CADTH

CADTH COMMON DRUG REVIEW

Patient Input

BENRALIZUMAB (Fasenra)

(AstraZeneca Canada Inc.)

Indication: asthma, severe eosinophilic

CADTH received patient input from:

Asthma Canada

The Ontario Lung Association

December 12, 2018

Name of the Drug and Indication	**Cinqair (reslizumab); Fasenra (benralizumab); Nucala (mepolizumab);**
Name of the Patient Group	**Asthma Canada**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

About Patient Group

Asthma Canada is the only national charity solely dedicated to enhancing the quality of life for people living with asthma and respiratory allergies. Asthma Canada has provided evidence-based health education programs and services to all Canadians affected by asthma for more than 40 years.

For more information, visit www.asthma.ca.

Information Gathering

Information for this Request for Advice was gathered through consultation with Asthma Canada's Scientific and Medical Advisory Committee, which plays an advisory role in Asthma Canada's knowledge translation framework for the public, healthcare professionals and government. The Committee members provide expert opinion based on evidence, editorial direction on materials and resources, and guidance on national initiatives and policies.

Background

Over the past few years, Asthma Canada has contributed patient input to: mepolizumab (Nucala), reslizumab (Cinqair), and benralizumab (Fasenra). In October 2018, CADTH called for patient input to contribute to a "Request for Advice" for these drugs, a document which prepared information for the Canadian Drug Expert Committee (CDEC) to respond to specific questions from the drug plan. The questions arose because the clinical criteria in the CDEC recommendations for the three drugs differ.

The specific questions from the drug plans for CDEC to answer are:

1. Should the clinical criteria in the CDEC recommendations for mepolizumab and/or reslizumab be updated to align with those that were specified in the more recent CDEC recommendation for benralizumab?
2. If the clinical criteria in the benralizumab recommendation should not be applied to the recommendations for mepolizumab and reslizumab, would it be appropriate for CDEC to establish new clinical criteria that are aligned for all three products?
3. If aligned criteria would not be appropriate for benralizumab, mepolizumab and reslizumab, could CDEC provide the rationale why different criteria are required for these drugs? Specifically, for

mepolizumab and reslizumab, is it appropriate to have to demonstrate reversibility (at least 12% and 200 mL) on pulmonary function tests (i.e., spirometry) as a clinical criterion for eligibility?

Asthma Canada was asked to weigh in on the following issues:

- Practical considerations for patients on blood eosinophil testing as compared to pulmonary function testing,
- Impact to patients if mepolizumab were not reimbursed if patients were using another biologic to treat asthma,
- Impact if mepolizumab and reslizumab were not reimbursed for patients who continue to smoke

Asthma Canada Recommendations

Eosinophil Level

Quebec has had consistent criteria for several years, which could act as a model to be adopted across Canada. The Quebec criteria have been reviewed by INESS and are largely considered to be reasonable. The Quebec requirements for mepolizumab and benralizumab are the same. However, the criteria for inclusion into the studies for reslizumab were quite different from the other two as a significant proportion of patients included were on moderate rather than high dose ICS/LABA and required a much higher eosinophil threshold (400) as compared with the other two. Therefore the 150-300 eosinophil threshold cannot be applied to reslizumab.
However, if CDEC is considering creating aligned criteria for the three drugs, they can look to standardized guidelines such as the one developed by CTS, which recommends a threshold of eos> 150 and on moderate-high dose ICS with LABA.

Reversibility Criteria

Quebec has not adopted a criteria of reversibility at the time of prescription. The general consensus amongst prescribers is that the 12% reversibility criteria is currently interfering with access and should not be included. Improvements in FEV1 is of little utility clinically in the study population where reduction of steroid use and exacerbation frequency are clearly the important clinical benefits being sought. The inclusion criteria in a study is never the criteria applied to using a drug in clinical practice. For instance, the McGill University Severe Asthma Center currently has close to 100 patients on anti-IL5 drugs and the majority have not demonstrated reversibility in the last year. Many patients with clear historical evidence of asthma but with remodeled airways, and usage of oral steroids have lost the ability to demonstrate reversibility, yet have frequent exacerbations and have clearly benefitted from anti-IL5 agents, by demonstrating symptomatic improvement, less steroid usage and fewer exacerbations. Historical evidence of reversibility or methacholine response and/or clinical diagnosis of asthma from a specialist should be sufficient criteria.

Preventing Wastage

In order to prevent wastage, non-responders should be taken off the medications in 4-6 months so that the medication is not used too long for no reason.

