Response to CADTH Draft Recommendations for Trikafta

Submitted by: CF Get Loud

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CF GET LOUD

SUMMARY

We appreciate that elexacaftor/tezacaftor/ivacaftor and ivacaftor (Trikafta) has been recommended for reimbursement for the treatment of patients 12 years and older who have at least one F508del mutation in the cystic fibrosis (CF) transmembrane conductance regulator (CFTR). However, we do not accept the conditions set out in the draft recommendation. We believe that these restrictions show a fundamental misunderstanding of the real scope of the disease and find them to be in conflict with several points raised in the Implementation Guidance of the Draft Recommendation: namely the many other clinical measures in addition to ppFEV1 such as BMI and reduction in the frequency of exacerbations.

In the Discussion Points, there is a clear acknowledgement that CF is complex and affects much more than the respiratory system: “CDEC concluded that ELX/TEZ/IVA potentially meets some very important unmet needs identified by patients”.
In addition to its effects on lung function, CF affects other organs and manifests in many other ways. The Draft Recommendation also noted the psychological challenges that CF creates for both the patients and families/caregiver. The conditions for initiation and renewal set out in the Draft Recommendation fall considerably short of such acknowledgements as they solely pertain to ppFEV1 with a complete disregard for the life-changing effects and quality of life improvements patients will benefit from.

It is our position that we should follow the physicians’ direction on the initiation, renewal and discontinuation of Trikafta. Canadian clinicians specialized in CF have developed the Canadian Clinical Consensus Guideline for Initiation, Monitoring and Discontinuation of CFTR Modulator Therapies for Patients with Cystic Fibrosis. They simply know best; and are the only ones in a position to be able to thoroughly make an individual assessment on each of their patients. They have studied this disease and have dedicated their careers to better understand everything about it.

We also appreciate that a reduction in price of at least 90% is required for Trikafta to be considered cost-effective at a $50,000 per QALY threshold. While we are aware of the role of the HTA process and its narrow focus, we fundamentally reject the $50,000 per QALY threshold set out by CADTH and similar HTA bodies as it poses problems that are much larger in scope. In the context of rare diseases, these processes do not properly weigh the benefits these life-saving medications can have on patients and reduce a human life year to a health economist analysis, fundamentally disregarding the value of a human life.
However, we are confident and believe that the pCPA and the manufacturer have already

established a successful framework for a mutually acceptable agreement based on their most recent negotiations of previous generation modulators.

FEEDBACK ON REIMBURSEMENT CONDITIONS

Initiation

Recommendation: ppFEV1 ≤ 90%

- **CF is not simply a lung disease.** It is a genetic disease that negatively affects multiple organs and systems including but not limited to the digestive system, sinuses and reproductive system. Creating initiation criteria exclusive to ppFEV1 will exclude patients that might not suffer primarily from lung disease but have other considerable challenges and significant loss in quality of life. It confirms our claim that CDEC does not fully understand the complex nature of cystic fibrosis.

- **Variability.** CF is a disease that greatly varies in severity from person to person. Many patients have 'normal' lung function but suffer from severe debilitating digestive issues including life-threatening bowel obstructions. Trikafta has significantly reduced digestive issues in CF patients. In fact, 1 in 5 babies are born with a life-threatening bowel obstruction in the small intestine called Meconium Ileus and have chronic bowel obstructions caused by thick, sticky mucus in the intestines.

- **CF can't wait.** Cystic fibrosis is a progressive disease. Most patients begin life with healthy lungs and pulmonary function levels of 120%. The current CADTH criteria require these patients to lose 30% of their lung function before they can benefit from a gene modulator that helps all aspects of the disease. CF is treated from the moment of diagnosis to try to minimize damage. Instead of patients staying as healthy as possible and using a preventative approach, they are being asked to allow CF to permanently scar their lungs and succumb to the devastation of structural changes to their lungs from the disease before being considered for Trikafta. Lung tissue is extremely delicate and often lost lung function cannot be recovered.

- **What about the children?** Limiting reimbursement to patients with less than 90% ppFEV1 will discriminate against children and teens. The FDA has already approved Trikafta for use in patients age 6 and over in the United States; we expect Health Canada to follow suit. We are concerned that the recommended initiation criteria will make it very difficult for children to start benefiting from Trikafta as soon as possible in order to prevent irreversible damage to their bodies (not just lungs).

