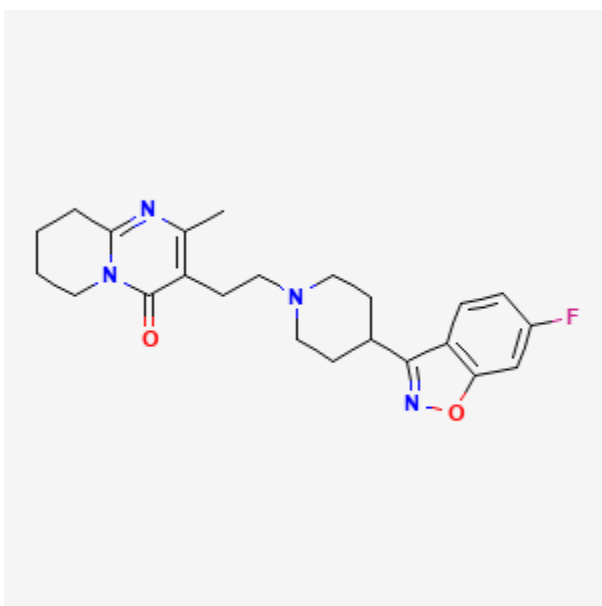




## Risperidone

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CASRN: 106266-06-2



## Drug Levels and Effects

### Summary of Use during Lactation

Limited information indicates that maternal risperidone doses of up to 6 mg daily produce low levels in milk. Sedation, failure to thrive, jitteriness, tremors, abnormal muscle movements and respiratory depression have been reported in infants exposed to risperidone in milk. Because there is little published experience with risperidone during breastfeeding and little long-term follow-up data, other agents may be preferred, especially while nursing a newborn or preterm infant. Systematic reviews of second-generation antipsychotics concluded that risperidone seemed to be a second-line agent during breastfeeding because of the limited data available and higher excretion into milk relative to other agents.[1-3] A safety scoring system finds risperidone to be possible to use cautiously during breastfeeding.[4] Monitor the infant for drowsiness, weight gain, tremors, respiratory

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rate, abnormal muscle movements, and developmental milestones, especially if other antipsychotics are used concurrently.

## Drug Levels

*Maternal Levels.* One mother taking risperidone 6 mg daily had milk and serum levels of risperidone and its active metabolite, 9-hydroxyrisperidone, measured over 24 hours. Results indicated that an exclusively breastfed infant would receive 0.84% of the maternal weight-adjusted dosage of risperidone and another 3.46% as 9-hydroxyrisperidone for a total of 4.3% of the maternal weight-adjusted dosage.[5]

Two breastfeeding women taking 2 mg twice daily and 1.5 mg daily in 2 divided doses, respectively, and another with risperidone-induced galactorrhea taking 3 mg once daily were studied. Both risperidone and 9-hydroxyrisperidone were measured in milk. Milk levels of the drugs were rather flat during the 12 to 24 hours after the dose. The mean dose that an exclusively breastfed infant would receive was calculated to be 3.3% (range 2.2 to 4.7%) of the maternal weight-adjusted dosage.[6]

A woman who was 1 week postpartum was started on oral risperidone 2 mg daily and increased to 3 mg once daily. On day 6 of therapy (dosage 2 mg daily) average milk levels at 3 hours after a dose were risperidone 2.5 mcg/L and 9-hydroxyrisperidone 10 mcg/L. On day 10 (dosage 2 mg daily) at 15 hours after a dose 9-hydroxyrisperidone averaged 1.2 mcg/L and risperidone was undetectable. On day 20 of therapy (dosage 3 mg daily) average milk levels at 16 hours after a dose were risperidone 0.1 mcg/L and 9-hydroxyrisperidone 2.5 mcg/L.[7]

A woman took risperidone during pregnancy and breastfeeding. At 3 months postpartum, she provided 6 foremilk samples over a 24-hour period after her daily dose while she was taking a dose of 1 mg daily. Milk was analyzed for risperidone and 9-hydroxyrisperidone by HPLC. Risperidone could not be detected in milk (assay limit not specified). Breastmilk 9-hydroxyrisperidone was about 3 mcg/L at 1 and 24 hours later; its concentration was about 4 mcg/L at 2, 4, 8, 18 and 23 hours after the dose. The authors estimated that a fully breastfed infant would receive 4.7% of the maternal weight-adjusted dosage as 9-hydroxyrisperidone.[8]

*Infant Levels.* In 2 breastfed infants (6 weeks and 3.3 months old) whose mothers were taking 2 mg twice daily and 1.5 mg daily in 2 divided doses, respectively, risperidone and 9-hydroxyrisperidone were both undetectable (<1 mcg/L) in the serums of the infants.[6]

An infant was breastfed 6 times daily during maternal therapy with risperidone 2 mg once daily. Fifteen hours after the mother's last dose, the infant's plasma levels of risperidone was undetectable and 9-hydroxyrisperidone was 0.1 mcg/L.[7]

An infant was exclusively breastfed on demand during maternal therapy with risperidone 1 mg daily. At 3 months of age, risperidone was undetectable in the infant's serum 6 hours after a maternal dose.[8]