Patient and Physician Choice

While inclusion criteria can be simplified, if not aligned, it is crucial to note that the three drugs are not the same and so it is important to preserve choice for patients and prescribing physicians. There has been evidence of patients failing on one biologic and then responding to another. There are potential advantages to each of the three drugs in terms of frequency of administration, self-injection, long-term experience, being weight-adjusted, differing mechanisms of action, etc. In an age of personalized medicine the physician needs access to all options so that they can decide what works best for each patient. *As one physician described, his practice is to start with mepolizumab since we have the most experience with it. However if eosinophil levels are very high or a faster response is needed benralizumab may be first. If the patient is on very high dose OCS i.e. > 15 mg daily, the data for benralizumab and reslizumab is perhaps a bit better although not clearly so. For obese patients reslizumab is a reasonable choice and benralizumab and reslizumab would be worthwhile alternatives to mepolizumab failures.*

Smoking

Smoking should not exclude those with asthma from optimal treatment. Smokers were excluded from the studies but they were also excluded from studies on all asthma medication available and are not prevented from using inhalers on that basis. The decision to be prescribed the biologic medications in question should be an individualized one between patient and physician. However, every effort should be made to first eliminate smoking.

Age Indication

The age indications of the biologic medications should also be reconsidered. Mepolizumab studies included children over the age of 12. The age indication for mepolizumab is 12 and older in the United States. However, it is indicated for 18 and older in Canada. There are many severe asthmatics who would benefit from this therapy who will not be able to access it if the age restriction continues. Standardized criteria would be ideal with as broad an age range as possible.

Equal Access throughout Canada

Every Canadian should have equal access to these drugs regardless of their province of residence. It is not helpful for every province to have slightly different criteria. This should not be the case, especially since there is consensus in Canada about how to treat severe asthma.

Conclusion

Asthma Canada supports the alignment of criteria for mepolizumab, reslizumab and benralizumab and views this as an opportunity to address problematic issues such the reversibility criteria, the age indication and patchwork access across the provinces. However, Asthma Canada strongly disapproves of any move to further restrict access such as denying currently available therapies to smoking asthmatics. Furthermore, Asthma Canada advises CADTH to ensure that patient and physician choice is preserved to allow for the best possible health outcomes.

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Fasenra (benralizumab) / Asthma, severe eosinophilic**
Name of the Patient Group	**The Ontario Lung Association**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

(The Ontario Lung Association is registered with the CADTH and pCODR) (www.lungontario.ca)

The Ontario Lung Association is a registered charity that assists and empowers people living with or caring for others with lung disease. It is a recognized leader, voice and primary resource in the prevention and control of respiratory illness, tobacco cessation and prevention, and air quality and its effects on lung health. The Association provides programs and services to patients and health-care providers, invests in lung research and advocates for improved policies on lung health. It is run by a board of directors and has approximately 50 employees, supported by thousands of dedicated volunteers. The Lung Association - Ontario is part of a federated model and works closely with 9 other provincial lung associations and the Canadian Lung Association.

2. Information Gathering

The information provided from the Ontario Lung Association in this submission was obtained from two phone interviews with women living with severe asthma (completed November 2018) and 91 on-line surveys completed by people living with a chronic lung condition and / or their caregivers (input received December 2018). Please note of the 91 surveys, nine of them were completed by people living with a diagnosis of asthma or severe asthma. Input from a certified respiratory educator was also obtained for this submission. All data gathered was from people residing in Canada.

3. Disease Experience

The symptoms and challenges that people experience as a result of Asthma are shortness of breath, fatigue, coughing (with or without mucus), wheezing, difficulty fighting infections and

weight loss. When asked whether this condition affected their day-to-day life, respondents indicated that it did indeed impact greatly their physical and leisure activities, and to a lesser extent, their work, ability to travel and socialize. A few direct quotes are:

- “Asthma affects all aspects of my day-to-day life. I struggle to keep my symptoms under control.”
- “I have to take my inhaler twice daily. I watch my triggers. I exercise daily to try and increase lung function.”
- “I am unable to lead an active life, as my asthma limits my ability to complete work tasks.”
- “It takes forever to do simple tasks.”
- “I cough a lot and have a lot of congestion, both of which cause me to be short of breath most of the time.”
- “Asthma severely affects my day to day life, restricting many activities and causing time off work.”
- “The cough is annoying and I can have difficulty swallowing.”
- “I become short of breath with any exertion….walking, carrying items, etc…”
- “My allergies to environmental triggers cause wheezing, shortness of breath.”

The aspects of the condition that are most important to control for people living with it are first - **shortness of breath** and second – **coughing and fatigue.** They would also like better control with wheezing and an increased ability to fight infections.

