



U.S. Food & Drug Administration

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## FDA Drug Safety Communication: Selective serotonin reuptake inhibitor (SSRI) antidepressant use during pregnancy and reports of a rare heart and lung condition in newborn babies

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### Safety Announcement

**[12-14-2011]** The U.S. Food and Drug Administration (FDA) is updating the public on the use of selective serotonin reuptake inhibitor (SSRI) antidepressants by women during pregnancy and the potential risk of a rare heart and lung condition known as persistent pulmonary hypertension of the newborn (PPHN). The initial [Public Health Advisory in July 2006](#)<sup>1</sup> on this potential risk was based on a single published study. Since then, there have been conflicting findings from new studies evaluating this potential risk, making it unclear whether use of SSRIs during pregnancy can cause PPHN.

**At this time, FDA advises health care professionals not to alter their current clinical practice of treating depression during pregnancy. Healthcare professionals should report any adverse events involving SSRIs to the [FDA MedWatch Program](#)**<sup>2</sup>.

FDA has reviewed the additional new study results and has concluded that, given the conflicting results from different studies, it is premature to reach any conclusion about a possible link between SSRI use in pregnancy and PPHN. FDA will update the SSRI drug labels to reflect the new data and the conflicting results. (See Data Summary).

PPHN occurs when a newborn baby does not adapt to breathing outside the womb. Newborns with PPHN may require intensive care support including a mechanical ventilator to increase their oxygen level. If severe, PPHN can result in multiple organ damage, including brain damage, and even death

### Facts about Selective Serotonin Reuptake Inhibitors (SSRIs):

- Marketed under various brand and generic drug names (see [Table 1](#)).
- Used to treat depression and other psychiatric disorders.
- Are commonly used drugs to treat depression during pregnancy in the United States.<sup>1,2</sup>
- There are no adequate and well-controlled studies of SSRIs in pregnant women.

### Additional Information for Patients

- **If you are pregnant or plan to become pregnant, talk with your healthcare professional if you are depressed or undergoing treatment for depression to determine your best treatment option during pregnancy.**
- Talk to your healthcare professional about the potential benefits and risks of taking an SSRI during

pregnancy.

- Do not stop taking an SSRI antidepressant without first talking to your healthcare professional. Stopping an SSRI antidepressant suddenly may cause unwanted side effects or a relapse of depression.
- Report any suspected side effects of SSRI use in pregnancy to your healthcare professional and to the FDA MedWatch program using the information in the "Contact Us" box at the bottom of the page.

### Additional Information for Healthcare Professionals

- It is unclear whether SSRI use during pregnancy can cause PPHN, because the available data are conflicting (see [Data Summary](#)).
- Healthcare professionals and their patients must weigh the small potential risk of PPHN that may be associated with SSRI use in pregnancy against the substantial risks associated with under-treatment or no treatment of depression during pregnancy.
- Untreated depression during pregnancy may lead to poor birth outcomes, including low birth weight, preterm delivery, lower Apgar Scores, poor prenatal care, failure to recognize or report signs of labor; and an increased risk of fetal abuse, neonaticide or maternal suicide.<sup>3,4</sup>
- The published joint 2009 American Psychiatric Association (APA) and American College of Obstetrics and Gynecology (ACOG) guidelines for the management of depression during pregnancy includes treatment paradigms for the appropriate management of depression in pregnancy.<sup>2</sup> The guidelines may be found here: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3103063/pdf/nihm><sup>3</sup>
- Report adverse events involving SSRIs to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page.

