



For more information about the Organization of Teratology Information Specialists or to find a service in your area, call (866) 626-6847 or visit us online at: www.OTISpregnancy.org.

Fluoxetine (Prozac®) and Pregnancy

This sheet talks about the risks that exposure to fluoxetine can have during pregnancy. With each pregnancy, all women have a 3% to 5% chance of having a baby with a birth defect. This information should not take the place of medical care and advice from your health care provider.

What is fluoxetine?

Fluoxetine is a medication commonly used to treat depression. Fluoxetine is also used to treat obsessive-compulsive disorders, eating disorders (bulimia nervosa), and Premenstrual Dysphoric Disorder (PMDD). Brand names for fluoxetine are Prozac® and Sarafem®. Fluoxetine belongs to the class of antidepressants known as selective serotonin reuptake inhibitors (SSRIs).

I am taking fluoxetine, but I would like to stop taking it before becoming pregnant. How long does fluoxetine stay in your body?

The liver breaks down fluoxetine. Each individual's ability to break down the medication is different. On average, fluoxetine has a half-life (time it takes to eliminate one half of the drug from the body) of two to three days, but may be found in your system for several weeks after you stop taking it. Studies have shown that the levels are fairly low after one to two weeks. An active metabolite of fluoxetine called norfluoxetine has a half-life of seven to sixteen days, but can remain in the body for a much longer time period. Please talk to your doctor before you stop taking fluoxetine. The benefits of taking the medication for your specific situation, and any possible adverse outcomes of not taking it, should be discussed with your doctor.

Can taking fluoxetine make it more difficult for me to become pregnant?

Animal studies have not shown any effect on fertility with the use of fluoxetine. There have been reports of lack of orgasm or delayed orgasm in women and men who take fluoxetine. There have also been reports of women who have had infertility problems, and who developed regular periods and ovulation after being treated with fluoxetine. Further studies are needed to determine fluoxetine's effect on fertility.

Can taking fluoxetine during my pregnancy cause birth defects?

Fluoxetine is one of the better-studied antidepressants in pregnancy. There are reports of nearly 2,000 pregnancies exposed to fluoxetine during the first trimester. No study found an increased risk for major

structural birth defects (those requiring surgery or reducing function). One study has identified an increased rate of three or more minor birth defects (those not medically or functionally significant) among children exposed to fluoxetine in the first trimester. When three or more minor birth defects are seen together, a major birth defect (including learning problems) occurs more often, although this was not seen in the fluoxetine study.

I need to take fluoxetine throughout my entire pregnancy. Will it cause withdrawal symptoms in my baby?

If you are taking fluoxetine during the third trimester until the time of delivery, your baby may experience some complications for the first few days of life requiring extra care. Symptoms of withdrawal such as problems breathing, jitteriness, increased muscle tone, irritability, altered sleep patterns, tremors and difficulty eating may occur. Your baby may need to stay in a special care nursery for several days until the withdrawal symptoms go away. While these problems occur at all doses of fluoxetine, they may occur more often with higher doses of fluoxetine.

Are there any other problems fluoxetine can cause when used in the third trimester?

Further research is needed to answer this question. One study found that third trimester use of fluoxetine compared to first trimester use increased the chances for premature delivery, higher rates of care in the newborn special-care nursery, and lower birth weight and length. In this study, women who stopped using fluoxetine by the end of the second trimester did not seem to be at an increased risk for these problems. Another study did not confirm these findings. Studies have shown that prematurity and other pregnancy complications may be related to the maternal depressive disorder itself rather than to the medication exposure.

One study showed that babies whose mothers take SSRIs like fluoxetine during the third trimester may be at an increased risk for pulmonary hypertension, a serious lung problem at birth. You should inform your obstetrician and your baby's pediatrician that you are taking fluoxetine so that any extra care can be readily provided.

Should I stop taking fluoxetine before the third trimester?

It is important to discuss with your doctor the risks associated with taking fluoxetine during pregnancy as compared to the risks of stopping fluoxetine. Studies have shown that when depression is left untreated during pregnancy, there may be increased risks for miscarriage, preeclampsia, preterm delivery, low birth weight, and a number of other harmful effects on the mother and the baby. Only you and your doctor know your medical history and can best determine whether or not you should stop taking fluoxetine during pregnancy. Some women can gradually wean off of fluoxetine before 28 weeks; for other women, the effects from stopping fluoxetine may be more harmful than the possible risks to the baby if they stay on fluoxetine. The benefits of taking fluoxetine for your specific situation and the potential risks to the baby should be considered before a decision is made.

Will taking fluoxetine have any effect on my baby's behavior and development?

Studies have begun to look at the possible long-term effects on infants exposed to fluoxetine during pregnancy. Fluoxetine affects the mother by changing chemical levels in the brain. These changes could also have an effect on fetal brain development. Two studies examining development in children at 16 months to 7 years of age, did not find differences between exposed and unexposed children. These studies are reassuring; however, more studies are needed before we can be certain of the effects on the fetal brain.

