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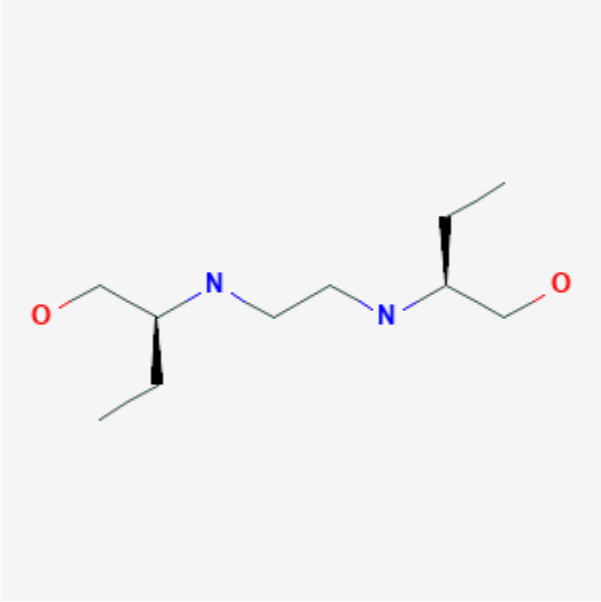
NLM Citation: Drugs and Lactation Database (LactMed) [Internet]. Bethesda (MD): National Library of Medicine (US); 2006-. Ethambutol. [Updated 2018 Oct 31].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Ethambutol

Revised: October 31, 2018.

CASRN: 74-55-5



Drug Levels and Effects

Summary of Use during Lactation

Limited information indicates that maternal doses of ethambutol up to 15 mg/kg daily produce low levels in milk and would not be expected to cause any adverse effects in breastfed infants, especially if the infant is older than 2 months. The amount of ethambutol in milk is insufficient to treat tuberculosis in the breastfed infant. The Centers for Disease Control and Prevention and other professional organizations state that breastfeeding should not be discouraged in women taking ethambutol.[1][2][3]

Drug Levels

Maternal Levels. Information available on ethambutol excretion into breastmilk is limited to 2 cases which were originally reported only as personal communications. One mother had milk levels measured twice while taking ethambutol 15 mg/kg daily. Milk levels were 1.5 mg/L 3 hours after the dose and 1.4 mg/L during a 2-hour

period after the dose, but collection methods were not stated. Another woman reportedly had a milk level of 4.6 mg/L which was similar to her plasma level, but her dosage and the milk collection time were not stated. Using these data, reviewers estimated that a breastfed infant would receive 0.51 to 0.86 mg/kg daily which is 3.4 to 5.7% of an infant's therapeutic dose.[4] Using the above sparse data, some authors have estimated that a fully breastfed infant would receive a maximum dose of 0.69 mg/kg daily,[5] which is 4.6% of the maternal weight-adjusted dosage.

A physiologically based pharmacokinetic model of ethambutol predicted that a fully breastfed infant would receive a dose of 0.08 mg/kg daily with a maternal dosage of 24.5 mg/kg daily, which is 0.3% of the weight-adjusted maternal dosage.[6]

Infant Levels. Measured infant serum levels have not been reported. A physiologically based pharmacokinetic model of ethambutol predicted that a fully breastfed infant would achieve a maximum serum concentration of 0.098 mg/L with a maternal dose of 24.5 mg/kg daily.[6]

Effects in Breastfed Infants

In one uncontrolled study, 6-beta-hydroxycortisol levels were measured in 10 male infants whose mothers had tuberculosis and took ethambutol 1 gram daily plus isoniazid 300 mg daily and the infants of mothers (apparently without tuberculosis) who took no chronic drug therapy. The infants of mothers taking the antituberculars had consistently lower 6-beta-hydroxycortisol levels on 8 occasions at 15-day intervals from 90 to 195 days of age, but these differences were statistically significant on days 120 and 195 only. The authors attributed the lower levels to inhibition of hepatic metabolism of cortisol to 6-beta-hydroxycortisol by the antitubercular drugs in milk.[7] However, ethambutol is not known to inhibit drug metabolism, so if the effect occurs it is more likely caused by isoniazid.

One woman taking rifampin 450 mg, isoniazid 300 mg and ethambutol 1200 mg daily during pregnancy and rifampin 450 mg and isoniazid 300 mg for the first 7 months of lactation (extent not stated). The infant was born with mildly elevated serum liver enzymes which persisted for to 1 (alanine transferase) to 2 years (aspartate transaminase), but had no other adverse reactions.[8]

Ethambutol was used as part of a seven-drug regimen to treat a pregnant woman with multidrug-resistant tuberculosis during the second and third trimesters of pregnancy and postpartum. The infant was breastfed (extent and duration not stated). At age 4.6 years, the child was developing normally except for a mild speech delay.[9]

Two mothers in Turkey were diagnosed with tuberculosis at the 30th and 34th weeks of pregnancy. They immediately started isoniazid 300 mg, rifampin 600 mg, pyridoxine 50 mg daily for 6 months, plus pyrazinamide 25 mg/kg and ethambutol 25 mg/kg daily for 2 months. Both mothers breastfed their infants (extent not stated). Their infants were given isoniazid 5 mg/kg daily for 3 months prophylactically. Tuberculin skin tests were negative after 3 months and neither infant had tuberculosis at 1 year of age. No adverse effects of the drugs were mentioned.[10]

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

Ethambutol

CAS Registry Number

74-55-5

Drug Class

Breast Feeding

Lactation

Antitubercular Agents