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Ethosuximide

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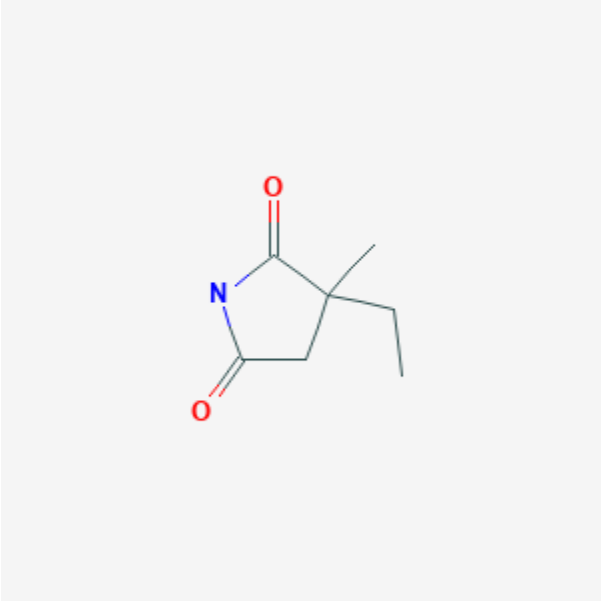
CASRN: 77-67-8



Drug Levels and Effects

Summary of Use during Lactation

Average ethosuximide dosages of 50 to 60% of the maternal weight-adjusted dosage are excreted in human milk and infant plasma levels of 25 to 30% of maternal levels are common. Although no adverse effects attributable solely to ethosuximide in breastmilk have been reported, monitor the infant for drowsiness, adequate weight gain, and developmental milestones, especially in younger, exclusively breastfed infants and when using combinations of anticonvulsants. Measurement of an infant serum level might help rule out toxicity if there is a concern.

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. An epileptic woman was taking primidone 250 mg and ethosuximide 500 mg orally every 12 hours. She did not nurse her infant, but had milk flow maintained to collect milk for study. Breastmilk ethosuximide levels were 55 to 70 mg/L on 4 occasions (times with respect to doses not stated) on days 3 to 5 postpartum.[1]

Four ethosuximide breastmilk levels were measured between days 3 and 32 postpartum at unstated times after the dose in an unstated number of women who were taking ethosuximide and other anticonvulsants in unstated dosages. Ethosuximide milk levels averaged 21.3 mg/L (range 18 to 24 mg/L), while maternal serum levels averaged 29.3 mg/L.[2]

An epileptic woman was taking oral ethosuximide 250 mg daily as a single agent during pregnancy and breastfeeding. Breastmilk samples were measured on several occasions during the first 4 months postpartum. Maternal serum and milk levels increased to higher levels between 1 and 2 months postpartum and then decreased, although the times of collection with respect to the doses were not reported. Milk levels on day 3 postpartum were about 31 mg/L, increased to about 55 mg/L at 1 month postpartum and decreased to about 42 mg/L at 4.5 months postpartum.[3]

Breastmilk ethosuximide levels were measured 1 to 4 times in 5 mothers who were taking ethosuximide alone (1 woman) or with other anticonvulsants (4 women). Ethosuximide milk levels averaged 49.5 mg/L (range 27 to 68.5 mg/L).[4] Using the average of the reported milk levels and maternal doses reported, exclusively breastfed infants would receive an average of 62% (range 32 to 113%) of the maternal weight-adjusted dosage.

Three women taking ethosuximide alone and one taking ethosuximide and phenytoin had colostrum levels that were 79 to 103% of maternal plasma levels; at 1.5 to 4.5 months postpartum, the average ratio was 1.[5]

A mother taking ethosuximide 1 gram daily during pregnancy and postpartum had breastmilk levels measured during the first week postpartum. The breastmilk concentration was 36 mg/L which was 92% of the maternal serum concentration.[6]

Two epileptic women who were taking ethosuximide had breastmilk samples measured. One mother who was taking ethosuximide 1 g daily plus carbamazepine 1.2 g daily had a breastmilk ethosuximide level of 33.9 mg/L at 2 weeks postpartum. The other mother taking ethosuximide monotherapy 750 mg daily had a milk level of 52.5 mg/L at 3.5 months postpartum.[7] Their infants would receive 35 and 57% of the maternal weight-adjusted dosage if they were exclusively breastfed.

Infant Levels. An exclusively breastfed infant whose mother was taking ethosuximide 250 mg daily began nursing (extent not stated) on day 2 postpartum and continued through 4.5 months of observation. Infant serum levels increased in parallel to maternal serum and breastmilk concentrations. The infant serum level was 22 mg/L on day 3 and reached a maximum of 29.5 mg/L at 1 month of age before decreasing to about 8.5 mg/L at 4.5 months of age. Intensive sampling of infant serum levels at 4 and 4.5 months of age found little fluctuation during the day and infant plasma levels were 24 to 30% of simultaneous maternal serum levels on the 2 days.[3]

Three fully breastfed infants whose mothers were taking ethosuximide had plasma levels that were 24 to 75% of their mother's average plasma levels. A fourth infant who was mostly formula-fed had undetectable plasma levels.[5]

The breastfed infant of a mother taking ethosuximide monotherapy 750 mg daily had a serum level of 16.9 mg/L which was 32% of the simultaneous maternal plasma level.[7]

Effects in Breastfed Infants

An infant whose mother was taking ethosuximide 250 mg daily began exclusive breastfeeding on day 2 postpartum and continued through 4.5 months of observation. The infant developed normally during this time and had no signs of an adverse reaction.[3]

Sedation, poor sucking and poor weight gain during the first 4 weeks of life occurred in a breastfed newborn whose mother was taking ethosuximide.[4] The reaction was possibly caused by ethosuximide in breastmilk; however, the mother was also taking primidone and valproic acid.

Three fully breastfed infants and a mostly formula-fed whose mothers were taking ethosuximide had no adverse reactions observed during the first 1.5 to 4.5 months of life.[5]

Effects on Lactation and Breastmilk

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

References

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Substance Identification

Substance Name

Ethosuximide

CAS Registry Number

77-67-8

Drug Class

Breast Feeding

Lactation

Anticonvulsants