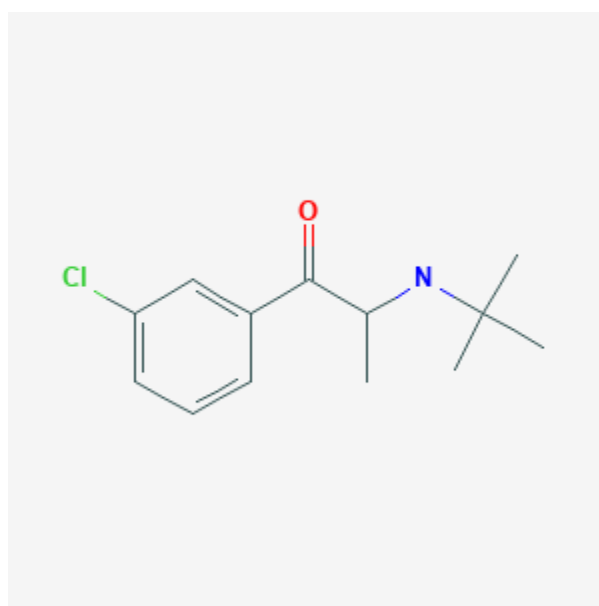




Bupropion

Revised: May 1, 2019.

CASRN: 34911-55-2



Drug Levels and Effects

Summary of Use during Lactation

Limited information indicates that maternal bupropion doses of up to 300 mg daily produce low levels in breastmilk and would not be expected to cause any adverse effects in breastfed infants. However, there is little reported use in breastfed newborn infants and case reports of a possible seizure in partially breastfed 6-month-olds. If bupropion is required by a nursing mother, it is not a reason to discontinue breastfeeding. However, another drug may be preferred, especially while nursing a newborn or preterm infant. Infants exposed to bupropion and an SSRI through breastfeeding should be closely monitored for vomiting, diarrhea, jitteriness, or sedation and possibly measurement of serum levels to rule out toxicity if there is a concern.

Drug Levels

Bupropion is metabolized to 3 metabolites (hydroxybupropion, erythrohydroxybupropion, threohydroxybupropion) with the antidepressant activity of each considered to be about 50% of bupropion's.[1]

Maternal Levels. A mother who was 14 months postpartum was taking bupropion 100 mg three times daily. Milk samples were obtained before and at 1, 2, 4 and 6 hours after the first daily dose of 100 mg. Peak bupropion levels of 181 and 189 mcg/L occurred at 1 and 2 hours after the dose, respectively. A peak hydroxybupropion level of 132 mcg/L occurred in milk 2 hours after the dose and peak threohydroxybupropion levels of 443 and 442 mcg/L occurred at 1 and 2 hours after the dose, respectively.[2]

Ten women who were an average of 12.5 months postpartum and who did not nurse their infants after the start of bupropion therapy took sustained-release bupropion 150 mg daily for 3 days, then 300 mg daily for 4 days. On the seventh day, breastmilk levels of the drug and metabolites were measured at a median 2.5 hours (range 1 to 12 hours) after the last dose. Breastmilk levels were as follows: bupropion 45.2 mcg/L (range 4 to 168 mcg/L); hydroxybupropion 104.6 mcg/L (range 9 to 242 mcg/L); erythrohydroxybupropion 72.1 mcg/L (range 25.4 to 143 mcg/L); and threohydroxybupropion 459 mcg/L (range 193 to 1052 mcg/L). There was no correlation between the amount of these drugs excreted in milk and maternal or infant age, maternal body mass or breastfeeding frequency prior to the study. The authors estimated that an exclusively breastfed infant would receive an average of 0.2% of the maternal weight-adjusted dosage of bupropion and an average of 2% of the maternal weight-adjusted dosage of bupropion plus metabolites with this maternal dosage regimen.[3]

