CADTH

CADTH COMMON DRUG REVIEW

Patient Input

benralizumab (Fasenra)

(AstraZeneca Canada Inc.)

Indication: Asthma, severe eosinophilic

CADTH received patient input from:
Asthma Canada
British Columbia Lung Groups

March 16, 2018

Patient Group Asthma Canada

1. About Your Patient Group

Asthma Canada is the only national, volunteer-driven 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.

2. Information Gathering

Information for this submission, was obtained through multiple sources, including an Asthma Canada online survey on the use of medications, the daily management of this chronic condition, and the impact that Severe Asthma has on quality of life. The survey was sent to the Asthma Canada Member Alliance (ACMA) members across Canada in November 2017 and 55 responses were received. A total of 87% of survey respondents had received a diagnosis of asthma and 9% identified themselves as caregivers.

Phone and email interviews were conducted with six participants involved in the Canadian benralizumab clinical trials (SIROCCO & CALIMA) in December 2017.

In addition, information was drawn from the study conducted by the Asthma Society of Canada in 2014, entitled "Severe Asthma: The Canadian Patient Journey". This study included Canadian adults 18 years or older who live with Severe Asthma as defined by their symptoms, their level of asthma control, and a review of their clinical profiles by a team of expert advisors. Twenty-four patients participated in in-depth personal interviews about their condition and its impact on their personal, social, medical, and economic circumstances. A complementary on-line quantitative survey of 200 individuals with Severe Asthma was conducted to validate and quantitate the in-person findings. Further details of the study population, investigators, and process are available on pages 28 to 31 of the full report.

Additional details of disease definitions and treatment options have been drawn from material published on Asthma Canada's website and US Prescribing Information for benralizumab and a PubMed search for relevant treatment guidelines and review articles.

3. Disease Experience

According to the Public Health Agency of Canada approximately 3.8 million Canadians live with asthma. Approximately 5% of Canadians with asthma have Severe Asthma. Recent guidelines and position papers published by the Canadian Thoracic Society (CTS) classifies Severe Asthma as a subset of asthma which remains poorly controlled despite adherence to best practices in terms of self-management and pharmacologic strategies.

Eosinophilic asthma is a subtype of asthma that is characterized by the presence of eosinophils in the inflamed tissues, which can be detected through examination of sputum. In contrast to more classic forms of asthma that tend to be linked to a particular allergic trigger and diagnosed earlier in life, many cases of eosinophilic asthma only appear in adulthood, in patients with few or no allergies.

Severe Asthma has many different effects and consequences that can impair patients' quality of life. In Asthma Canada's patient journey study, respondents identified several crucial areas where asthma had a major impact:

- **Physical activity**: Over 70% of survey respondents reported limitations to daily activities and exercise due to their asthma
- **Social interactions**: Almost 2/3 of respondents said that they have felt stigmatized because of their asthma at some point, and that asthma interferes with their social activities and interactions with others
- **Work/school productivity**: More than half of respondents mentioned that asthma has affected their attendance and/or performance at work or school

- **Emergency room visits and hospitalization**: About half of respondents had needed to visit an emergency room in the previous year because of asthma symptoms. One-third went more than once during this period, and one in five needed to be hospitalized

When asked how asthma affects their day-to-day life, more than three-quarters (79%) of survey participants who responded reported that it restricts the type or amount of physical activity they can engage in; more than a third of respondents (36%) cited lost productivity – either missing school or; 29% of respondents said that it has an impact on family or caregivers; and 14% of individuals reported experiencing negative stigma. Additional responses included experiencing anxiety and other mental health issues, decreased social life and inability to work.

When asked if there are activities that they are unable to engage in, 80% of survey participants identified physical activities such as exercising and spending time outdoors; 34% identified engaging in social activities; and 41% cited inability to sleep. A number of respondents provided additional information such as the inability to travel and visit family and friends who own pets. One respondent mentioned that they cannot work and "continue in my trade as an electrician." Some other comments included the following:

> *"I am taking injections to control asthma but still have problems breathing during physical exertion (stairs, walking and carrying something, walking up grades)"*
>
> *"I am hospitalized yearly and have many episodes throughout the year which requires prednisone. When I am sick, I am really sick and not controlled. I am on injections monthly, but I don't like how I need to nap daily. Most of the time, I am controlled, but when it's bad, it's really bad."*
>
> *"[I am] uncontrolled, despite max medications, medication changes, long-term steroids, I still have to sequester myself from people. My asthma remains uncontrolled and I don't have access or means to get the more expensive biologic drugs that might make a difference."*

When asked which aspects of asthma are most important to control, 52% of respondents indicated day-to-day symptoms; 36% identified asthma exacerbations or attacks; and 5% cited cost of medication.

