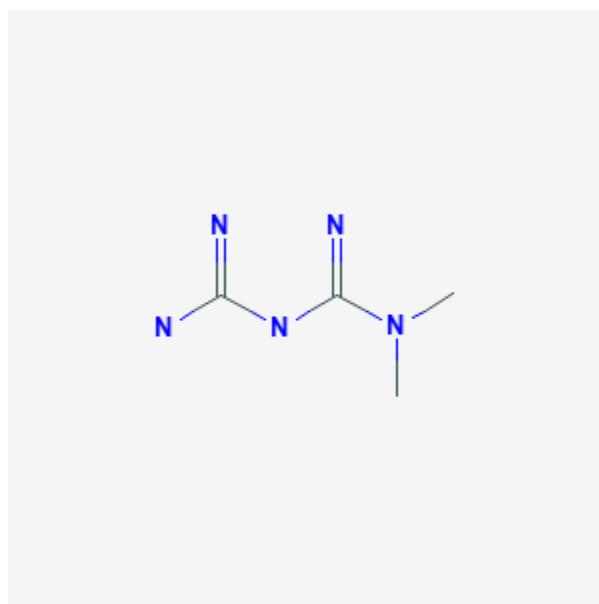




## Metformin

Revised: October 31, 2018.

CASRN: 657-24-9



## Drug Levels and Effects

### Summary of Use during Lactation

Data from well-conducted studies indicate that metformin levels in milk are low and infants would receive less than 0.5% of their mother's weight-adjusted dosage. Milk metformin levels are relatively constant during maternal metformin use, so timing of breastfeeding with respect to the administration times is of little benefit. Although the dose in milk is low, metformin is sometimes detectable in low levels in the serum of breastfed infants. One sizeable prospective study found no adverse effects in breastfed infants. Metformin should be used with caution while nursing newborn and premature infants and those with renal impairment.

### Drug Levels

*Maternal Levels.* Seven women (time postpartum not stated) were taking metformin with a median dose of 1500 mg daily (14 mg/kg daily; range 6.9 to 20 mg/kg daily) orally. Six of the women were taking an immediate-

release product 500 mg three times daily and one was taking 500 mg as a sustained-release product once daily. Six women had milk levels that varied little over 24 hours and averaged 270 mcg/L. One woman had a slight rise in the milk level to about 380 mcg/L at about 4 to 5 hours after the dose. The authors estimated that an exclusively breastfed infant would receive an average daily dosage of 0.04 mg/kg (range 0.02 to 0.06 mg/kg) or 0.28% (range 0.16 to 0.4%) of the maternal weight-adjusted dosage with this maternal dosage regimen.[1][2]

Two lactating women who were 14 and 14.5 months postpartum took a single dose of 500 mg of immediate-release metformin. Milk levels were relatively constant over the next 72 hours with average levels of 130 and 270 mcg/L; a slight peak occurred in one mother 12 hours after the dose. The authors estimated that their infants received 0.11 and 0.25% of the maternal weight-adjusted dosage. Three other mothers were studied in the same way for 12 or 24 hours and had results consistent with the 2 more completely studied mothers.[3]

Three women who had been taking immediate-release metformin 500 mg twice daily orally for at least several days were studied. Relatively stable milk levels averaging 130 to 270 mcg/L in the 3 mothers was found. The authors estimated that an exclusively breastfed infant would receive an average daily dosage of 29 mcg/kg (range 20 to 41 mcg/kg) or 0.2% (range 0.18 to 0.21%) of their mother's weight-adjusted dosage with this dosage regimen.[3]

Five women began metformin 500 mg twice daily on the first day postpartum. Trough and peak (2 hours after the dose) milk levels were collected 4 to 17 days postpartum. The average milk metformin levels were estimated to be 410 mcg/L. The authors estimated that an exclusively breastfed infant would receive an average of 0.65% of the maternal weight-adjusted dosage.[4]

Four women who were taking metformin during pregnancy and lactation provided breastmilk samples at 2- to 3-hour intervals over one dosage interval using a breast pump and emptying both breasts at each sampling time. The total amount of metformin excreted into milk was 0.13 mg with 1.5 grams daily (n = 1) and an average of 0.21 mg with 2 grams daily (n = 3). These values corresponded to daily infant dosages ranging from 0.024 to 0.050 mg/kg and an average of 0.25% (range 0.14 to 0.43%) of the weight-adjusted maternal dosage.[5]

*Infant Levels.* Serum levels were measured in 4 breastfed infants (ages and extent of nursing not stated) whose mothers were taking a median metformin dosage of 1.5 grams daily. In 2, metformin was undetectable (<10 mcg/L) 2.5 hours after the maternal dose, while in the other 2, levels of 50 and 80 mcg/L (10 and 15% of their mother's serum levels) were found at 6 and 5.3 hours after the maternal dose, respectively.[1][2]