- **Self harm.** We have already experienced first-hand that setting restrictive criteria for access such as this will result in patients self-harming as they weigh the benefits of being able to access a therapy. The only way Canadians have been able to access Trikafta over these past 18 months has been through the Compassionate Care program which had a threshold for consideration (<40%ppFEV1). We have heard and personally know instances where patients will weigh out the short term loss of lung function in order to benefit from the myriad of benefits Trikafta can bring about. No one should be forced into a position to invite a decline in lung function to access a life-saving medication.

- **Spirometry.** While pulmonary function tests are widely used as the most important measure of disease progression, they do not capture the whole picture and are not 100% effective at evaluating lung damage. Even in patients with a high FEV1, a CT scan will show extensive damage to the lower and smaller airways.

Renewal

Recommendation: Subsequent assessments for renewal of reimbursement should occur annually. Documented maintenance of ppFEV1 greater than 5% from baseline must be provided at each subsequent assessment for continued reimbursement.

- **CF does not happen in a vacuum.** CF Patients suffer from declining lung function for various reasons that are beyond the scope of treatment with a gene modulator. Unfortunately having CF does not preclude you from other natural or health events that can negatively affect your lung function such as aging, a cold, COVID, allergies, a collapsed lung due to impact, pregnancy, and other diseases. Trikafta cannot protect against external factors that will impact lung function. Not taking this into consideration is fundamentally flawed and resonates with a lack of understanding of the real-life experience of someone living with CF.

- **Permanent Damage.** Trikafta cannot change the permanent impact of the disease that will occur prior to its utilization. Adults with cystic fibrosis culture antibiotic-resistant bacteria that cause structural changes to their airways that cannot be reversed using a gene modulator. This is the impact of end-stage disease. Many CF patients experience a pneumothorax due to decades of damage creating delicate lung tissue, requiring chest tubes and thoracic surgery.

- **Trikafta is not a cure.** Although studies show Trikafta reduces lung infections by 60%, patients will still experience life-altering infections due to the aggressive nature of the disease that will deteriorate lung function.

- **Unnecessary stress.** Setting such narrow renewal criteria will have a considerable psychological impact on patients. Life with CF is already stressful enough and even a 1-2% decline in lung function can greatly affect the mental health of CF patients. To add insult to injury, they would now have to deal with the threat that they might lose access to a drug that has changed their lives for the better, on top of dealing with the inevitable disease progression.

- **Canadian Clinical Consensus Guidelines.** Canadian CF physicians have developed or endorsed the Canadian Clinical Consensus Guideline for Initiation, Monitoring and Discontinuation of CFTR Modulator Therapies for Patients with Cystic Fibrosis. As per those consensus guidelines, discontinuation should be limited to patients who have clinically significant adverse effects that persist or recur or patients who do not meet the criteria for response to the CFTR modulator as per the guidelines or are non-adherent.

Discontinuation

Recommendation: Patient has undergone transplantation.

- **CF is not just a lung disease.** A double lung transplant is a treatment for end-stage lung disease caused by cystic fibrosis but it is not a cure. CF patients that have received double lung transplants also suffer from digestive issues, CF related diabetes, low bone density, low BMI and sinus infections. In some cases, sinus infections can travel down to the new lungs and begin to negatively impact lung function. While we appreciate that

there is limited data on post-lung transplant patients, we stand by the fact that our doctors should be able to decide who will benefit from Trikafta.

- **Real World Evidence.** Transplant patients in the US have been benefiting from Trikafta since it was approved in October 2019. Their care teams have made the medical decision to prescribe Trikafta knowing full well the many benefits other than lung function.

OUR COMMUNITY'S VOICE

Each CF patient, their caregivers and their families are critical stakeholders in the evaluation for reimbursement. Their opinions and concerns regarding this matter are valuable and must be presented equitably. The CADTH open calls for input and feedback are not accessible to all stakeholders at this time as only feedback from patient groups can be submitted. All stakeholder experiences are unique and must be taken into consideration. As a grassroots patient group, we are responsible for helping elevate the voices in our community. We appreciate that having hundreds of submissions from patients and families is not ideal, we have the responsibility to make sure we communicate their worries and frustrations. Therefore, we have compiled testimonials from families across the country that are impacted by the draft recommendations.

