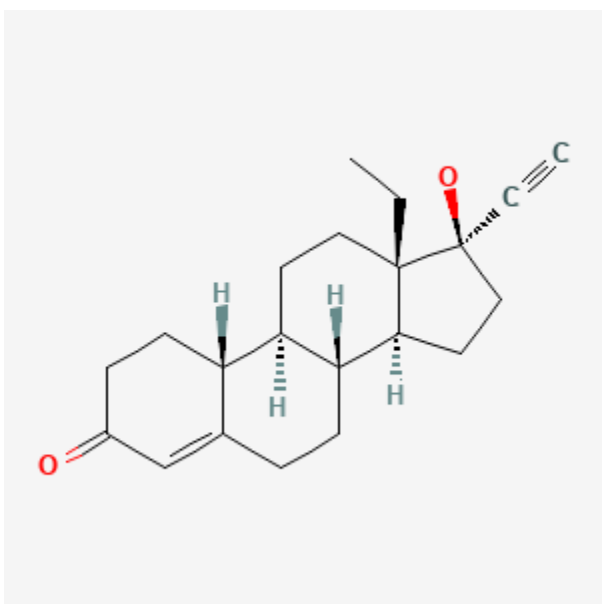




## Oral Levonorgestrel

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CASRN: 797-63-7



## Drug Levels and Effects

### Summary of Use during Lactation

This record contains information specific to oral levonorgestrel used alone for contraception. Those with an interest in a combination oral contraceptive should consult the record entitled, [Contraceptives, Oral, Combined](#).

Although nonhormonal methods are preferred during breastfeeding, progestin-only contraceptives such as levonorgestrel are considered the hormonal contraceptives of choice during lactation. Fair quality evidence indicates that levonorgestrel does not adversely affect the composition of milk, the growth and development of the infant or the milk supply. Expert opinion holds that the risks of progestin-only contraceptive products usually are acceptable for nursing mothers at any time postpartum.[1-3] Some evidence indicates that progestin-only contraceptives may offer protection against bone mineral density loss during lactation, or at least do not

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exacerbate it.[4-6] A large percentage of women who planned to breastfeed discontinued oral progestin-only contraceptives by 3 months postpartum[7] and progestin-only contraceptives often result in rapid repeat pregnancy.[8] Postcoital levonorgestrel appears to have no long-term adverse effects on breastfeeding or the infant.[9-12]

## Drug Levels

Levonorgestrel is a synthetic progestin that is the active isomer of the racemate norgestrel. It is considered to be twice as potent on a weight basis as the racemic mixture.

*Maternal Levels.* Fifteen women who were fully breastfeeding and 8 weeks postpartum were given oral levonorgestrel either alone in a dose of 30 mcg daily or in an estrogen-containing oral contraceptive in a dose of 150 mcg or 250 mcg daily. Five women received each dose for 10 days before breastmilk sample collection. With the 30 mcg dose, the drug was undetectable in all of the women in prenursing milk (<0.05 mcg/L) or postnursing milk (<0.1 mcg/L) at 3 to 23 hours after the dose. With the 150 mcg dose, the highest levels in milk were found 3 hours after the dose with foremilk and hindmilk levels of 0.34 and 0.54 mcg/L, respectively; levels decreased to 0.11 and 0.17 mcg/L, respectively, at 23 hours after the dose. With the 250 mcg dose, the highest levels in milk were found 3 hours after the dose with foremilk and hindmilk levels of 0.51 and 1.05 mcg/L, respectively; levels decreased to 0.22 and 0.38 mcg/L, respectively, at 23 hours after the dose. The authors estimated that fully breastfed infants would receive 0.4 to 0.5 mcg daily in breastmilk, or about 0.1% of the total (not weight-adjusted) maternal dose.[13]

