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Clonazepam

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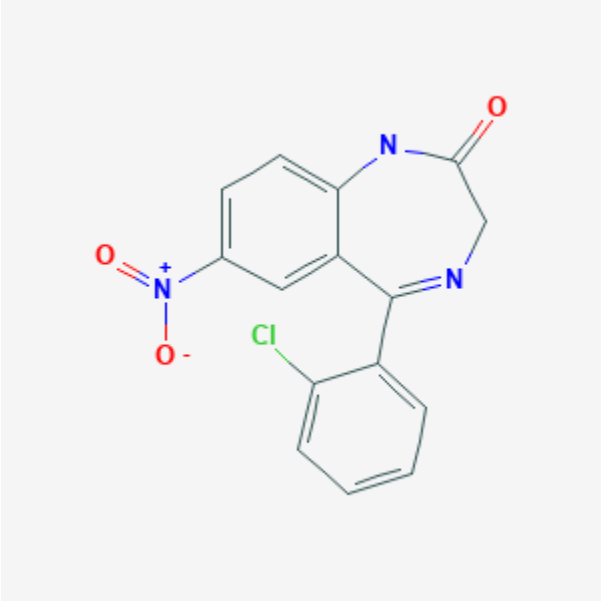
CASRN: 1622-61-3



Drug Levels and Effects

Summary of Use during Lactation

Maternal clonazepam occasionally causes sedation in their breastfed infants, especially when given with other central nervous system depressants. Monitor the infant for drowsiness, adequate weight gain, and developmental milestones, especially in younger, exclusively breastfed infants and when using combinations of psychotropic drugs. Monitoring of the infant's serum concentration may be indicated if excessive sedation occurs. Because it has a long half-life, a safer, shorter-acting drug should be used as rather than clonazepam.[1][2] An expert consensus guideline indicates that low-dose clonazepam is an acceptable choice for refractory restless leg syndrome during lactation.[3]

Drug Levels

In published reports of anticonvulsant use during breastfeeding, most women were taking a combination of anticonvulsants. Some other anticonvulsants (e.g., phenytoin, carbamazepine) stimulate the metabolism of other drugs including anticonvulsants, whereas others (e.g., valproic acid) inhibit the metabolism of other drugs. Therefore, the relationship of the maternal dosage to the concentration in breastmilk can be quite variable, making calculation of the weight-adjusted percentage of maternal dosage less meaningful than for other drugs in this database.

Maternal Levels. A breastfed newborn infant whose mother was taking clonazepam during pregnancy and lactation (dosage not stated) had serum levels that increased from about 23 mcg/L at 24 hours of age to 43 mcg/L at 96 hours of age.[4]

Repeated milk clonazepam levels were between 11 and 13 mcg/L in a woman taking clonazepam in an unstated dosage.[5]

A mother taking clonazepam 2 mg twice daily had severl milk level measurements on days 2 to 4 postpartum. The highest milk level was 10.7 mcg/L 4 hours after a dose. The authors calculated that an exclusively breastfed infant would receive a maximum of 2.5% of the maternal weight-adjusted dosage of clonazepam.[6]

A mother who was taking clonazepam 6 mg daily and carbamazepine 1400 mg daily had a milk clonazepam level of 12 mcg/L. No details on sampling times were provided.[7]

Infant Levels. One preterm infant had cord blood levels of 19 mcg/L and was not breastfed until 72 hours after delivery. The infant's serum clonazepam level was 2.9 mcg/L at 120 hours after birth, and 1 mcg/L at day 14. The mother's serum level was 32 mcg/L at delivery and repeated milk clonazepam levels were between 11 and 13 mcg/L.[5]

A newborn infant was breastfeeding during a maternal dosage of clonazepam 2 mg twice daily. A pooled sample of infant serum from days 2 to 4 of age contained 4.7 mcg/L of clonazepam.[6]

Ten of 11 breastfed infants whose mothers were taking clonazepam in dosages of 0.25 to 2 mg daily had no detectable (assay limit varied from 5 to 14 mcg/L) clonazepam or metabolites in serum. The infants' average age was 7.9 weeks, but 6 were under 1 month of age. One 1.9 week-old-infant whose mother was taking clonazepam 0.5 mg daily had a serum concentration of 22 mcg/L.[8]

One author reported a mother who was taking clonazepam 6 mg daily and carbamazepine 1400 mg daily. Her breastfed (extent not stated) infant had a serum clonazepam level of 20 mcg/L, while the mother's serum level was 50 mcg/L.[7]

Effects in Breastfed Infants

Excessive periodic breathing and prolonged apnea and cyanosis occurred in a newborn at 6 hours after birth at 36 weeks gestation and reoccurred repeatedly up to 10 days of age. The neonate was breastfed starting at 72 hours after delivery and her mother took clonazepam (dose not stated) during pregnancy and lactation. The repeated periodic breathing episodes continued up to 10 weeks of age and were possibly related to clonazepam in breastmilk. A neurodevelopmental examination was normal at 5 months of age.[5]

The infant of a mother taking clonazepam 1 mg daily during pregnancy and lactation was rated as highly apathetic and had decreased weight increase and slight neurologic signs at 4 weeks of age, but normal intelligence at 6 years of age.[9]

None of 11 infants whose mothers were taking clonazepam in dosages ranging from 0.25 to 2 mg daily (including 4 who were taking other psychotropic drugs also) had any side effects reported by their mothers. The infants' average age was 7.9 weeks, but 6 were under 1 month of age.[8]

One author reported a mother who was taking clonazepam 6 mg daily and carbamazepine 1400 mg daily. The infant had serum clonazepam levels of about 40% of the mother's serum level. Her infant was described as "somewhat lazy at the breast and tired."[7]

In a telephone follow-up study, 124 mothers who took a benzodiazepine while nursing reported whether their infants had any signs of sedation. Twenty-two mothers took clonazepam while breastfeeding and 1 reported sedation in her infant. She was taking clonazepam 0.25 mg twice daily, flurazepam 15 mg daily, 1 mg of bupropion daily, and 0.75 mg of risperidone daily.[10]

All adverse reactions in breastfed infants reported in France between January 1985 and June 2011 were compiled by a French pharmacovigilance center. Of 174 reports, clonazepam was reported to cause adverse reactions in 5 infants and to be one of the drugs most often suspected in serious adverse reactions, primarily sedation. One two-month old infant had well-documented hypotonia, somnolence and apnea caused by clonazepam in breastmilk.[11]

Effects on Lactation and Breastmilk

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

Alternate Drugs to Consider

(Sedative) Lorazepam, Oxazepam

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Substance Identification

Substance Name

Clonazepam

CAS Registry Number

1622-61-3

Drug Class

Breast Feeding

Lactation

Anticonvulsants

Benzodiazepines