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Natalizumab

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CASRN: 189261-10-7

Drug Levels and Effects

Summary of Use during Lactation

Measurable, but low, amounts of natalizumab are excreted into breastmilk in some, but not all, women. The time of the peak level in breastmilk is often in the first week after the dose, but might be as long as 6 months with repeated dosing. Because natalizumab is a large protein molecule with a molecular weight of about 149,000 Da, it is likely to be partially destroyed in the infant's gastrointestinal tract and absorption by the infant is probably minimal. Most expert guidelines do not recommend avoiding breastfeeding with natalizumab;[1-4] however, waiting for at least 2 weeks postpartum to resume therapy may minimize transfer to the infant.[5] No other precautions appear to be required during breastfeeding while using natalizumab and breastfeeding can resume immediately after injection.[5]

Drug Levels

Maternal Levels. A woman was started on natalizumab 300 mg intravenously while nursing her 11.5-month-old infant. Multiple milk levels were obtained almost daily over the 50 days after she received a dose on day 1 and another on day 29. Natalizumab was undetectable (<250 mcg/L) in breastmilk until day 14 when a concentration of 333 mcg/L was measured. A peak level of 1.01 mg/L was detected on day 20. On day 29, the natalizumab milk level was 491 mcg/L when the second dose was given. Milk levels increased to a maximum of 2.83 mg/L on day 50 when breastmilk collection ceased.[6]

Natalizumab was detected in the breastmilk in one of two mothers of newborn infants at a concentration of 1.89 mg/L just prior to a dose. The previous maternal dose had been given during pregnancy, but the maternal dose and time since the previous dose were not reported in the abstract. The other mother had no detectable natalizumab in breastmilk.[7]

Four women who were receiving natalizumab for multiple sclerosis donated breastmilk samples at various times after infusion of 300 mg of the drug up to 5.5 months postpartum. Concentrations of free natalizumab in breastmilk ranged from 2 to 412 mcg/L. One mother had no detectable natalizumab at any time and another had only trivial amounts at 6 time points. Variability in milk levels was considerable, but inversely correlated with the

time since the infusion. Regression indicated that on average, natalizumab was cleared from milk at about 35 days after a dose, although it was detectable at very low levels beyond this time in 2 samples.[8]

In a multi-center study of women with inflammatory bowel disease in pregnancy (the PIANO registry), 2 women receiving natalizumab provided milk samples at 1, 12, 24, and 48 hours after drug administration. One woman had natalizumab in breastmilk at 12 hours and 24 hours in concentrations of 0.26 and 0.46 mg/L, respectively.[2]

Three mothers provided milk samples at different time points during natalizumab therapy. Two provided multiple samples after their first dose postpartum. Peak levels were about 120 and 140 mcg/L and occurred 4 to 7 days after the dose (maternal dosage not provided). Milk natalizumab levels were undetectable on days 26 and 51 after the dose, respectively. Another mother provided milk samples at 13 to 15 days after her fourth dose postpartum. Levels were 40 to 50 mcg/L.[4]

Eleven women with relapsing-remitting multiple sclerosis were taking natalizumab during breastfeeding. All received 300 mg every 4 weeks during pregnancy, but one switched to every 6 weeks starting at week 30 of pregnancy. Eight of the 11 women provided at least 9 serial breastmilk samples after the first up to tenth (range 2 to 10 infusions) maintenance infusion after delivery. Samples were collected immediately before infusion, one day and several days after infusion. The other three patients provided 1, 3 or 4 breastmilk samples. A total of 178 breastmilk samples were obtained, with 8 patients donating 9 to 51 samples. The mean peak concentration of the 8 women was 0.126 mg/L and usually occurred in the first 8 days after the infusion. Their mean average concentration was 0.05 mg/L. No increases in milk natalizumab concentrations over time were seen. The average infant dosage was calculated to be 8 mcg/kg daily.[9]

Milk samples were collected from a woman with relapsing-remitting multiple sclerosis who had been treated with natalizumab for 14 years. Natalizumab was stopped 6 weeks before delivery and resumed 4 weeks postpartum, with an infusion every 6 weeks thereafter at an unspecified dosage. Eighteen milk samples were collected: before the first post-partum infusion and then weekly over the following 125 days with an average 8-day interval between samples. Free natalizumab was detectable in all the milk samples after the first dose, with a peak natalizumab concentration of 878 mcg/L after the first dose. The peak milk level was reached 1 week after each infusion. The mean milk concentration was 173.3 mcg/L.[10]

Infant Levels. Two nursing mothers who were taking natalizumab postpartum provided infant blood samples for analysis. One infant had a blood level taken 13 days after the mothers first dose postpartum and the second had two blood samples taken at 13 and 51 days after the maternal dose. Natalizumab was undetectable in all samples (lower limit of assay, maternal dosage and extent of breastfeeding not provided).[4]

Effects in Breastfed Infants

In a multi-center study of women with inflammatory bowel disease in pregnancy (the PIANO registry), 8 women received natalizumab while breastfeeding their infants. Among those who received natalizumab or another biologic agent while breastfeeding, infant growth, development or infection rate was no different from infants whose mothers received no treatment. An additional 68 women received a biologic agent plus a thiopurine. Infant outcomes were similar in this group.[2]

A retrospective cohort study from the German Multiple Sclerosis and Pregnancy Registry database identified 17 mothers who received natalizumab during breastfeeding. The first natalizumab infusion was administered after a median of 14 days (range 1–124 days) postpartum. Thirteen of the infants had also been exposed to natalizumab during the third trimester of pregnancy. More infants with third-trimester natalizumab exposure had a low birthweight and were hospitalized than unexposed children. Among the infants exposed only during breastfeeding, the mothers of 2 received the drug every 4 weeks and 2 received it every 6 weeks postpartum. They were breastfed for between 0.6 and 9.2 months. One of the 4 infants was a preterm infant who developed a

respiratory syncytial virus infection and the others had no infections. Two of the infants had normal blood counts postpartum and the two others were not tested.[4]

Effects on Lactation and Breastmilk

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

Alternate Drugs to Consider

(Inflammatory Bowel Disease) Budesonide, Infliximab, Mesalamine, Prednisone; (Multiple Sclerosis) Glatiramer, Immune Globulin, Interferon beta

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Substance Identification

Substance Name

Natalizumab

CAS Registry Number

189261-10-7

Drug Class

Breast Feeding

Lactation

Milk, Human

Antibodies, Monoclonal

Anti-Inflammatory Agents