

CADTH COMMON DRUG REVIEW

Patient Input

Fluticasone propionate

(Mfr.) Teva Canada Innovation

Indication: Indicated for the maintenance treatment of asthma as prophylactic therapy in patients 12 years of age and older. It is also indicated for patients requiring oral corticosteroid therapy for asthma.

CADTH received patient input for this review from:

Asthma Canada

The Lung Association – Ontario

April 6, 2018

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1. About Your Patient Group

Asthma Canada is the only national, volunteer-driven charity, solely devoted to enhancing the quality of life for people living with asthma and respiratory allergies. Asthma Canada (formerly the Asthma Society of Canada) has a 44-year reputation of providing health education programs and services to Canadians living with asthma and their caregivers, as well as healthcare professionals. Asthma Canada offers evidence based and age-appropriate asthma and allergy education, and disease management programs. Our vision is to empower every child and adult with asthma in Canada to live an active and symptom-free life. Our mission is to be a balanced voice for asthma in Canada, advancing optimal self-management, prevention, research, and health care.

Asthma Canada established the Asthma Canada Member Alliance – ACMA (formerly the National Asthma Patient Alliance), a grassroots patient/caregiver volunteer group of the organization with an outreach to more than 5,000 Canadians affected by asthma and respiratory allergies. The patient voice and face of Asthma Canada – ACMA leads asthma advocacy and education efforts across Canada. Asthma Canada, with the help of ACMA volunteers, aims to provide the patient perspective in asthma research, resources, and policy and strives to improve asthma care and quality of life for Canadians and their caregivers impacted by asthma and respiratory allergies.

For more information, visit www.asthma.ca.

2. Information Gathering

Information for this submission was obtained through multiple sources, one of which was a requested medical briefing provided by Teva Canada Innovation. Information about patient and caregiver experience was obtained through an Asthma Canada online survey with respect to the use of medications such as inhaled corticosteroids and combination controllers, the daily management of this chronic condition, and the impact that asthma has on quality of life. The survey was sent to ACMA members across Canada in July 2017 and 88 responses were received. A total of 85% of survey respondents had received a diagnosis of asthma and 13% identified themselves as caregivers of an individual who had been diagnosed with asthma.

Numerous studies published in peer-reviewed journals were also sourced for the purposes of this submission. In addition, information was drawn from the study conducted by the Asthma Society of Canada in 2014, entitled “Severe Asthma: The Canadian Patient Journey”.

3. Disease Experience

Asthma is the third most common chronic condition in Canada. Patients with persistent, moderate-to-Severe Asthma face greater difficulty in getting their asthma under control compared to patients with a more mild version of the disease. Statistics Canada and the Public Health Agency of Canada estimate about 3 million Canadians live with some degree of asthma, including 600,000 children. The Global Initiative for Asthma (GINA) guidelines state that asthma can be deemed “uncontrolled” if patients experience at least three of the following four symptoms during the past four weeks: daytime asthma symptoms more than twice a week; any night waking due to asthma; reliever medication needed more than twice a week (excluding taken before exercise); and any activity limitation due to asthma. It is estimated that 250,000 Canadians have Severe Asthma and, it is this population that will typically need to use a greater number of medications and a higher dosage of medications to achieve control of their disease. Patients with Severe Asthma are also more likely to need additional medical care and visit hospital emergency rooms more frequently because of exacerbations. In 2015, asthma attacks led to more than

70,000 visits to emergency rooms in Canada. For those who treat, care and live with asthma, the goal is to ensure that asthma is well controlled and that patients are able to live a symptom-free life.

Persistent moderate-to-Severe Asthma is a chronic condition that restricts engagement in social and physical activities, and progression of the disease leads to a deterioration in overall health. People living with asthma will often remark that the condition forces them to withdraw from participating in social activities on a regular basis because flare ups arise unpredictably. Staying active on a regular basis is a challenge because physical exercise exacerbates their asthma. Depression and anxiety can develop in patients with uncontrolled asthma because of the decline in quality of life they experience. Indeed, asthma has an adverse global impact on a patient. It first takes a physical toll, and is often followed by a social and financial toll. Patients will often say they want their old life and that the condition has put a strain and burden on their family, personal, and work life.

More than three-quarters (76% or 51 of 67) of survey participants who responded to the question of how asthma affects their day-to-day life reported that they restrict the type or amount of physical activity they engage in because of their asthma. Nearly three of 10 respondents (27% or 18 of 67) who answered that question cite lost productivity – either missing school or work – as a way in which asthma has impacted their daily life. A total of 13% of respondents said that it has an impact on family or caregivers. A total of 12% of individuals surveyed (8 of 67) reported experiencing negative stigma. Respondents provided additional various responses when asked how asthma affects their day-to-day life including experiencing anxiety and “avoidance of situations which will negatively impact my asthma” and not being able to be near individuals who are smoking or wearing perfume while at work for fear of an exacerbation.

