U.S. National Library of Medicine
National Center for Biotechnology Information

NLM Citation: Drugs and Lactation Database (LactMed®) [Internet]. Bethesda (MD): National Institute of Child Health and Human Development; 2006-. Rituximab. [Updated 2023 Dec 15].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Rituximab

Revised: December 15, 2023.

CASRN: 174722-31-7

Drug Levels and Effects

Summary of Use during Lactation

Rituximab is a genetically engineered chimeric murine/human monoclonal antibody that targets CD20, a B-cell-specific surface antigen. The amount in milk is very low. It is also likely to be partially destroyed in the infant's gastrointestinal tract and absorption by the infant is probably minimal.[1-3] Numerous breastfed infants apparently experienced no adverse effects during maternal use of rituximab, including no adverse effect on the CD19 +B cell count. The manufacturer recommends that breastfeeding be discontinued during rituximab therapy and for 6 months after the last dose. However, the American College of Rheumatology and others consider rituximab to be acceptable for use during breastfeeding;[4-7] however, waiting for at least 2 weeks postpartum to resume therapy may minimize transfer to the infant.[7] Breastfeeding can resume after the injection. One group recommends waiting for 4 hours after the pre-injection antihistamine dose before resuming breastfeeding.[7]

Drug Levels

Maternal Levels. A patient who had granulomatosis with polyangiitis received rituximab 1000 mg intravenously while exclusively breastfeeding her infant. Milk samples were collected daily for 4 days starting 7 days after the infusion. Milk rituximab concentrations averaged 0.5 mcg/L (range 0.4 to 0.6 mcg/L).[2]

A woman with ANCA-associated vasculitis was treated with rituximab 500 mg intravenously at week 19 postpartum. The median concentration of rituximab in milk samples collected on 4 consecutive days was 3 mcg/L (range 0 to 4 mcg/L). The relative infant dose to the infant was estimated to be 0.007%.[8]

An international, multicenter study of patients with multiple sclerosis or neuromyelitis optica spectrum disorder collected breastmilk samples from 26 women who were receiving rituximab.

Milk samples were collected at a mean of 2.6 months (range 0.1–36.0) postpartum. The women received 500 mg once (n = 2) or twice (n = 9) or 1000 mg once (n = 11) or twice (n = 4) and milk samples were collected before and up to 90 days after the dose. Where measurable, the peak concentration in milk usually occurred between 1

and 7 days after the dose. Milk concentrations were virtually undetectable at 90 days after a dose. For women who received a single 500 mg dose, the average milk concentration was 0.03 mg/L and the peak was 0.04 mg/L. For 10 women who receive a single 1000 mg dose, the average milk concentration was 0.04 mg/L and the peak was 0.07 mg/L. For women who received two 500 mg doses, the average milk concentration was 0.02 mg/L and the peak was 0.1 mg/L. For women who received two 1000 mg doses, the average milk concentration was 0.2 mg/L and the peak was 0.6 mg/L. Based on the average milk levels, infants would receive a dose between 0.003 and 0.03 mg/kg daily.[9]

Six mothers with relapsing-remitting multiple sclerosis received 500 or 1,000 mg of rituximab postpartum. Breastmilk was collected at six time points: pre infusion, two days after infusion, after one week, and after one, three and five half-lives of rituximab. The highest concentration reported was in one woman who had a milk concentration of 250 mcg/L. The median average concentration in the breastmilk of the 6 women was 41 mcg/L. [10]

Infant Levels. A woman received rituximab 375 mg/square meter once weekly for 4 weeks beginning at week 30 of gestation. Her infant was born at 40 weeks of gestation and was exclusively breastfed with no major health issues. At 4 months of age, trace amounts of rituximab heavy and light chains were detected, but not quantified, in the infant's serum. Whether the drug was acquired transplacentally or during breastfeeding was not determined.[11]

A woman with ANCA-associated vasculitis was treated with rituximab 500 mg intravenously at week 19 postpartum. She continued to breastfeed her infant (extent not stated). There was no detectable rituximab in the serum of the infant (assay limit not stated) at 4 and 24 hours after the maternal dose.[8]

Six nursing (extent not stated) mothers with relapsing-remitting multiple sclerosis received 500 or 1,000 mg of rituximab postpartum. Infant serum was collected at six time points: pre infusion, two days after infusion, after one week, and after one, three and five half-lives of rituximab. All of the measurements of rituximab concentration in the infants' serum were below 0.01 mcg/L, and most of them below the lower limit of quantification (<0.005 mcg/L).[10]

Effects in Breastfed Infants

A woman received rituximab 375 mg/square meter once weekly for 4 weeks beginning at week 30 of gestation. Her infant was born at 40 weeks of gestation and was exclusively breastfed with no major health issues. At 4 months of age, the infant's B-cell population and immunoglobulin levels did not appear to be affected.[11]

A woman received an IV infusion of 1000 mg of rituximab at about 3 months postpartum. Her infant who was fully breastfed had no serious infections during the lactation period and developed normally during a 1.5 year follow-up period.[2]

A retrospective cohort study from the German Multiple Sclerosis and Pregnancy Registry database identified 5 mothers who received rituximab during breastfeeding. Three mothers receive one dose of rituximab while nursing, one received 500 mg and two received 1000 mg. The infants breastfed for 1.6, 1.8 and 0.3 months, respectively. Infant blood counts were normal at 1 to 1.5 months after the mothers' doses. A blood count was not performed in the third infant. One infant developed omphalitis, but all had normal development. The fourth woman received rituximab 250 mg on day 55 postpartum and ocrelizumab 300 mg on day 333 postpartum. She breastfed for 22.9 months after the rituximab dose. Her infant had normal blood counts at 45 and 213 days after the rituximab dose, but had conjunctivitis and otitis media during this time.[12]

