WISCONSIN ASSOCIATION for Perinatal Care

ANTIDEPRESSANT MEDICATION CHART

(This chart is intended for clinicians who provide primary care to pregnant and postpartum women)

Data current as of December 2015

Antidepressants	Trade Name	Usual Daily Dose	Benefits	Maternal Risks	Fetal/Neonatal Risks	Breastfeeding: Relative infant dose=(RID)	Breastfeeding: Half-life ($t_{1/2}$)/ metabolites	Breastfeeding: Reported side effects in breastfed infants
DRUG CLASS: Selective Serotonin Reuptake Inhibitors (SSRIs)								
Citalopram	Celexa®	20-40mg	• Few interactions with other medications • No adverse morphologic consequences for infant found	• Side effects include nausea, insomnia, dizziness, and somnolence	• Behavioral consequences for infant unknown • Possible increased risk of growth restriction • Possible increased risk of neural tube defects and cardiac defects (ASD)	3.60%	• 1-2 days • 3 weak metabolites with little activity	• Somnolence • Decreased feeding • Weight loss
Escitalopram	Lexapro®	10-20mg	• Few interactions with other medications • No adverse morphologic consequences for infant found	• Side effects include nausea, insomnia, somnolence, dizziness, fatigue, diarrhea, sexual dysfunction, and dry mouth	• No systematic studies in human pregnancy • Morphologic and behavioral consequences for infant unknown • Possible increased risk of growth restriction	5.2-8%	• 1-2 days (drug and active metabolite)	• Somnolence • Decreased feeding • Weight loss
Fluoxetine	Prozac®	20-80mg	• More studies in human pregnancy, including meta-analysis and neurodevelopmental follow-up • No adverse behavioral consequences for infant found	• Side effects include nausea, drowsiness, and sexual dysfunction • Possible drug interactions	• More reports of neonatal side effects than some other antidepressants • Possible morphological consequences	1.6-14.6%	• Days to weeks (drug and active metabolites) • Serum levels similar to those in adults reported in some symptomatic infants	• Severe colic • Fussiness • Crying
Fluvoxamine	Luvox®	50-300mg	• No adverse morphologic consequences for infant found	• Side effects include nausea, drowsiness, anorexia, anxiety, and sexual dysfunction • Possible drug interactions	• Behavioral consequences for infant unknown	0.3-1.4%	• 12-24 hours • Major metabolite not active	• No reported concerns
Paroxetine	Paxil®	20-60mg	• None--avoid during pregnancy if possible	• May increase risk of miscarriage • Side effects include nausea, drowsiness, fatigue, dizziness, and sexual dysfunction.	• Behavioral consequences for infant unknown • Possible association with cardiovascular malformations in infant	1.2-2.8%	• Hours to days • No active metabolites	• Studies suggest minimal to no effect on breastfed infants
Sertraline	Zoloft®	50-200mg	• Relatively well-studied in human pregnancy • No adverse behavioral consequences for infants found • Fewer reports of neonatal side effects than other antidepressants	• Side effects include nausea, loose stools, tremors, insomnia, and sexual dysfunction • Possible drug interactions	• Possible specific association with cardiac septal defects, omphalocele, and craniosynostosis	0.4-2.2%	• 1-2 days (drug and weakly active metabolite) • Detectable levels in some infants, but no adverse effects	• Studies suggest minimal to no effect on breastfed infants

For additional information contact: Wisconsin Association for Perinatal Care | 211 S. Paterson St., Suite 250 | Madison, WI 53703 | www.perinatalweb.org Email: wapc@perinatalweb.org

