

FDA requests removal of strongest warning against using cholesterol-lowering statins during pregnancy; still advises most pregnant patients should stop taking statins
Breastfeeding not recommended in patients who require statins

7-20-2021 FDA Drug Safety Communication

What safety information is FDA announcing?

The U.S. Food and Drug Administration (FDA) is requesting removal of its strongest warning against using cholesterol-lowering statin medicines in pregnant patients. Despite the change, most patients should stop statins once they learn they are pregnant. We have conducted a comprehensive review of all available data and are requesting that statin manufacturers make this change to the prescribing information as part of FDA's ongoing effort to update the [pregnancy and breastfeeding information](#) for all prescription medicines.

Patients should not breastfeed when taking a statin because the medicine may pass into breast milk and pose a risk to the baby. Many can stop statins temporarily until breastfeeding ends. However, patients requiring ongoing statin treatment should not breastfeed and instead use infant formula or other alternatives.

What is FDA doing?

We are requesting revisions to the information about use in pregnancy in the prescribing information of the entire class of statin medicines. These changes include removing the contraindication against using these medicines in all pregnant patients. A contraindication is FDA's strongest warning and is only added when a medicine should not be used because the risk clearly outweighs any possible benefit. Because the benefits of statins may include prevention of serious or potentially fatal events in a small group of very high-risk pregnant patients, contraindicating these drugs in all pregnant women is not appropriate.

FDA expects removing the contraindication will enable health care professionals and patients to make individual decisions about benefit and risk, especially for those at very high risk of heart attack or stroke. This includes patients with homozygous familial hypercholesterolemia and those who have previously had a heart attack or stroke. Statins are safe to use in patients who are not pregnant but may become pregnant.

What are statins and how can they help me?

Statins are a class of prescription medicines that have been used for decades to lower low-density lipoprotein (LDL-C or "bad") cholesterol in the blood. Statins work by reducing the amount of cholesterol made by the liver and helping the liver remove cholesterol already in the blood. Statins also can lower the risk for heart attack and stroke in those who have heart disease or risk factors for it. These medicines may help stabilize the plaques that can build up inside blood vessel walls, which can interfere with blood flow to the heart and brain, leading to heart attack and stroke.

Medicines in the statin class include atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin. They are marketed as single-ingredient products and in

combination with other medicines (See FDA-Approved Statin Medicines below). They are available as brand-name and generic products.

What should patients do?

Patients taking statins should notify your health care professionals if you become pregnant or suspect you are pregnant. Your health care professional will be able to advise whether you should stop taking the medicine during pregnancy and whether you may stop your statin temporarily while breastfeeding. Patients who are at high risk of heart attack or stroke who require statins after giving birth should not breastfeed and should use alternatives such as infant formula.

What should health care professionals do?

Health care professionals should discontinue statin therapy in most pregnant patients, or they can consider the ongoing therapeutic needs of the individual patient, particularly those at very high risk for cardiovascular events during pregnancy. Because of the chronic nature of cardiovascular disease, treatment of hyperlipidemia is not generally necessary during pregnancy. Discuss with patients whether they may discontinue statins temporarily while breastfeeding. Advise those who require a statin because of their cardiovascular risk that breastfeeding is not recommended because the medicine may pass into breast milk.

We hope the revised language in the prescribing information will help reassure health care professionals that statins are safe to prescribe in patients who can become pregnant, and help them reassure patients with unintended statin exposure in early pregnancy or before pregnancy is recognized that the medicine is unlikely to harm the unborn baby.

What did FDA review?

When FDA approved the first statin in 1987, the medicine came with our strongest warning recommending against use during pregnancy and breastfeeding. This was based on several factors. These were safety signals from animal data at drug exposures higher than human doses, potential concern that lowering cholesterol may negatively affect the unborn baby or infant, and the perspective that short-term use during pregnancy and breastfeeding did not provide a substantial benefit to the mother. All statins approved subsequently have carried the same warning.

