

# Antidepressants for patients who are breastfeeding: What to consider

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**Consider a patient's previous response to medications, risks of untreated illness, and evidence regarding risks and benefits**

Ms. D, age 32, recently gave birth to her second child. Her psychiatric history includes major depressive disorder. She had been stable on mirtazapine 30 mg at bedtime for 3 years. Based on clinical stability and patient preference, Ms. D elected to taper off mirtazapine 1 month prior to delivery. Now at 1 month postdelivery, Ms. D notes the reemergence of her depressive symptoms; during her child's latest pediatrician visit, she scores 15 on the Edinburgh Postnatal Depression Scale (EPDS). She breastfeeds her baby and wants more information on the safety of taking an antidepressant while breastfeeding.

Ms. D discusses her previous use of mirtazapine with her treatment team. The team reviews the available resources with Ms. D and together they plan to make a shared decision regarding treatment of her depression at her next appointment.

The American Academy of Pediatrics<sup>1</sup> and World Health Organization<sup>2</sup> recommend exclusive breastfeeding of infants for their first 6 months of life and support it as a complement to other foods through and beyond age 2. Untreated conditions such as postpartum depression impact maternal

well-being and may interfere with parenting and child development. In fact, untreated maternal mental health leads to an increased risk of suicide, reduced maternal economic productivity, and worsened health for both mother and child.<sup>3</sup>

Because many women experience psychiatric symptoms before they become pregnant as well as during the perinatal period, questions often arise regarding the use of psychiatric medications—specifically antidepressants—and their safety in patients who are breastfeeding. Key considerations regarding medication management should include the patient's previous response to medications, the risks of untreated maternal mental illness, and evidence regarding risks and benefits in lactation. This article summarizes where to find evidence-based lactation information, how to interpret that information,

## Practice Points

- **Use multiple resources to research lactation safety data** for antidepressants when formulating a patient-centered recommendation.
- **Antidepressant use by patients who are breastfeeding should be considered on a case-by-case basis**, weighing the risks vs benefits for both the mother and infant, including the risk of untreated psychiatric illness.
- **If medications are used during lactation, monitor the infant for any changes in sleep, feeding, behavior, growth, and neurodevelopment.**

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Table 1

**Hale's Lactation Risk Categories**

Category	Notes
L1 Compatible	Drug which has been taken by a large number of breastfeeding mothers without any observed increase in adverse effects in the infant. Controlled studies in breastfeeding women fail to demonstrate a risk to the infant and the possibility of harm to the breastfeeding infant is remote or the product is not orally bioavailable in an infant
L2 Probably compatible	Drug which has been studied in a limited number of breastfeeding women without an increase in adverse effects in the infant and/or the evidence of a demonstrated risk which is likely to follow use of this medication in a breastfeeding woman is remote
L3 Probably compatible	There are no controlled studies in breastfeeding women; however, the risk of untoward effects to a breastfed infant is possible, or controlled studies show only minimal nonthreatening adverse effects. Drugs should be given only if the potential benefit justifies the potential risk to the infant
L4 Potentially hazardous	There is positive evidence of risk to a breastfed infant or to breastmilk production, but the benefits from use in breastfeeding mothers may be acceptable despite the risk to the infant (eg, if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective)
L5 Hazardous	Studies in breastfeeding mothers have demonstrated that there is significant and documented risk to the infant based on human experience, or it is a medication that has a high risk of causing significant damage to an infant. The risk of using the drug in breastfeeding women clearly outweighs any possible benefit from breastfeeding. The drug is contraindicated in women who are breastfeeding an infant

Source: Reference 7

and what information is available for select antidepressants.

**Locating lactation information**

Start by checking the manufacturer's medication labeling ("prescribing information") and medication information resources such as Micromedex ([www.micromedexsolutions.com](http://www.micromedexsolutions.com)) and Lexicomp ([www.wolterskluwer.com/en/solutions/lexicomp](http://www.wolterskluwer.com/en/solutions/lexicomp)). The updated labeling includes a risk/benefit assessment of available data on the risk for continued use of a medication during pregnancy compared to the risk if a medication is discontinued and the disorder goes untreated.<sup>4</sup> The "breastfeeding considerations" section of medication labeling include details regarding the presence of the medication and the amount of it in breastmilk, adverse events in infants exposed to the medication through breastmilk, and additional pertinent data as applicable. Lexicomp includes information regarding breastfeeding considerations, and a subscription may also include access to Briggs Drugs

in Pregnancy and Lactation's information pages. Micromedex includes its own lactation safety rating scale score.

