vs. time curve; a measure of the systemic exposure of a drug

in the 2nd and 3rd trimesters.

Contraindicated

Human exposures at any time in pregnancy, either to the drug itself or to drugs in the same class or with similar mechanisms of action, have been associated with developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death). Animal reproduction data, if available, confirm the risk. The drug should not be used in pregnancy.

No (Limited) Human Data—No Relevant Animal Data

There are no human pregnancy data or relevant data in animals, or the human pregnancy experience, that may or may not include the 1st trimester, is limited. The risk in pregnancy cannot be assessed.

Human Data Suggest Risk In 1st Trimester

Evidence (for the drug or similar drugs) suggests that there may be an embryo–fetal risk for developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death) in the 1st trimester but not in the 2nd and 3rd trimesters. The human pregnancy data outweigh any animal reproduction data.

Human Data Suggest Risk In 1st And 3rd Trimesters

Evidence (for the drug or similar drugs) suggests that there may be an embryo–fetal risk for developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death) in the 1st and 3rd trimesters but not in the 2nd trimester. The human pregnancy data outweigh any animal reproduction data.

Human Data Suggest Risk In 2nd And 3rd Trimesters

Evidence (for the drug or similar drugs) suggests that there may be a fetal risk for developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death) in the 2nd and 3rd trimesters but not in the 1st trimester. The human pregnancy data outweigh any animal reproduction data.

Human Data Suggest Risk In 3rd Trimester

Evidence (for the drug or similar drugs) suggests that there may be a fetal risk for developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death) in the 3rd trimester or close to delivery but not in the 1st or 2nd trimesters. The human pregnancy data outweigh any animal reproduction data.

Human (And Animal) Data Suggest Risk

The human data for the drug or drugs in the same class or with the same mechanism of action, and animal reproduction data if available, suggest that there may be a risk for developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death) throughout pregnancy. Usually, pregnancy exposure should be avoided, but the risk may be acceptable if the maternal condition requires the drug.

Definitions of Breastfeeding Recommendations in *Briggs Drugs in Pregnancy and Lactation*

Compatible

Either the drug is not excreted in clinically significant amounts into human breast milk or its use during lactation does not, or is not expected to, cause toxicity in a nursing infant.

Hold Breastfeeding

The drug may or may not be excreted into human breast milk, but the maternal benefit of therapy far outweighs the benefits of breast milk to an infant. Breastfeeding should be held until maternal therapy is completed and the drug has been eliminated (or reaches a low concentration) from her system.

No (Limited) Human Data—Probably Compatible

Either there are no human data or the human data are limited. The available data suggest that the drug does not represent a significant risk to a nursing infant.

No (Limited) Human Data—Potential Toxicity

Either there are no human data or the human data are limited. The characteristics of the drug suggest that it could represent a clinically significant risk to a nursing infant. Breastfeeding is not recommended.

Human Data Suggest Potential Toxicity

Human data suggest a risk to a nursing infant. The drug is best avoided during breastfeeding. Depending on the drug, short-term use by the mother may be possible, but the infant should be closely monitored for potential adverse effects.

No (Limited) Human Data—Potential Toxicity (Mother)

Either there are no human data or the human data are limited. The characteristics of the drug suggest that breastfeeding could represent a clinically significant risk to the mother such as further loss of essential vitamins or nutrients. Breastfeeding is not recommended.

Contraindicated

There may or may not be human experience, but the combined data suggest that the drug may cause severe toxicity in a nursing infant, or breastfeeding is contraindicated because of the maternal condition for which the drug is indicated. Women should not breastfeed if they are taking the drug or have the condition.

Reference

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