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Nelfinavir

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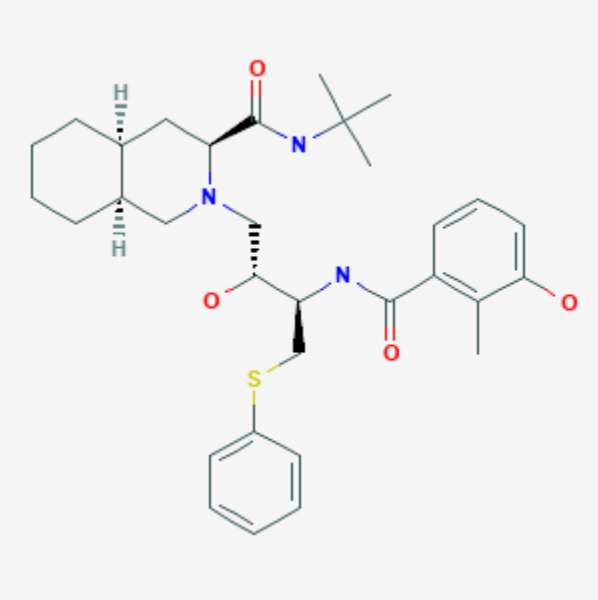

Drug Levels and Effects

Summary of Use during Lactation

In the United States and other developed countries, HIV-infected mothers should generally not breastfeed their infants. Published experience with nelfinavir during breastfeeding is limited. In countries in which no acceptable, feasible, sustainable and safe replacement feeding is available, World Health Organization guidelines recommend that all women with an HIV infection who are pregnant or breastfeeding should be maintained on antiretroviral therapy for at least the duration of risk for mother-to-child transmission. Mothers should exclusively breastfeed their infants for the first 6 months of life; breastfeeding with complementary feeding should continue through at least 12 months of life up to 24 months of life.[1] The first choice regimen for nursing mothers is tenofovir, efavirenz and either lamivudine or emtricitabine. If these drugs are unavailable, alternative regimens include: 1) zidovudine, lamivudine and efavirenz; 2) zidovudine, lamivudine and

nevirapine; or 3) tenofovir, nevirapine and either lamivudine or emtricitabine. Exclusively breastfed infants should also receive 6 weeks of prophylaxis with nevirapine.[2][3]

Drug Levels

Maternal Levels. Five women were receiving nelfinavir 1250 mg twice daily as part of a highly-active antiretroviral combination regimen. During the first 5 days postpartum milk was collected just before and 2 hours after the dose of nelfinavir. Breastmilk nelfinavir concentrations ranged between 6 and 24% of the maternal serum concentration. The M8 metabolite was not detectable in milk. Further details on the timing, or actual breastmilk concentrations were not provided.[4]

Twenty-six samples of breastmilk and maternal serum were obtained at 6, 12 and 24 weeks postpartum from mothers taking nelfinavir as part of a combination of antiretrovirals. The nelfinavir dosage the mothers were taking was not stated in the abstract. The median breastmilk concentrations of nelfinavir were 49 mcg/L at a median of 14 hours after the last dose at 6 weeks postpartum (10 samples), 51 mcg/L at a median of 14 hours after the last dose at 12 weeks postpartum (7 samples), and 184 mcg/L at a median of 16 hours after the last dose at 24 weeks postpartum (9 samples). Median milk concentrations were 8% (interquartile range 4 to 14%) of maternal plasma concentrations.[5] In a related study by the same authors, the nelfinavir milk to plasma ratio was found to be 0.21 in 29 patients.[6]

Twenty-six breastfeeding Kenyan mothers were receiving oral nelfinavir 1.25 grams twice daily in addition to zidovudine and lamivudine for HIV infection. Blood and breastmilk samples were collected at delivery, and at 2, 6, 14, and 24 weeks postpartum at various times after the previous dose of nelfinavir. The 104 breastmilk samples were analyzed for nelfinavir and its active metabolite, hydroxyl-t-butylamidenelfinavir (M8). Median breastmilk nelfinavir concentrations were 83 mcg/L at birth, 358 mcg/L at 2 weeks, 286 mcg/L at 6 weeks, 233 mcg/L at 14 weeks and 180 mcg/L at 24 weeks postpartum. The M8 metabolite was undetectable (<10 mcg/L) in most samples; the highest concentrations found at any time was 32 mcg/L. Nelfinavir levels in breastmilk tended to drop during the dosing interval but M8 levels were relatively stable.[7]

Infant Levels. The infants of postpartum mothers taking nelfinavir as part of a combination of antiretrovirals had undetectable serum nelfinavir concentrations by HPLC/MS analysis. The nelfinavir dosage the mothers were taking and times of infant plasma sampling were not stated in the abstract. Nelfinavir was not detectable in infant plasma at 6, 12 or 24 weeks of age.[5]

Twenty-six breastfeeding Kenyan mothers were receiving oral nelfinavir 1.25 grams twice daily in addition to zidovudine and lamivudine for HIV infection. Infant blood samples were obtained at various times between 2 and 24 weeks postpartum. Nelfinavir and M8 concentration were undetectable (<10 mcg/L) for 20 of the 28 infant blood samples. The highest concentrations detected were 30 mcg/L for nelfinavir and 32 mcg/L for M8 which are less than the MIC for the HIV virus.[7]

Effects in Breastfed Infants

A study compared the frequency of rash, hepatotoxicity, and hyperbilirubinemia among 464 breastfed infants whose mothers were taking either nelfinavir (n = 206) or nevirapine (n = 258) along with zidovudine and lamivudine for HIV infection during pregnancy and postpartum. Infants were examined during the first, second and sixth weeks postpartum. Moderate rash occurred in 7 (2.7%) of the infant exposed to nevirapine and one (0.5%) infant exposed to nelfinavir. Rash occurred at a median of 2 weeks postpartum. Four infants (1.9%) exposed to nelfinavir developed hepatotoxicity (3 moderate and 1 severe) and none exposed to nevirapine. Twenty-one infants (4.5%) developed high-risk hyperbilirubinemia, all prior to 48 hours of age, but there was no difference in exposure between the two drugs.[8]

Effects on Lactation and Breastmilk

Gynecomastia has been reported among men receiving highly active antiretroviral therapy. Gynecomastia is unilateral initially, but progresses to bilateral in about half of cases. No alterations in serum prolactin were noted and spontaneous resolution usually occurred within one year, even with continuation of the regimen.[9][10][11] Some case reports and in vitro studies have suggested that protease inhibitors might cause hyperprolactinemia and galactorrhea in some male patients,[12][13] although this has been disputed.[14] The relevance of these findings to nursing mothers is not known. The prolactin level in a mother with established lactation may not affect her ability to breastfeed.

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Substance Identification

Substance Name

Nelfinavir

CAS Registry Number

159989-64-7

Drug Class

Breast Feeding

Lactation

Anti-Infective Agents

Anti-HIV Agents

Antiviral Agents

Anti-Retroviral Agents

HIV Protease Inhibitors