



Re: Comments on the Draft Evidence Report titled “Modulator Treatments for Cystic Fibrosis: Effectiveness and Value”

To Whom it May Concern:

On behalf of the Boomer Esiason Foundation, I would like to express concern that ICER’s draft evidence report for the triple-combination therapy for cystic fibrosis (CF) does not share the complete picture of the value of the therapy for those living with CF.

CF is a deadly, progressive disease, and those living with CF have a projected life expectancy of 40 years. Patients living with CF must endure hours of therapy and take dozens of medicines each day just to stay “healthy.” For individuals with CF, such as my son, Gunnar, his standard for “healthy” means not spending weeks at a time in the hospital. His “healthy” is not typical. Breathing is a challenge every day.

Potentiators and CFTR correctors are innovative medicines used to treat CF. Previously, available CF medications could only treat patients with CF that had certain mutations. This meant that more than half of all patients with CF, including my son Gunnar, were still awaiting a treatment.

New treatments are able to harness the increased efficacy of combining the two classes of drugs, potentiators and CFTR correctors, and expand treatment options for patients. The most recent FDA-approved combination therapy is the first triple-combination medicine for CF. According to the FDA, the triple-combination therapy expands treatment so that over 90% of patients with CF now have a treatment option. Stunningly, this remarkable, groundbreaking achievement of biopharmacy and science is not mentioned in your 263-page report.

We are concerned about the accuracy of this draft evidence report for many reasons, but central to our concern is ICER’s use of the quality-adjusted-life year, or QALY. We believe that, as a 2018 article in Health Affairs said, “QALY calculations inherently privilege treatments that extend the lives of those who can be restored to perfect health, and disadvantage the many who seek life-extending treatments despite having a disability or chronic condition that is not curable.”

A number of organizations agree, including the National Council on Disability, which recently stated that QALY should not be used in coverage decisions.

My son’s experience brings the problems with QALY into focus. In his early 20s, Gunnar began slipping towards end-stage illness. Drug-resistant bacteria entered his lungs and his treatment arsenal began to fail. After graduating college, he was denied the opportunity to enter the workforce due to his health. Instead he spent his time in and out of the hospital, battling through nearly two dozen procedures and more than a year of intravenous antibiotic therapy.

Within a few hours of starting the triple-combination therapy, the viscosity of his usually thick, sticky mucus changed. Within a week, the constant cough he had lived with his entire life vanished. Within a month, his pulmonary function skyrocketed. He could finally breathe.

The triple-combination therapy under review put my son's life back on track. In a matter of days, he was allowed to look toward his future again. Today my son is in the first year of a joint MBA/MPH program at Dartmouth College, a far cry from the days of not having the strength to walk up a flight of stairs.

But ICER's report fundamentally fails to capture the monumental progress my son has achieved thanks to this triple-combination therapy. Increased pulmonary function is important, but it is the freedom to prepare for a fruitful future rather than to prepare for death that matters most. The larger point here is that the improvements that matter most to patients are not at the center of ICER's cost-effectiveness analysis.

Gunnar's isn't the only story like this. Thanks to decades of scientific and medical investigation, investment, research, development and risk taken on by countless individuals, tens of thousands of people with cystic fibrosis now have hope to manage their CF. ICER's report fundamentally discounts this fact, which only leads us to conclude that its motivation is not to support innovation and lifesaving therapy, but to limit access to it.

Sincerely,

*Boomer Esiason*

Boomer Esiason, Chairman



Re: Comments on the Draft Evidence Report titled “Modulator Treatments for Cystic Fibrosis: Effectiveness and Value”

To Whom it May Concern:

My husband and I had our worlds turned upside down when we discovered our baby had cystic fibrosis (CF). Today, my two beautiful daughters, Molly and Emily, both live with the disease. Their childhoods have been riddled with daily treatment, doctors’ visits, procedures and hospital stays. No child should have to endure the physical and mental stress my daughters have withstood, and thanks to new triple-combination CF therapies, many won’t have to.

But ICER’s flawed methodologies threaten access to lifesaving medications for thousands of people with PD who have no other treatment to turn to. I spoke to ICER officials on January 17<sup>th</sup>, 2020 about the concerns of the CF community and feel that those concerns have not been addressed in the current report. We feel that ICER does not understand the entire CF picture and certainly does not consider the multifaceted impacts of the disease in their reports.

