

## Appendix 1 (as submitted by the authors): Supplementary tables

Table S1. Summary of antihistamines of choice for allergy and urticaria.*							
Antihistamines (dose frequency)	Available in liquid form	Available in tablet form, (mg)†	Hepatic or renal dosing	Brand	Approximate price in CAD	Approximate price per unit	Considerations
Bilastine (1-2 times per day)	No	Yes (20)	No Δ	Blexten	\$38 (30 tabs)	\$1.00-1.27	By prescription only. Among least sedating. Lack of safety data in pregnancy/breastfeeding.
Cetirizine (1-2 times per day)	Yes (2 yr)‡ [6 mo]§	Yes (10)	5mg daily for either impairment	Reactine	\$17 (30 tabs) \$12 (118ml) \$24 (24x Fast Melt Jr) \$15 (118ml kids)	\$0.57 \$0.10/mL \$1.00 \$0.13/mL	Prescribed versions often have barriers to access (eg. EAP forms with very low approval rates; cost \$0.48-\$0.75 per 10 or 20 mg tablet)
				Allergy Relief	\$30 (48 tabs) \$47 (84 tabs)	\$0.62 \$0.56	
				Kirkland	\$19 (200 tabs)	\$0.10	
Desloratadine (1-2 times per day)	Yes (2 yr)‡ [6 mo]§	Yes (5)	No Δ	Aerius	\$40 (50 tabs) \$14 (100ml Kids version)	\$0.80 \$0.14/mL	Along with cetirizine, fexofenadine, and loratadine, among the most affordable.
				Allergy Control	\$38 (50 tabs)	\$0.76	
				Equate	\$28 (70 tabs)	\$0.40	
				Kirkland	\$19 (180 tabs)	\$0.11	
Fexofenadine (1-2 times per day)	No	Yes (120)	No Δ for either per manufacturer, but others suggest renal dosing	Allegra	\$17 (30 tabs)	\$0.57	Among least sedating (OR 0.59 [95% CI, 0.38 to 0.93] compared to most other 2 <sup>nd</sup> generation antihistamines <sup>5</sup> ).
Loratadine (1-2 times per day)	Yes (2 yr)‡ [1 yr]§	Yes (10)	No Δ for either per manufacturer, but others including WHO suggest renal and hepatic dosing <sup>3</sup>	Claritin	\$30 (50 tabs) \$13 (120ml Kids version)	\$0.60 \$0.11/mL	Prescribed versions often have barriers to access (eg. EAP forms with very low approval rates; \$0.63 per 10 mg).
				Allertin	\$43 (85 tabs)	\$0.51	
				Allergy Remedy	\$20 (30 tabs)	\$0.67	
Rupatadine (1-2 times per day)	Yes (2 yr)‡	Yes (10)	Use not recommended	Rupall	\$38 (30 tabs) \$27 (120ml)	\$1.00-1.27 \$0.22	By prescription only. Lack of safety data in pregnancy/breastfeeding.
For comparison: Diphenhydramine, a 1 <sup>st</sup> generation antihistamine (4-6 times per day)	X N/A [6 yr] <sup>¶</sup>	Yes (20)	No Δ for either per manufacturer	Benadryl Allergy	\$23 (60 caps) \$15 (20 chewables) \$13 (100 mL children liquid)	\$0.38 \$0.75 \$0.13/mL	Not recommended due to many and sometimes fatal adverse effects.  Rapid IV administration can cause vasodilation, hypotension and sedation.
				Allergy formula	\$12 (20 liquid caps)	\$0.58	

CI = confidence interval, EAP = exceptional access program, OR = odds ratio, Δ = change.

\*First-generation antihistamines (e.g., diphenhydramine [Benadryl], chlorpheniramine [Chlor-Tripolon], hydroxyzine [Atarax]) have worldwide concerns<sup>1-3</sup> about toxicity and drug-drug interaction, with no better efficacy, accessibility or affordability compared to the preferred second-generation antihistamines. Diphenhydramine is included only for comparison and is not an antihistamine of choice. Antihistamines should not be consumed with alcohol.

†Standard adult dose in parentheses of tablet column

‡ Youngest age of approval from Health Canada in parentheses of liquid form.  
§FDA approved and/or supporting RCT evidence for efficacy and safety starting at this age<sup>2,3</sup>

## References

1. Fein, M.N., Fischer, D.A., O'Keefe, A.W. *et al.* CSACI position statement: Newer generation H<sub>1</sub>-antihistamines are safer than first-generation H<sub>1</sub>-antihistamines and should be the first-line antihistamines for the treatment of allergic rhinitis and urticaria. *Allergy Asthma Clin Immunol* 15, 61 (2019). <https://doi.org/10.1186/s13223-019-0375-9>
2. Carson S, Lee N, Thakurta S. Drug Class Review: Newer Antihistamines: Final Report Update 2. Portland (OR): Oregon Health & Science University; May 2010.
3. Section 3: Antiallergics and Medicines Used in Anaphylaxis, Histamine-1 receptor antagonists – A critical evaluation to update Section 3, Developed by Harinder Chahal, For WHO Secretariat
4. Gilboa, S.M., Ailes, E.C., Pai, R.P. *et al.* Antihistamines and birth defects: a systematic review of the literature. *Expert Opinion on Drug Safety* 13, 1667–1667 (2014). <https://doi.org/10.1517/14740338.2014.970164>
5. Huang CZ, Jiang ZH, Wang J, Luo Y, Peng H. Antihistamine effects and safety of fexofenadine: a systematic review and Meta-analysis of randomized controlled trials. *BMC Pharmacol Toxicol.* 2019;20(1):72. Published 2019 Nov 29. doi:10.1186/s40360-019-0363-1