Two women with well-established lactation (exact time postpartum not stated) were given an oral contraceptive containing 150 mcg of levonorgestrel daily. Each had breastmilk levels measured on 2 occasions 10 to 12 hours after a dose between days 6 and 20 of use. The average of their levonorgestrel milk levels was 0.18 mcg/L (range 0.135 to 0.223 mcg/L).[14]

Milk levonorgestrel levels were measured in 4 women after daily ingestion of oral levonorgestrel 50 or 150 mcg started after 3 months postpartum. Peak milk levonorgestrel levels occurred between 1 and 3 hours and were in the ranges of 0.06 to 0.2 mcg/L after the 50 mcg dose and 0.35 to 0.45 mcg/L after the 150 mcg dose. After the 50 mcg dose, milk levels dropped to undetectable (<0.05 mcg/L) by 4 hours after the dose. After the 150 mcg dose, milk levels dropped to about 0.35 mcg/L at 4 hours after the dose and remained there for the next 2 hours.[15]

At 6 to 20 weeks postpartum, 10 women received single tablets containing 30 mcg of levonorgestrel and another 15 women received a single tablet of a combination oral contraceptive containing 250 mcg of levonorgestrel. At 2 to 2.5 hours after the dose, a foremilk sample was taken. The mothers breastfed their infants and then a hindmilk sample was taken. The 2 samples were pooled for assay. After the 30 mcg dose, milk levels averaged 0.05 mcg/L (range 0.03 to 0.076 mcg/L); after the 250 mcg dose, milk levels averaged 0.64 mcg/L (range 0.3 to 1.3 mcg/L). [16]

Twelve breastfeeding women averaging 11.1 weeks postpartum (range 6 and 12 weeks) received a single dose of 1.5 mg of levonorgestrel orally. Blood and milk samples were obtained over the next 72 hours. Peak milk levels of levonorgestrel occurred 3.9 hours after the dose; milk levels fell with a mean half-life in milk of 26 hours. The mean concentration in milk was 1.7 mcg/L during the first day, 0.4 mcg/L the second day and 0.2 mcg/L on the third day after the dose. The authors estimated that a fully breastfed infant would receive 1.6 mcg of levonorgestrel in the first 24 hours, 0.3 mcg in the second 24 hours, and 0.2 mcg in the third 24 hours after the dose.[17]

*Infant Levels.* Two 8-week old infants whose mothers were taking a combination oral contraceptive containing 250 mcg of levonorgestrel had plasma levels measured 5 hours after the maternal dose and 2 hours after nursing (i.e., nursed at the time of peak milk level). Plasma levels were 0.058 and 0.115 mcg/L in the 2 infants. A third infant whose mother was taking 30 mcg daily had undetectable (<0.005 mcg/L) plasma levonorgestrel. The

authors concluded that these results indicate that the infants are able to metabolize levonorgestrel and that no accumulation occurs in infant plasma.[13]

At 6 to 20 weeks postpartum, 10 women received single tablets containing 30 mcg of levonorgestrel and another 15 women received a single tablet of a combination oral contraceptive containing 250 mcg of levonorgestrel. At 2 to 2.5 hours after the dose, the mothers breastfed their infants; infant serum samples were taken 1.5 to 2 hours later at about 4 hours after the maternal dose. Infant serum levels after the 30 and 250 mcg doses averaged 0.019 and 0.078 mcg/L, respectively. These levels were 2% and 1%, respectively, of peak maternal serum levels drawn at 2 to 2.5 hours after the dose.[16]

Thirty mothers received 30 mcg oral levonorgestrel tablets daily for 5 weeks. Ten began at 4 weeks postpartum, 10 began at 12 weeks postpartum and 10 began at 24 weeks postpartum. Because of assay and serum sample size limitations, serum samples were obtained from some of the breastfed infants during the first and fifth weeks of maternal therapy as representative of the entire group. Based on infant serum levels, the authors concluded that absorption of the drug was not great until 12 weeks postpartum and metabolism was not well developed until 24 weeks postpartum.[18] The unusual and incomplete blood sampling scheme casts some doubt on the results of this study.