Several other resources can help guide clinicians toward patient-specific recommendations. From the National Library of Medicine, LactMed (<https://www.ncbi.nlm.nih.gov/books/NBK501922/>) allows clinicians to search for specific medications to see what information exists pertaining to medication levels in breastmilk and infant blood as well as potential adverse effects in the nursing infant and/or on lactation and breastmilk.<sup>5</sup> LactMed provides information regarding alternative medications to consider and references from which the information was gathered.

Another helpful resource is the InfantRisk Center from Texas Tech University Health Sciences Center, which includes a free call center for parents and clinicians who have questions about medications and breastfeeding (806-352-2519; Monday through Friday, 8 AM to 5 PM CST). The InfantRisk Center also offers smartphone apps for clinicians as well as

**Clinical Point**

In addition to providing information on medication levels in breastmilk, LactMed also suggests alternative medications



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### Clinical Point

Highly protein-bound medications do not tend to pass as easily into breastmilk and can minimize infant exposure

**Table 2**

### Select antidepressant breastfeeding information

Medication	RID range (%)	Hale's Lactation Risk Category <sup>a</sup>	Briggs Lactation Recommendation Category <sup>b</sup>	Comments
Amitriptyline	1.08 to 2.8	L2	Limited human data; potential toxicity	
Bupropion	0.1 to 2.0	L3	Limited human data; potential toxicity	Monitor for reduced milk supply
Citalopram	3.6 to 5.4	L2	Limited human data; potential toxicity	Monitor for somnolence in the infant
Duloxetine	0.1 to 1.1	L3	Limited human data; potential toxicity	
Escitalopram	5.2 to 7.9	L2	Limited human data; potential toxicity	
Fluoxetine	1.6 to 14.6	L2	Limited human data; potential toxicity	Long half-life due to active metabolite
Mirtazapine	1.6 to 6.3	L3	Limited human data; potential toxicity	
Nortriptyline	1.7 to 3.36	L2	Limited human data; potential toxicity	
Paroxetine	1.2 to 2.8	L2	Limited human data; potential toxicity	Plasma levels not detected in most infants
Sertraline	0.4 to 2.2	L2	Limited human data; potential toxicity	Plasma levels not detected in most infants
Trazodone	1.1 to 2.8	L2	Limited human data; potential toxicity	
Venlafaxine	6.8 to 8.1	L2	Limited human data; potential toxicity	
Vortioxetine	1.22 to 1.85	L3	No rating available	

<sup>a</sup>Table 1<sup>7</sup> (page 21) summarizes Hale's Lactation Risk Categories

<sup>b</sup>Limited human data; potential toxicity: Either there are no human data, or the human data are limited. The characteristics of the drug suggest that breastfeeding could represent a clinically significant risk to a nursing infant; breastfeeding is not recommended

RID: relative infant dose

Source: References 7,8

individuals who are pregnant or breast-feeding.<sup>6</sup> Two commonly referenced textbooks on medications and breastfeeding include *Hale's Medication and Mother's Milk 2023: A Manual of Lactational Pharmacology*<sup>7</sup> and *Briggs Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk*.<sup>8</sup>

### How to interpret the information

Medication levels in breastmilk are affected by several properties, such as the medication's molecular weight, protein binding, pKa, and volume of distribution.

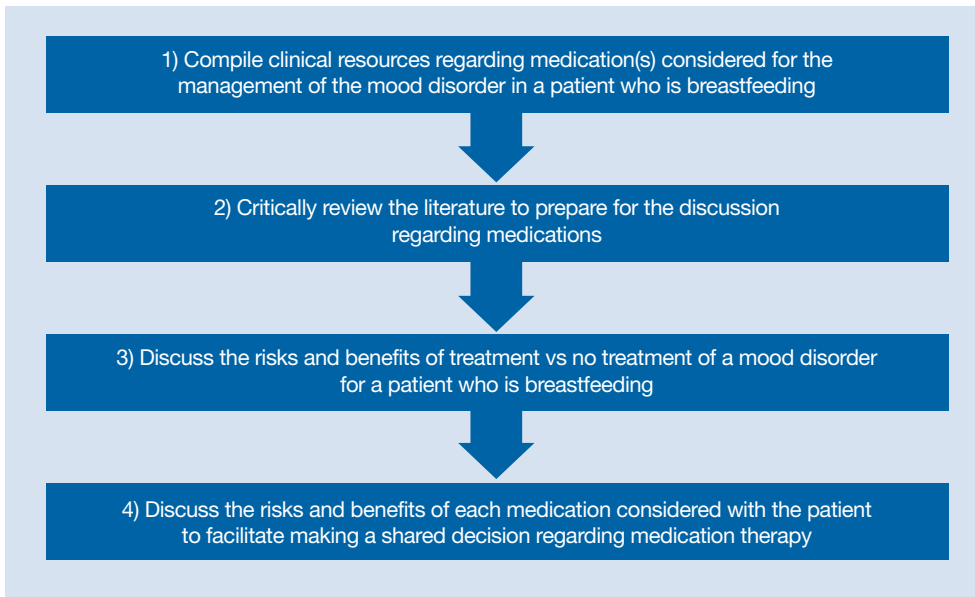
A few commonly used terms in lactation literature for medications include the relative infant dose (RID) and milk/plasma (M/P) ratio.