A woman was diagnosed with B-cell lymphoma at 27 weeks of pregnancy. Labor was induced at 34 4/7 weeks and treatment was begun with a standard regimen of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone in unspecified doses on a 21-day cycle, starting on day 2 postpartum. She pumped and discarded

her milk and fed her infant donor milk for the first 10 days of each cycle and then breastfed her infant for the remaining 10 days before the next treatment cycle. The 10-day period of breastfeeding abstinence was determined by using about 3 half-lives of vincristine. After completion of 4 cycles of chemotherapy, her infant was reportedly healthy and developing without any complications.[13]

A woman with ANCA-associated vasculitis was treated with rituximab 500 mg intravenously at week 19 postpartum. She continued to breastfeed her infant (extent not stated) for another 4 months. The infant did not experience any serious infections or allergies, developed normally during the following 2 years and received all recommended vaccinations.[8]

Six nursing (extent not stated) mothers with relapsing-remitting multiple sclerosis received 500 or 1000 mg of rituximab postpartum. Infants were followed for at least 5 half-lives of the drug. No apparent abnormalities in the CD19 +B cell count, white blood cell count, lymphocytes or immunoglobulin levels were detected in the infants after rituximab infusion.[10]

A multicenter study of women who were receiving either ocrelizumab (n = 30) or rituximab (n = 15) for multiple sclerosis or neuromyelitis optica spectrum disorder followed their infants. Forty-three women breastfed their infants (n = 27 exclusively, n = 16 partially) for a median of 6.4 months (range 0.3–11.7). In the first 12 months of life, all infants grew and developed normally compared to WHO standards and a group of infants who were not breastfed. Beyond minor infections common to infancy, no unexpectedly severe or frequent infections arose. Four infants between the ages of 2.1 and 6.2 months who were breastfed after maternal ocrelizumab or rituximab had IgG and CD19 levels within the normal range.[9]

Effects on Lactation and Breastmilk

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

Alternate Drugs to Consider

(Multiple Sclerosis) Glatiramer, Immune Globulin, Interferon Beta (Rheumatoid Arthritis) Adalimumab, Certolizumab Pegol, Etanercept, Infliximab, Tocilizumab

References

1. Pistilli B, Bellettini G, Giovannetti E, et al. Chemotherapy, targeted agents, antiemetics and growth-factors in human milk: How should we counsel cancer patients about breastfeeding? Cancer Treat Rev 2013;39:207-11. PubMed PMID: 23199900.
2. Bragnes Y, Boshuizen R, de Vries A, et al. Low level of rituximab in human breast milk in a patient treated during lactation. Rheumatology (Oxford) 2017;56:1047-8. PubMed PMID: 28339781.
3. Anderson PO. Monoclonal antibodies during breastfeeding. Breastfeed Med 2021;16:591-3. PubMed PMID: 33956488.
4. Sammaritano LR, Bermas BL, Chakravarty EE, et al. 2020 American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases. Arthritis Rheumatol 2020;72:529-56. PubMed PMID: 32090480.
5. Dobson R, Rog D, Ovadia C, et al. Anti-CD20 therapies in pregnancy and breast feeding: A review and ABN guidelines. Pract Neurol 2022;23:6-14. PubMed PMID: 35803727.
6. Russell MD, Dey M, Flint J, et al. British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: Immunomodulatory anti-rheumatic drugs and corticosteroids. Rheumatology (Oxford) 2023;62:e48-e88. PubMed PMID: 36318966.
7. Krysko KM, Dobson R, Alroughani R, et al. Family planning considerations in people with multiple sclerosis. Lancet Neurol 2023;22:350-66. PubMed PMID: 36931808.

8. Bosshard N, Zbinden A, Eriksson KK, Förger F. Rituximab and canakinumab use during lactation: No detectable serum levels in breastfed infants. Rheumatol Ther 2021;8:1043-8. PubMed PMID: 33999372.
9. Anderson A, Rowles W, Poole S, et al. Anti-CD20 monoclonal antibody therapy in postpartum women with neurological conditions. Ann Clin Transl Neurol 2023;10:2053-64. PubMed PMID: 37675826.
10. Rød BE, Torkildsen Ø, Myhr KM, et al. Safety of breast feeding during rituximab treatment in multiple sclerosis. J Neurol Neurosurg Psychiatry 2022;94:38-41. PubMed PMID: 35879056.
11. Jin J, Mills J, Conboy E, et al. In utero rituximab: Detection of rituximab in an infant at 4 months of age. Ann Allergy Asthma Immunol 2014;113:A14. Available at: http://www.sciencedirect.com/science/journal/10811206/113/5/supp/S
12. Ciplea AI, Langer-Gould A, de Vries, A, et al. Monoclonal antibody treatment during pregnancy and/or lactation in women with MS or neuromyelitis optica spectrum disorder. Neurol Neuroimmunol Neuroinflamm 2020;7:e723. doi:10.1212/nxi.0000000000000723 PubMed PMID: 32327455.
13. Hersey AE, Giglio P, Kurt H, et al. Diffuse large B-cell lymphoma during third-trimester pregnancy and lactation. Obstet Gynecol 2020;135:383-6. PubMed PMID: 31923071.

Substance Identification

Substance Name

Rituximab

CAS Registry Number

174722-31-7

Drug Class

Breast Feeding

Lactation

Milk, Human

Antibodies, Monoclonal

Antirheumatic Agents

Antineoplastic Agents