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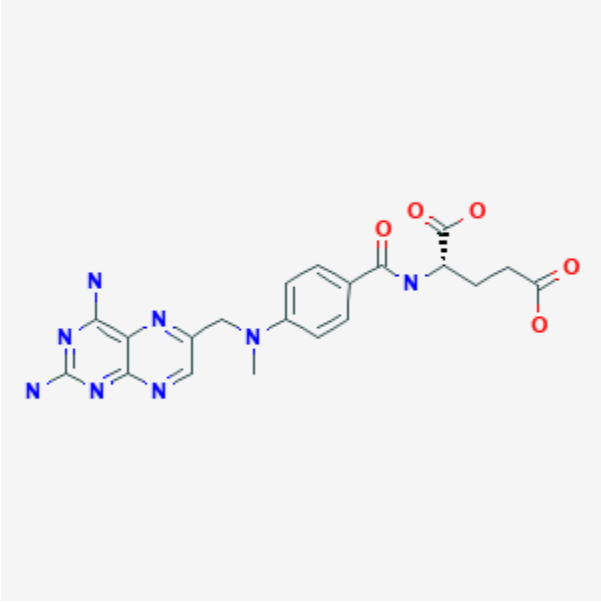
NLM Citation: Drugs and Lactation Database (LactMed) [Internet]. Bethesda (MD): National Library of Medicine (US); 2006-. Methotrexate. [Updated 2018 Oct 31].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Methotrexate

Revised: October 31, 2018.

CASRN: 59-05-2



Drug Levels and Effects

Summary of Use during Lactation

Most sources consider breastfeeding to be contraindicated during maternal high-dose antineoplastic drug therapy with methotrexate. An abstinence period of at least 1 week after chemotherapy doses of methotrexate has been suggested.[1] Chemotherapy may adversely affect the normal microbiome and chemical makeup of breastmilk.[2] Women who receive chemotherapy during pregnancy are more likely to have difficulty nursing their infant.[3]

Limited information indicates that a maternal dose of methotrexate up to 92 mg (1.12 mg/kg) produces low levels in milk, leading some authors to state that low single or weekly doses, such as those used for ectopic pregnancy or rheumatoid arthritis, are of low risk to the breastfed infant,[4][5][6][7][8] although some expert opinion warns against this use.[9][10][11][12][13] Withholding breastfeeding for 24 hours after a weekly low lose of methotrexate may decrease the infant's dose by 40%.[14][15] If breastfeeding during long-term, low-dose

methotrexate use is undertaken, monitoring of the infant's complete blood count and differential could be considered.

Drug Levels

Methotrexate is partially metabolized to the active metabolite, 7-hydroxymethotrexate, which is detectable in breastmilk.

Maternal Levels. One patient who was 1 month postpartum given 22.5 mg (15 mg/square meter) methotrexate daily by mouth for choriocarcinoma. Milk was collected at various times of the first 12 days of therapy. A peak milk level of 2.3 mcg/L occurred 10 hours after the first dose. However, the milk level was relatively constant during the period from 4 to 10 hours after the dose, after which it began to drop. Peak milk levels on the second and third days of administration were 2.7 mcg/L. The authors estimated that a cumulative amount of 0.32 mcg would be excreted in milk during the first 12 hours after this dose.[4]

A woman was given a single intramuscular dose of 65 mg (50 mg/square meter) of methotrexate for ectopic pregnancy. Six milk samples were obtained from 1 to 24 hours after the dose. Methotrexate was undetectable (<22.7 mcg/L) in all milk samples.[7]

A woman with rheumatoid arthritis received hydroxychloroquine, sulfasalazine and prednisone 10 mg daily during pregnancy and postpartum. On day 151 postpartum, methotrexate 25 mg was given subcutaneously. Breastmilk samples were obtained at 2, 12 and 24 hours after the dose. Milk levels were 0.05 micromolar (22.7 mcg/L) in all samples which was considered detectable, but not quantifiable. A fully breastfed infant would receive 3.4 mcg/kg in the first 24 hours after administration, or about 1% of the weight-adjusted maternal dosage.[8]

Two lactating women receiving subcutaneous methotrexate 25 mg once weekly donated 4 to 7 milk samples over a 1-week period between doses. Peak breastmilk methotrexate milk concentrations occurred between 1 and 12 hours after the dose and were 4 nmol/L (1.8 mcg/L). Peak breastmilk milk concentrations of the active metabolite, 7-hydroxymethotrexate, occurred at 24 hours after the dose and were 1.8 nmol/L (846 ng/L). Milk methotrexate concentrations were less than 2.5 nmol/L (1.1 mcg/L) during the rest of the dosing interval after the peak. One patient had undetectable (<91 ng/L) milk levels between 5 and 7 days after the dose. The authors estimated that if the peak methotrexate level were sustained throughout the feeding, the relative infant dose would be 0.5% of the weight-adjusted maternal dose and if breastfeeding were withheld for the first 24 hours after the dose, this value would decrease to 0.3% of the weight-adjusted maternal dose.[14]

A woman with placenta accretia received intramuscular methotrexate 92 mg (1.12 mg/kg) daily for 4 days, beginning on day 5 postpartum. On day 2 of therapy, she provided samples of breastmilk at baseline and 1, 2, 4, 8, 12, and 24 hours after the dose. The peak methotrexate milk concentration of 16.9 mcg/L occurred at 2 hours after the dose, which decreased to 4.9 mcg/L at 24 hours. The average methotrexate milk level over the 24-hour period was 8.6 mcg/L. The peak 7-hydroxymethotrexate milk concentration of 3 mcg/L occurred at 1 hour after the dose. The average 7-hydroxymethotrexate milk level over the 24-hour period was 1.5 mcg/L. The estimated daily dosages of methotrexate and 7-hydroxymethotrexate were estimated to be 1.2 mcg/kg and 0.2 mcg/kg, respectively. These represent infant dosages of 0.11% and 0.02% of maternal weight-adjusted dosages.[15]

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

Effects in Breastfed Infants

On day 151 postpartum, weekly methotrexate 25 mg subcutaneously begun a nursing mother. The estimated intake of the infant at that time was 3.4 mcg/kg in the first 24 hours after administration. The mother continued to breastfeed (extent not stated) for an additional 9 months while receiving subcutaneous methotrexate 25 mg weekly. No adverse effects were noted in the infant.[8]

Effects on Lactation and Breastmilk

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

Alternate Drugs to Consider

(Rheumatoid Arthritis) Auranofin, Etanercept, Gold Sodium Thiomalate, Hydroxychloroquine, Infliximab, Penicillamine, Sulfasalazine

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Substance Identification

Substance Name

Methotrexate

CAS Registry Number

59-05-2

Drug Class

Breast Feeding

Lactation

Abortifacient Agents, Nonsteroidal

Antimetabolites, Antineoplastic

Antirheumatic Agents

Folic Acid Antagonists

Immunosuppressive Agents