4. Experiences With Currently Available Treatments

In current Canadian practice, the cornerstones of asthma management are avoidance of triggers; long-term controller medications such as inhaled corticosteroids (ICS) which may or may not be used with add-ons such as leukotriene receptor antagonists and long-acting bronchodilators; and short-acting relievers. Oral corticosteroids (OCS) may be used for patients requiring a higher corticosteroid dose. This is particularly common in patients with severe eosinophilic asthma.

It is important to note that, by definition, a patient whose asthma has been classified as "Severe" has tried the standard options and is still experiencing symptoms of a severity and/or frequency that can drastically reduce quality of life. The definition of Severe Asthma therefore carries within it an unmet need for treatment options that go beyond the existing standard of care.

In addition, the distinctive nature of eosinophilic asthma means that some of the novel treatment options for other forms of asthma are not appropriate. One of the newer options for treatment of uncontrolled allergic asthma is omalizumab, an antibody that reduces patients' sensitivity to inhaled allergens by targeting immunoglobulin E. However, since many cases of eosinophilic asthma are non-allergic in nature, omalizumab will be of limited use in this population.

Financial considerations are an important barrier to optimal asthma medication use. In Asthma Canada's Severe Asthma study, about one third of patients reported that they had skipped filling a prescription for an asthma medication because they were unable to afford it. Many private insurers do not provide complete coverage for asthma medications, placing a significant portion of the burden on patients. Since many patients with Severe Asthma have low incomes (more than one-third of the study participants had household incomes under $50,000) and/or are unable to work because of their asthma, even having to pay a small percentage of the drug cost can be a significant financial concern.

The use of OCS in patients who fail to achieve adequate asthma control with ICS deserves special mention because of the short-term and long-term side effects of systemic corticosteroids. This issue is of particular concern in the population of patients with

severe eosinophilic asthma, where many patients depend on long-term OCS to provide some degree of inflammation control after other options prove to be inadequate (de Groot 2015).

OCS can have significant systemic adverse effects, both in terms of physical changes (e.g., cataracts, bone density changes, suppression of adrenal gland activity) and patients' psychological and emotional well-being (e.g., irritability, agitation, insomnia). Both types of effects can have a significant impact on patient health and quality of life; as such, the recommended practice is to use systemic steroids for as short a duration as possible, and to approach long-term use with caution and regular monitoring. Although this principle and the adverse effects of long-term OCS are well established, the burden of OCS use is not often evaluated in asthma clinical studies and is not well interrogated by the existing asthma-related and general health HRQOL scales, so the real impact of OCS use on patient experience and the improvements associated with OCS discontinuation may be even greater than we know. (Hyland 2015)

When asked about their current asthma management treatments, 88% of survey respondents cited combination therapies (ICS/LABA); 83% indicated relievers; 30% cited ICS; 25% indicated OCS; 18% cited leukotriene receptor antagonists; and 3% reported the use of long-acting beta-2 agonists. Some respondents reported using biologic therapies: 5% of respondents said they use anti-IgE biologics and 13% indicated using an anti-il-5 biologic.

When asked how effective current treatments are with controlling asthma, a total of 38% reported their currently available treatments as only somewhat effective, meaning they do not have control of their disease. For patients to live symptom-free, which is the goal of asthma management, their medications need to be consistently effective. According to the Severe Asthma: The Canadian Patient Journey, many patients report going through several years of trying different medications before finding the medication, or combination of medications, that will keep their asthma manageable. Some participants report having spent up to seven years experimenting with treatments before finding the right treatment; while others still have not found a treatment that works for them.

The three most common adverse effects reported by patients were weight gain due to medication, increased heart rate and hoarseness, each at 43%; followed closely by headaches reported by 37% of respondents; dry throat reported by 34%; difficulty sleeping reported by 31% mood or behavioural changes reported by 29%; upset stomach/nausea indicated by 20%; thrush reported by 17%; bad taste by 14%; and acne reported by 6% of respondents. Additional side effects included vaginal yeast infection and severe depression due to Prednisone, coughing, jitteriness from Ventolin use, fatigue, as well as nerve pain, muscle spasms, and burning feet and legs. Asked which adverse events were most bothersome and why, respondents supplied myriad answers. Below are some of the comments given by respondents:

> *"[I experience] mood swings, depression, tiredness, hand tremors, insomnia....all thanks to prednisone"*
>
> *"My weight has been steadily increasing despite diet and whatever limited exercise I'm able to do"*
>
> *"I have been on injections for 8 months, but still had one of my most severe attacks (1 week in isolation) despite this drug."*

When asked about obstacles in accessing current treatments, 53% reported cost as the leading obstacle; lack of awareness of new treatments was the second most common obstacle (47%) cited; an equal amount of respondents, 9%, cited inability to find an asthma specialist, and a doctor being unwilling to prescribe treatment.

