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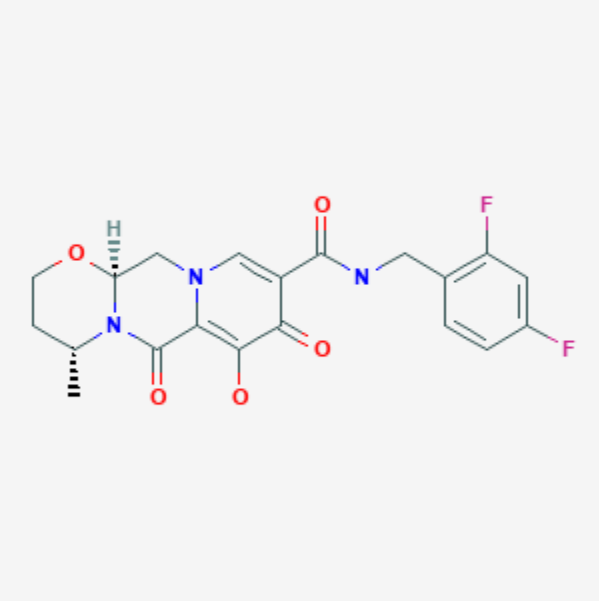
Dolutegravir

Revised: March 16, 2020.

CASRN: 1051375-16-6



Drug Levels and Effects

Summary of Use during Lactation

Dolutegravir is detectable in maternal milk and infant plasma during breastfeeding. It appears that elimination by newborn infants is prolonged. In the United States and other developed countries, HIV-infected mothers should generally not breastfeed their infants. No published information is available on the use of dolutegravir during breastfeeding. 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. An HIV-positive mother took a combination tablet containing dolutegravir 50 mg, abacavir sulfate 600 mg and lamivudine 300 mg (Triumeq) once daily. Her breastmilk dolutegravir concentrations were measured periodically over a 10-month period and averaged about 10 mg/L at 11 hours after the dose. The authors estimated a daily infant dosage of 15 mcg/kg of dolutegravir.[4]

Two HIV-positive women taking doultegravir (dose not stated, but presumably 50 mg daily) plus 2 unspecified nonnucleoside reverse transcriptase inhibitors donated two milk samples each. At 2 weeks postpartum, steady-state breastmilk dolutegravir levels in one woman were 154.2 mcg/L at 4 hours after the dose and 40.9 mcg/L at 24 hours after a dose. In the other woman, steady-state breastmilk dolutegravir levels were 116.3 mcg/L at 3 hours after the dose and 17.7 mcg/L at 24 hours after a dose. At 2 and 9 days, respectively, after discontinuing the drug, breastmilk levels were undetectable (<10 mcg/L).[5]

Twenty-nine pregnant HIV-positive women were randomized to receive an antiretroviral regimen containing oral dolutegravir 50 mg once daily. Of these, 17 women underwent extensive postpartum sampling of breastmilk and maternal serum at a median of 10 days postpartum. Median dolutegravir peak concentration in milk was 84.6 mcg/L and minimum of 22.3 mcg/L. Only one woman had 14 mcg/L of dolutegravir in milk at 48 hours; all other milk samples at 48, 72 and 96 hours after drug discontinuation were negative for dolutegravir.[6]

Infant Levels. An HIV-positive mother took a combination tablet containing dolutegravir 50 mg, abacavir sulfate 600 mg and lamivudine 300 mg (Triumeq) once daily. Her infant had a plasma dolutegravir concentration of 10 mg/L during the period of exclusive breastfeeding up to about 30 weeks postpartum. As supplemental feed was introduced, the plasma concentrations dropped to about 0.3 mg/L at 35 weeks and to 0 with no breastfeeding after about 50 weeks postpartum.[4]

Two HIV-positive women taking doultegravir (dose not stated, but presumably 50 mg daily) plus 2 unspecified nonnucleoside reverse transcriptase inhibitors breastfed their infants (extent not stated, but presumably exclusively). At 2 weeks postpartum, the plasma levels in one infant were 67.8 mcg/L and 75.5 mcg/L at 4 and 24 hours after the maternal dose, respectively. Two days after drug discontinuation, the infant had a plasma level of 58.6 mcg/L at a time when the maternal plasma level was 103.8 mcg/L. In the other infant, the plasma level was 16.3 mcg/L at 24 hours after the maternal dose.[5]

Seventeen women were receiving oral dolutegravir 50 mg daily as part of a study. Their breastfed infants had serum levels obtained at a median of 10 days postpartum. Their median dolutegravir peak serum concentration was 66.7 mcg/L and minimum was 60.9 mcg/L. After discontinuation of maternal dolutegravir, detectable concentrations were noted in 100%, 80% and 80% of breastfed infants at 48, 72 and 96 hours following final maternal dose, respectively. The ration of paired maternal and infant serum concentrations was 0.03 at the peak and 0.08 at the trough.[6]

Effects in Breastfed Infants

An HIV-positive mother took a combination tablet containing dolutegravir 50 mg, abacavir sulfate 600 mg and lamivudine 300 mg (Triumeq) once daily. Her infant was exclusively breastfed for about 30 weeks and partially breastfed for about 20 weeks more. No obvious side effects were noted.[4]

A study that randomized nursing mothers to anti-HIV regimens containing either dolutegravir (n = 29) or efavirenz (n = 31), the regimens were reportedly well tolerated by the infants and no difference in infant adverse reactions were noted between the two regimens.[7]

Effects on Lactation and Breastmilk

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

Alternate Drugs to Consider

Lamivudine, Nelfinavir, Nevirapine, Zidovudine

References

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Substance Identification

Substance Name

Dolutegravir

CAS Registry Number

1051375-16-6

Drug Class

Breast Feeding

Lactation

Anti-HIV Agents

Antiviral Agents

Anti-Retroviral Agents

HIV Integrase Inhibitors