Since then, multiple randomized trials and meta-analyses have demonstrated the benefit of statin therapy on the prevention of cardiovascular events. In addition, data from published observational studies of statin use in pregnant women have not identified a drug-associated risk of major birth defects when controlling for other risks such as diabetes and are insufficient to determine if there is a drug-associated risk of miscarriage.¹⁻¹⁵ Overall, animal data suggest limited potential of statins to cause birth defects or miscarriage and limited potential to affect nervous system development in an unborn baby. However, because statins decrease the body's ability to make cholesterol and possibly other substances, it is possible these medicines could harm an unborn baby when taken by a pregnant mother (See Data Summary for more details).

How do I report side effects from statins?

To help FDA track safety issues with medicines, we urge patients and health care professionals to report side effects involving statins or other medicines to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of the page.

How can I get new safety information on medicines I’m prescribing or taking?

You can sign up for [email alerts](#) about Drug Safety Communications on medicines or medical specialties of interest to you.

FDA-Approved Statin Medicines

Brand Name	Active Ingredient(s)
Lipitor	atorvastatin
Caduet	atorvastatin and amlodipine
Lescol XL	fluvastatin
Altoprev	lovastatin
Livalo	pitavastatin
Zypitamag	pitavastatin
Pravachol	pravastatin
Crestor	rosuvastatin
Ezallor Sprinkle	rosuvastatin
Roszet	rosuvastatin and ezetimibe
Zocor	simvastatin
Flolipid	simvastatin
Vytorin	simvastatin and ezetimibe

Facts about Statins

- Statins are a class of medicines used to lower cholesterol in the blood. Statins work by reducing the amount of cholesterol made by the liver and by helping the liver remove cholesterol already in the blood.
- Statins also can lower the risk for heart attack and stroke in patients who have heart disease or risk factors for it. These medicines may help stabilize the plaques that can build up inside blood vessel walls, which can interfere with blood flow to the heart and brain, leading to heart attack and stroke.
- Common side effects of statins include headache, nausea, muscle pain, diarrhea, and constipation.

Additional Information for Patients

- FDA is requesting that manufacturers of cholesterol-lowering statins remove FDA’s strongest warning in the current prescribing information, which states that statins should never be used in patients during pregnancy. However, most patients should still stop statins once they learn they are pregnant.

- Inform your health care professional if you become pregnant or suspect you are pregnant while taking a statin medicine. Your health care professional will be able to advise whether you should stop taking the medicine.
- Statins are safe to use if you are not pregnant but can become pregnant. If you are taking a statin before you know you are pregnant, it is unlikely to harm your unborn baby.
- Discuss with your health care professional if you are breastfeeding or plan to do so. Breastfeeding is not recommended in patients taking a statin. Your health care professional can help you determine whether it will be better for you to stop the statin temporarily while breastfeeding or whether you need to continue taking it and so should not breastfeed. If ongoing statin treatment is necessary, infant formula and other alternatives are available.
- Always consult with your health care professional about the use of all medicines during pregnancy or while breastfeeding.
- Talk to your health care professional if you have any questions or concerns about your statin medicine.
- To help FDA track safety issues with medicines, report side effects from statins or other medicines to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.
- You can sign up for [email alerts](#) about Drug Safety Communications on medicines or medical specialties of interest to you.

Additional Information for Health Care Professionals

- FDA is requesting that manufacturers of cholesterol-lowering statins remove the contraindication included in the current prescribing information stating these medicines should never be used in patients during pregnancy.
- Health care professionals should discontinue statin therapy in most pregnant patients. Alternatively, health care professionals should consider the ongoing therapeutic needs of the individual patient, especially patients at very high risk of cardiovascular events during pregnancy, such as patients with homozygous familial hypercholesterolemia or those with established cardiovascular disease.
- Statins are safe to prescribe in patients who are not pregnant but may become pregnant. Reassure patients who have an unintended exposure to statins in early pregnancy that it is unlikely to cause harm to the developing fetus.
- Treatment of hyperlipidemia is not generally necessary during pregnancy. Atherosclerosis is a chronic process and the temporary discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hyperlipidemia for most patients.
- There is insufficient evidence to determine whether statins can cause miscarriage.
- Observational studies have not identified an increase in birth defects associated with statin use during pregnancy after adjusting for potential confounders. Animal data suggest limited potential for statins to cause malformations, and limited potential to affect the developing nervous system or cause embryofetal death. Nevertheless, statins decrease the synthesis of cholesterol and possibly other biologically active substances derived from cholesterol.