## Effects in Breastfed Infants

One woman took risperidone 4 mg daily during breastfeeding. Her infant showed no developmental abnormalities on examinations up to 9 months of age. Another mother took risperidone 6 mg daily during breastfeeding. Her infant showed no developmental abnormalities on examinations up to 12 months of age.[9]

Two women taking risperidone 4 mg and 1.5 mg daily breastfed their infants of 3.3 months and 6 weeks of age, respectively, were achieving normal developmental milestones and had no adverse effects reported.[6]

A 1 week postpartum woman was started on risperidone 2 mg daily and increased after 10 days to a dosage of 3 mg daily. She breastfed her infant 6 times daily. The infant was observed for 5 weeks of inpatient therapy and

judged normal by a pediatric neurologist. No sedation or other adverse effects were observed in the infant. After 3 months of treatment with risperidone, the mother and infant were judged to be well.[7]

An infant had been exclusively breastfed for 3 months during maternal therapy with risperidone 1 mg daily. A pediatric examination found the infant to have no neurological or physical abnormalities, and appeared to interact appropriately.[8]

In a telephone follow-up study, 124 mothers who took a benzodiazepine while nursing reported whether their infants had any signs of sedation. One mother who was taking 0.75 mg of risperidone daily, flurazepam 15 mg daily, clonazepam 0.25 mg twice daily, and 1 mg of bupropion daily reported sedation in her breastfed infant. [10]

A woman diagnosed with schizophrenia was taking risperidone 1.5 mg daily during late pregnancy and postpartum while nursing (extent not stated) her full-term infant. At 2 weeks postpartum, haloperidol 0.8 mg daily was added because of a recurrence of symptoms. At these dosages, no adverse effects were seen in the infant. However, because of recurring symptoms, the dosage of haloperidol was increased to 1.5 mg daily. Three days later, the infant had excessive sedation, poor feeding, and slowing in motor movements. Pediatric assessment found no medical reason for these effects. Breastfeeding was discontinued and the infant's symptoms resolved completely in 5 days. The infant's symptoms were probably caused by the drug combination.[11]

A prospective cohort study of infants breastfed by mothers in an inpatient mother-baby psychiatric unit in India followed 7 infants who were exposed to risperidone in breastmilk; most received partial supplementation. One infant whose mother was taking risperidone 4 mg and lorazepam 2 mg developed sedation that resolved when lorazepam was discontinued. One infant whose mother received risperidone 4 mg daily, trihexyphenidyl 2 mg daily, and electroconvulsive therapy developed constipation. Infants were followed for 1 to 3 months after discharge. One infant had delayed weight development, one infant had delay in height, one infant mental delay, and a fourth infant had motor and mental delay.[12]

A woman with bipolar disorder was maintained on oral risperidone 2 mg at bedtime, long-acting injectable risperidone 50 mg intramuscular every 2 weeks, oral citalopram 20 mg daily, and oral benztropine 0.5 mg daily. She became pregnant and maintained the same regimen. Her infant was born at 35 weeks gestational age and was breastfed (extent and duration not stated). At 16 months of age, the infant was doing well and met his developmental milestones.[13]

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.[14] The number of women taking risperidone was not reported.

A preterm infant weighing 2.75 kg was born at 35 weeks gestation. The infant received bag and mask ventilation for 2 min and was kept on oxygen for the first 18 hours of life due to respiratory distress. The baby began breastfeeding on day 2 of life. On day 12, the mother was started on risperidone 1 mg daily for psychotic episodes. On day 13, the infant developed a respiratory rate of 16/min and no retractions and was placed on CPAP for 12 hours, with gradual weaning thereafter and was placed on formula. On day 15, the mother began breastfeeding again and the respiratory depression recurred. Feeding was changed to breastmilk expressed prior to the daily dose of risperidone and formula for 6 hours after each dose followed by direct breastfeeding. Over the next 2 days further episodes of respiratory depression occurred. The baby was discharged on day 24, with advice to continue the same feeding pattern. Respiratory depression was probably caused by risperidone in milk. [15]

A woman diagnosed with undifferentiated schizophrenia took risperidone 4 to 5 mg and trihexyphenidyl 2 mg daily throughout 5 pregnancies. She breastfed each infant for 20 to 24 months. No adverse developmental consequences were noted in any of the children. At the time of publication, the oldest three children, aged 26, 23 and 22 years, had completed their education and were employed, while the youngest two were 15 and 19 years old and were doing well academically in their education.[16]

## Effects on Lactation and Breastmilk

Risperidone has caused elevated prolactin serum levels, gynecomastia, and galactorrhea in patients taking the drug.[17-32] In one case, euprolactinemic gynecomastia and galactorrhea occurred in a 19-year-old man who was also taking fluvoxamine.[33] A meta-analysis of 3 studies found that the risk of gynecomastia with risperidone is 4.3 times greater than that of quetiapine.[34] The prolactin level in a mother with established lactation may not affect her ability to breastfeed.

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 primarily had 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.[14] The number of women taking risperidone was not reported.

## Alternate Drugs to Consider

(Antipsychotic) Haloperidol, Olanzapine, Quetiapine, Risperidone (Bipolar Disorder) Divalproex, Lithium, Olanzapine, Quetiapine, Valproic Acid

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## Substance Identification

### Substance Name

Risperidone

### CAS Registry Number

106266-06-2

### Drug Class

Breast Feeding

Lactation

Milk, Human

Antipsychotic Agents