Treatment decisions during pregnancy should be as collaborative as possible between health care providers and patients, and take into account the individualized risks and benefits of treatment options. In addition to the reproductive safety of psychopharmacologic treatments, the past course of illness and treatment responses should be strongly considered. Specifically, the potential risks of medications must be assessed along with the risks of untreated psychiatric disorders across pregnancy and the postpartum. Decision making around treatments for psychiatric disorders in pregnancy requires consideration of what is known about the medications in pregnancy, the course and severity of the woman's disorder being treated, and exposures to the baby of both untreated maternal illness and medication. Psychiatric mood and anxiety symptom burden during pregnancy is a major risk factor for serious postpartum illness.

Women who do not desire a pregnancy should be counseled about their family planning options; highly effective methods such as the intrauterine device and contraceptive implant may be of particular benefit to women on teratogenic medications who are not trying to get pregnant. However, unplanned pregnancies are common, and the reproductive safety of treatments should be kept in consideration when treating women of reproductive potential. General recommendations for healthy pregnancies should be included in the treatment plan, as some elements are particularly relevant for individuals with mood disorders. These include getting regular exercise, abstaining from tobacco, alcohol, and illicit substances, and maintaining a healthy diet and weight.

For specific recommendations on the treatment of mood disorders in pregnancy, visit ***floridamedicaidmentalhealth.org***.

Treatment Goals and Management

- Optimal functioning of the mother, aiming for remission of illness, with a goal of achieving or maintaining euthymia, and relapse prevention and associated risks of morbidity and mortality, including risk of suicide.
- Managing risk of medication exposure to the infant.
- Individualized consideration of risk/benefit ratio for treatment options, realizing that untreated illness itself poses risks to the mother and baby.
- Wherever possible, multidisciplinary management involving the patient's obstetrician, mental health clinician, primary health care provider, and pediatrician is recommended to facilitate care.
- Prioritize medications that have worked for the mother in the past.
- Minimize polypharmacy, if possible, as multiple exposures may increase risk to the fetus.
- Maximize non-pharmacologic therapies if effective, either without pharmacotherapy or to augment pharmacotherapy (Psychotherapy is the most important effective non-medication treatment for mood disorders during pregnancy and the postpartum)

Table 15.

The Safety of Psychotherapeutic Medication in Pregnancy and Lactation			
Safety and Management Issues*			
Medication Class	**Pregnancy**	**Birth Defects and Other Neonatal Outcomes**	**Lactation****
Benzodiazepines	Ultrasonography for facial morphology	Possible increased incidence of cleft lip or palate Floppy infant syndrome Withdrawal syndrome	Infant sedation reported
SSRIs, SNRIs***, and tricyclic antidepressants	Decreased serum concentrations across pregnancy	No conclusive evidence of birth defects, with the exception of paroxetine Potential increased risk of congenital and cardiac defects in first trimester exposure to paroxetine[†] Prenatal antidepressant exposure syndrome	No conclusive evidence of adverse outcomes
Lithium	Ultrasonography, fetal echocardiography, or both for heart development Decreased serum concentrations across pregnancy Delivery - intravenous fluids; increased risk for lithium toxicity in mother	Increased incidence of cardiac malformations Increased risk for lithium toxicity in infant	Is incompatible with breastfeeding due to relatively high levels found in neonates, and multiple adverse event reports

Table 15. ***(continued)***

The Safety of Psychotherapeutic Medication in Pregnancy and Lactation *(continued)*			
Safety and Management Issues*			
Medication Class	**Pregnancy**	**Birth Defects and Other Neonatal Outcomes**	**Lactation****
Antiepileptic drugs	Decreased serum concentrations across pregnancy Folate supplementation and Vitamin K for some drugs	Valproic acid in the first trimester is associated with numerous neural tube defects and congenital malformations. Carbamazepine in the first trimester is associated with fetal carbamazepine syndrome – dysmorphic features and major malformations Neonatal symptoms Long-term adverse neurobehavioral outcomes	Carbamazepine has relatively higher levels in breast milk, with measurable levels in the infant
First and second generation antipsychotics	Avoid anticholinergic medications for side-effects	No conclusive evidence of birth defects Potential higher risk of preterm birth, low birthweight, and postnatal symptoms (e.g., jitteriness, somnolence)	Breastfeeding is not recommended for mothers on clozapine due to relatively high levels in breast milk that may affect the infant's complete blood count (CBC)

Note: SSRIs = Selective serotonin reuptake inhibitors; SNRIs = Serotonin–norepinephrine reuptake inhibitors.

