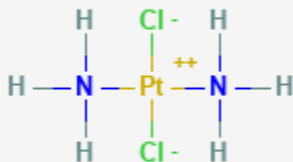




## Cisplatin

Revised: February 28, 2019.

CASRN: 15663-27-1



## Drug Levels and Effects

### Summary of Use during Lactation

Most sources consider breastfeeding to be contraindicated during maternal antineoplastic drug therapy, especially alkylating agents such as cisplatin.[1] Excretion of platinum into milk occurs, but results from 3 cases are inconsistent. The exact form and toxicity of platinum excreted into breastmilk are also not known. The nursing infant would receive any platinum compounds orally rather than intravenously and oral absorption of oral platinum compounds by infants is not known. 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.

## Drug Levels

*Maternal Levels.* Platinum was not detected (<100 mcg/L) in the milk of one patient at any time after an IV infusion of 100 mg/sq. m (130 mg) of cisplatin.[3]

In another patient, trough milk platinum was 900 mcg/L at 19.5 hr after her second daily dose of cisplatin 20 mg/sq. m infused intravenously over 4 hours. The simultaneous plasma platinum level was 800 mcg/L.[4] Note: the original report stated a cisplatin dose of 30 mg/sq. m, but this was later corrected to 20 mg/sq. m in a published erratum.

A patient was given cisplatin 60 mg/sq. m (100 mg) infused intravenously over 3 hours. Samples from two cycles of therapy found average peak milk platinum concentrations of about 125 mcg/L occurred at 30 minutes after the dose and about 112 mcg/L at 18 hours after the dose. Milk platinum levels were about 10% of simultaneous plasma levels at all time points over the 18-hour sampling periods of two cycles.[5]

Three patients with cervical cancer received cisplatin 20 mg/sq. m during pregnancy as part of their treatment. All women had a cesarean section and hysterectomy between 31 and 35 weeks of gestation, followed by another course of chemotherapy. Breastmilk samples "in the first days of lactation" were obtained and analyzed, although the time since the last cisplatin dose and the time since surgery were not specified. Cisplatin concentrations in breastmilk samples were 0.2, 1.4, and 5.5 mg/L, which were 0.9%, 2.3% and 9% of concentrations in maternal blood at the time of surgery.[6]

Two women were treated with unspecified doses of cisplatin for treatment of cervical cancer every 2 weeks during pregnancy. The time of the last dose before delivery was not clearly specified in the abstract. Breastmilk samples were obtained daily on days 1 to 4 postpartum. Cisplatin was measured by flameless atomic absorption spectrophotometry. Platinum was undetectable (lower limit of assay not specified) in all of the samples.[7]

A woman was given her first dose of 70 mg (40 mg/sq. m) of cisplatin intravenously at 6 weeks postpartum for treatment of cervical cancer discovered during pregnancy. Fifteen milk samples were obtained between 4 and 70 hours after the dose. Total platinum was measured in milk. The first sample at 4.25 hours after the dose contained about 16 mcg/L of platinum. Concentrations fell with a half-life of 10.2 hours until 17 hours after the dose. Between 17 and 57 hours after the dose, platinum was detectable (>2.5 mcg/L), but not quantifiable (<5 mcg/L) in milk. Platinum was undetectable (<2.5 mcg/L) at 66 and 70 hours after the dose. The authors estimated that a breastfed infant would be exposed systemically to between 0.08 and 0.12% of a therapeutic dose and that resumption of breastfeeding would be possible at 72 hours after a dose of this size.[8]

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

## Effects in Breastfed Infants

Two women were treated with unspecified doses of cisplatin for treatment of cervical cancer every 2 weeks during pregnancy. They both breastfed their newborn infants. Follow-up examinations of the infants, including Bayley scale test, neurology, and echocardiography at age of 20 and 35 months revealed normal findings.[7]

## Effects on Lactation and Breastmilk

A study of adolescent males who had received chemotherapy for childhood malignancies found that having received cisplatin was associated with elevated serum prolactin concentrations.[9] Another study of survivors of testicular cancer found that about 6% of those treated with cisplatin had abnormally high prolactin levels and 2% had abnormally low prolactin levels.[10]

A telephone follow-up study was conducted on 74 women who received cancer chemotherapy at one center during the second or third trimester of pregnancy to determine if they were successful at breastfeeding

postpartum. Only 34% of the women were able to exclusively breastfeed their infants, and 66% of the women reported experiencing breastfeeding difficulties. This was in comparison to a 91% breastfeeding success rate in 22 other mothers diagnosed during pregnancy, but not treated with chemotherapy. Other statistically significant correlations included: 1. mothers with breastfeeding difficulties had an average of 5.5 cycles of chemotherapy compared with 3.8 cycles among mothers who had no difficulties; and 2. mothers with breastfeeding difficulties received their first cycle of chemotherapy on average 3.4 weeks earlier in pregnancy. Of the 3 women who received a cisplatin-containing regimen, 1 had breastfeeding difficulties.[11]

## 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. Urbaniak C, McMillan A, Angelini M et al. Effect of chemotherapy on the microbiota and metabolome of human milk, a case report. *Microbiome.* 2014;2:24. PubMed PMID: 25061513.
3. Egan PC, Costanza ME, Dodion P et al. Doxorubicin and cisplatin excretion into human milk. *Cancer Treat Rep.* 1985;69:1387-9. PubMed PMID: 4075315.
4. de Vries EG, van der Zee AG, Uges DR, Sleijfer DT. Excretion of platinum into breast milk. *Lancet.* 1989;1(8636):497. Letter. Erratum in *Lancet* 1989 Apr 8;1(8641):798. PubMed PMID: 2563865.
5. Ben-Baruch G, Menczer J, Goshen R et al. Cisplatin excretion in human milk. *J Natl Cancer Inst.* 1992;84:451-2. Letter. PubMed PMID: 1538424.
6. Lanowska M, Kohler C, Oppelt P et al. Addressing concerns about cisplatin application during pregnancy. *J Perinat Med.* 2011;39:279-85. PubMed PMID: 21391877.
7. Tesfaye H, Halaska MJ, Branova P et al. Breast-fed infants whose mothers were on platinum based chemotherapy: Cases with promising outcomes. *Ther Drug Monit.* 2013;35:693. Abstract. DOI: [10.1097/FTD.0b013e3182a8ef2b](https://doi.org/10.1097/FTD.0b013e3182a8ef2b).
8. Hays KE, Ryu RJ, Swisher EM et al. Duration of cisplatin excretion in breast milk. *J Hum Lact.* 2013;29:469-72. PubMed PMID: 23492761.
9. Siimes MA, Ropponen P, Aalberg V et al. Prolactinemia in adolescent males surviving malignancies in childhood: impaired dating activity. *J Adolesc Health.* 1993;14:543-7. PubMed PMID: 8312290.
10. Wiechno P, Demkow T, Kubiak K et al. The quality of life and hormonal disturbances in testicular cancer survivors in cisplatin era. *Eur Urol.* 2007;52:1448-54. PubMed PMID: 17544206.
11. Stopenski S, Aslam A, Zhang X et al. After chemotherapy treatment for maternal cancer during pregnancy, is breastfeeding possible? *Breastfeed Med.* 2017;12:91-7. PubMed PMID: 28170295.

## Substance Identification

### Substance Name

Cisplatin

### CAS Registry Number

15663-27-1

### Drug Class

Breast Feeding

Lactation

Antineoplastic Agents