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DRUG CLASS: Tricyclic antidepressants (TSAs)								
Amitriptyline	Elavil®	25-300mg	• More studies in human pregnancy, including neurodevelopmental follow-up • No adverse morphologic consequences for infant found • No adverse behavioral consequences for infant found • May be useful if sedation desired	• Side effects include sedation, weight gain, dry mouth, constipation, and orthostatic hypotension--baseline ECG recommended • Possible drug interactions	• Fetal and neonatal side effects include tachycardia and urinary retention	1.9-2.8%	• 1-2 days (drug and active metabolite, nortriptyline)	• No reported adverse events in infants found • Monitor for sedation and poor feeding
Desipramine	Norpramin®	100-300mg	• More studies in human pregnancy, including neurodevelopmental follow-up • No adverse morphologic consequences for infant found • No adverse behavioral consequences for infant found • May be useful if sedation desired	• Side effects include sedation, weight gain, dry mouth, constipation, and orthostatic hypotension--baseline ECG recommended • Possible drug interactions	• Fetal and neonatal side effects include tachycardia and urinary retention	0.2-0.9%	• 1-2 days (drug and active metabolite) • Not detected in infants	• No reported adverse events in infants found
Nortriptyline	Pamelor®	50-150mg	• More studies in human pregnancy, including neurodevelopmental follow-up • No adverse morphologic consequences for infant found • No adverse behavioral consequences for infant found • May be useful if sedation desired	• Side effects include sedation, weight gain, dry mouth, constipation, and orthostatic hypotension--baseline ECG recommended • Possible drug interactions	• Fetal and neonatal side effects include tachycardia and urinary retention	1.7-3.1%	• ≥1 day • No active metabolites	• No reported adverse events in infants found
DRUG CLASS: Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)								
Desvenlafaxine	Pristiq®	50-100mg	• Balanced antidepressant; may be effective when selective agents are not • No adverse morphologic consequences for infant found	• May increase risk of miscarriage • Side effects include hypertension, nausea, sweating, dry mouth, dizziness, insomnia, somnolence, and sexual dysfunction	• No behavioral studies in human pregnancy • Possible neonatal risk of respiratory distress, cyanosis, apnea, seizures, temperature instability, and feeding difficulties	5.9-9.3%	• 10-11 hours • No active metabolites	• Monitor for excessive sedation and adequate weight gain
Duloxetine	Cymbalta®	40-60mg	• Balanced antidepressant; may be effective when selective agents are not • Low cord to maternal serum ratio suggests limited transfer across the placenta	• Side effects include nausea, dry mouth, constipation, diarrhea, vomiting, decreased appetite, fatigue, dizziness, somnolence, tremors, sweating, blurred vision, and insomnia	• No systematic studies in human pregnancy • Morphologic and behavioral consequences for infant not reported	0.10%	• 8-20 hours • No active metabolites	• No reported adverse events in infants found
Venlafaxine	Effexor®	75-375mg	• Balanced antidepressant; may be effective when selective agents are not • No adverse morphologic consequences for infant found	• May increase risk of miscarriage • Side effects include hypertension, nausea, sweating, dry mouth, dizziness, insomnia, somnolence, and sexual dysfunction	• No behavioral studies in human pregnancy • Possible neonatal risk of respiratory distress, cyanosis, apnea, seizures, temperature instability, and feeding difficulties	6.8-8.1%	• Approx 5 hrs (11 hrs for active metabolite, desvenlafaxine)	• Detectable plasma levels in several breastfed infants were not associated with any adverse effects • Monitor for excessive sedation and adequate weight gain

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DRUG CLASS: Other								
Aripiprazole	Abilify®	2-15mg	• No adverse morphologic consequences for infant reported	• Side effects include headache, extrapyramidal reaction, sedation, dizziness, nausea, agitation, insomnia, weight gain	• May increase risk of prematurity and fetal growth restriction	1%	• 3-5 days	• Somnolence
Bupropion	Wellbutrin® Zyban®	300-450mg	• Helps with smoking cessation (never tested in pregnancy)	• May increase risk of miscarriage • Side effects include dizziness, headache, dry mouth, sweating, tremor, agitation, insomnia, and rare seizures • Possible drug interactions	• Behavioral consequences for infant • Possible increased risk of CHD • Possible increased risk of fetal cardiac arrhythmia	0.6-2%	• Approx 1 day • Plasma levels undetectable in breastfed infant	• One reported case of seizure in a 6 month old
Gabapentin	Neurontin®	900-2400mg	• No adverse morphologic consequences for infant reported	• Side effects include somnolence and dizziness	• May increase risk of prematurity and low birth weight	1.3-6.6%	• Approx 14 hrs • Drug excreted unchanged	• Drowsiness • Poor weight gain
Mirtazapine	Remeron®	15-45mg	• No adverse morphologic consequences for infant found • Helps restore appetite in women who are not gaining weight • Less likely to exacerbate nausea and vomiting	• May increase risk of miscarriage • Side effects include somnolence, nausea, weight gain, and dizziness	• Behavioral consequences for infant unknown • May increase risk of preterm birth • Possible hypothermia	1.6-6.3%	• 1-2 days (drug and active metabolite) • Very low plasma level detected in 1 of 3 infants tested	• No adverse effects reported • Observe for sedation
Quetiapine	Seroquel®	100-800mg	• No adverse morphologic consequences for infant reported • Low transplacental passage	• Side effects include drowsiness, headache, weight gain, increased triglycerides and cholesterol, dry mouth • Avoid concomitant use with other drugs that prolong QT interval		<1.0%	• 6-12 hours (drug and active metabolite)	• No adverse effects reported

Breastfeeding and Medications: Maternal Considerations

1. Avoid random switching of medications based on data alone. Choose drugs for which published data is available, rather than those recently introduced.
2. Most drugs are quite safe in breastfeeding mothers.
3. If the Relative Infant Dose (RID) is less than 10%, most medications are relatively safe to use. The RID of the vast majority of drugs is <1%.
4. Choose drugs with a short half-life, high protein binding, low oral availability, or high molecular weight.
5. Medications used in the first 3-4 days postpartum generally produce sub-clinical levels in the infant due to the limited volume of milk.
6. Avoid using medications when possible. Herbal drugs, high dose vitamins, unusual supplements, etc. that are not necessary should be avoided.