Four women were taking bupropion SR 150 mg or 300 mg for depression or smoking cessation. Maternal milk and serum concentrations were measured before a dose at steady-state and 2 hours after the dose; 2 women had samples taken on 2 separate occasions. Milk bupropion concentrations standardized to a 150 mg dose averaged 64.1 mcg/L (range <10 to 120 mcg/L); metabolites were not measured. The average infant dose (normalized to a 150 mg maternal dose) was estimated to be 21.5 mcg/day (range 5.1 to 31.1 mcg/day) which averaged 5.1% (range 1.4 to 10.6%) of the maternal weight-adjusted dosage.[4]

The mother of a 6.5-month-old had been taking escitalopram 10 mg daily since birth and had begun extended-release bupropion 150 mg daily 3 weeks earlier. Stored milk samples from between 6 and 6.25 months postpartum contained bupropion in concentrations ranging from 15.8 mcg/L to 24.4 mcg/L and hydroxybupropion in concentrations ranging from 46 mcg/L to 87 mcg/L.[5]

Infant Levels. Bupropion and its metabolites were undetectable (<5 mcg/L for bupropion and <20 mcg/L for its metabolites) in one 14-month-old infant 3.7 hours after nursing and 9.5 hours after the mother's last dose. The infant was nursing twice daily and his mother was taking 100 mg three times a day.[2]

One 15-week postpartum mother was taking immediate-release bupropion 75 mg twice daily. After 2 weeks of therapy and full breastfeeding, serum levels of bupropion (<5 mcg/L) and hydroxybupropion (<100 mcg/L) were undetectable in her infant 2 hours after nursing and after the mother's dose. Another mother who was 29-weeks postpartum was taking sustained-release bupropion 150 mg daily. After 10.5 weeks of therapy and approximately 80% breastfeeding, serum levels of bupropion (<10 mcg/L) and hydroxybupropion (<200 mcg/L) were undetectable in her infant 3.25 hours after nursing and after the mother's dose.[6]

Three breastfed infants ranging in age from 14 to 56 days whose mothers were taking bupropion 150 or 300 mg of bupropion SR had their urine collected 2 hours after a maternal dose; 1 infant had urine collected on 2 occasions. Only one of the infants' urine samples had detectable amounts (>10 mcg/L) of bupropion at 41 mcg/L; metabolites were not measured.[4]

The mother of a 6.5-month-old had been taking escitalopram 10 mg daily since birth and had begun extended-release bupropion 150 mg daily 3 weeks earlier. Her baby was partially breastfed, receiving pumped breastmilk,

formula and solid foods. At 6.5 months of age, after having been breastfed 8 hours after the mother's morning dose of bupropion, the infant was admitted to the emergency department with a seizure and vomiting. The infant's serum at this time contained a detectable, but non-quantifiable level of bupropion (<4.8 mcg/L) and a serum hydroxybupropion level of 11.2 mcg/L. The following morning the infant's serum hydroxybupropion level was 17.1 mcg/L.[5]

Effects in Breastfed Infants

Three partially to fully breastfed infants who were 15 weeks to 14 months of age had no clinically detectable adverse effects during maternal bupropion therapy. Dosages were 100 mg 3 times daily of the immediate-release product in one mother, and 150 mg daily in the other two, one as the SR product and one as the immediate-release product.[2][6]

Two women of 8 in an open-label clinical trial of bupropion SR for postpartum depression breastfed their infants. The median dosage of bupropion SR in the 8 women was 262.5 mg (range 37.5-300 mg). Seven women completed the 8-week study and 1 took the drug for 6 weeks. No specific details were given on the 2 women who breastfed their infants, but neither noted any adverse effects in their infants.[7]

A woman who started taking sustained-release bupropion 150 mg daily fed her 6-month-old infant by breastfeeding and stored breastmilk in addition to solid foods. After 3 days and 2 doses of the drug, the infant had symptoms consistent with a seizure, but no infant serum levels were obtained. The seizure was possibly related to the bupropion in breastmilk.[8]

