

How to use antihistamines

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1 Antihistamines are among the most commonly and incorrectly used medicines worldwide

Antihistamine use is most strongly supported for treating allergic rhinoconjunctivitis (“hay fever”) and urticaria (hives).¹⁻³ Avoid off-label usage for conditions where antihistamines have questionable utility, such as in managing asthma, eczema, cough or insomnia.

2 First-generation antihistamines are associated with substantial and sometimes fatal adverse effects

First-generation antihistamines (e.g., diphenhydramine [Benadryl], chlorpheniramine [Chlor-Tripolon], hydroxyzine [Atarax]) cause sedation, injury and impairment in sleep, and psychomotor and cognitive function, including impairing performance at school.¹⁻³ Overdose can result in death from anticholinergic and anti- α -adrenergic effects, and QT prolongation (including torsades de pointes). First-generation antihistamines are on the Beers list of potentially inappropriate medications for older persons.³

3 Newer antihistamines are safer, as affordable and as efficacious as first-generation antihistamines

Compared with first-generation antihistamines, systematic reviews of randomized controlled trials have found newer antihistamines to be safer (e.g., 4% sedation v. 28%),²⁻⁴ longer lasting (12–24 h v. 4–6 h dosing) and faster acting (50 v. 80 min).¹ The World Health Organization replaced chlorpheniramine with loratadine on its essential medicines list in 2013 for these reasons (see Table 1 and Appendix 1, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.201959/tab-related-content for preferred antihistamines).³ Bilastine and fexofenadine are the least sedating options. However, no antihistamine should be consumed with alcohol.

4 Antihistamines should not be used instead of epinephrine to treat anaphylaxis

Oral antihistamines can be used in addition to, but should not replace, epinephrine for the treatment of anaphylaxis.^{1,3} Intravenous diphenhydramine can cause vasodilation and sedation, which can worsen hypotension and confound assessment of patients with anaphylaxis.^{1,3}

5 Most antihistamines are safe during pregnancy and breastfeeding

Systematic reviews of observational studies show no association with adverse fetal or maternal outcomes with antihistamine use during pregnancy or breastfeeding, and they are also safe for children.^{2,3,5} There is inadequate evidence regarding the newest antihistamines (rupatadine, bilastine) to support their use in pregnancy.

Table 1: Summary of preferred antihistamines for allergy and urticaria

| Antihistamine (standard single adult dose, mg) | Available in liquid form? | Prescription required? | Approval for children? | | Evidence for safety during pregnancy/breastfeeding |
|--|---------------------------|------------------------|------------------------|------------|--|
| | | | HC (age) | FDA* (age) | |
| Bilastine (20) | No | Yes | N/A | N/A | Lack of data |
| Cetirizine (10)† | Yes | No‡ | Yes (2 yr) | Yes (6 mo) | Yes |
| Desloratadine (5)† | Yes | No | Yes (2 yr) | Yes (6 mo) | Yes |
| Fexofenadine(180)† | No | No | N/A | N/A | Yes |
| Loratadine (10)† | Yes | No‡ | Yes (2 yr) | Yes (1 yr) | Yes |
| Rupatadine (10) | Yes | Yes | Yes (2 yr) | N/A | Lack of data |

Note: FDA = Food and Drug Administration, HC = Health Canada, N/A = not applicable.
 *FDA and/or supporting randomized controlled trial evidence for efficacy and safety.
 †Most affordable (see Appendix 1, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.201959/tab-related-content).
 ‡Prescription not required, but can be prescribed and covered by some provincial plans as an affordable route of accessing this medication. However, prescriptions often have barriers to access (e.g., Exceptional Access Program forms with very low approval rates).

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