Common Drug Review
Patient Group Input Submissions

Ivacaftor + lumacaftor (Orkambi) Cystic Fibrosis, F508del CFTR mutation

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

CADTH received patient group input for this review on or before December 18, 2015

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.

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Cystic Fibrosis Canada

Section 1 – General Information

Name of the drug CADTH is reviewing and indication(s) of interest		Orkambi (ivacaftor + lumacaftor) / Cystic Fibrosis (F508del homozygous > 12yrs)
Name of the patient group		Cystic Fibrosis Canada
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Permission is granted to post this submission		Yes

1.1 Submitting Organization

Cystic Fibrosis Canada (CF Canada) is a charitable non-profit corporation with a mission to help people with cystic fibrosis (CF). CF Canada funds research towards the goal of a cure or control for CF, supports high quality CF care, and promotes public awareness of CF. Since its establishment, CF Canada has invested more than $226 million in leading research, innovation and care.

1.2 Conflict of Interest Declarations

For the 2015/16 financial year, CF Canada received financial contributions from Mylan, Gilead, Hoffman-La Roche, Merck, Insmed, Vertex and Rx&D. Contributions from pharmaceutical companies accounted for less than 2 percent of the organization's gross revenue in 2015/16. No one compiling this submission has a conflict of interest.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

CF Canada reached out to CF patients and their families with the assistance of CF clinics and through the use of social media. CF Canada's national patient data registry was also a credible, reliable and authoritative source of information.

2.2 Impact of Condition on Patients

CF is the most common fatal genetic disorder in Canada. It is estimated that one in every 3,600 children born in Canada has CF. There are currently over 4,000 people with CF in Canada. The disease affects all exocrine glands of the body and results in the production of thick, sticky mucus amongst other clinical symptoms. The principal clinical impacts are on the lungs and digestive systems. Eighty-five percent of

Canadian CF patients lack pancreatic enzymes and have difficulty digesting fats and proteins. Fat and nutrient absorption are also impacted and patients struggle to maintain a healthy weight and are typically deficient in vitamins. The most significant clinical impact however is in the lungs, where patients have difficulty in clearing secretions from the lungs, which in combination with aberrant inflammation leads to persistent infections with cycles of inflammation that are ineffective in clearing infections and lead to progressive scarring of the airways and a decline in lung function. This eventually leads to respiratory failure which is the main cause of death in CF. Of the 40 CF patients who died in 2013, half were under 35 years old. There is no cure. A demanding treatment routine combined with regular visits to specialized CF clinics, acute infections and episodic flare-ups called exacerbations that lead to frequent hospitalizations have a significant impact on day-to-day quality of life affecting life decisions including education, career, travel, relationships, and family planning.

Adults living with CF have shared how the disease impacts them:
"For the last 10 years I have been short of breath from simply walking upstairs. Recently I have been needing oxygen and have not been able to keep up with normal daily activities." Female CF patient, 47 years old

"When you have a life-threatening illness, you can let fear overtake your life or you overcome fear and fight back with every bone in your body. The hospital stays, the hours of treatments and everything else that goes along with managing cystic fibrosis can take a toll on your emotional stamina." – Male CF patient, 27 years old

"I have experienced many health crises related to cystic fibrosis leaving me with no other option but to consider a double-lung transplant. In 2011 my lung function reached an all-time low sitting at 26 percent and my family and I were faced with the difficult reality of having to make a decision. At this point I was so exhausted I couldn't even perform basic tasks." – Female CF patient, 27 years old

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"My biggest challenge with cystic fibrosis has been the insecurity of what the disease holds for my future." – Female CF patient, 42 years old

"I lost three friends in three months, while they waited for a lung transplant. It's not right to bury your friends all under the age of 25. I've been to more funerals than weddings in my life." - Female CF patient, 23 years old

"I struggled to keep up with work and uni, and had to spend up to 2 hours a day on exhausting, never ending, treatments. For 20 years I had about 3 hospital admissions a year. This meant I had over 60 hospital admissions, equaling more than 3 years of my life in hospital." - Female CF patient, 29 years old
"Growing up, I spent a lot of my life trying to show everyone that I was tough and that I could handle CF because I didn't want their worry or their pity. I have to live my life knowing that it's most likely going to be shorter than my parents' lives. Shorter than my younger brother's life. No one should have to live like that. Now that I'm an adult living with CF, the realities of the disease are catching up to me. My health is worse than it's ever been before. Not having enough breath to do the things I want to do on a daily basis is incredibly frustrating. I want to have enough breath to run up the stairs. To hike down to the dock and

go fishing with my dad. To clean the house. CF is slowly stealing my life from me. I have dreams. I want to get married and not break my husband's heart when the CF stops mine." Female CF patient, 22 years old.

