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Dipyrone

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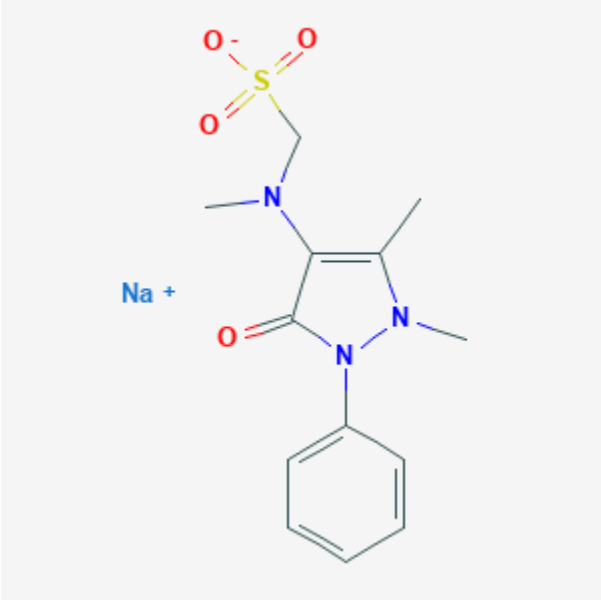
CASRN: 68-89-3



Drug Levels and Effects

Summary of Use during Lactation

Dipyrone is not approved for marketing in the United States by the U.S. Food and Drug Administration or in Canada and many European countries because of its adverse reactions, including agranulocytosis. However, it is widely used in other countries during labor and breastfeeding.[1][2][3][4] After ingestion by the mother, dipyrone and its metabolites appear in breastmilk in rather large amounts. It is found in the blood and urine of breastfed infants and can cause pharmacological effects in the breastfed infant. One case of cyanotic episodes in a breastfed infant was attributed to dipyrone in breastmilk. The drug and metabolites are eliminated from the breastmilk by 48 hours after a dose and one manufacturer recommends no breastfeeding for 48 hours after a dose.[5] Safer alternatives are available for analgesia during breastfeeding.

Drug Levels

Maternal Levels. A woman took 3 doses of dipyrone 500 mg orally, over a 16-hour period. The dipyrone concentration in breastmilk was 4.3 mg/L 24 hours after the last dose.[6]

Ten women who were 3 to 5 days postpartum were given a single dose of 1 gram of dipyrone orally. Milk concentrations of its four metabolites were measured in breastmilk. In 8 of the patients, milk samples were taken once between 2.5 to 5.5 hours after the dose; all 4 metabolites were detected in the milk of all mothers. The total concentration of all the metabolites averaged 20.5 mg/L at the times sampled. In 2 of the women, milk samples were obtained before drug administration and before each feeding for 3 days. By 48 hours after the dose all metabolites were absent from breastmilk.[7] Using data from the 2 mothers with extensive sampling, an exclusively breastfed infant would receive an average of 6.8% of the maternal weight-adjusted dipyrone dosage in the form of metabolites.

In a survey of breastmilk in a rural Chilean hospital, dipyrone was detectable in the breastmilk of 8 out of 15 mothers tested.[1]

Infant Levels. Dipyrone was detected in a breastfed infant's serum and urine after his mother took 1500 mg of dipyrone over a 16-hour period. The infant's dipyrone serum concentration was 3.2 mg/L and urine concentration was 3.74 mg/L.[6]

Effects in Breastfed Infants

A 42-day-old breastfed infant had 2 cyanotic episodes within 30 minutes after his mother took 3 doses of dipyrone 500 mg orally, 18, 7 and 2 hours before the first episode. A third episode occurred 24 hours after admission to the hospital. Dipyrone was detected in the mother's breastmilk 24 hours after the last dose and in the infant's serum and urine. No explanation could be found for the cyanotic episodes other than dipyrone and after suspending maternal dipyrone intake, no further episodes occurred in the infant up to age 3 years. The reaction is rated as possibly caused by dipyrone in breastmilk.[6]

In a blinded study, mothers who were at least 3 days postpartum and requesting analgesia for postpartum uterine pain were given either 1 gram of dipyrone or placebo. The infants of mothers who received dipyrone cried fewer times and for shorter durations in the 14 hours after drug administration than the infants of mothers who received placebo. This effect was more apparent in infants who demand fed than in those who fed on a fixed schedule.[8] Although this study appears to demonstrate a pharmacologic effect in the infants from dipyrone in milk, there is no clear explanation for the change in infant behavior.

A multicenter case-control study in Brazil compared 231 children who developed leukemia before 2 years of age with 411 children with various other nonmalignant diseases. Mothers were interviewed to ascertain their analgesic use during pregnancy and lactation. Nursing mothers who took dipyrone during the three months after delivery had a 2-fold risk of having a child with acute lymphocytic leukemia and a 3.87-fold risk in having rearrangement of the MLL gene in infants under one year of age.[9]

Effects on Lactation and Breastmilk

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

Alternate Drugs to Consider

Acetaminophen, Ibuprofen, Morphine

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Substance Identification

Substance Name

Dipyrone

CAS Registry Number

68-89-3

Drug Class

Breast Feeding

Lactation

Analgesic Agents

Nonsteroidal Antiinflammatory Agents