An uncontrolled online survey compiled data on 930 mothers who nursed their infants while taking an antidepressant. Infant drug discontinuation symptoms (e.g., irritability, low body temperature, uncontrollable crying, eating and sleeping disorders) were reported in about 10% of infants. Mothers who took antidepressants only during breastfeeding were much less likely to notice symptoms of drug discontinuation in their infants than those who took the drug in pregnancy and lactation.[9]

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 bupropion 1 mg daily, flurazepam 15 mg daily, clonazepam 0.25 mg twice daily, and risperidone 0.75 mg daily reported sedation in her breastfed infant.[10]

A 6.5-month-old infant developed severe vomiting and an apparent tonic seizure after being breastfed by her mother. The mother had been taking escitalopram 10 mg daily since birth and had begun extended-release bupropion 150 mg daily 3 weeks earlier. The seizure occurred 8 hours after the mother's morning dose of bupropion. The infant's mother had noted disturbances in sleep behavior, unusual movements, and unresponsiveness followed by sleep on several previous occasions. The baby was partially breastfed, also receiving pumped breastmilk, formula, and solid foods. Breastfeeding was discontinued and the baby was discharged after being asymptomatic for 48 hours. The seizure was probably drug-related, most likely caused by bupropion and hydroxybupropion in breastmilk, but a contribution by escitalopram cannot be ruled out.[5]

A retrospective database study compared women who took bupropion with no SSRI (n = 29) women who took an SSRI but no bupropion (n = 54), and women who took a combination of bupropion and a SSRI (n = 23) during breastfeeding. There were 5 (17%) adverse events reported by the mothers in their infants in the bupropion group, 4 (7%) in the SSRI group and 7 (30%) in the combination group. The proportion of adverse events was significantly higher in the combination group compared to the SSRI group. The reported adverse events included vomiting, diarrhea, jitteriness, sleepiness, hypotony and a seizure (reported in the SSRI group). No seizures were reported in infants exposed to bupropion (alone or with an SSRI) through breastfeeding. There was no statistically significant difference among the groups with regards to average daily weight gain in the first 6 months after birth. therefore seizures are probably not a major concern in these infants.[11]

Effects on Lactation and Breastmilk

A 34-year-old non-pregnant woman diagnosed with depression was started on bupropion 150 mg daily. During the second week of therapy, she presented with galactorrhea and an elevated serum prolactin level of 98 mcg/L. A cranial MRI found no abnormalities. Bupropion was discontinued and the galactorrhea disappeared in 2 days. One week later, her serum prolactin level was 3 mcg/L. Fluoxetine 20 mg daily was started and continued for 4 months with no signs of galactorrhea.[12]

An observational study looked at outcomes of 2859 women who took an antidepressant during the 2 years prior to pregnancy. Compared to women who did not take an antidepressant during pregnancy, mothers who took an antidepressant during all 3 trimesters of pregnancy were 37% less likely to be breastfeeding upon hospital discharge. Mothers who took an antidepressant only during the third trimester were 75% less likely to be breastfeeding at discharge. Those who took an antidepressant only during the first and second trimesters did not have a reduced likelihood of breastfeeding at discharge.[13] The antidepressants used by the mothers were not specified.

A retrospective cohort study of hospital electronic medical records from 2001 to 2008 compared women who had been dispensed an antidepressant during late gestation (n = 575) to those who had a psychiatric illness but did not receive an antidepressant (n = 1552) and mothers who did not have a psychiatric diagnosis (n = 30,535). Women who received an antidepressant were 37% less likely to be breastfeeding at discharge than women without a psychiatric diagnosis, but no less likely to be breastfeeding than untreated mothers with a psychiatric diagnosis.[14] None of the mothers were taking bupropion.

Alternate Drugs to Consider

Nortriptyline, Paroxetine, Sertraline

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Substance Identification

Substance Name

Bupropion

CAS Registry Number

34911-55-2

Drug Class

Breast Feeding

Lactation

Antidepressive Agents

Antidepressive Agents, Second-Generation

Anti-Obesity Agents