



Common Drug Review *Patient Group Input Submissions*

reslizumab (Cinqair) for Asthma, eosinophilic

Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.

Asthma Society of Canada/National Asthma Patient Alliance — permission granted to post

British Columbia Lung Groups— permission granted to post

CADTH received patient group input for this review on or before June 23, 2016

CADTH posts all patient input submissions to the Common Drug Review received on or after February 1, 2014 for which permission has been given by the submitter. This includes patient input received from individual patients and caregivers as part of that pilot project.

The views expressed in each submission are those of the submitting organization or individual; not necessarily the views of CADTH or of other organizations. While CADTH formats the patient input submissions for posting, it does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no personal information is included in the submission. The name of the submitting patient group and all conflict of interest information are included in the posted patient group submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

Asthma Society of Canada/National Asthma Patient Alliance

Section 1 — General Information

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|---|--|
| Name of the drug CADTH is reviewing and indication(s) of interest | Reslizumab |
| Name of the patient group | Asthma Society of Canada/ National Asthma Patient Alliance |
| Name of the primary contact for this submission: | [REDACTED] |
| Position or title with patient group | [REDACTED] |
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| Website | www.asthma.ca |
| Permission is granted to post this submission | Yes |

1.1 Submitting Organization

The Asthma Society of Canada (ASC) is a registered charitable organization whose mission is to be the balanced voice for asthma in Canada, advancing optimal self-management, prevention, research, and health care. Its vision is to empower every child and adult in Canada with asthma to live an active and symptom-free life. The ASC is based in Toronto under the direction of a volunteer Board of Directors, and provides its services directly to people with asthma through Web sites, e-mail, and the Asthma & Allergy HelpLine. Individuals with asthma are invited to join the National Asthma Patient Alliance (NAPA), the ASC's grassroots patient group providing asthma support, education, and advocacy. NAPA has an outreach to over 5,000 asthma and allergy patients, caregivers, and other interested participants, from all regions of Canada.

1.2 Conflict of Interest Declarations

We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements:

The patient research that forms a significant part of this submission was supported by educational grants from Novartis Pharmaceuticals Canada Inc., Roche Canada and Boston Scientific Ltd. Additional funding for the Asthma Society of Canada comes from GlaxoSmithKline, AstraZeneca, Boehringer-

Ingelheim, Merck, Teva Innovation Canada, Sanofi and Pfizer. We do not have any conflicts of interest with regard to corporate members and joint working arrangements.

We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission:

The ASC requested and received a medical briefing from Teva Canada Innovation previously with regard to Reslizumab. We did not receive any additional assistance in compiling this submission.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

The majority of the patient impact information in this section is drawn from a study conducted by the Asthma Society of Canada in 2014, entitled “Severe Asthma: The Canadian Patient Journey”. A copy of the full study report can be [viewed here](#). 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 the ASC’s Web site and US Prescribing Information for reslizumab, interviews with clinical trial participants through Clinical Score LLC and a PubMed search for relevant treatment guidelines and review articles.

2.2 Impact of Condition on Patients

Definitions and statistics

Asthma is a chronic disease characterized by inflammation in the airways. Symptoms of asthma include wheezing, coughing, shortness of breath, and a sensation of tightness in the chest. Asthma symptoms can occur in both a low-grade chronic manner and also as more sudden, severe attacks known as exacerbations, which can be triggered by a variety of allergic and non-allergic causes. Information from Statistics Canada and the Public Health Agency of Canada shows that approximately 3 million Canadians live with some degree of asthma, with approximately 150,000 to 250,000 of these cases being classified as Severe Asthma. (Life and Breath: Respiratory Disease in Canada)

Although no universally accepted dividing line has been established between “severe” and non-severe asthma, the recent international guidelines of the European Respiratory Society and the American Thoracic Society (Chung 2014) recommend classifying patients’ asthma as severe if it is still uncontrolled in spite of optimal use of long-term controller and short-acting reliever medications (see section 2.3 for more detail on medication types). According to the guidelines of the Global Initiative for Asthma (GINA), asthma can be considered “uncontrolled” if during the past 4 weeks the patient has experienced **at least 3** of the following: (GINA Global Strategy for Asthma Management and Prevention):

- Daytime asthma symptoms more than twice a week
- Any night waking due to asthma
- Reliever medication needed more than twice a week (not including reliever taken before exercising)

- Any activity limitation due to asthma

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. The initial approach to treatment is similar as in patients with allergic asthma – inhaled controller and reliever medications – but often also extends to oral corticosteroids if initial inhaled corticosteroid treatment is inadequate. Even with the use of inhaled and/or oral steroids, many cases of eosinophilic asthma remain uncontrolled and therefore classified as “severe”. (de Groot 2015)

