



## NZF is changing the way that pregnancy and breast-feeding advice for medicines is presented

From 1 October, 2018, the New Zealand Formulary (NZF) will replace the current pregnancy and breast-feeding advice, which is based on a five-letter classification system, with more comprehensive information from *Drugs in Pregnancy and Lactation*. This move is in line with international recommendations.

### Why change pregnancy and breast-feeding advice?

For many decades pregnancy categories have been used to indicate the safety of prescribing medicines to pregnant or breast-feeding women. The New Zealand Formulary used a pregnancy category system from the Therapeutic Goods Administration (TGA) Australia, based on A, B, C, D or X classifications, and breast-feeding information from the Therapeutic Guidelines Limited (TGL), Australia.<sup>1,2</sup>

The system of using pregnancy categories has several limitations, including that:<sup>1,3</sup>

- It does not provide information about risks across different trimesters of pregnancy
- Medicines with a wide range of associated risks could be included in the same category
- The categories imply a grading system, which could lead to prescribing based on the risk category rather than an understanding of the evidence of risks and benefits for a particular patient
- The single-letter classification system does not provide enough information to support informed decision making by prescribers and patients

As a result of these limitations, there is an international movement away from using pregnancy safety categories, and instead providing descriptions of the underlying evidence, degree of severity, timing of effects on the developing fetus and also indicating areas where there is a lack of evidence.


## New pregnancy and breast-feeding advice

From 1 October, 2018, the NZF will include advice on the safety of medicines in pregnancy and breast-feeding from *Drugs in Pregnancy and Lactation* (used by permission from Wolters Kluwer Health).<sup>4</sup> This information will be available in an expandable section in a medicine monograph.

For example, the current information regarding the safety of prescribing metronidazole in women who are pregnant is classified as “B2”:

**Pregnancy** systemic use: **B2**; topical use: **B2**; manufacturer advises avoidance of high-dose regimens

From 1 October, 2018, the pregnancy information for systemic use of metronidazole will show two headers: “Human Data Suggest Low Risk” and “Pregnancy Summary”:


**Pregnancy** Human Data Suggest Low Risk ☺ Pregnancy Summary ☺ 

Clicking on the arrow icon ☺ to the right of “Human Data Suggest Low Risk” will open a description of this risk category:

**Pregnancy** Human Data Suggest Low Risk ☺ Pregnancy Summary ☺

**Human Data Suggest Low Risk**

There is limited human pregnancy experience, either for the drug itself or drugs in the same class or 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 outweighs any animal reproduction data.




Clicking on the arrow icon to the right of “Pregnancy Summary” ☺ will open a brief overview of the evidence regarding the safety of using metronidazole during pregnancy, including available information on risks during different trimesters:

**Pregnancy** Human Data Suggest Low Risk ☺ Pregnancy Summary ☺

**Pregnancy Summary**

Although some of the available reports have arrived at conflicting conclusions as to the safety of metronidazole in pregnancy, most of the published evidence suggests that the anti-infective does not represent a significant risk of structural defects to the fetus. At present, it is not possible to assess the risk to the fetus from the carcinogenic potential of metronidazole. The answer to the question of transplacental carcinogenic potential of metronidazole has major public health implications, but may never be answered because of the rarity of childhood cancers and the inability to identify potentially confounding environmental factors in older children and adults. The manufacturer considers metronidazole to be contraindicated during the 1st trimester in patients with trichomoniasis or bacterial vaginosis (1). The use of metronidazole for trichomoniasis or vaginosis during the 2nd and 3rd trimesters is acceptable. For other indications, metronidazole can be used during pregnancy if there are no other alternatives with established safety profiles.

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As another example, the current information regarding the safety of prescribing paracetamol in women who are pregnant or breast-feeding is “A”; not known to be harmful, with a compatible rating for breast-feeding:

<b>Pregnancy</b>	A; not known to be harmful
<b>Breast-feeding</b>	compatible eTG complete

From 1 October, 2018, the updated pregnancy information will show “Human Data Suggest Low Risk” and “Pregnancy Summary” and the breast-feeding information will show “Compatible”. Clicking on the arrow icons next to any of these headings will reveal further information:

<b>Pregnancy</b>	Human Data Suggest Low Risk ↕ Pregnancy Summary ↕  Wolters Kluwer <b>Further pregnancy advice</b> generally considered compatible for short-term use if clinically indicated; frequent use should be avoided unless potential benefit outweighs risk
<b>Breast-feeding</b>	Compatible ↕  Wolters Kluwer

<b>Pregnancy</b>	Human Data Suggest Low Risk ↕ Pregnancy Summary ↕
	<div style="border: 1px solid #ccc; padding: 5px;"> <p><b>Pregnancy Summary</b></p> <p>Acetaminophen is commonly used in all stages of pregnancy. Although originally thought not to cause risk in offspring, some recent reports have questioned this assessment, especially with frequent maternal use or in cases where genetic variability exists. Additional data are needed to confirm these risks, but, as with all drug use in pregnancy, routine use of acetaminophen should be avoided.</p> <p style="text-align: right; font-size: small;">Drugs in Pregnancy and Lactation ©2017 Wolters Kluwer Health. All rights reserved.</p> </div> <p> Wolters Kluwer  <b>Further pregnancy advice</b> generally considered compatible for short-term use if clinically indicated; frequent use should be avoided unless potential benefit outweighs risk</p>
<b>Breast-feeding</b>	Compatible ↕  Wolters Kluwer