Therefore, statins may cause fetal harm when administered to pregnant patients. Counsel pregnant women of this potential risk.

- Some statins have been shown to pass into human milk and may cause harm to the breastfed infant based on the mechanism of action.
- Advise patients who can become pregnant to inform their health care professionals of a known or suspected pregnancy, or if they are breastfeeding or plan to do so, to discuss whether their statin should be discontinued.
- To help FDA track safety issues with medicines, report adverse events involving statins or other medicines to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of [this page](#).
- You can sign up for [email alerts](#) about Drug Safety Communications on medicines or medical specialties of interest to you.

Data Summary

FDA reviewed data from case series and prospective and retrospective observational cohort studies over decades of use of statins in pregnant women.¹⁻¹⁵ Multiple larger, well-designed, and controlled observational studies did not find an increase in major birth defects associated with use of statins during pregnancy. The most recent 2015 Medicaid cohort linkage study of 1,152 statin-exposed pregnant women compared to 886,996 controls did not find a significant teratogenic effect from maternal use of statins in the first trimester of pregnancy, after adjusting for potential confounders.² Propensity score-based methods were used to control for maternal age, diabetes, hypertension, obesity, and alcohol and tobacco use. The relative risk of congenital malformations between the group with statin use and the group with no statin use in the first trimester was 1.07 (95% confidence interval (CI) 0.85 to 1.37) after controlling for confounders, particularly pre-existing diabetes. There were also no statistically significant increases in any of the organ-specific malformations assessed after accounting for confounders. In the majority of pregnancies, statin treatment was initiated prior to pregnancy and was discontinued at some point in the first trimester when pregnancy was identified. Study limitations included reliance on physician coding to define the presence of a malformation, lack of control for certain confounders such as body mass index, use of prescription dispensing as verification for the use of a statin, and lack of information on non-live births.

Published data from prospective and retrospective observational cohort studies with statin use in pregnant women are insufficient to determine if there is a drug-associated risk of miscarriage. Many older studies did not report or discuss the rate of miscarriage; however, three studies included miscarriage in their analyses and did not find an increased risk once adjustments were made for confounders.^{3, 9, 10} In 2009, McGrogan et al.⁸ reported an adjusted risk ratio for terminations of 2.48 (95% CI 1.65-3.73). However, this study did not differentiate between elective terminations and miscarriage, and an increased rate of elective terminations would be expected in a study of pregnant women exposed to a drug contraindicated during pregnancy. In a meta-analysis of six small observational studies of statin exposure in pregnant women, Zarek et al.⁴ reported a risk ratio of miscarriage of 1.35 (95% CI 1.04-1.75). However, many of the studies included in the analysis, which were older and included the McGrogan 2009 study, did not control for multiple confounders that are known to increase the risk of miscarriage. In 2017,

McGrogan et al.¹ published a retrospective cohort study specifically looking at fetal loss as a primary outcome. The authors compared 281 statin-exposed pregnant women versus 2,643 controls. The cohorts were matched for maternal age, diabetes mellitus, hypertension and body mass index, and free text was used to help identify type of loss (i.e., miscarriage vs. elective termination). They found a miscarriage rate of 25% in statin-exposed versus 21% for controls. The adjusted hazard ratio was 1.64 (95% CI 1.1-2.46). Although there was an attempt to control for the presence of diabetes, the authors acknowledged there might still be some confounding because the study was not controlled for the type or severity of diabetes, which can influence rate of miscarriage. They also acknowledged the possibility of residual misclassification regarding smoking and alcohol use based on changed behavior patterns during pregnancy.

FDA also re-reviewed nonclinical data from statin development programs. The totality of the data suggests a limited potential for statins to cause malformations or embryofetal lethality, and limited potential to affect nervous system development during human embryofetal development and during the pre- and post-natal period.

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