As a general rule, financial challenges are a significant barrier to optimal health outcomes. This is no less true for patients with asthma. Many insurance carriers do not provide complete, or even partial, coverage of asthma medications, meaning many patients with asthma cannot afford their medications. The expense of medications and the fact that many patients with asthma may have low incomes, in part because they may be unable to work because of their asthma, causes additional stress for many patients and their families (*Severe Asthma: The Canadian Patient Journey*). Even paying for a small percentage of the cost of a drug may present financial difficulties for patients. When asked for details, some responses included:

> *"At this point, when my asthma is controlled I don't have financial difficulties. I work full time. Before my [Benralizumab] clinical trial I had to take extra time off because I had daily symptoms and was not able to sleep. It resulted in decreased income."*
>
> *"Sometimes I cannot afford [medication] and ask if doctor might have a sample or I go without"*

"The most effective inhaler I tried isn't covered by my health plan so I am using something that isn't as effective."

"[Asthma] caused me to not be able to work, then not have insurance, but cost of medications keeps rising, while income diminishes."

5. Improved Outcomes

Treatment success for patients with asthma ideally means being brought under control so they can live life to the fullest without fear of an exacerbation. Getting asthma under control so that patients experience fewer symptoms and ideally no symptoms, is the primary objective for all patients with asthma. When survey participants were asked if there were needs that were not being met by their current treatments, 49% of respondents indicated that they continued to experience poor symptom control; 29% reported that many doses were needed daily making it difficult to manage their asthma on a day-to-day basis; 26% indicated that they continued to require frequent hospitalization and doctors' visits; and 17% indicated that their current treatment was unaffordable. These responses indicate that current asthma treatments are not fully leading to optimal control in many patients. Some respondents gave specific responses, some of which can be found below:

"Moderate symptom control, but still limitations day to day."

"Severe attacks during colds. Constant coughing up of phlegm."

Asthma affects not only the individuals living with asthma but has a pronounced impact on caregivers, whether caregivers are family members, spouses, parents, siblings, educators, or close friends. Caregivers have a constant fear and worry that their loved one or close friend will experience an asthma exacerbation. The condition takes an emotional toll on caregivers. When asked about the challenges caregivers face when caring for people with asthma, 71% of respondents reported worry and fear of exacerbation/asthma attack; 57% indicated missed work/school days was challenging; 51% said the potential for hospital visits/admissions were substantial concerns; and 46% indicated cost and financial burden. Some of their responses appear here:

"[Caregivers] never get a chance to do what they want. Lack of sport and social activities and worry about sick person can be very depressing"

"Lack of control, ability to help. Once an attack begins you feel/are helpless."

Caring for a patient with asthma can be taxing on an individual in terms of responsibilities and more difficult if the patient requires more medications to achieve control. Survey respondents defined the burden that asthma treatments have on the daily routine or lifestyle of caregivers, citing lack of sleep (66%), frequent doctor's appointments (59%), and managing multiple medications (50%).

"I care for my mother who has asthma and Alzheimer's. Impact to me has been worry that she has issues with lack of adherence to her daily meds and possible technique issues due to her memory disease. My mother lives 6 hours away from my home town. Thus, I travel monthly to see her. So, there is cost of travel, my absence from my family and friends while gone, absence of my regular routine in taking care of myself when I am home etc. Luckily I am retired and have time to travel to support my mother in her care of her asthma and allergic rhinitis (saline wash, nasal corticosteroid use, avoidance of triggers)."

"Drugs are costly as is the cost of having to give up a full time career to be available 24/7 to care for my child."

6. Experience With Drug Under Review

Asthma Canada interviewed six participants involved in the Canadian benralizumab clinical trials (SIROCCO & CALIMA) in December 2017.

Feedback received was overwhelming positive, with patients indicating that they experience no negative effects from the drug and that their asthma symptoms were negligible with no need to use their rescue inhaler. Benralizumab was successful in reducing asthma. Some of the feedback include:

"I have tried every asthma medication available in Ontario. Benralizumab is the only drug that has worked long-term, without any side effects… The only disadvantage is that I have to travel to Hamilton every month from Wasaga Beach [2.5 hours] to receive my injection … It is difficult to describe the impact that this drug has had. For anyone who has a disease or chronic condition of any kind, living with the symptoms, fear, sickness, depression, etc. is as debilitating to family and friends as it is to the individual. To have a condition, that gradually worsened with age, virtually disappear is literally a miracle to me and my family. My life is no longer limited in any capacity by asthma. I literally almost died in 2011, and would have left behind my husband and 2 small children. Knowing that my life is no longer impacted by my asthma is like having a new lease on life."