Can I take fluoxetine while breastfeeding?

Fluoxetine and its breakdown product, norfluoxetine, are found in breast milk in amounts estimated to be 10 to 20 percent of the amount of the drug in the mother's blood.

There are several small studies and case reports regarding the use of fluoxetine during breastfeeding. Most reports found no problems in breastfed babies. However, in a small number of cases, irritability, vomiting, diarrhea, and/or decreased sleep were seen in newborns. These symptoms were thought to be due to the mother's use of fluoxetine while breastfeeding. One study noted a slight decrease in weight gain; however, this decrease would likely only be significant if the infant's weight gain were already of concern. One small study showed that babies whose mothers took fluoxetine while breastfeeding scored no differently on neurodevelopmental tests than other babies. More studies need to be done to determine if breastfeeding while taking fluoxetine causes any long-term effects on learning or behavior.

Other antidepressants like paroxetine or sertraline get into breast milk in lower amounts than fluoxetine and therefore may be better to use while breastfeeding. It is important to discuss the risks and benefits of taking fluoxetine while breastfeeding with your health care provider.

OTIS is currently conducting a study looking at women who take antidepressants during pregnancy and choose to continue or discontinue their medication. If you are interested in taking part in this study, please call 1-877-875-7333.

June 2006.

Copyright by OTIS.

Reproduced by permission.



References:

- Addis A and Koren G. 1997. Safety of fluoxetine during the first trimester of pregnancy: meta-analytical review of epidemiological data. *Teratology* [abstract]. 55:37.
- Bonari L, et al. 2004. Perinatal risks of untreated depression during pregnancy. *Can J Psychiatry* 49(11):726-735.
- Burch KJ and Wells BG. 1992. Fluoxetine/Norfluoxetine concentrations in human milk. *Pediatrics* 89:676-677.
- Chambers C, et al. 1996. Outcomes in pregnant women taking fluoxetine. *NEJM* 335(14):1010-1015.
- Chambers CD, et al. 1999. Weight gain in infants breastfed by mothers who take fluoxetine. *Pediatrics* 104(5):11-15.
- Chambers C, et al. 2006. Selective serotonin-reuptake inhibitors and risk of persistent pulmonary hypertension of the newborn. *N Engl J Med* 354(6):579-587.
- Goldstein DJ, et al. 1997. Effects of first-trimester fluoxetine exposure on the newborn. *Obstet Gynecol* 89:713-718.
- Hale, TW. 2004. *Medications and Mother's Milk*, Eleventh Edition. Pharmasoft Medical Publishing: Amarillo, TX.
- Isenberg KE. 1990. Excretion of fluoxetine in human breast milk. *J Clin Psychiatry* 51:169.
- Kristensen JH, et al. 1999. Distribution and excretion of fluoxetine and norfluoxetine in human milk. *Br J Clin Pharmacol* 48(4):521-527.
- Lester BM, et al. 1993. Possible association between fluoxetine hydrochloride and colic in an infant. *J Am Acad Child Adolesc Psychiatry* 6:1253-1255.
- Levinson-Castiel R, et al. 2006. Neonatal abstinence syndrome after in utero exposure to selective serotonin reuptake inhibitors in term infants. *Arch Pediatr Adolesc Med* 160:173-176
- Mattson SN, et al. 1999. Neurobehavioral follow-up of children prenatally exposed to fluoxetine [abstract]. *Teratology* 59:376.
- Nulman I, et al. 1997. Neurodevelopment of children exposed in utero to antidepressant drugs. *NEJM* 336(4):258-262.
- Pastuszak A, et al. 1993. Pregnancy outcome following first trimester exposure to fluoxetine (Prozac). *JAMA* 269(17):2246-2248.
- Sanz E, et al. 2005. Selective serotonin reuptake inhibitors in pregnant women and neonatal withdrawal syndrome: a database analysis. *Lancet* 365:482-487.
- Strain, SL. 1994. Fluoxetine-initiated ovulatory cycles in two clomiphene-resistant women. *J Am J Psychiatry* 151(4):620.
- Taddio A, Ito S, and Koren G. 1996. Excretion of fluoxetine and its metabolite, norfluoxetine, in human breastmilk. *J Clin Pharmacol* 36(1):42-47.
- Warnock, JK, et al. 1995. Onset of menses in two adult patients with Prader-Willi syndrome treated with fluoxetine. *Psychopharmacology Bulletin* 31(2):239-42.
- Yoshida, K, et al. 1998. Fluoxetine in breastmilk and developmental outcome of breastfed infants. *Br J Psychiatry* 172:175-178.

If you have questions about the information on this fact sheet or other exposures during pregnancy, call OTIS at 1-866-626-6847.