The Bonnell Foundation: Living with cystic fibrosis and our CF Task Force of Michigan work closely with the CF community. Every day, we witness the devastating effects of CF firsthand, as well as the tremendous relief the triple-combination therapy provides to us and our loved ones. We believe that ICER’s report undervalues the modulator therapies and fails to consider the intangible benefits of the medication.

The most impactful changes for most patients, including my daughters, cannot be captured with a number. Things like being able to go to school, play soccer, or just hang out with friends are what bring meaning to my daughters’ lives. These CFTR modulators have changed the face of CF for my girls, and our CF community, taking CF from a deadly disease to a chronic illness. Having a treatment that works has brought so much hope to our lives. But none of this is taken into consideration by ICER because hope or the chance to live a more normal childhood cannot be quantified and calculated.

The CF community also believes ICER wrongly gave Trikafta a low rating based on “a lack of evidence.” As a rare and deadly disease, CF therapies will always face limited clinical trial data. To weaponize a lack of evidence against a CF therapy is to discriminate against rare diseases.

Additionally, the FDA granted the therapy orphan drug status; citing limited evidence as a problem undermines the very purpose of the Orphan Drug Act.

There is ample evidence to suggest Trikafta will provide benefits for thousands of patients who currently have no or few options. Trikafta has already provided huge, lifesaving benefits to the CF community and I'm thankful to it for giving my daughters a better life. I think about how if I had been born with CF, I would have died around the age my daughters are now. Instead, my daughters' continue to move full steam ahead.

ICER's low rating is an unjust one that could have profound repercussions for patients by blocking access. We hope ICER will reevaluate their methodology and consider the benefits that matter most to patients as well as the nature of CF as a rare disease. Please, ICER, do not make medication access for the CF community any harder than it already is.

With much hope for the CF future,

Laura Bonnell

The Bonnell Foundation: living with cystic fibrosis

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March 24, 2020

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Re: Modulator Treatments for Cystic Fibrosis: Effectiveness and Value Draft Evidence Report

Dear Dr. Pearson,

On behalf of the 30,000 individuals living with cystic fibrosis in the United States, we write to provide public comment on the *Modulator Treatments for Cystic Fibrosis: Effectiveness and Value Draft Evidence Report*. These disease-modifying therapies are transformative and represent tremendous potential to benefit people with CF by altering the course of cystic fibrosis. We appreciate that ICER incorporated several important points of feedback we provided during the review process; however we continue to have serious reservations about the model ICER used to generate this assessment. In its final report, the CF Foundation urges ICER to better characterize the potential benefit of long-term modulator use and the limitations of the economic model to capture this benefit; better reflect the impact of this chronic life-threatening disease on daily life; and highlight the limitations of the model in capturing the complexity and heterogeneity of CF.

### **Modulators mark a significant advancement in cystic fibrosis treatment**

As noted in the draft report, modulator therapies “substantially improve patient outcomes” when added to best supportive care. These treatments are the first to target the underlying defect in the CFTR protein caused by specific mutations of the *CFTR* gene. Although each available modulator provides clinically significant benefits to people with cystic fibrosis who are eligible, two modulator drug products — ivacaftor (Kalydeco®) and elexacaftor/tezacaftor/ivacaftor (Trikafta™) — demonstrate such a high magnitude of treatment benefit that CF clinical experts consider them “highly effective modulator therapies” (HEMTs). HEMTs demonstrate dramatic benefits compared to existing therapies across key clinical outcome measures including lung function, growth, risk of pulmonary exacerbations, sweat chloride concentrations, and quality of life. Given the individualized nature of cystic fibrosis, CF clinicians, in consultation with patients, are best positioned to determine which treatment will be most effective for each individual.

### **Potential benefits from long-term and early initiation of CFTR modulators**

Short of a cure for cystic fibrosis, modulators have the potential to dramatically alter the course of this chronic, life-shortening disease, particularly for those who start treatment at a young age. People with CF who start modulator treatment at a young age may be able to restore CFTR protein function to normal levels, thus preventing organ damage, halting the progression of the disease and avoiding future damage. An early start on modulators could have long-term benefits in sustaining health by 1) reducing the rate of lung function decline through prevention of

structural damage to the lungs; and 2) improving nutrient absorption and weight gain through preservation of exocrine pancreatic function and normalization of intestinal pH. For these people, we anticipate a life span that approximates that of the general population. Additionally, we anticipate that eventually most, if not all, of the cost associated with current “standard of care” treatments can potentially be eliminated. While studies focused on examining the impact of early initiation of modulators are underway, we urge ICER to incorporate the potential benefit of early use of these therapies in the relevant sections of the report.

