

PAROXETINE

Trade: Paxil

Can/Aus/UK: Paxil , Aropax 20 , Seroxat

Uses: Antidepressant, serotonin reuptake inhibitor

LRC: L2

AAP: Drugs whose effect on nursing infants is unknown but may be of concern

Paroxetine is a typical serotonin reuptake inhibitor. Although it undergoes hepatic metabolism, the metabolites are not active. Paroxetine is exceedingly lipophilic and distributes throughout the body with only 1% remaining in plasma. In one case report of a mother receiving 20 mg/day paroxetine at steady state[1], the breastmilk level at peak (4 hours) was 7.6 $\mu\text{g/L}$. While the maternal paroxetine dose was 333 $\mu\text{g/kg}$, the maximum daily dose to the infant was estimated at 1.14 $\mu\text{g/kg}$ or 0.34% of the maternal dose. In two studies of 6 and 4 nursing mothers respectively[2], the mean dose of paroxetine received by the infants in the first study was 1.13% (range 0.5-1.7) of the weight adjusted maternal dose. The mean M/P (AUC) was 0.39 (range 0.32-0.51) while the predicted M/P was 0.22. In the second study, the mean dose of paroxetine received by the infants was 1.25% (range 0.38-2.24%) of the weight adjusted maternal dose with a mean M/P of 0.96 (range 0.31-3.33). The drug was not detected in the plasma of 7 of the 8 infants studied and was detected (<4 mg/L) in only one infant. No adverse effects were observed in any of the infants. In a recent study of 16 mothers by Stowe, paroxetine levels in milk were low and varied according to maternal dose.[3] Milk/plasma ratios varied from 0.056 to 1.3. Milk levels ranged from approximately 17 $\mu\text{g/L}$, 45 $\mu\text{g/L}$, 70 $\mu\text{g/L}$, 92 $\mu\text{g/L}$, and 101 $\mu\text{g/L}$ in mothers receiving a dose of 10, 20, 30, 40, and 50 mg/day respectively. Levels of paroxetine were below the limit of detection (<2 ng/mL) in all 16 infants. In a study of 6 women receiving 20-40 mg/day, the milk/plasma ratio ranged from 0.39 to 1.11 but averaged 0.69.[4] The average estimated dose to the infants ranged from 0.7 to 2.9% of the weight-adjusted maternal dose. In a seventh patient, and based on area-under-the-curve data, the milk/plasma ratio was 0.69 at a dose of 20 mg and 0.72 at a dose of 40 mg/day. The estimated dose to the infant was 1.0% and 2.0% of the weight-adjusted maternal dose at 20 and 40 mg respectively. Paroxetine levels in milk averaged 44.3 and 78.5 $\mu\text{g/L}$ over 6 hours following 20 and 40 mg doses respectively. No adverse reactions or unusual behaviors were noted in any of the infants. In another study of 24 breastfeeding mothers who received an average dose of 17.6 mg/d (range 10-40 mg/d) the average level of paroxetine in maternal serum and milk was 45.2 ng/mL and 19.2 ng/mL respectively.[5] The average milk/plasma ratio was 0.53. The authors estimated the average infant dose to be 2.88 $\mu\text{g/kg/d}$ or 2.88% of the weight-adjusted maternal dose. All infant serum levels were below the limit of detection. Yet another study of 16 mothers taking an average of 18.75 mg/day showed that paroxetine was undetectable in any of the breastfeeding infants exposed to paroxetine.[8] A pooled analysis of 68 breastfeeding mothers taking between 10-50 mg/day reported breastmilk levels between 0-153 $\mu\text{g/mL}$, with an average of 28 $\mu\text{g/mL}$. No untoward effects were noted in any of these infants exposed to paroxetine through breastmilk. One infant did experience lethargy and poor weight gain, but this infant had prenatal exposure.[9] These studies generally conclude that paroxetine can be considered relatively 'safe' for breastfeeding infants as the absolute dose transferred is quite low. Plasma levels in the infant were generally undetectable. Recent data suggests that a neonatal withdrawal syndrome may occur in newborns exposed in utero to paroxetine[6,10] although there is significant difficulty in differentiating between withdrawal and toxicity.[7] Symptoms include jitteriness, vomiting, irritability, hypoglycemia, and necrotizing enterocolitis. Suicide ideation and withdrawal symptoms seem worse with this product and it should not be used in adolescent patients due to the risk of suicide. In addition, the Swedish birth registries have found that pregnant women who consumed Paroxetine were 1.5-2.0 times more likely to give birth to a baby with severe heart defects. Paroxetine is no longer recommended for use in pregnancy. While all of these complications may arise in pregnancy and in adolescents, paroxetine is still a suitable SSRI for breastfeeding women simply because the clinical dose consumed by the infant via breastmilk is exceedingly low. This said, it is still probably smart to use sertraline or another SSRI at this time.

Pregnancy Risk

Category:

D

Lactation Risk

Category:

L2

Adult Concerns: Sedation, headache, dry mouth, dizziness, nausea, insomnia, constipation, seizures. Use in children and adolescents suggests increased risk of suicide. New data may suggest an increased risk of congenital malformations if

this product is used during the first trimester. Some caution is recommended.

Pediatric Concerns: Numerous studies suggest minimal to no effect on breastfed infants. A neonatal withdrawal effect (early postnatally) may following in utero exposure. Most studies show minimal to no plasma levels in breastfed infants. Severe heart defects have been reported in infants exposed in utero to paroxetine.

Drug Interactions: Decreased effect with phenobarbital and phenytoin. Increased toxicity with alcohol, cimetidine, MAO inhibitors (serotonergic syndrome). Increased effect with fluoxetine, tricyclic antidepressants, sertraline, phenothiazines, warfarin.

Theoretic Infant Dose: 15.15 ug/Kg/Day

Relative Infant Dose: 2.1%

Adult Dose: 20-50 mg daily.

Alternatives: Sertraline

T_{1/2} = 21 hours	M/P = 0.056-1.3
PHL =	PB = 95 %
T_{max} = 5-8 hours	Oral = Complete
MW = 329	pKa =
Vd = 3-28	

References:

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8. Hendrick V, Fukuchi A, Altshuler L, Widawski M, Wertheimer A, Brunhuber MV. Use of sertraline, paroxetine and fluvoxamine by nursing women. *Br J Psychiatry* 2001; 179:163-166.
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