Impact of severe (uncontrolled) asthma on patients

Severe Asthma has many different effects and consequences that can impair patients’ quality of life. In the ASC’s recent patient journey study, respondents identified several crucial areas where asthma had a major impact: (Severe Asthma: The Canadian Patient Journey)

- **Physical activity:** Over 70% of survey respondents reported limitations to daily activities and exercise due to their asthma, even though 89% agreed that, ideally, asthma should not be a reason for avoiding physical exertion
- **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, with about 40% of these saying it affected them “a great deal”
 - About 30% of respondents mentioned that asthma had caused them to miss days of work or school in the previous year; of these, about 2/3 missed 5 days or more, and about 1/3 reported missing more than 10 days
- **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

Patient quotes:

“I’m just so tired that I can’t do anything anymore. Severe Asthma has changed everything.”

“I can’t even take my son hiking because of my health. My limitations affect other people and it makes me angry that I can’t do the things other can and that I used to be able to do.”

2.3 Patients’ Experiences With Current Therapy

In current Canadian practice, the cornerstones of asthma management are:

- Identification and avoidance of triggers that worsen symptoms and/or cause exacerbations
- Long-term controller medication(s) taken on a regular, ongoing basis to reduce inflammation and reactivity in the airways. The most common controllers are inhaled corticosteroids (ICS) delivered through a “puffer”; these can be used with or without other add-ons such as leukotriene receptor antagonists and long-acting bronchodilators. For patients requiring a higher corticosteroid dose than

an inhaler can deliver, oral corticosteroids (OCS) may be used; this is particularly common in patients with severe eosinophilic asthma

- A short-acting reliever (bronchodilator) taken as needed through a puffer to provide rapid relief of exacerbations or severe symptoms

While these measures are adequate to control asthma symptoms and exacerbations in patients with milder disease, 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 as outlined in section 2.2. 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 to the unmet needs experienced by all patients with Severe Asthma, 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.

There is another targeted biologic available for the treatment of eosinophilic asthma in Nucala (mepolizumab) which is currently undergoing a similar review. However, in contrast, reslizumab provides an IV delivered drug which is targeted for patients showing a higher level of eosinophils and has shown results in a shorter time period. Therefore, if a targeted biologic approach is to be used in eosinophilic asthma, it will be necessary to focus on non-allergic targets that are more specific to the eosinophilic pathology, as well as a treatment which demonstrates a quicker impact, such as reslizumab.

Patients’ use of current therapies

The ASC’s recent patient research reveals that many patients do not use their medications appropriately and are not well equipped to manage their Severe Asthma. Many respondents do not carry their short-acting reliever medication with them, and more than half admit to not regularly taking their long-term controller medication. Most often this was due to patients’ perception that they were asymptomatic and did not need to continue taking their controller medication. This indicates both a lack of understanding regarding the purpose and goals of controller treatment, as well as perhaps a misperception on the patients’ part that their asthma is well controlled. Other reasons cited for not using medications as directed included lack of efficacy (repeated exacerbations despite past use) and unpleasant side effects. (Severe Asthma: The Canadian Patient Journey)

Financial barriers to optimal asthma control

Financial considerations are another important barrier to optimal asthma medication use. In the ASC’s survey, 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 survey respondents 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. (Severe Asthma: The Canadian Patient Journey)

Patient quotes:

"I have prescription coverage that will cover birth control, but it won't cover my inhaler. Sometimes I just want to give up."

"My doctors help me with the cost by giving me samples of most of my inhalers, but when I have to pay for them...I have to take on extra work to help pay for my medication."

Patient quotes:

Specific concerns with oral corticosteroids

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).

Since the activity of ICS is mainly localized to the lungs and airways, the risk of systemic side effects is low and they can be used long-term with few serious safety concerns. On the other hand, 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)

Even so, clinical studies in patients with Severe Asthma have demonstrated that patient quality of life, as measured by validated HRQOL scales, improves significantly when a non-OCS add-on medication is introduced that allows patients to stop the OCS. (Nelson 1999, Schmier 2003) Regarding reslizumab specifically, a study presented at The American Thoracic Society's International Congress in 2016 showed that over a 52-week treatment period, patients with inadequately controlled asthma and with elevated blood eosinophil levels treated with reslizumab required fewer new systemic corticosteroid prescriptions. These patients, compared with placebo, had a lower systemic corticosteroid burden as assessed by corticosteroids initiated after first dose of the study drug. Although these analyses did not assess change in maintenance systemic corticosteroids in patients with corticosteroid-dependent asthma, they suggest that reslizumab reduces the overall need for systemic corticosteroids in patients with moderate-to-severe eosinophilic asthma. (Bardin 2016)