**Long-term and real-world data are not yet available for several of these therapies, seriously limiting the utility and reliability of the report**

The first CFTR modulator, ivacaftor, became available to patients in January 2012, with the most recent approved therapy, elexacaftor/tezacaftor/ivacaftor, receiving U.S. Food and Drug Administration (FDA) approval in October 2019. ICER’s review of CFTR modulators so close to the approval date does not allow enough time to collect sufficient data to support a lifetime economic model. Without long-term data, these therapies might be significantly undervalued in ICER’s economic model. Although we appreciate ICER’s recognition of this limitation in the draft report, we are nonetheless concerned that the results of the economic modeling may be incorrectly interpreted or used by payers, the public, and other stakeholders.

It is also important to note that ICER’s decision to only include studies that have at least 100 participants disregards additional meaningful data. This participant threshold is unreasonable for a rare disease population. Given that each of the three therapies evaluated by ICER is under the rare or ultra-rare condition framework, the high participant threshold for included studies limits the data that contributed to this report.

There is a concerted effort underway in the CF research community to understand the long-term and real-world impacts of modulators on health status, quality of life, health care resource utilization, and other factors. The Cystic Fibrosis Foundation is sponsoring several studies – randomized clinical trial as well as real world research – to evaluate the safety of withdrawing symptomatic treatments, such as dornase alfa, among individuals taking elexacaftor/tezacaftor/ivacaftor. Results from these studies may impact the findings of ICER’s report. For more information on these studies, please see the CF Foundation’s [Research We Fund Highlights Report](#).

**Model limitations**

Several of the remaining assumptions and data inputs, or lack thereof, impose significant limitations to the model. Below, we highlight discrete aspects of this model that do not accurately reflect the value of CFTR modulators.

*Quality-adjusted life years should not be the primary health outcome measurement*

We would like to again express our concerns about the use of quality-adjusted life-years (QALY) as the primary measure of the cost-effectiveness analysis as QALYs do not account for patient-reported outcomes. We appreciate that ICER acknowledges such limitations and has included additional health outcome measurements such as life years (LYs) and equal value life years gained (evLYGs). However, the lack of patient relevant information in these models cannot be overstated. Furthermore, the QALY looks solely at longevity. The length of life for a person with

CF is determined primarily by the degree and decline of lung disease; therefore, by definition, this endpoint disregards all benefits outside of FEV<sub>1</sub>. QALYs cannot adequately inform coverage decisions or value assessments as they exclude patient experience and other benefits outside of lung function, thus severely limiting this model.

#### *Inappropriate data inputs*

As we have stated previously, the costs derived from Lieu et al. and Ouyang et al. are not valid estimates for current standard of care. These papers are outdated and should not be generalized in the model. Further, while only utility scores by ppFEV<sub>1</sub> are available, we know that modulators have clinical and quality of life benefits beyond lung function. The utility values derived from Schechter et. al are not an adequate measure for modulator therapies as these were developed for use with inhaled antibiotics and are mediated through FEV<sub>1</sub>.<sup>1</sup> This approach does not account for the clinical and quality of life data necessary for evaluating modulators, which have impact beyond the lungs, thereby imposing significant limitations to the model.

Additionally, the use of cost data from different types of payers (private vs. public) for disease management and lung transplant costs poses a noticeable limitation. Costs for private and public payers vary significantly for health care services and therapies. Using a mixture of Truven data and Medicare-specific numbers in the same model causes the resulting cost of CF to be incomparable to what is seen in the real-world and biases model outputs.

#### *Chronic therapy outcomes should not be discounted 3% per year*

We disagree with the application of a three percent annual discount rate on health outcomes. This discount rate assumes that one year of life today is valued higher than a year of life in the future. This assumption is philosophical in nature and not grounded in patient experience. While we appreciate the addition of undiscounted scenarios in the Appendix, we have concerns with the use of this discount in the base-case as that is not an appropriate perspective when evaluating chronic disease-modifying therapies.

#### *Lack of long-term data*

The timing of this review, and therefore the model, does not account for the anticipated long-term benefits of modulators. As experts in the pathophysiology of CF, we believe that early initiation and long-term use of modulators will have profound implications, altering the course of this disease by preventing downstream disease sequelae including loss of exocrine pancreatic function, structural damage to the lungs, risk of CF liver disease and failure, and CF-related diabetes, which in turn, will have a profound effect on costs to the patient and the system.