2.3 Patients' Experiences With Current Therapy

Most CF patients take pancreatic enzymes, multi-vitamins and nutritional supplements to maintain normal growth. CF patients work tirelessly every day to improve the clearance of secretions from their lungs. This is done by performing airway clearance techniques at least twice a day for about 30-45 minutes per session. Inhaled medications are used to open the airways while inhaled antibiotic treatments are used to control infections. The total time spent on maintaining lung health is well over two hours each day. Patients frequently have periods of infection and acute inflammation called exacerbations that require a hospital stay of at least two weeks. Eventually the ongoing cycles of infection and inflammation destroy the lungs. Lung transplantation may help people with end-stage cystic fibrosis regain health; however following a transplant, the extended median life expectancy is only 34 months.

People have shared how they live with current therapy regimens:

"Her day starts with a ventolin puffer, 25 minutes of physiotherapy and then a mask that lasts for 30minutes. Throughout the day she must have her enzymes to digest when she consumes food. At 4:30 p.m. she does breathing exercises that lasts 30 minutes to relieve sputum from her chest and once again follows the same procedure that she dealt with in the morning which lasts 55 minutes. During the evening hours we will hook her up to a feeding machine that goes through the night. Once we wake up this procedure starts over. At least 1-2 times a year [she] gets pseudomonas and requires two additional masks (that take 35 minutes) into this already hectic schedule" Father of a 7 year old CF patient

"I notice a lack of lung capacity as I age. My older sister died of CF 5 years ago at the age of 36. She left behind a loving husband and young children. I saw through her life that good care won't stop the progression of the disease." – Female CF patient, 31 years old.

"A typical day at home: 6:00-7:30 AM: intravenous (IV) antibiotics (2x40 mins). They connect with my picc-line. It's rather tedious because of the many steps of the procedure: disinfect, flush with saline, connect the antibiotic, wait 40 minutes, flush with saline again, connect the next antibiotic, wait 40 minutes... etc. Very often, my Mum, Dad or sister will do this for me while I sleep in, so I can catch a bit more sleep. 8:00-9:00 AM: wake-up routine; asthma meds, inhaled antibiotics and enzymes, pep-mask physiotherapy, wash all the nebulizers, prep any meds that need to be reconstituted.
9:00-10:00 AM: breakfast; meal routine: check blood sugar, take insulin, have breakfast, morning pills (the usuals + check calendar for the ones on a variable schedule), scandishake, after-breakfast meds, if any (check calendar). 1:00-2:00 PM: lunch; repeat meal routine; 2:00-4:00 PM: IV antibiotics (3x40 mins), (concurrent) 3:00-3:10 PM: inhaled antibiotics. 4:00-5:00 PM: exercise. 6:00-7:00 PM: supper; repeat meal routine. 8:00-9:00 PM: clapping physiotherapy. 9:00-9:30 PM: bedtime routine; asthma meds, inhaled antibiotic, bedtime meds (check calendar). 10:00-11:30 PM: IV medications (2x40 mins) Fairly often, my Mum, Dad or sister will do this one for me too so I can go to bed a bit earlier.
Juggling the timing of everything is a bit of a headache, mostly because I need to space out eating with physiotherapy (doing physio or exercise tends to give me coughing fits, which makes me throw up if I've eaten too recently). On most days I've also got a limited amount of energy, so I've got to manage my activities to make sure I don't crash before the end of the day. Other regular tasks include: keeping medical appointments (1/week or more); preparing pills in advance (it saves time at meals); speaking

with my pharmacist 2-3 x a week to order meds, arrange delivery...and…staying on top of insurance reimbursements (3-4 hours / month or so)." Female CF Patient, 27 yrs old.