2.4 Impact on Caregivers

Since the focus of this application is a medication that is indicated for adult patients only, it will not go into detail regarding the significant challenges for parent caregivers of children with asthma. In terms of the impact on people who must live with and/or care for an adult with Severe Asthma, the burden of helping with acute exacerbations, trips to the hospital, and other aspects of Severe Asthma has not been specifically quantitated, but based on the comments from patients regarding their interactions with others, the following could be anticipated:

- Inability to do certain physical activities with their family member who has Severe Asthma

- Interruptions to sleep – 80% of survey respondents with Severe Asthma reported that asthma caused sleep disruptions for either themselves or their family members in the past 3 months
- Heightened stress and anxiety due to the constant need to be on alert for asthma exacerbations
- Stress, time, and financial impact (e.g., time off work) associated with accompanying the family member to the emergency room

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

Information on reslizumab was gathered through a PubMed search of the published literature, a detailed reading of the US Prescribing Information and interview with clinical trial participants.

3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?

a) Based on no experience using the drug:

For patients with severe (uncontrolled) asthma, the major marker of treatment success is for their asthma to be brought under control so that it no longer qualifies as “severe”. Depending on the patient’s particular clinical profile, this could involve improvements in lung capacity, reductions in the number of exacerbations (particularly those involving hospitalization), and less frequent and/or less severe airway symptoms overall. For patients with severe eosinophilic asthma, many of whom still have uncontrolled asthma in spite of using standard medications (and potentially OCS), the prospect of a targeted therapy that could address their specific disease in the same way that omalizumab does for allergic asthma is likely to be attractive and encouraging.

In the ASC’s survey, patients with Severe Asthma identified their top unmet needs in asthma care generally; these are not specific to reslizumab 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: (Severe Asthma: The Canadian Patient Journey)

- 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

b) Based on patients’ experiences with the new drug as part of a clinical trial or through a manufacturer’s compassionate supply:

While there were no clinical trials for reslizumab in Canada, the ASC contacted 15 trial participants, through Clinical Score LLC, located in the United States of America. Two participants elected to provide feedback for the purpose of this submission.

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. Reslizumab was successful in reducing asthma symptoms including shortness of breath, wheezing, coughing, sore throat and tiredness.

While participants indicated some concern at having to have the medication delivered by infusion at the Doctor’s office, there was positive response to only needing to receive a dose monthly.

Patient quotes:

“From experience, I expect, except for one day out of each month, that I will forget I have asthma.”

“Asthma does take its toll, and it is more than just a physical burden to carry... I expect that burden to be lifted forever with [this treatment].”

Section 4 — Additional Information

References

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9. Bel EH, Wenzel SE, Thompson PJ, et al. N Engl J Med. 2014 Sep 25;371(13):1189-97. Epub 2014 Sep 8.
10. Bardin P, Murphy K, Garin M. Effect of Reslizumab treatment on rescue systemic corticosteroid use in patients with asthma and elevated blood eosinophils: results from a pooled analysis of two phase 3, placebo-controlled trials. Poster session presented at: American Thoracic Society. International Congress; 2016 May 13-18; San Francisco, CA.

British Columbia Lung Groups

Section 1 — General Information

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| Name of the drug CADTH is reviewing and indication(s) of interest | TBC Reslizumab |
| Name of the patient group | British Columbia Lung Groups |
| Name of the primary contact for this submission: | [REDACTED] |
| Position or title with patient group | [REDACTED] |
| Email | [REDACTED] |
| Telephone number(s) | [REDACTED] |
| Name of author (if different) | |
| Patient group's contact information: Email | |
| Telephone | ablog@bc.lung.ca |
| Address | 604-731-5864/778.867.3676 |
| Website | 2675 Oak Street, Vancouver, BC V6H 2K2 |

1.1 Submitting Organization

The Mission of the British Columbia Lung Association (BCLA) is to improve lung health and to lead lung health initiatives. Our Vision is healthy lungs for everyone. Our role is to improve respiratory health and overall quality of life through programs, education, research, training, treatment, advocacy and prevention of lung disease.

The BCLA is a major Canadian charitable organization with more than a century of experience and leadership in lung disease prevention, treatment and management. Today its areas of interest and expertise include the entire scope of respiratory diseases including Asthma, COPD, lung cancer, sleep apnea, idiopathic pulmonary fibrosis, alpha 1 antytrysin and tuberculosis. We work together with the Canadian Lung Association and other partners to help the one in five Canadians who have breathing problems.

