

INFORMATION FOR CLINICIANS ON ANTIDEPRESSANTS DURING PREGNANCY & BREAST FEEDING – SEPTEMBER 2010

This chart is produced by the University of Illinois at Chicago (UIC) Perinatal Mental Health Project as a summary of research on antidepressants in human pregnancy and breastfeeding.

Sources of data:

▪ **Pregnancy data:** Data summarized here are from controlled studies in human pregnancy. The Food and Drug Administration (FDA) Pregnancy Risk Categories, as found in the Physicians' Desk Reference¹, are based on both animal and human studies. No antidepressants are yet specifically FDA-approved for use during pregnancy. All antidepressants cross the placenta, so there are none that are 'Category A' ('no risk'). Medications that are non-teratogenic in animal studies but have never been studied in humans are classified as 'Category B'. Since teratogenicity does not generalize across species, a 'Category B' classification does not imply greater safety in human pregnancy than a 'Category C' or 'D' classification. Several medications have been shifted from 'Category B' to 'Category C' or 'Category D' as their risks became better known.

▪ **Breastfeeding data:** Data about antidepressant effects on breastfeeding babies are predominantly from case reports and case series. For medications with no reported side effects, that does not necessarily mean the medication is "safe"; often it means there are few case reports available. Reported percents of maternal dose to breastfeeding babies are weight-adjusted estimates that include the agent and its active metabolite(s).

*Specific references are available on request.

General guideline:

▪ Optimal treatment is based on individual patient characteristics and clinical judgment, especially weighing medication risks against risks of untreated illness. Risks of untreated perinatal depression may include preterm birth and other obstetric complications, increased risk of infection and difficult temperament in the infant, impaired parenting, and psychological effects such as impaired cognitive development, emotional and behavioral problems and increased reactivity to stress in children.

Antidepressants as a group may be associated with following risks:

- Increased risk of preterm birth and lower gestational age at birth, but without adverse effects on birth weight or Apgar scores
- Increased risk of miscarriage, but rates within norms of the general population.

SSRI antidepressants as a group (citalopram, escitalopram, fluoxetine, paroxetine, sertraline) may be associated with the following risks:

- Neonatal side effects, including respiratory distress, excessive crying, changes in sleep and behavioral state, difficulty sleeping, increased or decreased muscle tone, hyperreflexia, seizures, and/or cardiac arrhythmias.
- Most studies have found no increased risk of gestational hypertension. One retrospective study² found a possible increased risk of gestational Hypertension.
- Possible increased risk of persistent pulmonary hypertension in the newborn with exposure later in pregnancy.
- Most studies have found no increased risk of birth defects. One retrospective study³ found a possible increased risk of anencephaly, craniosynostosis, and omphalocele; another⁴ found an increased risk of anomalies in general, although absolute risks were small.
- Delay in lactation, however the delay was only for 14 hours on average.

For questions, references, or permission to reprint, call the UIC Perinatal Mental Health Project at 1-800-573-6121

