Singulair slam

On behalf of Merck Frosst Canada, I am replying to the recent article on montelukast (Singulair) reprinted in the January issue of Canadian Family Physician. This article originally appeared as a drug review from the Association Mieux Prescrire (AMP) in France. It does not represent the data from clinical trials with montelukast in asthma fairly and, more importantly, does not reflect Canadian indications or Canadian medical opinion. I bring to your attention the following points.

1. The article states that there are two indications for montelukast: “as adjunctive treatment for mild-to-moderate chronic asthma when regular inhaled steroid therapy and short-acting inhaled \( \beta_2 \) stimulants ‘on demand’ are inadequate; and in prevention of effort-induced asthma.” This indication means that montelukast should be used only for uncontrolled patients already using inhaled steroids or for patients with exercise-induced asthma. These are the indications for montelukast use in France, not in Canada.

2. In Canada, montelukast is indicated for prevention and prophylaxis of chronic asthma in patients 6 years of age and older, including those who are acetylsalicylic acid-sensitive and who have exercise-induced asthma. Montelukast is effective alone or in combination with other agents used in maintenance therapy for asthma. Montelukast can be used concomitantly with additive effects to control asthma or to reduce the inhaled corticosteroid dose while maintaining control.

3. In this article much discussion is on the role of leukotriene antagonists (LTRAs) according to different international guidelines on asthma. The authors leave the impression that there is no clear consensus on the role of LTRAs in asthma according to these different guidelines. Given that this article was published in a Canadian journal in 2000, why is there no reference to the new Canadian asthma guidelines published in November 1999?

4. Montelukast, as part of the LTRA class, is included in the Canadian Asthma Consensus Report 1999 and is given a clear role in the treatment of asthma. These new asthma guidelines were written by Canadian opinion leaders who had access to the same information as those writing the article in Prescrire. The Canadian Asthma Consensus Group describes two important roles for LTRAs:
   - as an alternative to increased doses of inhaled steroids, LTRAs may be used as adjunct therapy to moderate or higher doses of inhaled steroids to achieve control of persistent asthma symptoms, and
   - for patients who cannot or will not use inhaled steroids, LTRAs should be the primary treatment choice.

5. This article also discusses the lack of comparative studies with montelukast. The authors mention oral \( \beta_2 \) stimulants, short-acting \( \beta_2 \)-agonists, and theophylline as examples. These medications are either not directly comparable or are used infrequently in Canada. Comparisons with montelukast and other medications, such as inhaled corticosteroids, sodium cromoglycate, or long-acting \( \beta_2 \)-agonists have been made and either been published or presented in abstract form.

6. The article states that montelukast is very well tolerated but might be associated with Churg-Strauss syndrome. Although reports of Churg-Strauss syndrome have been uncovered while patients are taking montelukast, this is true with any medication used in the chronic treatment of asthma. In fact, the most widely prescribed inhaled steroid in Canada, fluticasone, and the latest asthma therapy, fluticasone and salmeterol in combination (Advair), both include precautions related to Churg-Strauss syndrome in their Canadian product monographs.

7. Last, according to our medical translators, the conclusion in the article that “Montelukast. No current use for asthma” is not the correct translation of “Montelukast. L’utilité de ce produit dans l’asthme reste à préciser.” The English should have been: “Montelukast. Role in asthma remains to be determined.” In the original French version, the authors conclude that the role of montelukast is not yet clear, while the English translation wrongly concludes that there is no place for this product in asthma. Given these points, we believe this article does not reflect the Canadian situation for montelukast, which was researched and developed in Canada and now sold around the world.
yours is a Canadian journal for Canadian physicians, we believe a fairer description and review of our product in the Canadian context is required.

— Dr Ernest Pregent
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References

Response
Thank you for your letter.

It is true that articles published in La revue Prescrire are mainly written for health professionals working in France. Versions published in Canadian Family Physician are not rewritten in the light of Canadian indications, a point we should have underlined. According to the Physicians’ Desk Reference,1 the indication is limited to “prophylaxis and chronic treatment of asthma in adults and pediatric patients 6 years of age and older,” with no mention of failure of short-acting β₂-stimulants or of exercise-onset asthma.1

The Canadian recommendations to which you refer are probably those published in late November 1999,2 which could not have been included in our article published in January 2000. In addition, the summary of the recommendations of the Canadian Asthma Consensus Group states that they met in May 1998. The literature search on which the article in La revue Prescrire was based was terminated in early 1999, as stated at the head of the references section.

Regarding leukotriene antagonists, the report states that “their potential for modifying the natural evolution of the disease has yet to be confirmed. [T]heir use as monotherapy cannot be promoted in most circumstances.”2 The consensus conference proposed that adjunctive leukotriene antagonists be considered as an alternative to increasing the dose of inhaled glucocorticoids, with only level 2 evidence. They further proposed that patients who remain symptomatic despite moderate-dose inhaled glucocorticoids should receive theophylline to control asthma similarly to high-dose inhaled glucocorticoids (level 2 evidence).2 A sound comparison of montelukast and theophylline is thus fully warranted, even on the basis of the Canadian recommendations.

We think a sound comparison with short-acting β₂-stimulants for prevention of exercise-onset asthma is also fully justified, as is a comparison with oral β₂-stimulants, which can be useful when first-line treatments fail. The fact that these drugs are rarely used in Canada has nothing to do with their efficacy, and patients finding themselves in unusual circumstances also have a right to strictly assessed treatments.

The fact that the risk of the Churg-Strauss syndrome cannot be ruled out with other asthma treatments does not affect the persistent doubt regarding montelukast, as stated in the Physicians’ Desk Reference, for example.3

We recognize that the English translation of the French subtitle “No current use for asthma” was clumsy. The rest of the translation and particularly the opinion “judgment reserved,” however, closely reflects the nuances in our conclusion.

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References

Conflicting message in the title

This letter concerns the article1 on montelukast in the January issue. In this review article, the authors mention the role of leukotriene receptor antagonists (LTRAs) in asthma management in relation to a number of international guidelines. There was no mention of the role of LTRAs in asthma management in Canada. I believe this might be related to the time line between the publication of the most recent Canadian guidelines in November 19992 and the publication of this review.1 Therefore, the role of LTRAs based on Canadian recommendations requires further clarification.

I was puzzled by the message conveyed in the title of the article1 “Montelukast. No current use for asthma,” and the rating “judgment reserved” assigned by the editors of Prescrire. Based on the Prescrire rating system, a rating of judgment reserved indicates that “The editors postpone their judgment until better data and a more thorough evaluation of the drug are available.” Given this definition, the title should be modified accordingly because it explicitly passes judgment, and it does not reflect Canadian recommendations on the use of LTRAs. Current Canadian guidelines2 on asthma management suggest the use of LTRAs:

1. Leukotriene receptor antagonists may be considered as an alternative to increased doses of inhaled glucocorticosteroids (ICS) and therefore should be used as a potential addition to therapy to moderate or higher doses of ICS to achieve control of persistent asthma symptoms.
2. There is insufficient evidence to recommend LTRAs for regular therapy in place of ICS; however, for patients who choose not to use ICS, LTRAs should be the primary treatment of choice.