4. Experiences With Currently Available Treatments

Treatments tried by those who completed the survey and were interviewed included: Symbicort, Ventolin, Pulmicort Bricanyal, Fasenra, Trelegy, Spiriva, Prednisone, and Singular. Nasonex, Reactine and other antihistamines are used for allergies as needed.

Current treatments do provide some relief for: fatigue, shortness of breath, cough, low energy, poor appetite and the inability to fight infection, but patients indicated they want to experience greater assistance with managing all of these symptoms. The side effects indicated from using the above-mentioned dugs include: hoarse voice, dry mouth, increased mucus, low energy/ fatigue, appetite loss, impact on mood and being shaky. One person mentioned concerns over an increased heart rate from daily inhaler use.

When asked about whether the treatments affected their life in any other way, some respondents indicated that the cost burden was an issue, as was the time required to travel to health-care settings, the time required off work for these appointments and the changes to their daily routine to accommodate treatment. One respondent indicated that their work requires them to move every three years and changing physicians makes things difficult – would like a seamless referral system.

One of the respondents was part of a trial for Fasenra that started three years ago, and she stated this medication has made a tremendous difference in her quality of life. Before Fasenra, she was taking about six medications, did not feel well, was able to do her job but nothing else as she was “exhausted” at the end of each work day. She has been living with severe asthma for more than 30 years. Since starting Fasenra, she has been weaned off of almost all other

medications, has experienced an increase in energy and lung capacity and no longer has difficulty sleeping.

She accesses this medication at an injection site about every eight weeks which she finds to be easy to manage. She did indicate that if her drug plan did not provide coverage, she would not be able to afford this medication.

5. Improved Outcomes

Key treatment outcomes of asthma that patients would most like addressed are: reduced shortness of breath, reduced coughing, reduced fatigue and improved appetite. They would like an increased ability to fight infections and to have a higher energy level. Ideally, patients would experience an improved quality of life and improved lung function.

Administration of medication, side effects and cost burden were the three most commonly mentioned things that are evaluated when considering new therapies. “I am extremely fortunate that my insurance covers my medication, otherwise I would be unable to afford it. It has made a huge difference in my quality of life.”

“The turboinhaler mechanism didn’t bother me until I had to start taking more of it. Now that I am taking more doses, an easier mechanism (a tablet, or something) would be preferable. I just find it a bit time-consuming and cumbersome.”

The main trade-offs for people when discussing options with their doctor are cost and likelihood of effectiveness. “My doctor once said that I could try adding another medication into the mix to help with management, but noted that it was more expensive and only worked in a relatively small percentage of patients. That didn’t seem worth it.”

For the one respondent who is taking Fasenra, she has experienced many positive outcomes as a result of this medication. She has experienced an increase in energy and lung capacity and no longer has difficulty sleeping. She is able to play with her grandkids, be outside and take part in active activities such as kayaking. Additionally, she has experienced reduced blood pressure, lost some weight and “feels like a different person.” She attributes all of these positive outcomes to the use of Fasenra.

6. Experience With Drug Under Review

One of the respondents was part of a clinical trial for Fasenra that started three years ago at St. Joseph’s. She stated this medication has made a tremendous difference in her quality of life – “everything is better.” Before Fasenra, she was taking about six medications and did not feel well most of the time. She has been living with severe asthma for more than 30 years and it was slowing robbing her of her independence and enjoyment of life.

She accesses this medication at an injection site about every eight weeks which she finds to be easy to manage. She did indicate that if her drug plan did not provide coverage, she would not be able to afford this medication. The cost of this treatment would absolutely be a barrier if it were not to be covered.

The positive results were noticed by her almost immediately, with increased energy being at the top of the list. She no longer experiences issues with scents, which used to be a big trigger for her, or with weather changes. She describes herself as almost being “symptom-free.”

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

   No – not applicable

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   No – not applicable

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AstraZeneca Canada Inc.				X

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Peter Glazier
Position: VP Marketing, Development & Public Affairs
Patient Group: The Lung Association - Ontario
Date: December 12, 2018

CADTH

1. **Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.**

   We did not receive any external assistance in compiling this submission.

2. **Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.**

   We did not receive any additional assistance in compiling this submission.

3. **List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.**

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AstraZeneca				X
GlaxoSmithKline				X
Merck			X	
Novartis				X
Teva				X
Boehringer Ingelheim	X			
Trudell		X		

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: **Mehnaz Rahman**
Position: **Manager, Programs and Services**
Patient Group: **Asthma Canada**
Date: **December 18, 2018**