Survey participants were asked if there are activities they are unable to engage in because of their asthma. Physical activities, such as exercising and spending time outdoors, was cited by 50 of 63 respondents (79%), and social activities, including engaging in group outings or participating in organizations or meetings was cited by 20 of 63 respondents (32%). Three out of 10 respondents to that question (19 of 63 or 30%) said asthma interfered with their sleep. A total of 16 of 63 (25%) cited other activities in which they could not participate because of asthma. Some of those activities included being around people who smoke, visiting with friends or family who have pets, and scuba diving.

“I stay away from being outside. I stay away from crowds.”

“There are a great deal of things I cannot do for any length of time. The one thing I miss the most is dancing.”

“Wow, where do I begin, sick day from work, lead to loss finances, plus strains employer-employee relations, flare up usually result in increased medication usage, hospitalization, etc effecting your family, work life and social life (assuming you had any to begin with).”

When asked what aspect of asthma is the most important to control, 59% of respondents (40 of 68) said day-to-day symptoms were the most important to control. Asthma exacerbations (asthma attacks) were cited by 32% of respondents (22 of 68) as the aspect of the illness that is the most important to control followed by the amount of medications needed (cited by 7%).

4. Experiences with Currently Available Treatments

The most common currently available treatments that feature most prominently in treatment regimens, cited by respondents, were monotherapies and combination therapies. Nearly three-quarters of individuals who reported their specific medication usage (50 of 67) indicated the use of reliever medications. A total of 46 of 67 respondents (69%) reported usage of combination therapies, consisting of inhaled corticosteroids and long-acting beta-2 agonists (ICS/LABA). A total of 37% or 25 of 67 respondents reported use of inhaled corticosteroids (ICS). One quarter or respondents (25% or 17 of 67) said they use leukotriene receptor antagonists. Systemic corticosteroids were used by 16% or 11 of 67 respondents. Two respondents (3%) cited the use of long-acting beta-2 agonists. Some respondents reported using biologic therapies: four or 6% of respondents said they use anti-IgE biologics and one (1%) respondent indicated using an anti-il-5 biologic.

When asked how effective current treatments are with controlling asthma, a total of 25% (17 of 67) 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 most common adverse event, with 21 of 55 respondents (38%) reporting, was an increase in weight due to medication. This was found to be more difficult to accept than other side effects. A third of respondents (18 of 55 or 33%) said an increase in heart rate was the most bothersome side effect. Closely behind was dry throat (17 of 55 or 31%). Equal numbers of patients (13 or 24%) complained of hoarseness and difficulty sleeping and 10 of 55 (18%) indicated thrush and headaches were the most difficult side effects. Mood or behaviour changes were cited by eight (15%) respondents as negative adverse events. Other side effects that patients complained of included bad taste (13% or 7 respondents), upset stomach (9% or five respondents), and acne (4% or two respondents). Some respondents had very specific comments about the side effects they experienced while taking their therapies:

"Sometimes after use, I must lie down because the steroids make me so shaky I can't stand up."

Respondents were asked about concerns about the side effects of inhaled corticosteroids and combination therapies (inhaled corticosteroids and long acting beta agonists). Asked which adverse events were most bothersome and why, respondents supplied myriad answers. Below are some of the comments given by respondents:

"I really don't like the increased heart rate from my rescue inhaler. It's a terrible feeling and usually results in headache after, but I also know that taking it is lifesaving, so I try not to complain."

"The bone loss. Having been taking corticosteroids for 30 years – borderline for osteoporosis."

When asked about difficulties or obstacles in accessing current treatments, 19 of 52 respondents (37%) reported cost as the leading obstacle to accessing treatment. Lack of awareness of new treatments was the second most common obstacle (18 of 52 or 35%) cited as impeding access to treatment. Inability to find an asthma specialist was cited by four or 8% of respondents, and a doctor being unwilling to prescribe treatment was reported by two or 4% of respondents. A total of 23 or 44% of respondents reported "other" obstacles to accessing treatment. Here are some specific responses:

"Zenhale is not covered by OHIP or my work supplemental insurer. Symbicort is, but not available in Canada as an MDI inhaler and I have 'reflux laryngitis' and also experience sore throat/hoarseness with Symbicort turboinhaler use. My hiatal hernia was caused by severe coughing several years ago...feel like I am between a rock and a hard place. Also, have been on medication for cardiac arrhythmia and heavy use of my rescue inhalers causes bouts of tachycardia and even triggered a-fib."

