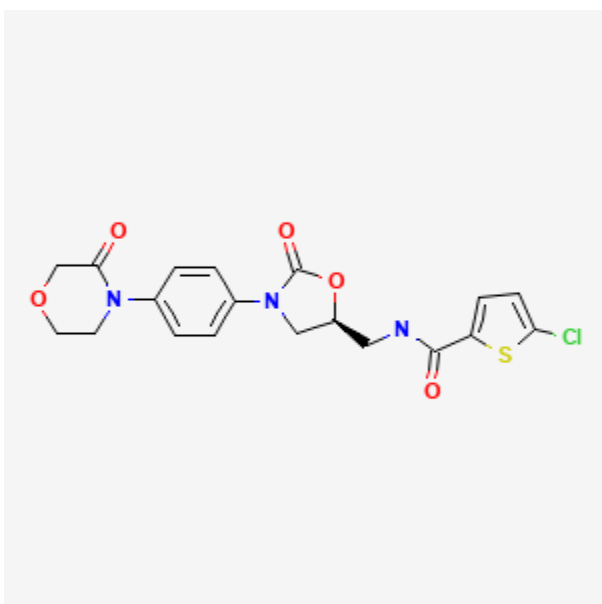




Rivaroxaban

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CASRN: 366789-02-8



Drug Levels and Effects

Summary of Use during Lactation

Several case reports and one thorough pharmacokinetic analysis consistently indicate that maternal doses of rivaroxaban of 15 to 30 mg daily produce low levels in milk that are considerably below doses (<2%) required for anticoagulation in infants. Plasma rivaroxaban levels in two breastfed infants were undetectable. If the mother requires rivaroxaban, it is not a reason to discontinue breastfeeding.[1]

Drug Levels

Maternal Levels. A 40-year-old woman developed bilateral pulmonary embolism and peripartum cardiomyopathy following cesarean section. She initially received enoxaparin, but was switched to oral

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rivaroxaban 15 mg twice daily after 2 days. On day 3 of rivaroxaban, complete milk collections from both breasts were obtained before and at 3, 6, and 10 hours after the morning dose. Blood samples were taken at the same times. The authors calculated that a fully breastfed infant would receive 2.4 mcg/kg over the 10-hour period, which would be 1.3% of the maternal weight-adjusted dosage.[2]

A 38-year-old woman with antiphospholipid syndrome began rivaroxaban 15 mg (0.19 mg/kg) daily at 5 days postpartum for prophylaxis of deep vein thrombosis. On two separate days, 7 samples of milk were taken over a 24-hour period. Values were similar at the same times on each day. A mean peak value of 53.9 mcg/L occurred at 6 hours after the dose and the average milk concentration was 22.7 mcg/L. The half-life in milk was 4.7 hours. The estimated daily dose that a fully breastfed infant would receive was 3.4 mcg/kg daily, which corresponded to 1.8% of the maternal weight-adjusted dosage.[3]

Two postpartum women were prescribed rivaroxaban, one for stroke and the other for a pulmonary embolism. Each began therapy with 15 mg twice daily for 21 days, then 20 mg daily. Both patients provided several steady-state milk samples over the dosage interval during each regimen. After the 15 mg dose, a mean peak value of 300 mcg/L occurred 1 hour after the dose and the average milk concentration was 160 mcg/L. The estimated daily dose that a fully breastfed infant would receive was 10 mcg/kg every 12 hours, which corresponded to 5% of the maternal weight-adjusted dosage. After the 20 mg dose, the mean peak value of 260 mcg/L occurred 2 hours after the dose and the average milk concentration was 70 mcg/L. The estimated daily dose that a fully breastfed infant would receive was 10 mcg/kg daily, which corresponded to 4% of the maternal weight-adjusted dosage.[4]

Two nursing mothers who were 8 months postpartum received a single oral dose of 20 mg of rivaroxaban. Blood and milk samples were obtained before the dose and at 2.5, 6, 10, 12, and 24 hours after the dose. The peak rivaroxaban milk level of about 90 mcg/L occurred at 2.5 hours after the dose. The average milk level over 24 hours was 28.9 mcg/L, which corresponds to a daily infant dosage of 4.3 mcg/kg daily and a relative infant dose of 1.63% of the maternal weight-adjusted dosage. The daily dosage of rivaroxaban in milk is about 0.7% of the estimated infant daily dosage required for anticoagulation.[5]

Two mothers receiving rivaroxaban 15 mg (0.22 and 0.25 mg/kg) daily beginning 3 days postpartum. Trough milk samples on day 5 postpartum taken just before a dose were 6.7 and 116.2 mcg/L; approximate peak milk samples taken 2 hours after breastfeeding were 39 and 59.2 mcg/L. These values were entered into a population pharmacokinetic model to obtain maternal plasma and milk pharmacokinetic parameters. Using a daily dosage of 150 mL/kg of milk, and the average concentrations of rivaroxaban in milk, the infants' daily dosages would be 0.0018 and 0.0031 mg/kg, which translate into relative infant dosages of 0.82 and 1.27%, respectively in the two mothers' infants.[6]

Infant Levels. Three newborn infants (1 pair of twins) were breastfed by two mothers receiving rivaroxaban 15 mg daily (0.22 and 0.25 mg/kg daily) beginning 3 days postpartum. Infant blood samples on day 5 postpartum taken 2 hours after breastfeeding and 4 hours after the mothers' daily doses contained undetectable (<2.5 mcg/L) levels of rivaroxaban.[6]

Effects in Breastfed Infants

A 38-year-old woman with antiphospholipid syndrome began rivaroxaban 15 mg (0.19 mg/kg) daily at 5 days postpartum for prophylaxis of deep vein thrombosis. She partially breast-fed her infant (at least 50%). No apparent evidence of bleeding was noted in the infant at 1- and 3-month check-ups and development was normal at 18 months of age.[3]

Two mothers received rivaroxaban 15 mg (0.22 and 0.25 mg/kg) daily beginning 3 days postpartum for prophylaxis of deep vein thrombosis. At 3 months postpartum, their infants continued to be breastfed (extent not stated) and had no health problems or bleeding events.[6]

Effects on Lactation and Breastmilk

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

Alternate Drugs to Consider

Acenocoumarol, Dabigatran, Dalteparin, Enoxaparin, Heparin, Warfarin

References

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Substance Identification

Substance Name

Rivaroxaban

CAS Registry Number

366789-02-8

Drug Class

Breast Feeding

Lactation

Milk, Human

Anticoagulants

Antithrombins