Common symptoms of allergic rhinitis include nasal congestion, discharge, and itching, as well as eye involvement such as conjunctival redness, swelling, and excessive lacrimation. The symptoms are typically triggered by airborne allergens (eg, pollens from trees, grasses, weeds); however, household allergens such as dust mites or animal dander are also common triggers. Allergic diseases are estimated to affect 20% to 30% of women of childbearing age, making them the most common medical conditions to complicate pregnancy. Furthermore, during pregnancy, up to 10% to 30% of women with pre-existing allergic rhinitis have reported increased symptoms. Possible explanations include increased circulating blood volume, nasal vascular engorgement, and increased secretions from nasal mucosa due to hormonal influences.

First-generation antihistamines
Antihistamines targeting histamine–type 1 (H₁) receptors are commonly used to treat allergic rhinitis. Examples of first-generation antihistamines are brompheniramine, chlorpheniramine, dimenhydrinate, diphenhydramine, doxylamine, hydroxyzine, and pheniramine. Most—with the exception of doxylamine and dimenhydrinate, both used for the treatment of nausea and vomiting, and hydroxyzine (prescription-only)—are commonly found in over-the-counter allergy and cold medications. None of the medications in this class of drugs has been reported to increase fetal risk when used at any time during pregnancy. Epidemiologic data support safety in early pregnancy, with a meta-analysis involving more than 200,000 participants concluding that there was no increase in any type of congenital malformation.

Second-generation antihistamines
At present, medications from this class of drugs are preferred because they do not cause central nervous system adverse effects (eg, drowsiness) and because they are available without prescription. Examples of second-generation antihistamines are cetirizine, desloratadine, fexofenadine, and loratadine.

Cetirizine. Cetirizine is the active metabolite of hydroxyzine. A small prospective, comparative study conducted by Motherisk following 120 women exposed to hydroxyzine and 39 to cetirizine (37 in first trimester) did not find differences in pregnancy outcomes between the exposed and comparison groups. Pregnancy outcomes from the
Swedish Medical Birth Registry (1995 to 1999) of 17766 women exposed to antihistamine drugs, 917 of whom used cetirizine, did not show increased risk of malformations or adverse delivery outcomes compared with the general population. In 2004 another study examining 144 first-trimester exposures to cetirizine confirmed the previous results, with no adverse pregnancy outcomes attributed to the drug. The most recent data were from the Berlin teratogen information service, with 196 women exposed in any trimester (11% in the first trimester), also showing no increased risk of birth defects or other adverse outcomes.

**Fexofenadine.** Fexofenadine is an active metabolite of terfenadine, a second-generation H₁ blocker that is no longer available on the Canadian market owing to clinically significant QT prolongation. Although animal studies failed to show teratogenicity, decreases in pup weight and survival were observed. There are no human data on fexofenadine; however, limited data from terfenadine did not find an increased risk of major malformations.

**Loratadine and desloratadine.** Desloratadine is a major metabolite of loratadine; therefore, data pertaining to safety of loratadine might be extrapolated to desloratadine. A Swedish registry study involving 292 loratadine-exposed women did not suggest an increased risk of major malformations. A Motherisk study prospectively following 161 loratadine-exposed women and an equal number of unexposed controls confirmed the safety of loratadine use in pregnancy. Another study comparing 210 pregnant women exposed to loratadine and 267 women exposed to other antihistamines with 929 women in a control group also failed to show an association with loratadine. However, a further analysis from the Swedish registry reported an increased risk of hypospadias, although this association has not been confirmed by the other studies. Furthermore, a recent meta-analysis conducted by Motherisk comparing 2694 male infants exposed to loratadine in utero with 450413 unexposed controls also failed to confirm such an association.

**Antihistamines and breastfeeding.** Although the data regarding the use of first-generation antihistamines and breastfeeding is limited, only minimal amounts of these drugs have been reported to be secreted in breast milk. In a telephone follow-up study conducted by Motherisk, 10% of mothers reported irritability and colicky symptoms in their infants exposed to various antihistamines, and drowsiness was reported in 1.6% of infants. None of the reactions required medical attention. Therefore, short-term or occasional use of the older generation antihistamines would not be expected to be a concern during breastfeeding.

Among the second-generation H₁ blockers, data on drug concentration in breast milk are available for loratadine, desloratadine, and fexofenadine. The pharmacokinetics of loratadine and its metabolite desloratadine in breast milk were studied in 6 lactating women after a single oral dose of 40 mg of loratadine, which is 4 times the current standard therapeutic dose. Assuming the breast milk intake by an infant is 150 mL/kg daily, the maximum infant loratadine-equivalent dose based on the highest concentration of loratadine and desloratadine in breast milk was estimated to be 7.3 µg/kg daily (ie, 1.1% of the daily dose given to the mother in mg/kg). The pharmacokinetics of fexofenadine in breast milk were studied in 4 lactating women taking 60 mg of terfenadine every 12 hours. The maximum infant dose of fexofenadine based on the highest concentration of fexofenadine in breast milk would be 9 µg/kg daily (ie, 0.45% of the daily dose given to the mother in mg/kg). Considering the minimal exposure of a nursing infant to the drugs through breast milk, maternal use of loratadine, desloratadine, or fexofenadine in a standard therapeutic dose is unlikely to result in adverse effects in nursing infants and is considered to be compatible with breastfeeding.

**Conclusion**

Although seasonal allergy is not a life-threatening medical condition, it can be extremely troublesome for pregnant women and breastfeeding mothers. Based on the current body of evidence, which is large, first-generation H₁ blockers are not associated with an increased risk of major malformations or any other adverse fetal effects. Although there is less evidence on second-generation H₁ blockers, they have also not been associated with an increased risk of adverse pregnancy outcomes. In addition, none of the antihistamines is excreted in the breast milk in an appreciable amount so as to have any adverse effects on the breastfeeding infant. Therefore, pregnant and breastfeeding women can be reassured that they can alleviate their symptoms without posing an increased risk to their fetuses or infants.

**Competing interests**

None declared.

**References**


Motherisk questions are prepared by the Motherisk Team at the Hospital for Sick Children in Toronto, Ont. Ms So, Ms Bozzo, and Dr Inoue are members and Ms Einarson is Assistant Director of the Motherisk Program.

Do you have questions about the effects of drugs, chemicals, radiation, or infections in women who are pregnant or breastfeeding? We invite you to submit them to the Motherisk Program by fax at 416 813-7562; they will be addressed in future Motherisk Updates.

Published Motherisk Updates are available on the Canadian Family Physician website (www.cfp.ca) and also on the Motherisk website (www.motherisk.org).