### Data Summary

It is well documented in the medical literature that SSRIs are used during pregnancy.<sup>1,2</sup> In general, most epidemiology studies show that adverse events in pregnant patients are similar to those in non-pregnant patients, and many studies find no major fetal abnormalities in excess of the 1-3% found in the general population.<sup>5</sup> Two studies suggest an increased risk for PPHN with SSRI use in pregnancy.<sup>3,6</sup> Three other studies do not support this association and the potential risk with SSRI use during pregnancy remains unknown.<sup>5,7,8</sup>

PPHN affects between 1 and 2 infants per 1000 live births in the general population, a relatively uncommon event, but one associated with significant infant morbidity and mortality as well as long term sequelae.<sup>7,8,9</sup> A neonate with primary PPHN is typically a term or late-preterm infant who presents within hours after birth with severe respiratory failure and who often requires mechanical ventilation. These neonates have no radiographic lung abnormalities and no evidence of parenchymal lung disease. Secondary PPHN may be associated with other problems with the fetus, such as meconium aspiration, neonatal infection or congenital heart malformations.<sup>8,9,10</sup>

The 2006 study by Chambers et al. found a six-fold increase in PPHN among neonates whose mothers were exposed to an SSRI after 20 weeks of gestation, and provided the rationale for the current SSRI product label warning under Usage in Pregnancy: *Nonteratogenic Effects* stating, "Infants exposed to SSRIs in late pregnancy may have an increased risk for persistent pulmonary hypertension of the newborn (PPHN)."<sup>3</sup> A more recent study by Källén, et al. also found a statistically significant association between SSRI use and PPHN, although the majority of exposures occur during the first trimester of pregnancy.<sup>6</sup> The results of these two studies reporting an increase in risk are interpreted by some to show a strong association between SSRI use in pregnancy and the development of PPHN.

A review of the published literature also identified three studies reporting no increase in risk of PPHN.<sup>5,7,8</sup> The 2006 study by Wichman et al. is a retrospective cohort study of obstetric deliveries within a defined geographic area conducted by the Mayo Clinic. The study identified 16 neonates with PPHN and no exposures to an SSRI in utero.<sup>5</sup> The 2009 study by Andrade et al. is a well-designed retrospective cohort study from four health plans in an ongoing HMO research network study of birth outcomes. The authors found no association between SSRI exposure during the third trimester of pregnancy and PPHN.<sup>7</sup> Lastly, the smaller 2011 retrospective case-control study by Wilson et al. identified 58 neonates with PPHN and no SSRI exposure in utero.<sup>8</sup>

Design features in each of the above five published studies preclude the demonstration, either individually or collectively, of a definitive association between SSRI use and PPHN. Each study incorporates a different study design, different method of collecting exposure information during gestation, and gives incomplete attention

to potentially important factors including Cesarean delivery. FDA recommends caution be used when interpreting results of studies with statistical associations, as statistical significance in an epidemiologic study does not always correlate with clinical significance and good clinical decision making.<sup>11,12</sup>

At present, FDA does not find sufficient evidence to conclude that SSRI use in pregnancy causes PPHN, and therefore recommends that health care providers treat depression during pregnancy as clinically appropriate. FDA will update the SSRI labels as any new data regarding SSRI use and PPHN become available.

## References

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**Table 1: Selective Serotonin Reuptake Inhibitor (SSRI) Drugs**

Generic name	Found in Brand name(s)
Citalopram	Celexa
Escitalopram	Lexapro
Fluoxetine	Prozac, Sarafem, Symbyax
Fluvoxamine	Luvox, Luvox CR
Paroxetine	Paxil, Paxil CR, Pexeva
Sertraline	Zoloft
Vilazodone	Viibryd

## Related Information

- [Public Health Advisory: Treatment Challenges of Depression in Pregnancy and the Possibility of](#)

[Persistent Pulmonary Hypertension in Newborns](#)<sup>5</sup>  
7/2006

- [The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists](#)<sup>6</sup>
- [FDA Drug Safety Podcast for Healthcare Professionals: Selective serotonin reuptake inhibitor \(SSRI\) antidepressant use during pregnancy and reports of a rare heart and lung condition in newborn babies](#)<sup>7</sup>  
12/14/2011
- [Comunicado de la FDA sobre la seguridad de los medicamentos: El uso de antidepresivos con inhibidor selectivo de recaptación de serotonina \(SSRI por sus siglas en inglés\) durante el embarazo y reportes de afecciones cardíacas y pulmonares poco comunes en recién nacidos](#)<sup>8</sup>
- [Selective Serotonin Reuptake Inhibitors \(SSRIs\) Information](#)<sup>9</sup>

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