Allergic rhinitis: prescription antihistamine treatments

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The Impact of Allergic Rhinitis

The prevalence of allergic rhinitis (AR) is estimated at 20% of the Canadian population and rising.[1,2] The symptoms of AR, typically nasal congestion, rhinorrhea, sneezing and nasal itching, negatively impact a patient's quality of life.[2] Additionally, AR is a risk factor for the development of asthma and untreated AR is associated with asthma exacerbations.[2]

Comparing Second Generation Antihistamines

In light of the Canadian Society of Allergy and Clinical Immunology's (CSACI) recent position paper[3] against the routine use of 1st generation antihistamines and their recommendation for the use of 2nd generation as first-line treatment for AR, a review of the currently available prescription therapeutic options in Canada is timely.

Second generation antihistamines are available both over-the-counter and by prescription. Until as recently as 2017, the only available 2nd generation prescription strength AH was cetirizine (Reactine®). Two new 2nd generation prescriptions are now available, bilastine (Blexten®) and rupatadine (Rupall®).

The international Allergic Rhinitis and Its Impact on Asthma (ARIA) Guideline[4] classify 2nd generation antihistamines into 2 categories:

- 2nd generation antihistamines that do not cause sedation and do not interact with cytochrome P450
- 2nd generation antihistamines that cause some sedation and/or interact with cytochrome P450

ASK THE EXPERT

When should patients be referred to an allergist?

I recommend referring patients to an allergist for the following reasons:

- Patients have symptoms of AR that are not adequately responding to medical therapy
- To deal with other allergic comorbidities like asthma
- The patient or referring nurse practitioner (NP) would like to identify allergic triggers for proper allergen avoidance
- The patient is having side effects to medical therapy or does not wish to take medical therapy
- Consideration by the patient and/or NP of immunotherapy to treat AR

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ARIA Guidelines recommend a 2nd generation AH that does not cause sedation and does not interact with the cytochrome P450 system as a first-line treatment option for all severities of intermittent AR and mild persistent AR.[4] (Figure 1)

Sedation

The sedation rates from the product monographs of each of the available prescription 2nd generation AHs are shown in figure 2.[5-7] Both bilastine and rupatadine demonstrated a lower rate of somnolence than cetirizine, with bilastine's rate of somnolence being comparable to placebo.[5-7]

Interaction with cytochrome P450

Comparing the metabolism of the prescription antihistamines, rupatadine is metabolized by the cytochrome P450 system, cetirizine is less extensively metabolized and bilastine is not metabolized, meaning it does not interact with other drugs metabolized via the CYP450.[5-7] Bilastine can therefore be given to patients with kidney or liver impairment without dose adjustment whereas the dose of cetirizine needs to be adjusted and rupatadine is not recommended in patients with kidney or liver impairment.[5-7]

Figure 1. ARIA 2010 Treatment Recommendations for Allergic Rhinitis in Adults[4]

	Recommended	Suggested	Not Suggested
Allergen avoidance			
Animal dander			
Indoor moulds			
Occupational allergens			
First generation oral H_1-antihistamines			
Second generation oral H_1-antihistamines			
New generation H_1-antihistamines that do not cause sedation and do not interact with cytochrome P450			
New generation H_1-antihistamines that cause some sedation and/or interact with cytochrome P450			

Pharmacodynamics

Bilastine's onset of action is 1 hour post-dose and lasts for 26 hours.[5] Cetirizine's onset is within 20-60 minutes and lasts for at least 24 hours post-dose.[6] Similarly, onset of action of rupatadine occurs within 1-2 hours post-dose.[7]

QT prolongation

The potential for QT prolongation is a class effect of all antihistamines. As such, all 2nd generation AHs are contraindicated in patients with a history of QT prolongation including congenital long QT syndromes, and/or torsade de pointes.[5-7]

Indications and Contraindications of Prescription 2nd Generation Antihistamines[5-7]

Indications

	Allergic Rhinitis
OD Bilastine 20 mg	Seasonal allergic rhinitis ≥ 12 yrs
OD Cetirizine 20 mg	Seasonal allergic rhinitis & perennial allergic rhinitis ≥ 12 yrs
OD Rupatadine* 10 mg	Seasonal allergic rhinitis & perennial allergic rhinitis ≥ 12 yrs