Three women 2, 5 and 14 months postpartum who had been taking immediate-release metformin 500 mg twice daily orally for at least several days were studied. Metformin was undetectable (<5 mcg/L) in the serum of the 2 infants (extent of nursing not stated) aged 2 and 14 months in whom it was measured.[2]

## Effects in Breastfed Infants

Seven infants aged 5 to 25 months whose mothers were taking metformin (start date and duration not stated) were judged to be healthy with growth and development progressing as expected. Two of the infants also had normal Denver Developmental Screening tests.[1]

Three infants aged 2, 5 and 14 months whose mothers were taking metformin 500 mg twice daily had no detectable adverse effects from metformin.[3]

In 3 breastfed (extent not stated) infants aged 10 to 11 days postpartum whose mothers were taking an average metformin dosage of 9.6 mg/kg (range 7.5 to 12.4 mg/kg) daily, none of the infants had low blood glucose levels. Their mothers reported no adverse reactions in the infants.[4]

Ninety-two mothers of 111 infants were treated with metformin in a mean dosage of 2.2 grams daily (range 1.5 to 2.55 mg daily) throughout pregnancy and postpartum. A 6-month, nonrandomized, prospective trial followed

61 predominantly breastfed and 50 formula-fed infants of these women. No differences in 3- and 6-month outcomes were found by blinded observers between the 2 groups of infants in height, weight, motor-social development or rates of illness.[6][7]

## Effects on Lactation and Breastmilk

In a study of 250 women who received metformin 500 mg to 2 grams daily in either the immediate- or extended-release formulation for polycystic ovary syndrome, information on breastfeeding was available on 164 women. Of these, 97 (59%) were successful at breastfeeding, 27 (17%) failed, and 40 (27%) made no attempt to breastfeed. Of the 124 who attempted to breastfeed, 78% were successful. Failures were attributed to poor milk production in 4 women, demands of multiple births, infant prematurity, cleft palate and mastitis.[8]

In a follow-up to a placebo-controlled study on metformin use during pregnancy in women with polycystic ovary syndrome, women were asked about the duration and extent of breastfeeding. No difference in breastfeeding in the duration of exclusive or partial breastfeeding was observed between the women who received metformin during pregnancy and those who received placebo.[9]

## Alternate Drugs to Consider

Acarbose, Glipizide, Glyburide, Insulin, Miglitol

## References

1. Hale TW, Kristensen JH, Hackett LP et al. Transfer of metformin into human milk. *Diabetologia*. 2002;45:1509-14. PubMed PMID: 12436333.
2. Hale T, Kristensen J, Hackett L et al. Transfer of metformin into human milk. *Adv Exp Med Biol*. 2004;554:435-6. PubMed PMID: 15384618.
3. Gardiner SJ, Kirkpatrick CM, Begg EJ et al. Transfer of metformin into human milk. *Clin Pharmacol Ther*. 2003;73:71-7. PubMed PMID: 12545145.
4. Briggs GG, Ambrose PJ, Nageotte MP et al. Excretion of metformin into breast milk and the effect on nursing infants. *Obstet Gynecol*. 2005;105:1437-41. PubMed PMID: 15932841.
5. Eyal S, Easterling TR, Carr D et al. Pharmacokinetics of metformin during pregnancy. *Drug Metab Dispos*. 2010;38:833-40. PubMed PMID: 20118196.
6. Glueck CJ, Salehi M, Sieve L, Wang P. Growth, motor, and social development in breast- and formula-fed infants of metformin-treated women with polycystic ovary syndrome. *J Investig Med* 2006;54 (suppl 2):S376. Abstract 21. DOI: [10.2310/6650.2005.x0015](https://doi.org/10.2310/6650.2005.x0015).
7. Glueck CJ, Salehi M, Sieve L, Wang P. Growth, motor, and social development in breast- and formula-fed infants of metformin-treated women with polycystic ovary syndrome. *J Pediatr*. 2006;148:628-32.e2. PubMed PMID: 16737874.
8. Thatcher SS, Jackson EM. Pregnancy outcome in infertile patients with polycystic ovary syndrome who were treated with metformin. *Fertil Steril*. 2006;85:1002-9. PubMed PMID: 16580387.
9. Vanky E, Nordskar J, Leithe H et al. Breast size increment during pregnancy and breastfeeding in mothers with polycystic ovary syndrome: a follow-up study of a randomised controlled trial on metformin versus placebo. *BJOG*. 2012;119:1403-9. PubMed PMID: 22827167.

## Substance Identification

### Substance Name

Metformin

## CAS Registry Number

657-24-9

## Drug Class

Breast Feeding

Lactation

Hypoglycemic Agents

Biguanides