"My daughter gets up at 5 to take all of her medication which starts with her Creon to eat breakfast then anti-biotic then Ventolin mask then the vest for 20 minutes then Advair puffer then a Tobi mask and vitamins. When she is done all this then she is ready to start preparing to get ready for school. When she is done school which is around 3:30 she has about 1 hour to herself if she doesn't have homework so she starts same routine as morning. By the time she is done this she is almost ready for bed because she gets up so early just so she can attend school and have some time with her friends. Children living with CF don't really ever live like other kids." Mother of a 16 yr old daughter with CF

FACT: In 2013, CF patients spent a cumulative total of almost 25,000 days in hospital, attended over 16,500 clinic visits, and underwent 676 courses of home IV therapy. (2013 Canadian CF Registry Annual Report)

2.4 Impact on Caregivers

Whether as a parent, spouse, grandparent, child, sibling or friend, being a caregiver for a CF patient can have significant emotional, psychological, physical and financial impacts. Caregivers have shared their stories on how the disease has impacted them and their families:

"It is devastating to have two children with a life threatening disease. It is difficult to imagine and breaks my heart to think of when my children fully grasp the information about cystic fibrosis in the way we do. They are used to the treatments from young ages, but the disease still affects their ability to have a normal childhood – shortened time with friends, early mornings to fit in treatment before school and even with daily therapy to manage the disease we still have hospitalizations which are very disruptive to the whole family. When one of them is hospitalized we have to find childcare for our other children, my husband has to take time off work, and we have to put everyone's life on hold."

"When two of my children were first diagnosed, the doctor told me I'd never go back to work again. It is a full-time job keeping my children healthy. From helping with their physio to clear mucus, frequent CF clinic visits, hospital stays, and on top of that ensuring our third child does not feel left out as a healthy child." - Mother of an 8-year-old girl and a 3-year-old boy with CF

"My 11 year old daughter spends in excess of 26 hours a week trying to stay healthy. The fight against CF is all encompassing for the family. It requires giving up 2 to 7 hours every day for her therapies. The physical therapies take a toll on my and my wife's bodies. We both have repetitive strain injuries and arthritis in our hands, wrists and shoulder. This commitment requires scheduling all meals and everyone's activities around her therapies. We restrict our social activities to prevent passing on colds and flus. Each day that a control for cystic fibrosis is not available to her is a day that her lungs are deteriorating. All the treatments that she has access to only try to mitigate her existing health problems, none address the root cause. Without the availability of drugs that fix the basic defect in cystic fibrosis, our daughter and others like her will lose their valiant fight as they pass away while gasping for air." – Father of a 13 year old CF patient.

"On April 1st, 2011 my son and daughter were both diagnosed with Cystic Fibrosis. It remains the most devastating news I have ever received. My 9 yr old son has already spend in total over 6 months of his life in the hospital. Each time he is away from school, his friends, his extra-curricular activities, his bed, his family. He is stuck in a hospital room attached to cords and tubes. He's not allowed to leave his room

due to infection control. It's complete isolation. Being away from home for 2 weeks at a time affects the whole family. My daughter has developed separation anxiety." Parent of two CF children.

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

See 2.1.

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

A number of people living with CF and their family have described their expectations of how Orkambi can help improve their health and quality of life. Based on their understanding of this drug, they expect improved lung function, weight gain and in many cases, avoiding the need for lung transplantation. Those who have been on Orkambi, either through clinical trials or private insurance, have reported improvements in lung function and weight gain. The improvements in health have also led to better quality of life and ability to function normally.

a) Based on no experience using the drug:

"Among my many other roles, I am a wife, a mother, and a healthcare professional. I am also a woman living and sometimes struggling with cystic fibrosis. Gaining access to Orkambi gives me hope that I will have the opportunity to grow old with my husband, watch my children mature into adults, and choose when I am ready to retire because I have had a full and satisfying career, and not because my illness demanded it." Female CF patient, mid-thirties

"I work in cystic fibrosis and so am exposed to different stories. I am also the parent of a daughter with CF. In August 2013 two young women were preparing to participate in the Orkambi trial. My daughter, who was 27 at the time, and a 12yr old. My daughter's lung capacity (as measured by FEV1) was ~43% of normal, the 12yr old's was ~ 85%, similar to what my daughter's was at that age. My daughter was an excellent patient, highly adherent to therapy and very physically active. She did aerobic activities to stay healthy, biking, swing dancing and running. May 2013 we ran a 5km race together. Five days before starting the Orkambi trial she had a hemoptysis and was pulled from the trial. The 12yr old started on Orkambi. Six weeks later my daughter's doctor tried to get her back on the trial before it closed but her FEV1 had dropped to 39%, below the inclusion criteria of 40%. She was excluded. My daughter's health rapidly deteriorated, with hemoptyses at an increasing pace. By March she was on the lung transplant list near her home. By May we'd moved her to a larger transplant program to speed the process. In July 2014 the 12yr old's FEV1s had risen from 85 to 99%. In late July 2014 my daughter died from complications from too many hemoptyses before ever getting a transplant. This is the difference a drug like Orkambi can make. It's not for everyone but can be the difference between a 12yr old who can look forward to a long and productive life vs dying at 27yr in the prime of life in the middle of doing a PhD at a world-renowned university." Father of a CF patient.