Appendix: Comments from CF key stakeholders across Canada

Testimonials From CF Families:

Courtney Masters, CF patient, Ontario

"My lung function used to be over 90%, so I would not have qualified for Trikafta, given the new recommendations by CADTH. While my lung function was great, my GI issues were severe; so severe, I ended up sedentary for nearly two years, after which my PFT dropped by 40%. Five years later, I have only been able to gain 20% back. To disqualify someone based on lung function is so blatantly discriminatory, it is mind boggling to think this recommendation was actually made public."

Stephanie Stavros, CF Patient, Ontario

"Born in 1983 with meconium ileus, I have had severe digestive issue for 36 years. Prior to being prescribed Trikafta, I would have monthly bowel obstructions and frequent emergency hospital admissions. One bowel obstruction nearly took my life in 2015. My life was focused around pain management, special diets, feeding tubes and hospital admissions. Since starting Trikafta a 18 months ago, I no longer experience severe digestive issues. For the first time in my life, I digest fatty foods and I have a normal BMI. My liver levels and my bone density have improved due to proper digestion and I no longer need pain management."

Cheryl Ann Smith, CF Parent, Manitoba

"My son has decent lung function baseline 94% but horrible GI effects, extreme difficulty gaining weight and CF Related Diabetes. We have been dreaming of Trikafta hoping for some relief but am discouraged that his access may be contingent on his lung function declining. So if he falls below 90 and increases to above 90, will he lose access?"

Anonymous, CF mother, British Columbia

"My teenage son is already threatening to stop doing his treatments so that he will be able to qualify for Trikafta and it's breaking my heart.

Anonymous, CF Double Lung Transplant Patient, Ontario

"Since having my transplant, I have had multiple, painful sinus surgeries. During my last appointment, we discussed removing more bone in my face to ease the pressure. I asked my doctor about the possibility of Trikafta if it comes to Canada and he gushed about how he's seen all the proof of complete sinus improvement with it. So needless to say I have some renewed motivation to fight to change the restrictions around its use in Canada."

Sabrina Lamontagne, CF Patient, Québec

"Comment une organisation qui se vente d'émettre ses recommandations sur des preuves d'évidences peut conclure a des recommandations en ayant une compréhension aussi limitée de la maladie. La fibrose kystique ne se résume pas a un VEMS et le Trikafta n'est pas une cure. Même sous Trikafta nous avons malheureusement encore la Fibrose Kystique. Je suis très déçu de la lecture de ses recommandations. Ça sonne a mes oreilles comme un brouillon fait sur le coin d'une table. Dans ses conditions, je perdrai l'accès au Trikafta dans un avenir rapproché. Le Trikafta m'ayant permis d'éviter la greffe pulmonaire et un retour sur le marché du travail puisque ma santé s'était améliorée. La perte d'accès me sonne comme une condamnation a moyen terme :("

Lindsay Collicott, CF Patient, Ontario

"The draft recommendations are misguided and dangerous for CF patients. CF is a multi organ disease so only taking lung function into account for eligibility of trikafta is extremely problematic. Moreover, requiring a significant increase on trikafta or else risking being taken off it is extremely dangerous. Speaking from personal experience, I have been on trikafta, on compassionate care, for over a year. I have not seen an increase like others but have become overall more stable. I have gained weight, I have stayed off of antibiotics, and I've had no hospitalizations, where prior to being on trikafta, my weight and lung function had been gradually decreasing every year, I was on IV antibiotics twice in two years, and my quality of life was decreasing to the point where I had been evaluated for a lung transplant. Being on trikafta has allowed me to maintain lung function while also gaining back my quality of life and therefore my life expectancy. I beg you to reconsider these recommendations and involve CF patients, their doctors, and other CF experts in the review process. We are the ones who understand the intricacies of CF and know how it affects every CF patient differently."