**Many challenges exist in interpreting and evaluating evidence regarding adverse effects of psychotropic medication use during pregnancy. Key limitations include lack of well-conducted robust studies in pregnant women. Use of registry data and cohort designs has inherent flaws of lack of control for confounding variables such as psychiatric diagnoses, comorbid health conditions, obesity, tobacco use and use of alcohol and illicit substances.*

***Most medications can cross into breast milk but their levels vary. Formula feeding is an alternative that can allow the mother to use whichever medication works best for her.*

****Little is currently known about the safety of SNRIs, compared to SSRIs.*

†*Data also suggest that the risks of malformations associated with paroxetine use are inconsistent.*

Psychotherapeutic Medications Associated with Risks in Pregnancy

- Avoid benzodiazepines if possible, although the decision should be made on a case by case basis. There is inconsistent data suggesting that in the first trimester, there may be a small increased risk of oral clefts, and high doses in late pregnancy may be associated with a floppy infant syndrome at birth and withdrawal afterwards.
- Valproate exposure in pregnancy is associated with an increased risk of fetal anomalies, including neural tube defects, fetal valproate syndrome, and long-term adverse neurocognitive effects. It should be avoided in pregnancy, especially during the first trimester.
- Carbamazepine exposure in pregnancy is associated with fetal carbamazepine syndrome.
- It should be avoided during pregnancy, if possible, especially during the first trimester.
- Lithium exposure in pregnancy is associated with a small increase in a congenital cardiac malformation known as Epstein's anomaly. Risk of Ebstein's anomaly is estimated at 1/20,000 (0.005%) in the general population. The relative risk of developing Ebstein's anomaly has been estimated at 7.7 in patients exposed to lithium in utero compared to those not exposed to lithium in utero.
- Paroxetine use in pregnant women and women planning pregnancy should be avoided, if possible. Fetal echocardiography should be considered for women who are exposed to paroxetine in early pregnancy.

Note. The U.S. Food and Drug Administration's (FDA) new labeling is detailed in the Pregnancy and Lactation Labeling Rule (PLLR) or "final rule" at ***https://www.fda.gov/vaccines-blood-biologics/biologics-rules/pregnancy-and-lactation-labeling-final-rule****. The use of letter labeling (i.e., A, B, C, D, X) for pregnancy categories has been phased out by the FDA. This change was based on the major limitations of the letter category system.*

Psychotherapeutic Medications Use and Breastfeeding

The concentration of medication in breast milk depends on maternal drug plasma concentration, maternal pharmacogenomics, maternal plasma protein binding, size of the drug molecule, the degree of drug ionization, and the drug's lipid solubility. Risk of adverse effects on the baby during breastfeeding depends on the timing of the maternal dose, toxicity, oral bioavailability, volume of breast milk ingested, relative infant dose, and age of the infant. Breastfeeding an infant before the mother takes a medication dose results in the infant receiving the lowest possible drug concentration, but this principle does not apply to medications with a long half-life. Furthermore, premature babies and neonates have a lower ability to metabolize and excrete drugs. In infants who have been exposed to drugs in utero, exposure to drugs through breastmilk can augment these serum drug concentrations.

Most medications can cross into breast milk, but breast milk levels vary by medication. Recommendations regarding breastfeeding depend on the specific medications, known adverse effects, and assessment of benefits versus risks to both the mother and child. Generally, breastfeed babies should be monitored for unusual signs and symptoms (e.g., sleepiness, irritability, jaundice) if the mother is taking medications while breastfeeding.

Special Populations: Women of Childbearing Age *(continued)*

Psychotherapeutic medications found in relatively high concentrations in breastfed infants include lithium, carbamazepine, and clozapine. Although some sources state that lithium is contraindicated during pregnancy, other studies do not consider lithium an absolute contraindication to breastfeeding, particularly in babies over two months old with mothers on lithium monotherapy. In studies, most breastfed infants exposed to carbamazepine through breastmilk had no adverse reactions, but sedation, poor sucking, withdrawal, and three cases of hepatic dysfunction have been reported. Published reports have indicated sedation and adverse hematological effects in breastfeed infants of mothers taking clozapine. Because there is limited published experience with clozapine during breastfeeding, other medications are preferred.

For more information on treatment considerations in women of reproductive age, view the online Florida Medicaid Best Practice Psychotherapeutic Medications Guidelines at ***floridamedicaidmentalhealth.org***.

For updated data on medications during lactation and breastfeeding, visit the U.S. National Library of Medicine LactMed Database at: ***https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm***.

Treatment guidelines are available on our Program website: floridamedicaidmentalhealth.org

- Monitoring Physical Health and Side-Effects of Psychotherapeutic Medications in Adults and Children: An Integrated Approach
- Best Practice Psychotherapeutic Medication Guidelines for Adults
- Autism Spectrum Disorder & Intellectual Developmental Disorder: Psychotherapeutic Medication Recommendations for Target Symptoms in Children and Adolescents
- Best Practice Recommendations for Women of Reproductive Age with Severe Mental Illness and Comorbid Substance Use Disorders
- Best Practice Psychotherapeutic Medication Guidelines for Children and Adolescents

If you would like hard copies of the guidelines, please email sabrinasingh@usf.edu