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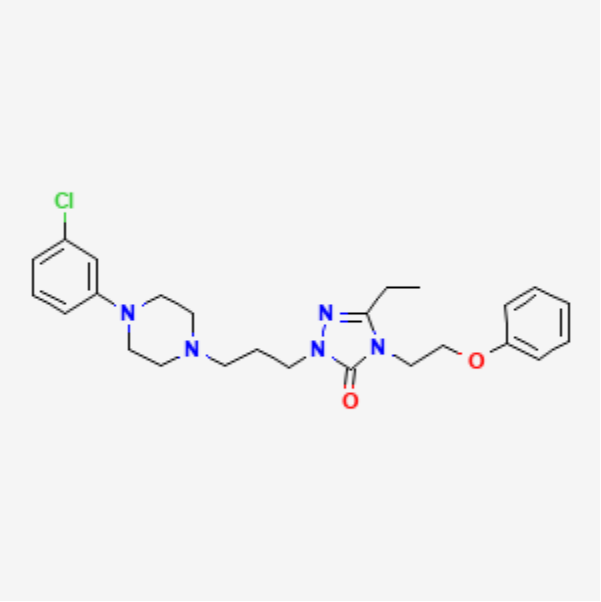
Nefazodone

Revised: January 15, 2024.

CASRN: 83366-66-9



Drug Levels and Effects

Summary of Use during Lactation

Limited information indicates that usual doses of nefazodone produce low but variable levels in milk that would not be expected to cause adverse effects in a breastfed infant, especially if the infant is older than 2 months. However, adverse effects in a breastfed preterm infant have been reported. If nefazodone is required by the mother of an older infant, it is not a reason to discontinue breastfeeding, but until more data become available, other drugs may be preferred, especially while nursing a newborn or preterm infant.

Drug Levels

Nefazodone is metabolized to 4 metabolites, but only hydroxynefazodone is thought to be active as an antidepressant. Its antidepressant activity is considered to be equal to that of nefazodone.[1]

Maternal Levels. The trough milk levels of nefazodone and its metabolites were measured 10 to 15 hours after the previous dose in 3 women who had been taking nefazodone for at least 3 weeks. Dosages were 200 mg twice daily, 50 mg twice daily, and for the third, 50 mg in the morning and 100 mg in the evening. Milk nefazodone levels were 57, 687, and 213 mcg/L, respectively; milk hydroxynefazodone was not quantifiable (<50 mcg/L) in the first 2 mothers and 104 mcg/L in the third.[2] Using the trough milk level data, the estimated minimum intake of these infants would be 0.24, 6.2 and 2% of the maternal weight-adjusted dosage of nefazodone and its active metabolite.

In another paper by the same authors, it appears that 2 of the above mothers were studied again in more detail. One mother who was 21 weeks postpartum had been taking nefazodone 50 mg in the morning and 100 mg in the evening for 6 days. The other mother who was 4 weeks postpartum had been taking nefazodone 200 mg twice daily for 7 months. Four or 5 milk levels were analyzed for drug and metabolites, but values do not appear in the published paper. No metabolites appeared in the milk of the first mother; only nefazodone and hydroxynefazodone were found in the milk of the second mother. The authors estimated that the first infant would receive 0.28 mg/kg daily or 0.4% of the maternal weight-adjusted dosage and the second would receive 0.54 mg/kg daily or 2.2% of the maternal weight-adjusted dosage.[3]

A woman was taking nefazodone 200 mg in the morning and 100 mg in the evening. The highest milk levels of nefazodone occurred 1 to 3 hours after the morning dose, with the highest level of 358 mcg/L occurring 3 hours after the dose. Hydroxynefazodone levels were consistently much lower with a peak level of 32 mcg/L at 2 hours after the dose. The authors estimated that an exclusively breastfed infant would receive 0.34% of the maternal weight-adjusted dosage of nefazodone and its active metabolite with this maternal dosage regimen. Two inactive metabolites would contribute an additional 0.11% of maternal dosage.[4]

Infant Levels. Relevant published information was not found as of the revision date.