Adapted from Hale, T.W. & Rowe, H.E. (2014). *Medications and Mothers' Milk* (16th ed.)

Breastfeeding and Medications: Neonatal Considerations

1. Evaluate the infant for risks: Premature infants and neonates in general are at greater risk than older infants are.
2. Inquire about the infant: Always inquire about the infant's age, size, and stability. This is perhaps the most important criteria to be evaluated prior to using the medication.
4. Infant stability: Unstable infants with poor GI stability may increase the risk of using medications.
5. Pediatric approved drugs: These generally are less hazardous if long-term history of safety is recognized.

Adapted from Hale, T.W. & Rowe, H.E. (2014). *Medications and Mothers' Milk* (16th ed.)

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Notes

(1) Dosage information: www.medscape.com (Accessed December 14, 2015.).

Table based on Wisner, K.L., Parry, B.L., & Piontek, C.M. (2002). Clinical Practice. Postpartum Depression. *New England Journal of Medicine*, 347(3), 194-199 and related articles.

Breastfeeding information from Hale, T.W. & Rowe, H.E. (2014). *Medications and Mothers' Milk* (16th ed.) and Micromedex® Healthcare Series. 1974-2010. Greenwood Village, CO: Thomson Healthcare.

Clinicians may consider initiating treatment with these agents at half of the lowest recommended therapeutic dose. Treatment decisions should be based on patient characteristics and clinical judgment. Recommended dosages can be found in the most recent editions of the *Physician's Desk Reference* and the *Drug Information Handbook*.

(2) Reported side effects in breastfeeding infants are based on case reports and case series.

(3) Medications vary in the amount and quality of data available about effects in human pregnancy. A better-studied medication may have more reported side effects than a less-studied medication because more is known about it, not necessarily because it is riskier.

(4) Data presented here are based on reports from and studies during human pregnancy. The Food and Drug Administration's Pregnancy Risk Categories, as found in the *Physician's Desk Reference*, are based on a combination of animal and human studies.

Comments

This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.

- Risks of antidepressants during pregnancy and lactation must be weighed against the risks of untreated symptoms. Treatment should be individualized.
- Monitor for dose adjustment through pregnancy. The dose of the medication may need to be increased to maintain response.
- All antidepressants, if abruptly discontinued during pregnancy or at the time of birth, can lead to discontinuation side effects. Discontinuation side effects can be minimized by a partial dose taper during the last month of pregnancy, if the patient is asymptomatic, with a return to full dose after delivery to prevent postpartum recurrence.
- If a patient is on other medications, consult with a pharmacist or other appropriate specialists for interaction information.
- See also ACOG Practice Bulletin No. 92: Use of psychiatric medications during pregnancy and lactation. (2008/Reaffirmed 2014) *Obstetrics and Gynecology*, 111(5), 1001-1020.
- As a class, SSRI antidepressants may be associated with an increased risk of miscarriage; gestational age decreased by an average of one week; and increased risk of persistent pulmonary hypertension in the newborn with exposure after 20 weeks gestation.
- For more information on SSRIs and pregnancy, see:

Byatt N et al. (2013). Antidepressant use in pregnancy: a critical review focused on risks and controversies. *Acta Psychiatrica Scandinavica*, 127, 94-114.

Deligiannidis KM et al. (2014). Pharmacotherapy for mood disorders in pregnancy: A review of pharmacokinetic changes and clinical recommendations for therapeutic drug monitoring. *Journal of Clinical Psychopharmacology*, 34(2), 244-255.

Grigoriadis S et al. (2013). Antidepressant exposure during pregnancy and congenital malformations: Is there an association? A systematic review and meta-analysis of the best evidence. *Journal of Clinical Psychiatry*, 74(4), e293-e308.

Huybrechts KF et al. (2014). Antidepressant use in pregnancy and the risk of cardiac defects. *New England Journal of Medicine*, 370(25), 2397-2407.

Reefhuis J et al. (2015). Specific SSRIs and birth defects: bayesian analysis to interpret new data in the context of previous reports. *BMJ*, 350, h3190.

Wemakor A et al. (2015). Selective serotonin reuptake inhibitor antidepressant use in first trimester pregnancy and risk of specific congenital anomalies: a European register-based study. *European Journal of Epidemiolology, 30*(11), 1187-1198.

This chart was compiled by a multidisciplinary work group of leaders in their respective disciplines including OB/GYN, family practice, psychiatry, nursing, genetics, and pharmacy, practicing in Wisconsin and representing WAPC and/or the Wisconsin Section of the American Congress of Obstetricians and Gynecologists.

Updated December 2015

Funded in part by the MCH Title V Services Block Grant through the MCHB/HRSA/U.S. DHHS and the Perinatal Foundation.

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