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Antidepressant	Advantages During Pregnancy	Teratogenicity	Other Disadvantages During Pregnancy	Estimated % of Maternal Dose to Breastfeeding Baby	Reported Side Effects to Breastfeeding Babies
Bupropion	<input type="checkbox"/> Fewer sexual side effects <input type="checkbox"/> Less risk of weight gain <input type="checkbox"/> Helps with smoking cessation	<u>Morphologic</u> – limited evidence of cardiac malformations <u>Behavioral</u> – limited evidence of increased risk of ADHD	<input type="checkbox"/> Limited data available <input type="checkbox"/> Lowers seizure threshold <input type="checkbox"/> Can cause insomnia <input type="checkbox"/> May increase risk of miscarriage	2.0%	Seizures
Citalopram	<input type="checkbox"/> Few interactions with other medications	<u>Morphologic</u> – none found <u>Behavioral</u> – none found	<input type="checkbox"/> Limited data available	0.7% -9.0%	Uneasy sleep, drowsiness, irritability, weight loss
Desipramine	<input type="checkbox"/> More studies in human pregnancy, including neurodevelopmental follow-up	<u>Morphologic</u> – none found <u>Behavioral</u> – none found	<input type="checkbox"/> Maternal side effects additive to pregnancy effects (sedation, constipation, tachycardia) <input type="checkbox"/> Orthostatic hypotension, risking decreased placental perfusion <input type="checkbox"/> Fetal and neonatal side effects: tachycardia, urinary retention	1.0%	None
Duloxetine	<input type="checkbox"/> Also treats diabetic peripheral neuropathic pain	<u>Morphologic</u> – unknown <u>Behavioral</u> – unknown	<input type="checkbox"/> No systematic studies in human pregnancy	0.1%	Unknown
Escitalopram	<input type="checkbox"/> Few interactions with other medications	<u>Morphologic</u> – unknown <u>Behavioral</u> – unknown	<input type="checkbox"/> No systematic studies in human pregnancy	3.9% - 7.9%	Enterocolitis
Fluoxetine	<input type="checkbox"/> More studies in human pregnancy, including meta-analysis and neurodevelopmental follow-up	<u>Morphologic</u> – unlikely increased risk of cardiovascular malformations* <u>Behavioral</u> – none found	<input type="checkbox"/> More reports of neonatal side effects than most other antidepressants	1.2% - 12.0%	Excessive crying, irritability, vomiting, watery stools, difficulty sleeping, tremor, somnolence, hypotonia, decreased weight gain, hyperglycemia
Mirtazapine	<input type="checkbox"/> Fewer sexual side effects <input type="checkbox"/> Helps restore appetite in women who are not gaining weight <input type="checkbox"/> Less likely to exacerbate nausea and vomiting	<u>Morphologic</u> – none found <u>Behavioral</u> – unknown	<input type="checkbox"/> Limited data available <input type="checkbox"/> Can cause excessive weight gain <input type="checkbox"/> Tends to be sedating <input type="checkbox"/> May increase risk of preterm birth	0.6% - 2.8%	None
Nortriptyline	<input type="checkbox"/> More studies in human pregnancy, including neurodevelopmental follow-up	<u>Morphologic</u> – none found <u>Behavioral</u> – none found	<input type="checkbox"/> Maternal side effects additive to pregnancy effects (sedation, constipation, tachycardia) <input type="checkbox"/> Orthostatic hypotension, risking decreased placental perfusion <input type="checkbox"/> Fetal and neonatal side effects: tachycardia, urinary retention	1.3%	None

Paroxetine	<input type="checkbox"/> None specific, but may be optimal for some individual patients	<u>Morphologic</u> – Possible increased risk of cardio vascular malformations <u>Behavioral</u> – unknown	<input type="checkbox"/> More reports of neonatal side effects than most other antidepressants ACOG recommends fetal echo for all exposed fetuses	0.1% -4.3%	Irritability, sleepiness, constipation, SIADH
Sertraline	<input type="checkbox"/> Relatively well-studied in human pregnancy <input type="checkbox"/> Fewer reports of neonatal side effects than other antidepressants	<u>Morphologic</u> – unlikely increased risk of omphalocele and septal defects* <u>Behavioral</u> – none found	<input type="checkbox"/> None specific	0.4% -2.3%	Benign sleep myoclonus, agitation
Venlafaxine	<input type="checkbox"/> None specific, but may be optimal for some individual patients	<u>Morphologic</u> – none found <u>Behavioral</u> – unknown	<input type="checkbox"/> Limited data available	5.2% -7.6%	Decreased weight gain
Desvenlafaxine	<input type="checkbox"/> None specific, but may be optimal for some individual patients	<u>Morphologic</u> – unknown <u>Behavioral</u> – unknown	<input type="checkbox"/> No systematic studies in human pregnancy	Unknown	Unknown

* Findings from one study at variance with other data, perhaps due to methodological flaws

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1. Physician’s Desk Reference. Thomson Reuters. Montvale, NJ.
2. Toh et al. Selective serotonin reuptake inhibitor use and risk of gestational hypertension. Am J Psychiatry. 2009 Mar;166(3):320-8.
3. Alwan, S. et al. Use of selective serotonin-reuptake inhibitors in pregnancy and the risk of birth defects. N Engl J Med. 2007 Jun 28; 356(26):2684-92.
4. Wogelius et al. Maternal use of selective serotonin reuptake inhibitors and risk of congenital malformations. Epidemiology. 2006 Nov;17(6):701-4.
5. Suri et al. Effects of Antenatal Depression and Antidepressant treatment on gestational age at birth and risk of preterm birth. Am J Psychiatry. 2007 Aug; 164:1206-1213.
6. Figueroa. Use of antidepressants during pregnancy and risk of Attention-Deficit/Hyperactivity Disorder in the offspring. JDBP. 2010 Oct. Vol 31, No.8.
7. Alwan et al. Maternal use of Bupropion and risk of congenital heart defects. Am J Obstet Gynecol 2010.