"As I have delta F508 homozygous, Orkambi would be a great benefit to me. Having fewer exacerbation or infections and weight gain would certainly be an improvement and a reduction in lung bacteria would certainly make life much easier. I hope that this drug can become part of my treatment in the near future. Any improvement in my breathing would have a significant impact on my quality of life." Female CF Patient, 49 yrs old.

"I feel like I could benefit from this combination drug as this is my mutation and I have had several hospitalizations especially in the last 2 years. This has affected my life hugely as I have been unable to complete my education." Female CF Patient, 21 yrs old.

"Having a pill like ORKAMBI would make the simple things many people take for granted easier. I could have weeks without being sick due to mucus build up, instead of days. I would be able to stay off antibiotics longer, and decrease my risk of becoming resistant to even more antibiotics. Having a less amount of mucus, as well as thinner mucus will greatly improve my scattered lung functions. ORKAMBI could help patients from having to receive a lung transplant at an early age, as well as make life for younger patients less stressful as they get older." Female CF patient

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

"I started taking Orkambi about 2 years ago and since then I don't get sick as often and I feel much better. I can now keep up with everyone on the soccer field and during other sports and my lungs don't hurt anymore. I actually like going to the hospital for check ups now, because my pulmonary function test FEV1 results are always so good! As I high-school student, it's important that I stay healthy so that I don't miss too many classes." Female CF patient, 14 years old

"In March 2015 we were offered the opportunity to participate in a CF study. There was only one spot offered, so we chose our most "sickly" child, our son, to participate. This was not easy, especially when we had to explain to our daughter why we didn't choose her. We didn't know what to expect and anything better than his deteriorating health condition was a welcome change. I was astounded to find that 7 hours after his first Orkambi dose our son, that only coughed when he was sick, had a productive cough, he was clearing out the mucous in the lungs that the antibiotics couldn't remove! The drug has changed my son's life. He is no longer deteriorating, he is thriving! The chronic, four year rattle in his lower right lobe disappeared immediately and no doctor has heard it since. He no longer rolls on the floor in abdominal agony, the pain is gone. His PFTs have increased. He has put on more weight. He sleeps better and wakes up energized, not sluggish like before. People are even noticing more colour in his face, he looks like a healthy 9 year old boy, not like the sickly, pale looking boy that existed pre-Orkambi. This is our first winter on Orkambi and to date he has not had a single sinus infection and has not needed antibiotics. My daughter is not on Orkambi. She is still rolling on the ground while my son now looks on. They both need access to this drug in Canada. I am a first-hand witness of the immense benefits of Orkambi and I know it will save my children's lives. This is a first generation drug that delays the progression of CF much more effectively than what all the physio and antibiotics can do alone." Mother of a boy, 9 and a girl, 7 with CF.

"We have been so very fortunate to see first-hand how well the Orkambi medication works. Prior to enrolling as a Phase 3 trial study participant in August 2013, our daughter's lung function had reached a new low. Within a short period of time (weeks), she had re-gained much of her lung function (PFT results now in the mid-90's percentile), and was feeling considerably more 'normal'. We are confident that Orkambi has helped to slow down or stop any further lung degradation and our daughter continues to thrive as a young woman, with a very bright and healthy future." Father of a 14 yr old patient.

(translated from French) "One day, the doctors told me that I had to have a transplant. To me, this was very bad news. After two years on the transplant waiting list, I could not bring myself to believe that I was ready for this procedure. I got off the list and was accepted [into a clinical trial on Orkambi]. The very first month, I saw a big difference! My secretions were clearer. I started having more energy and

less fatigue, and this never stopped. Before, it was harder to get over a cold. With the medication, I feel as though my body is stronger! I have gotten over infections that were much more invasive in the past. My forced expired volume in one second (FEV1) is stable. I had to stop taking the medication for one week during a stay in the hospital, and my functions went down by 10% during this period. I cannot picture my life without this medication. It has had many positive effects on me. Indeed, it has increased my energy, boosted my immune system, improved my quality of life, stabilized my FEV1 and decreased the number of pulmonary exacerbations that I experience." Female Patient, 34 yrs old

Section 4 — Additional Information

In July 2015 Orkambi obtained approval from the FDA in the USA for use in people with two copies of the F508del mutation ages 12 and older. The European Commission approved Orkambi for the same population in the EU in November 2015.