RID provides information about relative medication exposure for the infant. It is calculated by dividing the infant's dose of a medication via breastmilk (mg/kg/d) by the mother's dose (mg/kg/d).<sup>7</sup> Most consider an RID <10% to be safe.<sup>7</sup>

M/P is the ratio of medication concentration in the mother's milk divided by the medication concentration in the mother's plasma. A ratio <1 is preferable

## Figure

## Discussing antidepressant use with patients who are breastfeeding



## Clinical Point

A relative infant dose  $<10\%$  and a milk/plasma ratio  $<1$  are preferable and generally considered safe

and generally indicates that a low level of medication has been transferred to human milk.<sup>7</sup>

Another factor that can be evaluated is protein binding. Medications that are highly protein-bound do not tend to pass as easily into breastmilk and can minimize infant exposure.

Several risk categorization systems are available, depending upon the resource used to obtain lactation information. One common system is Hale's Lactation Risk Categories, with 5 safety levels ranging from L1 (breastfeeding compatible) to L5 (hazardous) (*Table 1*,<sup>7</sup> *page 21*). Briggs et al<sup>8</sup> utilize 7 categories to summarize recommendations ranging from breastfeeding-compatible to contraindicated; however, it is important to read the full medication monograph in the context of the rating provided. *Table 2*,<sup>8</sup> (*page 22*) provides breastfeeding information from Hale's<sup>7</sup> and from Briggs et al<sup>8</sup> for some commonly used antidepressants.

In addition to interpreting available literature, it is also important to consider patient-specific factors, including (but not

limited to) the severity of the patient's psychiatric disorder and their previous response to medication. If a mother achieved remission on a particular antidepressant in the past, it may be preferable to restart that agent rather than trial a new medication.

## CASE CONTINUED

Two weeks later and following the use of a variety of resources, Ms. D's treatment team finds that mirtazapine is rated Probably Compatible (L3 in Hale's Lactation Risk Categories), with an M/P ratio of 0.76.<sup>7</sup> The RID of mirtazapine ranges from 1.6% to 6.3%, and limited data from infants exposed to maternal use of mirtazapine during breastfeeding have not shown adverse effects.<sup>5</sup> The treatment team administers the EDPS to Ms. D again and she scores 18. Given Ms. D's previous remission with mirtazapine, current severity of depressive symptoms, and the risk/benefit assessment from lactation resources, the decision is made to restart mirtazapine 15 mg/d at bedtime with the option to titrate up if indicated. Ms. D plans to continue breastfeeding and will monitor

continued on page 48

Savvy Psychopharmacology  
continued from page 23

for signs of any adverse effects in her infant. The **Figure (page 23)** provides a summary of navigating this individualized decision with patients.

## References

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## Related Resources

- MotherToBaby. Medication fact sheets, option to contact for no-charge consultation, free patient education information materials. [www.mothertobaby.org](http://www.mothertobaby.org)
- Reprotox. Summaries on effects of medications on pregnancy, reproduction, and development (subscription required). [www.reprotox.org](http://www.reprotox.org)

## Drug Brand Names

Bupropion • Wellbutrin	Nortriptyline • Pamelor
Citalopram • Celexa	Paroxetine • Paxil
Duloxetine • Cymbalta	Sertraline • Zoloft
Escitalopram • Lexapro	Trazodone • Oleptro
Fluoxetine • Prozac	Venlafaxine • Effexor
Mirtazapine • Remeron	Vortioxetine • Trintellix

## Clinical Point

Take into account the severity of the patient's psychiatric disorder and their previous response to medication

September 29, 2022. <https://www.infantrisk.com/infantrisk-center-resources>

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