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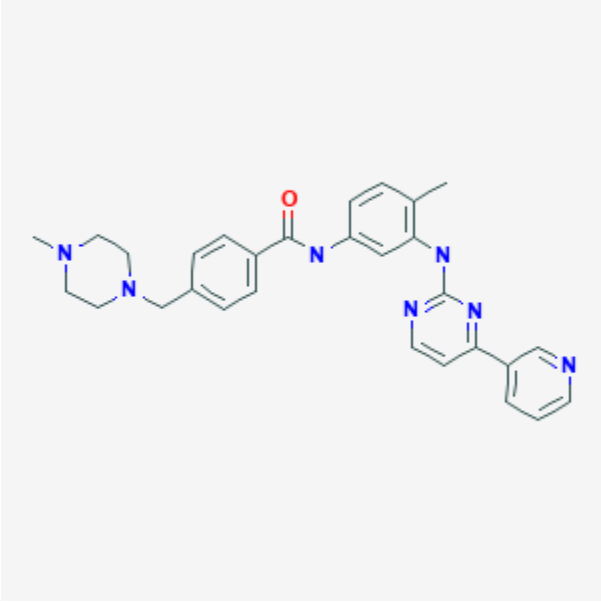
Imatinib

Revised: October 31, 2018.

CASRN: 152459-95-5



Drug Levels and Effects

Summary of Use during Lactation

Limited information indicates that maternal doses of imatinib up to 400 mg daily produce low levels of the drug and its active metabolite in milk. Although a few breastfed infants apparently experienced no adverse effects during maternal use of imatinib, no long-term data are available. Until more data are available, imatinib should be used only with careful monitoring during breastfeeding. The manufacturer and some authors recommend that breastfeeding be discontinued during imatinib therapy and for 1 month after therapy.[1][2]

Drug Levels

Imatinib is metabolized to an equally active metabolite, CGP 74588. The half-lives of the drug and its active metabolite are 18 and 40 hours, respectively, so accumulation might occur in the infant.

Maternal Levels. A woman receiving oral imatinib 400 mg daily for chronic myeloid leukemia breastfed her infant. During week 4 postpartum, serum and milk levels of imatinib and CGP 74588 were measured before and at several times during the 9 hours after the dose. The highest concentrations of imatinib and its metabolite were at 2 and 4 hours after the dose. Peak concentrations of imatinib ranged between 1.1 and 1.4 mg/L and were 0.8 mg/L for the metabolite. The concentrations of both were 25 to 50% lower 9 hours after the dose. Milk and serum levels were also measured during the second month of breastfeeding with similar results (details not reported).[3] Using these data, the estimated maximum dosage of the drug and metabolite that a fully breastfed infant would receive is 0.3 mg/kg daily or 4.5% of the maternal weight-adjusted dosage.

A woman who was 7 days postpartum and had been taking imatinib 400 mg daily since the middle of her pregnancy had a single milk sample analyzed for the drug an its metabolite. Milk concentration 15 hours after a dose was 596 mcg/L for imatinib and 1513 mcg/L for the metabolite. The authors estimated that a fully breastfed infant would receive between 1.2 and 2 mg of the drug and metabolite daily with this maternal dose.[4]

A woman who took imatinib 400 mg daily during pregnancy and postpartum delivered a normal infant, but did not breastfeed. Breastmilk imatinib concentrations were measured on the 7th, 14th, 15th and 16th days postpartum at times ranging from 10 to 16 hours after the previous dose. Breastmilk concentrations ranged between 1.4 and 2.6 mg/L.[5]

A woman with chronic myeloid leukemia was begun on imatinib 400 mg daily immediately after delivery. She did not breastfeed, but 5 breastmilk samples were obtained over the 7 days after the first dose, on days 1, 2, 3 and 7 postpartum, apparently 3 hours after the daily doses (exact times not stated). Imatinib milk levels were about half of maternal plasma levels and ranged from 151 to 1153 mcg/L. Milk levels of the metabolite, N-desmethylimatinib were about 3 times those in maternal plasma and ranged from 409 to 1052 mcg/L.[6]

A woman received imatinib 400 mg daily beginning in week 30 of pregnancy. Colostrum and milk samples obtained during the first 5 days postpartum contained an average of 0.233 mg/L of imatinib and 0.529 mg/L of n-desmethylimatinib, the active metabolite. The authors estimated that an exclusively breastfed infant would ingest a mean of 0.12 mg/kg daily of the active drug (imatinib plus metabolite).[7] This would be approximately 1.8% of the weight-adjusted maternal dosage.

A woman with chronic myeloid leukemia began treatment with imatinib 400 mg daily in week 28 of pregnancy. The drug was discontinued 72 hours prior to the scheduled induction of labor. A breastmilk was taken postpartum at 99 hours after the last dose. The concentration of imatinib in breastmilk was 18.9 mcg/L and the concentration of n-desmethylimatinib was 658 mcg/L, both using control breastmilk as a standard.[2]

Two women with Ph+ chronic myelocytic leukemia were taking imatinib before pregnancy, but stopped until breastfeeding ceased. Each received one dose of imatinib orally and took milk samples at 1, 2, 4, 6, 8, 12 and 24 hours after the dose. One patient received imatinib 400 mg and had a peak milk concentration of 1.4 mg/L at 4 hours after the dose and 0.42 mg/L at 8 hours after the dose. The other patient received imatinib 400 mg on day 1 and imatinib at 600 mg on day 2 of milk collection. She had a peak milk concentration of 0.42 mg/L at 8 hours after the 400 mg dose and a peak concentration of 1.4 mg/L at 6 hours after the 600 mg dose.[8]

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

Effects in Breastfed Infants

A woman receiving oral imatinib 400 mg daily for chronic myeloid leukemia breastfed her infant. No adverse effects were noted in the infant during the first 2 months of nursing.[3]

One woman with chronic myelogenous leukemia received imatinib 400 mg daily throughout pregnancy and during breastfeeding (extent not stated) for nearly 6 months postpartum. Her infant reportedly grew and developed normally.[9]

A woman with chronic myeloid leukemia received imatinib 400 mg daily starting at week 8 of pregnancy and continuing throughout 8 months of breastfeeding (extent not stated). The infant was healthy, but an atrial septal defect was repaired at 30 months of age. It was thought to be unrelated to imatinib therapy.[10]

Effects on Lactation and Breastmilk

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

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Substance Identification

Substance Name

Imatinib

CAS Registry Number

152459-95-5

Drug Class

Breast Feeding

Lactation

Antineoplastic Agents

Enzyme Inhibitors

Protein Kinase Inhibitors

Signal Transduction Inhibitors

Tyrosine Kinase Inhibitors