"My current therapy is Benralizumab, I have no adverse effects and I am fully happy. My life is back to normal."

"Benra[lizumab] was amazing, it was like I didn't have asthma. And the adverse effects were minimal if anything. It's not like prednisone which have crippling side effect… Having Benra[lizumab] would make my life easier. I cannot explain what it was like not having asthma for the first time in my life. Not always worrying where my inhaler was, not needing to plan my life around avoiding triggers. A wonderful secondary effect was my nasal polyps shrunk and I got my sense of smell back. I want benra[lizimab] back."

"The asthma study I participated in was Benralizumab. I wish with all my heart that I could afford it when it comes to market, as my severe asthma was noticeably better while I was on the injectable drug, but I can't afford."

In Asthma Canada's Severe Asthma Study, patients with Severe Asthma identified their top unmet needs in asthma care generally; these are not specific to benralizumab or any other novel agent, but give an overall indication of areas that could be addressed to make a major impact on patients' lives. The top 5 goals that respondents would like to achieve are:

- Function normally while completing household activities, walking, and enjoying life
- Not have to visit the emergency department or be admitted to hospital
- Sleep without nighttime symptoms
- Exercise without asthma symptoms
- Go to work

7. Anything Else?

The drug has been approved by other regulatory bodies in other jurisdictions. An expansion of choice of medications and unrestricted access to those medications for people living with asthma will ultimately decrease the burden of the disease in the daily lives of patients and in the daily lives of their caregivers. A broadened selection of medications will allow people living with asthma to live their lives as richly and symptom-free as possible and could save lives.

Appendix: Patient Group Conflict of Interest Declaration

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

   Asthma Canada requested and received a medical briefing from AstraZeneca on benralizumab.

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: March 2, 2018

Patient Group British Columbia Lung Groups

1. About Your Patient Group

Website: www.bc.lung.ca

For more than 100 years, the British Columbia Lung Association has led the fight for healthy lungs. Our mission is to improve the lung health of all British Columbians. We support people affected by lung conditions, such as Better Breather groups for patients with COPD, asthma, lung cancer, pulmonary fibrosis, sleep apnea and other lung disease. We fund vital research in subject areas such as asthma, pulmonary rehabilitation, Tuberculosis, air quality issues, tobacco cessation, radon awareness and more. We are the leading organization working to prevent and improve lung health for British Columbians.

2. Information Gathering

The information for all of the remaining sections was gathered through consultations, telephone interview and patients personal experience.

The information was gathered by telephone interview from 7 female patients and 3 male patients who are on the medication

3. Disease Experience

The symptoms experienced by all were shortness of breath, chronic cough, wheezing, shortness of breath or tightness on the chest, fatigue as a result of their asthma. Other symptoms were depression and frustration as now they are not able to be active and do things that they were once able to do. Depression plays a key factor when you are restricted from doing things or limit their activities.

They are hopeful when a new choice of medication is discovered so that they can try the new medication if the other or current medications they are on is/are not working for them.

Of critical importance to the treatment of severe asthma are medicines that will help reduce or stop the progression of the disease and subsequent hospitalizations. Additional therapies are needed that go beyond symptomatic relief.

4. Experiences With Currently Available Treatments

The individuals interviewed with severe asthma understand there is no cure for asthma but it can be controlled and they do understand that the drug slows the progression and gives them relief of their symptoms. Statements from most of the patients interviewed said" it gives them a chance to work again and have less admission to hospital" They can sleep better and feels less tired.

Another individual expressed the need for anything that would lessen the need at different times for oxygen, to help the panic breathing mode when you exert yourself. "It is frightening when you can't get enough oxygen to be able to stand up -you have to wait until you can get back to a reasonable state". When you cannot breathe, nothing else matters.

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

- Availability(Access to the new medication) very important to the patients.-inclusion in BC Formulary
- Symptom relief
- Better quality of life
- Less or tolerable side effects(Side effects minor nasal problems)
- Less admission to ER or hospital admission
- Live as normal as possible without shortness of breath and chronic coughing

6. Experience With Drug Under Review

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways?

- Private Insurance
- Clinical trials
- Less side effects from new medication
- Was able to live a normal life with the new medication, absence of Shortness of Breath & Chronic coughing
- Reduced flare-ups with asthma
- Less admission to hospital

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

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

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
Glaxo Smith Kline Educational grant			20,000	
AstraZeneca Educational Grant	2000			
Boehringer Ingelheim Educational grant			37,000	

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: Kelly Ablog Morrant

Position: Vice President, Advocacy & partnerships

Patient Group:British Columbia Lung Groups

Date: March 12, 2018