As a general rule, financial challenges act as 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 if financial difficulties were experienced as a result of asthma, more than one in six respondents (16 of 59 or 17%) reported experiencing such difficulties. Here are some of the responses:

"Loss of work due to asthma attacks, illness or having to travel for my medical appointments results in loss of income."

"Yes, even with coverage I still have to pay out of pocket about \$80-\$100 per month. If I didn't have my

husband's benefits, it would be around \$500."

"Sometimes as I have limited budget but by being careful, am able to get by."

5. Improved Outcomes

Treatment success for patients with asthma ideally means being brought under control so they can live life to the fullest every day 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. Survey participants were asked if there were needs that were not being met by their current treatments. Seventeen of 45 (38%) said the reality that many doses were needed daily made it difficult to manage their asthma on a day-to-day basis, making it a time-consuming burden that can interfere with day-to-day activities. Fourteen of 45 (31%) respondents indicated optimal symptom control was not being achieved with their current therapies, describing their symptom control as "poor". The lack of affordability of current treatment, which can result in limited access to available medications, was cited by 8 (18%) of respondents as failing to permit effective self-management of their asthma. Six respondents (13%) indicated current treatments were resulting in frequent hospitalization/doctor visits, making asthma a condition that interfered with daily life for patients and caregivers. Fourteen respondents (31%) gave specific responses, some of which can be found below:

"Meds are for control, not cure."

Patients supplied numerous responses when asked what they would look for in a new controller inhaler.

"I think inhalers could be made easier to use. It was hard for me as a child to learn, and I see adults who are newly diagnosed struggling to use them properly. It would also be great if there was less hoarseness and dry throat after using the inhaler. I feel self-conscious when my voice changes after using an inhaler."

"My son is only 6. He uses the spacer with the mask for Flovent and Ventolin. He breaks out in a terrible rash around his mouth and gets made fun at school but because he has to take it daily it never goes away! I really wish there was another way! He also doesn't like to sit still to take 20 breaths which is what it takes for both doses!"

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. A total of 59 respondents answered with respect to the challenges caregivers face in caring for people with asthma. Two-thirds (68%) of respondents reported worry and fear of exacerbation/attack in their loved ones. About half of respondents (49%) said the potential for hospital visits/admissions were substantial concerns. Four out of every ten who responded (41%) said missed work/school was a considerable challenge. Cost and financial difficulty/burden was cited by 22 respondents (37%). Eleven respondents (19%) cited specific challenges that caregivers face. Some of their responses appear here:

"Missed personal time, missed fun activities."

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 impact that asthma treatments have on the daily routine or lifestyle of caregivers. Thirty-one of 50 respondents (62%) said managing multiple medications or multiple doses has an impact on the caregivers' daily routine or lifestyle. Twenty-three of 50 (46%) said they are impacted by asthma treatments because the treatments affect the frequency of doctor's appointments, and as a result, impact the daily routine or lifestyle of caregivers. Twenty-two (44%) said asthma treatments have an impact on caregivers' sleep. Eleven respondents (22%) cited other specific impacts that asthma treatments had on caregivers' lifestyle including stress and worry. These are some of the responses:

"It is all up to me."

Being a caregiver for a patient with asthma can impact many aspects of family, social and work life and be an added stress financially. A huge effect of asthma on caregivers is the worry and fear they face that their loved on will suffer an exacerbation of an asthma attack. A total of 38 of 88 respondents described how being a caregiver impacts these aspects, here are some descriptions:

"I finished my child and youth care worker course last August. My son started kindergarten in September, and he missed over 53 days of school this year. I still haven't been able to go back to work. I owe students loans and can't pay them. We barely get from one month to the other with child support and help from family. I make too much to qualify for assistance but not enough to live."

"It has had a significant impact on our daily lives, especially at the beginning, before symptoms were controlled. At the time, there were frequent, long term hospitalizations, impacting family life, work etc. Today, symptoms are controlled, with infrequent flares that generally don't require hospitalization or too much time missed from school and activities."

