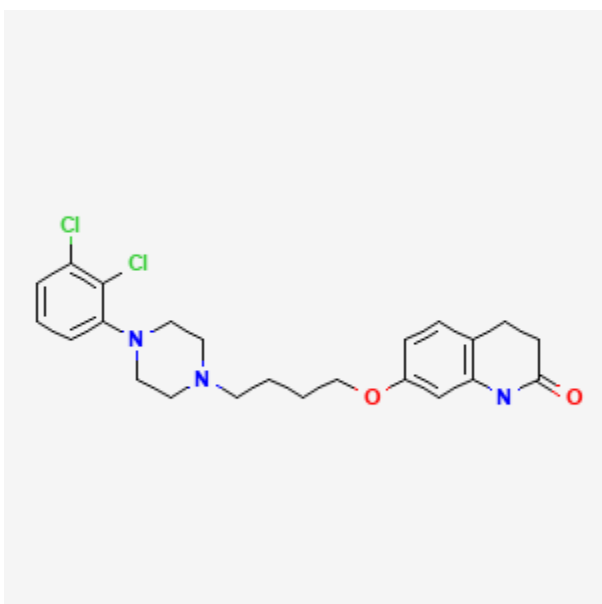




Aripiprazole

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Drug Levels and Effects

Summary of Use during Lactation

Limited information indicates that maternal doses of aripiprazole up to 15 mg daily produce low levels in milk. Aripiprazole can lower serum prolactin in a dose-related manner. Cases of lactation cessation have occurred, but cases of gynecomastia and galactorrhea have also been reported. Weight loss and poor weight gain have been reported in breastfed infants whose mothers were taking aripiprazole. Until more data become available, an alternate drug may be preferred, especially while nursing a newborn or preterm infant.[1]

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Drug Levels

Maternal Levels. A woman who was 6 months postpartum was taking aripiprazole 15 mg by mouth daily. Milk levels after 11 and 12 days of therapy (times not stated) at that dose were 13 and 14 mcg/L.[2]

A woman took aripiprazole 15 mg daily by mouth during pregnancy and postpartum. At 3 days postpartum, aripiprazole was not detectable in colostrum because of an unknown substance that interfered with the assay. On day 27 postpartum, 3 additional milk samples were collected 30 minutes before the dose (24 hours after the last dose), and 4 and 10 hours after the dose. The drug and its metabolite were undetectable (<10 mcg/L) in all samples. The authors estimated that a fully breastfed infant would receive less than 0.7% of the maternal weight-adjusted dosage.[3]

A woman was taking aripiprazole 18 mg daily. On day 6 postpartum, a breastmilk sample (time not reported) contained a concentration of aripiprazole of 38.7 mcg/L.[4]

A woman took aripiprazole 10 mg daily by mouth beginning in week 9 of pregnancy and continuing postpartum. Mid-nursing milk samples were obtained at 8 and 10 weeks postpartum over a 24-hour period after the dose. Aripiprazole and dehydroaripiprazole were measured in the milk. On the first sampling day, mean milk concentrations were 52.6 mcg/L of aripiprazole and 8.8 mcg/L for the metabolite. On the second day, mean milk concentrations were 53.6 and 6.3 mcg/L, respectively. The authors calculated that a 5 kg infant would receive a daily dose of 47 mcg daily and the weight-adjusted dosage would be 8.3% of the maternal dosage.[5]

An abstract reported that a relative infant dose of 12.7% was found in nursing mother(s) taking aripiprazole who provided 8 milk samples over 24 hours, but other details were not supplied.[6]

Infant Levels. A woman was taking aripiprazole 18 mg daily during pregnancy and postpartum. On day 6 her breastfed infant had a serum concentration of 7.6 mcg/L, although some portion of the concentration could have been residual from transplacental transmission because of the drug's on half-life.[4]

Effects in Breastfed Infants

A woman took aripiprazole 15 mg daily by mouth during pregnancy and postpartum. She breastfed her infant (amount not stated) and at 3 months of age, the infant was growing normally.[3]

A woman took aripiprazole 10 mg daily by mouth beginning in week 9 of pregnancy and continuing postpartum. She exclusively breastfed her infant for 6 weeks, then was partially breastfed. At 4 months of age the infant was still breastfeeding and had normal psychomotor and behavioral development and had reached the expected milestones for her age.[5]

A 12-day-old exclusively breastfed male infant presented with severe weight loss and hypernatremic dehydration because of inadequate milk intake and a 30% weight loss since birth. The infant's mother was being treated for bipolar disorder with lamotrigine 250 mg orally once daily, aripiprazole 15 mg orally once daily, and sertraline 100 mg orally once daily. She was also taking levothyroxine 50 mcg once daily, a prenatal multivitamin, and folic acid. On initial evaluation in the emergency department, he was pale, with marbled skin, dry mucous membranes, decreased skin turgor, and bluish feet with prolonged capillary refill. The right foot eventually became darker with blackened toes and he developed gangrene of the right lower limb, which did not respond to medical therapy and required amputation of all five toes and surgical debridement of the metatarsals. Necrosis was attributed to arterial microthrombi caused by disseminated intravascular coagulation after severe dehydration. The authors considered the mother's medications as a possible cause of the dehydration and related problems.[7]

A woman with paranoid schizophrenia had been receiving long-acting injectable aripiprazole 400 mg every 28 days for 32 months when pregnancy was confirmed. The dose was lowered to 300 mg every 28 days and after

delivery she breastfed her infant (extent and duration not stated). At 3 years of age, the infant's growth and development were normal.[8]

Patients enlisted in the National Pregnancy Registry for Atypical Antipsychotics who were taking a second-generation antipsychotic drug while breastfeeding (n = 576) were compared to control breastfeeding patients who were not treated with a second-generation antipsychotic (n = 818). Of the patients who were taking a second-generation antipsychotic drug, 60.4% were on more than one psychotropic. A review of the pediatric medical records, no adverse effects were noted among infants exposed or not exposed to second-generation antipsychotic monotherapy or to polytherapy.[9] The number of women taking aripiprazole was not reported.