Effects in Breastfed Infants

Drowsiness, lethargy, poor feeding and low body temperature occurred in a 2.1 kg breastfed 9-week-old infant who was born preterm at 27 weeks to a mother taking a dose of 300 mg of nefazodone daily. The symptoms were probably caused by nefazodone in breastmilk.[4]

Effects on Lactation and Breastmilk

An observational study looked at outcomes of 2859 women who took an antidepressant during the 2 years prior to pregnancy. Compared to women who did not take an antidepressant during pregnancy, mothers who took an antidepressant during all 3 trimesters of pregnancy were 37% less likely to be breastfeeding upon hospital discharge. Mothers who took an antidepressant only during the third trimester were 75% less likely to be breastfeeding at discharge. Those who took an antidepressant only during the first and second trimesters did not have a reduced likelihood of breastfeeding at discharge.[5] The antidepressants used by the mothers were not specified.

A retrospective cohort study of hospital electronic medical records from 2001 to 2008 compared women who had been dispensed an antidepressant during late gestation (n = 575) to those who had a psychiatric illness but did not receive an antidepressant (n = 1552) and mothers who did not have a psychiatric diagnosis (n = 30,535). Women who received an antidepressant were 37% less likely to be breastfeeding at discharge than women

without a psychiatric diagnosis, but no less likely to be breastfeeding than untreated mothers with a psychiatric diagnosis.[6] None of the mothers were taking nefazodone.

In a study of 80,882 Norwegian mother-infant pairs from 1999 to 2008, new postpartum antidepressant use was reported by 392 women and 201 reported that they continued antidepressants from pregnancy. Compared with the unexposed comparison group, late pregnancy antidepressant use was associated with a 7% reduced likelihood of breastfeeding initiation, but with no effect on breastfeeding duration or exclusivity. Compared with the unexposed comparison group, new or restarted antidepressant use was associated with a 63% reduced likelihood of predominant, and a 51% reduced likelihood of any breastfeeding at 6 months, as well as a 2.6-fold increased risk of abrupt breastfeeding discontinuation. Specific antidepressants were not mentioned.[7]

Alternate Drugs to Consider

Nortriptyline, Paroxetine, Sertraline

References

1. Weissman AM, Levy BT, Hartz AJ, et al. Pooled analysis of antidepressant levels in lactating mothers, breast milk, and nursing infants. Am J Psychiatry 2004;161:1066-78. PubMed PMID: 15169695.
2. Dodd S, Buist A, Burrows GD, et al. Determination of nefazodone and its pharmacologically active metabolites in human blood and breast milk by high-performance liquid chromatography. J Chromatogr B Biomed Sci Appl 1999;730:249-55. PubMed PMID: 10448960.
3. Dodd S, Maguire KP, Burrows GD, Norman TR. Nefazodone in the breast milk of nursing mothers: A report of two patients. J Clin Psychopharmacol 2000;20:717-8. PubMed PMID: 11106156.
4. Yapp P, Ilett KF, Kristensen JH, et al. Drowsiness and poor feeding in a breast-fed infant: Association with nefazodone and its metabolites. Ann Pharmacother 2000;34:1269-72. PubMed PMID: 11098340.
5. Venkatesh KK, Castro VM, Perlis RH, Kaimal AJ. Impact of antidepressant treatment during pregnancy on obstetric outcomes among women previously treated for depression: An observational cohort study. J Perinatol 2017;37:1003-9. PubMed PMID: 28682318.
6. Leggett C, Costi L, Morrison JL, et al. Antidepressant use in late gestation and breastfeeding rates at discharge from hospital. J Hum Lact 2017;33:701-9. PubMed PMID: 28984528.
7. Grzeskowiak LE, Saha MR, Nordeng H, et al. Perinatal antidepressant use and breastfeeding outcomes: Findings from the Norwegian Mother, Father and Child Cohort Study. Acta Obstet Gynecol Scand 2022;101:344-54. PubMed PMID: 35170756.

Substance Identification

Substance Name

Nefazodone

CAS Registry Number

83366-66-9

Drug Class

Breast Feeding

Lactation

Milk, Human

Antidepressive Agents

Serotonin and Noradrenaline Reuptake Inhibitors