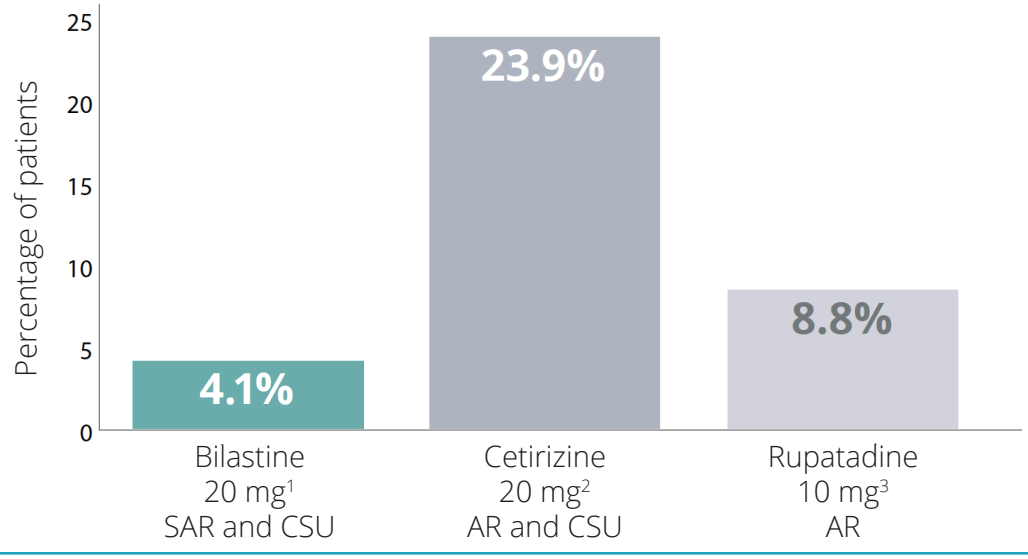
* Children 2-11 years of age, dosage based on weight

Contraindications*

Bilastine	· History of QT prolongation and/or torsade de pointes
Cetirizine	· Renal impairment: CrCl < 10 ml/min
Rupatadine	· History of QT prolongation and/or torsade de pointes · Use with CYP3A4 inhibitors · Use with other QTc-prolonging drugs

* All are contraindicated in patients with a hypersensitivity to the drug or to any ingredient in the formulation or component of the container.

Figure 2. Somnolence rates of the prescription 2nd generation AHs from product monographs[5-7]



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Metabolism

Bilastine[5]	Cetirizine[6]	Rupatadine[7]
· Not metabolized	· Less extensively metabolized than other antihistamines	· Metabolized by cytochrome P450 (CYP 3A4) · Metabolites include desloratadine

Dosing in kidney and liver disease

Bilastine[5]	Cetirizine[6]	Rupatadine[7]
· No dose adjustment for patients with kidney or liver impairment	· Dose adjustment in patients with moderate kidney or liver impairment	· Not recommended in patients with kidney or liver impairment

Overview of Bilastine: a novel 2nd generation antihistamine

Bilastine is a novel 2nd generation antihistamine used by over 113 million patients in over 118 countries around the world. Bilastine has been available in Canada since January 2017 and is also approved in Europe for children 6 to 11 years age for seasonal and perennial allergic rhino-conjuctivitis.

Efficacy in AR

Two phase III studies investigated the efficacy and safety of bilastine compared to cetirizine and desloratadine.[8-9] There was no significant difference in the change in total symptom score between the bilastine and cetirizine treatment arms or bilastine and desloratadine arms. However, bilastine demonstrated a significantly lower incidence of somnolence and fatigue compared to cetirizine.

Safety and Tolerability

At the recommended dose of 20 mg once daily, bilastine's treatment-emergent adverse reactions, including somnolence, were equal to placebo.[5] At doses up to double the recommended dose (40 mg), bilastine, did not affect psychomotor performance and did not affect driving performance in a standard car driving test.[5]

Bilastine's cardiac safety was assessed in a robust QT study and showed no clinically significant impact on the QTc interval at both therapeutic and supratherapeutic doses.[5]

Conclusion

The use of 1st generation AHs is no longer recommended by the CSACI and ARIA guidelines.[2,3] In their place, ARIA guidelines recommend a 2nd generation AH that is non-sedating and does not interact with the cytochrome P450 system.[4]

Bilastine is the only prescription 2nd generation antihistamine available in Canada that meets both these criteria.

Bilastine has shown comparable efficacy to other 2nd generation AHs with sedation less than cetirizine and comparable to placebo.[5]

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