<b>Pregnancy</b>	Human Data Suggest Low Risk ↕ Pregnancy Summary ↕  Wolters Kluwer <b>Further pregnancy advice</b> generally considered compatible for short-term use if clinically indicated; frequent use should be avoided unless potential benefit outweighs risk
<b>Breast-feeding</b>	Compatible ↕
	<div style="border: 1px solid #ccc; padding: 5px;"> <p><b>Compatible</b></p> <p>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.</p> </div> <p> Wolters Kluwer</p>

### The NZF or NZFC may provide additional advice



For some medicines additional information will be included with a “Further pregnancy advice” or “Further breast-feeding advice” header.

For example, the prescribing recommendations on the use of morphine or allopurinol during breast-feeding will show “Limited Human Data – Potential Toxicity” with additional advice below under the “Further breast-feeding advice” headers:



Advice for allopurinol use in women who are breast-feeding:

<b>Pregnancy</b>	Limited Human Data—No Relevant Animal Data ↕ Pregnancy Summary ↕  Wolters Kluwer
<b>Breast-feeding</b>	Limited Human Data—Potential Toxicity ↕  Wolters Kluwer <b>Further breast-feeding advice</b> present in milk; manufacturer advises caution—potential risk of adverse effects, including hypersensitivity

Advice for morphine use in women who are breast-feeding:

<b>Pregnancy</b>	Human Data Suggest Risk ☹️ Pregnancy Summary ☺️  Wolters Kluwer <b>Further pregnancy advice</b> respiratory depression can occur in the neonate if opioid analgesics are used during labour or delivery; babies born to mothers who have been chronic opioid users during pregnancy can suffer from neonatal abstinence syndrome
<b>Breast-feeding</b>	Limited Human Data—Potential Toxicity ☹️  Wolters Kluwer <b>Further breast-feeding advice</b> manufacturer advises avoid—present in milk; if necessary, use lowest dose for shortest period and monitor infants for drowsiness, adequate weight gain, respiratory problems, limpness, constipation, and developmental milestones; breastfed infants exposed to opioids for long periods should be monitored for withdrawal symptoms on sudden discontinuation

Clicking on the “Limited Human Data – Potential Toxicity” header will open a description of this risk category:

<b>Pregnancy</b>	Human Data Suggest Risk ☹️ Pregnancy Summary ☺️  Wolters Kluwer <b>Further pregnancy advice</b> respiratory depression can occur in the neonate if opioid analgesics are used during labour or delivery; babies born to mothers who have been chronic opioid users during pregnancy can suffer from neonatal abstinence syndrome
<b>Breast-feeding</b>	Limited Human Data—Potential Toxicity ☹️ <div style="border: 1px solid #ccc; padding: 5px; margin: 5px 0;"><b>Limited Human Data—Potential Toxicity</b> No (Limited) Human Data—Potential Toxicity: Either there is 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.</div>  Wolters Kluwer <b>Further breast-feeding advice</b> manufacturer advises avoid—present in milk; if necessary, use lowest dose for shortest period and monitor infants for drowsiness, adequate weight gain, respiratory problems, limpness, constipation, and developmental milestones; breastfed infants exposed to opioids for long periods should be monitored for withdrawal symptoms on sudden discontinuation

### Alternative advice will be included if medicine information is not available

For some medicines the NZF or NZFC will provide alternative advice if information regarding its safety in pregnancy or breast-feeding is not available in *Drugs in Pregnancy and Lactation*.

### From 1 October, 2018, contraception advice will be included under a separate header

Medicine monographs will now also include a “Contraception and conception” section, which will contain information about any precautionary measures for women or men of childbearing age due to potential teratogenicity, including:

- Recommendations on the type of contraception
- Potential interactions with contraceptives
- Duration of continuing with contraception after a medicine has been stopped

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#### References:

1. Temming LA, Cahill AG, Riley LE. Clinical management of medications in pregnancy and lactation. *Am J Obstet Gynecol* 2016;214:698–702. doi:10.1016/j.ajog.2016.01.187
2. Therapeutic Goods Administration (TGA). Australian categorisation system for prescribing medicines in pregnancy. Therapeutic Goods Administration (TGA) 2011. Available from: <https://www.tga.gov.au/australian-categorisation-system-prescribing-medicines-pregnancy> (Accessed Aug, 2018).
3. Mosley JF, Smith LL, Dezan MD. An overview of upcoming changes in pregnancy and lactation labeling information. *Pharm Pract (Granada)* 2015;13:605.
4. Briggs G, Freeman R, Towers C, et al. *Drugs in pregnancy and lactation*. 11th edition. Wolters Kluwer 2017. Available from: [www.lww.co.uk/drugs-in-pregnancy-and-lactation-11e](http://www.lww.co.uk/drugs-in-pregnancy-and-lactation-11e) (Accessed Aug, 2018).