6. Experience with Drug Under Review

Inhaled corticosteroids are a mainstay of asthma treatment aimed at achieving control through daily use. Improper use of controller inhalers can lead to sub-optimal outcomes as can the need to coordinate inhalation with actuation. Survey participants were asked for their impressions about the availability of a controller inhaler that follows a simple, three-step process that administers a consistent low dose, and includes active metering, such as fluticasone propionate. A total of 58 of 76 respondents (76%) said the availability of such a controller inhaler would improve the lives for people with asthma. Additionally, 70% said they would be more likely to take their medication regularly if it followed these parameters. Asked if respondents would be willing to experience adverse events from a new controller inhaler, one out of five (15 or 20%) said they would and 34 (45%) said they were unsure.

Patients supplied a variety of answers when asked how satisfied they were with their current medication and what they would look for in a new combination inhaler. Below are some of the responses that were given:

"I would look for better control."

"Always looking for something easier, especially if it is better."

"Not satisfied. I want better symptom control and ease of use."

"I would look for one that doesn't need mouth rinsing after use. This is inconvenient during the day when I have to take it and rinse my mouth and use the restroom."

"...I think inhalers could be made easier to use. It was hard for me as a child to learn (to use them) and I see adults who are newly diagnosed struggling to use them properly. It would also be great if there was less hoarseness and dry throat after using the inhaler. I feel self-conscious when my voice changes after using an inhaler."

"I am satisfied with my current medication because that's all I can get. If I had a med that would last longer than twice a day, maybe once a day med, I would be happier. I wish I could do something more physical like walking, vacuuming, swimming, dancing more than just 5 minutes. I want to be able to do something physical without running out of breath so quickly."

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.

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 Teva Canada Innovation with regard to RespiClick – fluticasone propionate / salmeterol xinafoate.

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
Pfizer			X	
Roche	X			
Sanofi			X	
Teva				X
Boehringer Ingelheim	X			
Parsons	X			
Trudell		X		
Innovative Medicines Canada		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: Jenna Reynolds

Position: Director, Programs and Services

Patient Group: Asthma Canada

Date: October 17, 2017

1. About Your Patient Group

The Lung Association - Ontario 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.

www.lungontario.ca

2. Information Gathering

The information provided in this submission was obtained from two phone interviews (completed in October 2017), five on-line surveys (completed in 2016), as well as input from a certified respiratory educator. All of these individuals are people living in Ontario, Canada, and all are living with Asthma.

The first phone interview was with a woman, in her 50's, who has a diagnosis of chronic severe asthma with mild COPD. She has been living with the disease for 22 years. The second phone interview was also with a woman, in her 30's, who has been living with asthma for ten years. Both indicated that their asthma symptoms have been particularly bad this calendar year.

3. Disease Experience

The symptoms and challenges that people experience as a result of Asthma are coughing (with or without mucus), wheezing, shortness of breath, difficulty fighting infections and weight loss. When asked whether this condition affected their day-to-day life, respondents indicated that it did indeed impact both their physical and leisure activities, as well as their work, ability to travel and socialize. One person had a recent (Jan. 2017) ten day hospital stay for her asthma and since then has only been able to re-gain 50 – 60% of her lung capacity. Another respondent indicated that their asthma impacted their independence, financial situation, and relationships with family and friends. A few direct quotes are:

- “Asthma affects all aspects of my day-to-day life. I can no longer curl or cross country ski, both of which I miss doing very much, as it provided me with a social network.”
- “My asthma has been poorly managed since Feb. 2016, which has had all sorts of impacts. For me the biggest problem has been exercise – I usually do quite a lot and I've had to scale way back. I can't run much, which I'm normally good at, and weights feel much heavier and harder to lift.”
- “I cough a lot and have a lot of congestion, both of which cause me to be short of breath most of the time.”
- “If I get any kind of respiratory infection it tends to become very severe (my cough scares people) and takes about a month to go away.”
- “My asthma can cause some pain and tightness in my chest.”

The aspects of the condition that are most important to control for people living with it are first - shortness of breath and second – coughing. They would also like better control with wheezing and fatigue, to better manage their weight loss and have 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, Alvesco with salbutamol, Xolair injections, Spiriva, and Breo Ellipta. Prednisone was used in emergency situations and Nasonex / other antihistamines 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 drugs include: hoarse voice, 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.

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.

“The turboinhaler mechanism didn’t bother me until I had to start taking more of it. Now that I’m 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.”

6. Experience with Drug Under Review

No patients within this evidence group submission have used the drug fluticasone propionate.

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.

- 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
- 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
- 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
Boehringer Ingelheim				x
Innovative Medicines Canada	x			
GSK				x
Novartis				x
Pfizer				x
Sanofi Pasteur				x
Merck Canada				x
Roche Canada			x	
Teva Canada			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: Vice President, Marketing, Development and Public Affairs
 Patient Group: The Lung Association - Ontario
 Date: October 24, 2017