Ilka Bond, CF Parent, Ontario

“My son has CF and he is suffering for 34 years. We've been waiting for medication like Trikafta for so long, living in fear every day. His lung function suddenly decline from 60% to 43% in the last 7months. He cultures antibiotic-resistant bacteria as do many CF patients, the lungs have scars, as well the heart and the liver have some damages too. With this antibiotic- resistant bacteria will be a miracle his lung function not to decline, never mind the 5% CADTH is requesting to be eligible for Trikafta. He was born with a bowel obstruction in the small intestine called Meconium Ileus. My son has severe GI issues, flashing the intestines periodically. He developed a CF related diabetes, it's extremely difficult to gain weight. He has heartburn daily. Patients on Trikafta are gaining weight, becoming healthier. What I don't understand is WHY CADTH is putting restrictions on life-saving medication Trikafta??? CF is not only a lung illness, CF is a multi-organ disease. It puzzles me Why CADTH is placing blanket restrictions on CF patients when we all know that each patient's disease is individually unique. Why some patients will be discriminated because of these restrictions? We know that Trikafta is making corrections not only in the lungs but other organs too. CADTH we are not numbers, we are human beings. Step-up and show that you are human beings too and have compassion and humanity. My opinion is that the final decision should be made by the CF clinics and doctors who are treating the patients.”

Lucy Mcneil, CF Parent, Ontario

“Cystic fibrosis is a disease that progresses & watching your child suffer everyday is heartbreaking , Trikafta is the closest cf treatment to finding a cure for our Canadian cfers they have literally been dying for this breakthrough,it's given them hope to look toward a quality of life instead of waiting on transplant lists.TheCADTH recommendations it's unacceptable to wait for ones health to become more sick we need our children to live some quality of life they fight to live and fight for our govt to hear us help us Canadian cfers we matter too. Fund our miracle drug we need this hope to be a reality a chance to seeing a future”

Marilyn Nieboer, CF Supporter, Ontario

“As a nurse health educator we teach it is better to prevent disease than to cure it. We treat high blood pressure to avoid a stroke or heart attack, we treat diabetes to avoid blindness and amputation and we treat cancer before it invades the body. We now have Trikafta and we can prevent the disease from doing damage. Less infections, less admissions, less bronchiectasis (scarring in lungs), less exacerbation, less digestive issues, less abnormal widening of the bronchial tubes, lessen the high risk of CF related diabetes or reverse insulin dependency, less

time connected to feeding tubes (7 hours every night), increase energy and weight gain, increase overall mental health, increase life expectancy. Someday in the future we will look back and think how could Canada be so slow to help those who suffer. The question today is how many young lives will die in the meanwhile. This IS life or death. I want my granddaughter to live a long happy life. She deserves this."

Julie Hanna, CF Parent, Ontario

"The CADTH recommendations are so infuriating. Are there prescribing criteria for diabetic requiring insulin? If the dr. says they require insulin, a prescription is all they need! Enough said! The CF patients deserve the same respect and consideration. With these limitations, it only leads to patients neglecting care or figuring out work arounds in order to get access. As we all know, CF affects the whole body and my understanding is the modulators are a cellular treatement that affects multiple organs as well. Why are we basing access on ONE test? A personal example of a major flaw in this, my son has been hovering in the 30-40 range for PFT for at least a year now. After a successful two weeks on IVs and A LOT of hard work on his part, he went into clinic on the last day of IVs and did another PFT. To everyone's shock, he blew a 57. He wasn't overly excited knowing full well that was the IV mask and that in two weeks, he'd be full again and it would plummet. So, if he gains provincial access, is this the number the take and base all future success of the modulator? This is a scary position to be in. Rather than be happy he hit that number I am scared for him due to these ridiculous CADTH recommendations. Hasn't our community fought enough? Haven't we had enough stress and anxiety? Must we claw our way...every step of the way...to take care of our loved one? Isn't CANADA the country with exceptional health care that puts Canadian well-being as a priority? I'm not seeing this. We can and MUST do better! My son, with the hope of a Trikafta future, was out home shopping last night! He's been saving every penny of his adult work life for this dream! He can finally see a glimmer of HOPE! Look at the boost to our economy if we can support these fierce warriors and have them healthy enough to contribute to our economy. If nothing else, look at this factor! Money talks!"