Effects on Lactation and Breastmilk

Unlike the phenothiazines, aripiprazole has a minimal effect on serum prolactin levels and it has been used to reverse hyperprolactinemia in nonlactating patients taking other antipsychotics.[10-21] Case reports of both decreased lactation in nursing mothers and cases of hyperprolactinemia and galactorrhea in patients taking aripiprazole have been reported.[22-31] The maternal prolactin level in a mother with established lactation may not affect her ability to breastfeed.

One woman began taking aripiprazole 10 mg daily at week 20 of pregnancy. She underwent a cesarean section delivery at term, but was unable to establish lactation. The authors suggested that more data are needed to determine if aripiprazole adversely affects lactation.[32]

A woman took aripiprazole 10 mg daily by mouth beginning in week 9 of pregnancy and continuing postpartum. She exclusively breastfed her infant for 6 weeks, but then began supplementation because of insufficient milk production. Her serum prolactin was 35 to 40 mcg/L, which is lower than expected for a nursing mother. The authors speculated that the aripiprazole might have been the cause of her low serum prolactin and diminished her milk supply.[5]

A woman with bipolar disorder was taking lithium during pregnancy and postpartum. At 10 days postpartum, her infant's serum lithium level was 0.26 mmol/L, so lithium was discontinued. Quetiapine was begun, but discontinued because of maternal sedation. Aripiprazole 2.5 mg daily was begun and within 24 hours, the mother noted a marked decrease in milk supply. After 2 weeks of working with a lactation consultant, she continued to have lactation difficulties and she switched back to lithium. Within 48 hours, her milk supply improved markedly.[33]

A retrospective study of outpatients receiving an average aripiprazole dose of 17.3 mg daily (n = 20) or another antipsychotic (n = 141) found that those receiving such high-dose aripiprazole had an 81% chance of having hypoprolactinemia. Patients not treated with aripiprazole had only a 2.9% chance of having hypoprolactinemia. [34]

The breastfeeding mother of a 5-week-old infant was diagnosed with bipolar disorder, panic attacks and anxiety disorder. She was started on hydroxyzine 50 mg at an unspecified interval and took it for 3 to 5 days with no effect on milk production. She then started on aripiprazole 5 mg at an unspecified interval. After 5 days, she reported a decrease in milk production that required supplementation with formula. Nine days after stopping both drugs, her milk supply returned to normal. The decreased milk supply was possibly caused by the medications, with aripiprazole most likely.[27]

A woman with chronic depression was treated throughout pregnancy with extended-release venlafaxine 225 mg daily. She gave birth by cesarean section at 36.5 weeks and began to breastfeed her infant. The infant was not nursing adequately, but the mother pumped milk after each feeding and used it to supplement the infant. It was estimated that she was producing at least 900 mL of milk daily. By 8 days postpartum, she began to experience depression and aripiprazole 2 mg daily, which she had taken before pregnancy, was added to her regimen. After

3 days of combined therapy, she noticed a decrease in milk supply, and within 21 days, lactation had ceased completely. Either aripiprazole or the combination with venlafaxine possibly caused a decrease in milk supply. [28]

A woman with major depressive disorder received duloxetine 40 mg twice daily. After 2 weeks, she developed menstrual irregularities and a milky discharge from her breasts. Her serum prolactin was elevated at 205 mcg/L. The duloxetine dosage was decreased to 60 mg once daily and aripiprazole was begun at 2.5 mg daily and then increased to 5 mg daily. Within 2 weeks, galactorrhea had stopped and the serum prolactin had decreased to 118 mcg/L. Six weeks later, serum prolactin was 39 mcg/L. The combination was continued for another 39 weeks with no return of galactorrhea. [35]

A postpartum woman was given sertraline 200 mg daily for anxiety, depressive symptoms, hypochondriacal thoughts and checking compulsions, which interfered with bonding. Two months later aripiprazole 5 mg daily was added. Two to three days later the patient reported decreased milk production. Prolactin levels decreased from a previous 30.18 mcg/L to 5.02 mcg/L. Milk production normalized in less than a week after stopping aripiprazole. [36]

Patients enlisted in the National Pregnancy Registry for Atypical Antipsychotics who were taking a second-generation antipsychotic drug while breastfeeding (n = 576) were compared to control breastfeeding patients who had primarily diagnoses of major depressive disorder and anxiety disorders, most often treated with SSRI or SNRI antidepressants, but not with a second-generation antipsychotic (n = 818). Among women on a second-generation antipsychotic, 60.4% were on more than one psychotropic compared with 24.4% among women in the control group. Of the women on a second-generation antipsychotic, 59.3% reported “ever breastfeeding” compared to 88.2% of women in the control group. At 3 months postpartum, 23% of women on a second-generation antipsychotic were exclusively breastfeeding compared to 47% of women in the control group. [9] The number of women taking aripiprazole was not reported.

Two women took aripiprazole during pregnancy and postpartum for schizophrenia in doses of 10 and 20 mg daily. Neither mother could breastfeed her infant because of little to no milk production. [37]

Alternate Drugs to Consider

Haloperidol, Olanzapine, Quetiapine, Risperidone

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Substance Identification

Substance Name

Aripiprazole

CAS Registry Number

129722-12-9

Drug Class

Breast Feeding

Lactation

Milk, Human

Antipsychotic Agents