

Metronidazole in Pregnancy and Breastfeeding

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There is inconsistent advice regarding the use of metronidazole in pregnant and breastfeeding women. Historically, its safety in pregnancy and breastfeeding has been controversial due to data from animal studies showing that metronidazole is potentially carcinogenic and mutagenic. However, there is no substantial evidence of these effects in humans.⁽¹⁻⁴⁾

Pregnancy

Metronidazole can be taken during all stages of pregnancy including the first trimester.

Data suggest that it poses low risk in pregnancy.^(1,4-6) On the basis of over 3,000 analysed pregnancies, metronidazole is not considered teratogenic in humans.⁽²⁾

A retrospective cohort study found no association between metronidazole treatment and preterm birth, low birth weight, or congenital malformations in 2,829 mother/infant pairs where 922 mothers took metronidazole.⁽⁷⁾

As with all medicines in pregnancy, only use if clearly indicated and at the recommended dose.

Pharmacokinetic parameters

Metronidazole ^(4,8-10)	
Half-life, $t_{1/2}$ (active metabolite)	8 hours (prolonged in neonates) (10 hours)
Oral availability (F)	100%
Tmax (oral dose)	1-2 hours
Protein binding	< 20%
Relative Infant Dose (RID)*	12-14%

* The RID is the dose received via breast milk (mg/kg/day) relative to the mother's dose (mg/kg/day).

Breastfeeding

Metronidazole at standard doses is considered safe to use when breastfeeding healthy, full-term infants. Caution is required in preterm infants or where high dose metronidazole is used.

Metronidazole transfers into breast milk in relatively high amounts. The relative infant dose (RID) is 12-14% (up to 24% in some studies). For drugs that are not overtly toxic, a RID < 10% suggests safety in breastfeeding full-term, healthy infants. While the RID seems high, metronidazole is used in infants at therapeutic doses of 15-30 mg/kg/day. In comparison, infants whose mothers take 1200 mg/day receive < 3 mg/kg/day via breast milk.^(3,11,12)

Breastfeeding continued

Oral doses of 400-600 mg BD for 7-10 days are reasonable. Intravenous administration (e.g. 500 mg IV BD) produces similar maternal plasma and milk concentrations to equivalent oral doses, and is also considered reasonable. Vaginal and topical routes are associated with less exposure in infants than oral or IV routes.^(1,3,11,12)

Numerous studies have shown virtually no untoward effects in breastfed infants. Monitor the infant for changes in bowel habit, vomiting, skin rash, thrush and poor feeding as a precaution.^(2,10,11)

It has been suggested that metronidazole may give a bitter or metallic taste to milk that deters infants from feeding; however, this is not supported by published evidence.⁽¹¹⁾

Metronidazole exposure should be avoided in premature breastfed infants ($t_{1/2}$ up to 74 hours), and in infants with low birth weight or renal or hepatic impairment.^(2,11) For these infants, give an alternative antibiotic to the mother, otherwise use pasteurised donor milk (if available) or infant formula and discard expressed milk during the metronidazole course. Seek expert advice.

Dose for bacterial vaginosis or trichomoniasis^(2,10,11,13-15)

Metronidazole oral 400 mg BD for 7 days.

Metronidazole gel 0.75%, one full applicator (5 g) intravaginally, once a day for 5 days (not funded).

Vaginal administration of metronidazole is safe as exposure is reduced.

Metronidazole oral 2 g stat dose can be used; however, the 7 day regimen is preferred. If breastfeeding, consider delaying for 12 hours following the 2 g stat dose to reduce infant exposure, but this is not essential.

Refer to local guidelines.

Safety of other nitroimidazoles e.g. ornidazole

Ornidazole has not been studied in pregnancy or breastfeeding. Metronidazole should be used in preference to ornidazole.

Key Points

1. Metronidazole can be taken during all stages of pregnancy including the first trimester.
2. Metronidazole is considered safe to use when breastfeeding healthy, full-term infants. As the RID is greater than the usual safety cut-off of 10 %, high doses are not recommended.
3. Metronidazole oral 400 mg BD for 7 days is the preferred regimen for bacterial vaginosis or trichomoniasis in pregnant or breastfeeding women.

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