Sue Alonzi, CF Patient, Ontario

"Being granted Trikafta on compassionate grounds my quality of life has completely changed for the better!! Better bmi, lung function, no coughing, no sinus issues, no hospitalizations, minimal gi issues all resulting in better mental health. CADTH recommendations are looking at one piece of the daily CF challenges. This is discriminatory by making decisions based on FEV1 less than 90% and maintaining a 5% lung function improvement (this is beyond stressful in itself we can do all the necessary treatments but exacerbations do happen beyond our control).

Trikafta has the power to grant access to our lives! Let clinicians decide who benefits from this medicine!”

Melanie Morin-Pelletier, CF Patient, Ontario

“I am 41 yo with CF. I spent a week in hospital last fall coughing mouthfuls of blood every day. I came back from hell, spent weeks on IV antibiotics and worked so hard to get my PFTs over 90. Now you tell me that I am « too healthy » to get a medication that will same my life? The damage to my lungs is real. PFTs are just a small part of the story, not the whole story. Your actual recommendations will likely end with my son losing his mom.”

Lesley Chown, CF Parent, Ontario

“My 12 year old daughter has CF and severe autism. She is not able to complete a PFT test due to her cognitive abilities. She was discharged from the hospital last week from a CF chest infection and was coughing up blood— but she isn’t going to be able to access Trikafta? My 15 year old son has CF - his PFT’s are under 90, but shouldn’t his physician determine if he should stay on the medication? His BMI is low as well, this medication could help him in so many ways!”

Stephanie Whaley, CF Parent, Ontario

“I am absolutely heartbroken and angered by these bogus recommendations. I feel as though science was completely ignored for the majority of the population. Cystic Fibrosis is a multi organ disease, when you search it that is evident in the information that pops up. My nine year old would understand that means the disease effects more than one organ. I have never heard of an oncologist telling their patients that the tumour needs to get a bit bigger in order for them to decide whether it's worth the money to remove it and treat it. Every time my CF daughter has an infection it creates scare tissue that never goes away. The damage is irreversible and after 14 years of having bowel surgeries, sinus surgeries and reoccurring lung infections (yes those are several different body parts affected by this disease not just the lungs) you are wanting her to create more damage in order to justify the cost and access to this medication. I have never wished this disease on anyone, but clearly this panel is the type of human that maybe needs to experience a day in the life to understand. Shame on all of them, they better hope Karma doesn't catch up to them or their family members because I guarantee if their loved one was touched by this horrible MULTI-ORGAN disease, their tune would change for access as preventive so their loved one doesn't have to go through a fraction of what current CF Canadians go through. Disgusting Canada - DO BETTER”

Carli Kennedy, CF Parent, Ontario

“Extreme anger and now sadness. My daughter was just recently given a 2nd chance at life and was given Trikafta for compassionate reasons. I honestly don't think anyone can comprehend the miracle this drug is. 12 HOURS my daughter went from DYING...unable to walk up stairs, non stop vomiting, never ending coughing with bleeding, gasping for breath sitting, to NOT coughing, to sleeping so soundly I panicked! After one month she went backcountry camping with her sister and friend. A month earlier she could not go to the store for 15 minutes without needing the rest of the day to recover! I think it is impossible for administrators to understand how life changing this drug is beyond "clinical data" I promise you none of the almighty tests would have looked any different after those first hours but watching your child not suffer and have life pour back into her eyes is undeniable. It is 100% cruel to not make this drug accessiblesible and worse take it away by numbers alone. Why wait until the damage is irreversible. My son has amazing lung function I am crushed that he will not have access and that the plan is for them to wait until damage has happened. We need to change how we evaluate drugs. I understand we need to keep big pharma in check and public dollars accountable etc etc. But cost analysis is much more than just numbers. These are human beings. They are our future, they have so much to contribute to society. This is not an everyday drug this is life changing and I mean LIFE CHANGING!!! I don't know how to convey this so people understand. Thank you for continuing to fight.”

Michelle Matta, CF Patient, Ontario

‘We need more flexibility on the recommendations for prescribing Trikafta. As a CF patient who has had a lung transplant, the lung volume restrictions (as well as the requirement for seeing a lung volume increase) exclude patients like myself. I am treated with in-office polypectomies quarterly for nasal polyps and frequent sinus infections that are debilitating and affect my ability to work, to participate in life, and risk the outcome of my transplant. My ENT has informed me of studies coming out of other countries indicating that Trikafta in both pre and post transplant individuals can virtually eliminate sinus problems.’