## Effects in Breastfed Infants

One study found serum thyroid stimulating hormone levels to be lower in the infants exposed to levonorgestrel than in control infants.[19]

A nonrandomized trial compared 250 breastfed infants whose mothers received 30 mcg daily of oral levonorgestrel initiated 7 days postpartum to 250 infants whose mothers received nonhormonal contraception. No differences in height and weight gain were seen during the 9-month study period between the 2 groups.[20]

Multicenter, nonrandomized studies followed infants whose mothers received levonorgestrel contraception during breastfeeding, either as oral tablets of 37.5 mcg daily (n = 246) or as Norplant (n = 453). No adverse effects on infant growth through the first year were found in comparison to standard measurements.[21,22]

In a cohort study of 71 nursing women who took levonorgestrel as a postcoital contraceptive, none noticed any adverse effect in their infants.[9]

In a cohort study, breastfed infants of women (n = 100) who used at least one dose of levonorgestrel as a postcoital contraceptive in addition to the lactational-amenorrhea method (LAM) of birth control were compared to infants whose mothers used LAM only (n = 100). No statistically significant differences were found between the groups in weight, length, head circumference, chest circumference, and mid-arm circumference at 3 and 6 months postpartum, nor in the Denver Developmental Screening Test results at 6 months postpartum.[12]

## Effects on Lactation and Breastmilk

Among a cohort study of 71 women who took levonorgestrel as a postcoital contraceptive during nursing, none reported any obvious decrease in milk supply after the drug was used.[9]

A study of 1158 postpartum randomized women using the lactational amenorrhea method (LAM) for birth control randomized to be given levonorgestrel as a postcoital contraceptive or given nothing. No difference in the duration of breastfeeding was found between women who used the levonorgestrel and those who did not. [10]

In a nonrandomized, nonblinded study comparing women who were breastfeeding at discharge, 102 postpartum women received depot medroxyprogesterone acetate (dosage not stated) in the early postpartum period (average 51.9 hours postpartum; range 6.25 to 132 hours), 181 received another progestin-only contraceptive and 138

used nonhormonal contraception. No differences in breastfeeding rates were seen at 2 and 6 weeks, but women receiving any hormonal contraceptive were breastfeeding at a lower rate (72.1% vs 77.6%) at 4 weeks postpartum. The authors concluded that progestin-only contraception initiated in the early postpartum period had no adverse effects on breastfeeding rates.[23]

A study analyzed data from a prospective cohort study of U.S. women from May 2005 through June 2007. Women were followed from the third trimester of pregnancy throughout the first year postpartum. Data from the subset of women who professed that intended to breastfeed for 3 months or longer postpartum during their third trimester of pregnancy and who were using a contraceptive at 3 months postpartum were analyzed (n = 1349). Women who intended to breastfeed for at least 4 months and were taking a progestin-only oral contraceptive, such as levonorgestrel, were 3.15 times more likely to be breastfeeding (exclusive or nonexclusive) at 4 months than women who used a nonhormonal contraceptive. Women who said they would breastfeed for 3 to 4 months had 4-month breastfeeding rates equivalent to those using a nonhormonal contraceptive. These rates were much higher than those of women who were taking an estrogen-containing, combined oral contraceptive.[24]

In a cohort study, women (n = 100) who used at least one dose of levonorgestrel as a postcoital contraceptive in addition to the lactational-amenorrhea method (LAM) of birth control were compared to mothers used LAM only (n = 100). No difference was found in the mothers' subjective opinions of their milk supplies.[12]

## Alternate Drugs to Consider

Etonogestrel, Intrauterine Copper Contraceptive, Medroxyprogesterone Acetate, Norethindrone

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## Substance Identification

### Substance Name

Oral Levonorgestrel

### CAS Registry Number

797-63-7

### Drug Class

Breast Feeding

Lactation

Milk, Human

Contraceptive Agents, Female

Contraceptives, Oral, Synthetic

Contraceptives, Postcoital