Our staff and volunteers include health professionals and interested individuals and patients with a broad range of training and experience in lung disease and lung health that enables our organization to develop and lead programs of education and health promotion at the highest standard. The BC Lung Association provides approximately \$1.2 million each year to internationally recognized physicians and scientist doing research in BC on lung diseases. All funding proposals go through a rigorous national peer review system so that the most promising research can be explored. This world class research is discovering the causes of lung disease, finding new treatments, and giving hope for a future free of lung disease

1.2 Conflict of Interest Declarations

- a) *We have the following declaration(s) of conflict of interest in respect of corporate members and joint working sponsorship, or funding arrangements:*

The BC Lung Association has multiple sources of funding for programs and operations and is supported by individual and corporate donations, and through service contracts with government organizations. Funding sources include: direct mail campaigns such as our Christmas Seals campaign, memorial giving, bequests, special events and service contracts with government organizations. From time to time we have received unrestricted educational grants from the following pharmaceutical companies: Astrazeneca, Boehringer Ingelheim, GlaxoSmithKline, Merck Frosst, Novartis & Pfizer. Our relations and interactions with pharmaceutical companies remain transparent, and policy positions of the BC Lung Association are developed without industry influence.

- b) *We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission:*

Neither the principal author, Kelly Ablog Marrant, nor the BC Lung Association, has any conflicts to declare in respect to the compiling of this submission with TEVA Canada Innovation.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

The British Columbia Lung Association is significantly invested and involved in both Asthma research and provision of patient services and programs. We have Certified Educators on staff who provide expert consultations to respiratory patients, their family members and caregivers dealing with Asthma and other with lung disease.

2.2 Impact of Condition on Patients

The symptoms experienced by all were shortness of breath, chronic cough (a dry cough) wheezing, shortness of breath or tightness on the chest and fatigue as a result of severe Asthma, Other symptoms include depression and frustration because they are no longer able to be active and do the things they were once able to do. Depression plays a factor when you are restricted from doing things. It adds to the negativity.

Patients who report negative experiences with the diagnostic process are much more likely to experience a negative mindset with respect to Asthma

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

2.3 Patients' Experiences With Current Therapy

Some of their medication works for them but there are some that does not work so they are very grateful when a new medication is available for them to try to relieve their symptoms.

UNMET NEEDS:

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. New treatments are urgently needed that will work to improve overall lung function. New treatment options are required as the disease progresses such as the medication mentioned .TBC (Reslizumab) a medication for severe eosinophilic asthma, this medication is for patients who have a history of severe attacks or exacerbations, it controls asthma related symptoms and improve pulmonary symptoms in patients with eosinophilic asthma despite receiving their current medication.

2.4 Impact on Caregivers

Patients identify a need for balanced information starting at the point of diagnosis, which also impacts caregivers.

A major area of impact identified by patients with Asthma with obvious effects on parents & caregivers is physical activity. The impact is most noticeable on patients' progressive inability to perform day to day tasks as they begin to notice that they struggle to cope with tasks that they had previously taken for granted (e.g. negotiating a staircase that they climb daily or plain walking on the street or walking around the house) due to frequent asthma attacks & exacerbations.

The first aspect of life where patients start to make adjustments/compromises are in leisure activities, daily activities of living and absence in school attendance for children. Typically there is an emotional cost to patients, parents and caregivers, as even the most optimistic people begin to come to terms with the progressive nature of the condition. At worst the impact on mobility due to breathlessness & wheezing can lead to isolation and depression, which is self-reinforcing. As the patient's condition deteriorates, they tend to stay at home more which means that their fitness levels further deteriorate and their body's ability to use oxygen efficiently is further compromised. As the condition progresses, further compromises are made in the patient's independence, with huge implications for caregivers. If the patient is working or has an active social life, this will start to be affected along with an impact on their family life.

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

The British Columbia Lung Association is significantly invested and involved in both Asthma research and provision of patient services and programs. We have Certified Educators on staff who provide expert consultations to respiratory patients, to children, their family members and caregivers dealing with Asthma and other with lung disease. The vast knowledge and experience garnered through research, best practice guidelines and direct involvement with patients is the basis of the information provided in Section 3. Additional information is taken from several support group meetings we currently have with our lung patients with Asthma in the Province of BC

3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had to Date With the New Drug?

a) *Based on no experience using the drug:*

UNMET NEEDS:

This would be a new medication to try as often times the other medication they are on does not work for them. When it is effective it improves their quality of life.

The individuals interviewed with Asthma understand that 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 for their symptoms. One statement from a patient said "it gives them the chance to work again" & less admission to hospital. 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"

Section 4 — Additional Information

Please provide any additional information that would be helpful to CADTH, CDEC, and participating drug plans. This could include suggestions for improving the patient input process, indicating whether the questions are clear, etc.