Ana Dujakovic, CF Patient, Nova Scotia

“If criteria are to be required they need to encompass ALL possible potential improvements in CF including quality of life improvements which are subjective experiences by the patient and are probably the number 1 way to see if a drug is helping someone. CF folks and their doctors know their bodies best and are often acutely aware if something is helping, hurting, or not making any difference. Also, my lung function varies wildly due to also having asthma which many CF patients have. Due to my asthma, my CF vs asthma symptoms can never be perfectly

differentiated since both affect my lungs. Therefore I may have some asthma issues one day and be denied my life saving medication just because I had an allergy trigger that day that I may not even be aware of. This is absolutely unfair criteria and in my opinion was unscientific and unethical."

Cheryl Smith, CF Parent, Manitoba

"We have been dreaming of access to Trikafta to help my son with frequent painful G.I. symptoms caused by his cystic fibrosis. He works hard to preserve his lung function with time consuming daily lung clearance treatments. Since his lung function is a baseline 94% , he would have to lose function in order to access the medication that we have been waiting for. Health Canada approved it for all cf patients with at least one copy of the Df508 gene, everyone who has that gene should be eligible to receive this drug. Cf is unique to each person, lung function is not the only measure of suffering and should therefore not be the measure to determine appropriateness of access"

Esther Segui, CF Parent, British Columbia

"CADTH's draft recommendations were heartbreaking. It was made clear to me that these recommendations were made by individuals who are not familiar with this disease. I would love to help educate, and help CADTH understand why their criteria for Trikafta reimbursement isn't attainable for an individual with CF. First of all, CF effects many organs in the body, not just the lungs. Many people live with CF, and their lung function isn't bad, however they are still living in and out of hospitals because of the other health concerns that come along with CF (GI issues, CF related diabetes, bowel obstructions, etc.) In regards to lung function, and needing to obtain certain lung functions in order to qualify and be accepted for reimbursement on this drug is unethical. I'd like to explain why...firstly, it's discrimination. Secondly, Trikafta doesn't eradicate CF completely, so although it makes living with the disease much more manageable, losing lung function is a guarantee. It will still happen over time from colds, flu's, pregnancy, and just in general over time. Expecting someone to maintain/gain lung function every year in order to stay on this life saving drug, is going to put unnecessary stress, anxiety and depression on people, because it's not possible. Loss of lung function will always happen until an actual cure is found! Please don't put our patients in a place where they feel pressured to self harm themselves (not doing breathing treatments) in order to qualify for this medication! There are so many ways Trikafta can benefit people with CF, lung function is just a small aspect."

Lisa Grono, CF Parent, Alberta

"Logan has Lung function >90% and has Cf-related liver disease, pseudomonas, aspergillis, staph aureus, 15 sinus/polyp surgeries, pancreatic insufficiency, coughs like he smokes 20 packs of cigarettes per day, sees a psychologist to deal with his fatal disease and has PICC lines/ IV lines, and has had too many specialist appointments to count yet this 14 year old CHILD is NOT 'sick' enough to access his miracle medicine! When they took our daughter from us to do her Bronchoscopy the doctors said she would be back in 30mins. 41/2 hrs later she was still intubated under general anesthetic in the OR. The mucus in her tiny lungs was so thick and sticky they described it to be "cement" and said it would be impossible to cough up. To help her breathe they had to spend 41/2 hrs literally pulling thick sticky infected mucus from her lungs. They instilled a mucolytic directly onto the mucus abs then tried to suck the mucus out with suction catheters only every time it would clog up the catheter so they had to cut the catheters and take them out with for forceps. And her FEV1 is currently 117% so according to cadth my tiny girl should be left to suffer like this with no access to life saving medicine."

Patient Group Conflict of Interest Declaration

Our group has compiled data from advocacy initiatives held since January of 2020 and participated in by the Canadian CF community. No additional help outside of our patient group was received to complete this submission. Our group did not receive any help to collect or analyze the data used in this submission. Our group has not had any financial payment from any company or organization since our inception. We are a patient and family volunteer group.

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.