#### **Societal outcomes must be better incorporated into the report.**

We thank ICER for expanding their outreach to the CF community and their increased diligence in adding the patient perspective to the report. However, ICER has demonstrated that there is no process to incorporate critical patient-reported outcomes or the patient and caregiver experience into the economic model. This is a failing of the model, and thus will create a report that is not inclusive of the true impact of these therapies. As you have heard from people with CF, families, caregivers, and clinicians, CFTR modulators have great potential to dramatically change the trajectory of this disease and, more importantly, individual lives.

### **Lumacaftor/ivacaftor and tezacaftor/ivacaftor access remain important treatment options**

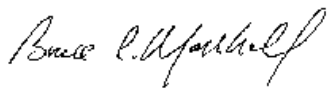
Access to lumacaftor/ivacaftor and tezacaftor/ivacaftor remains essential, though they are not considered HEMTs. These treatments are important therapeutic options for people with CF, especially for young children not yet eligible for elexacaftor/tezacaftor/ivacaftor per the FDA label. Further, the clinical impacts of CFTR modulators vary person-to-person and having multiple treatment options available is imperative to extend disease-modifying treatment to as many people with CF as possible. Ultimately, CF clinicians, in consultation with their patients, are best positioned to determine which treatment will be most effective for each individual.

### **Coverage policy landscape of CFTR modulators**

We appreciate ICER's attention to coverage policies for CFTR modulators as the value of these therapies is only realized if patients can access them. While many of the plans reviewed in ICER's evidence report provide coverage aligned with the FDA's label, there are multiple plans included that have implemented more restrictive coverage criteria. Many of these criteria are clinically inappropriate, administratively burdensome, and create unnecessary barriers to access. ICER's previous report on CFTR modulators stated that "public and private payers should continue to affirm their commitment to provide access to important clinical advances for CF and should remove superfluous requirements for coverage approval and continuation."<sup>ii</sup> This statement from ICER's earlier analysis summarizes these important facts and should be included in the current report.

Finally, we would like to stress that this report should not be the only source of data used by payers to determine coverage decisions. Although cost-effectiveness analyses can be informative, they must be used carefully and as part of a holistic evaluation of the value a treatment provides.

Thank you again for the opportunity to comment on the draft report.



Bruce C. Marshall, MD  
Chief Medical Officer  
Executive Vice President of Clinical Affairs



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Senior Vice President of Policy and Advocacy

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<sup>i</sup> Schechter MS, Trueman D, Farquharson R, Higuchi K, Daines CL. Inhaled aztreonam versus inhaled tobramycin in cystic fibrosis. An economic evaluation. *Annals of the American Thoracic Society*. 2015;12(7):1030-1038.

<sup>ii</sup> Balk E, Trikalinos T, Kuntz K, et al. Modulator Treatments for Cystic Fibrosis: Effectiveness and Value; Final Evidence Report and Meeting Summary. Boston, MA: Institute for Clinical and Economic Review; June 7 2018



Submitted electronically to: [publiccomments@icer-review.org](mailto:publiccomments@icer-review.org)

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Re: Comments on the Draft Evidence Report titled: “Modulator Treatments for Cystic Fibrosis: Effectiveness and Value”

Dear Dr. Pearson:

As a 43-year old adult who has fought to live successfully with cystic fibrosis (CF) since diagnosis at birth, I advocated for the CF community with complete opposition to the methodology and intent of ICER’s review of CFTR modulator therapies, particularly Trikafta.

Because I am undoubtedly convinced that this process is a pretense for a clearly pre-determined mission of de-valuing high cost medications, I cannot justify a concerted investment of my time and effort in response to this report as I feel it is largely a waste of breath and words.

The evidence of this belief is the report referencing the incorporation of input from community organizations, yet a complete absence that ALL organizations expressed disapproval and objection to the work of ICER. That is manipulation. The interest being served by this report and process is clearly not that of the patient’s. A collective objection was made overtly clear on the January 17, 2020 phone call between ICER and CF community representatives, which was completely discarded by the report.

While the report appears comprehensive from the attempt at incorporating the lived experiences of physical, psychological, social, emotional, treatment burden and quality of life benefits, there is no clear numerical factoring of these outcomes in the QALY assessment process. The severe limitation of selected endpoints in and of itself disqualifies the legitimacy of this statistical analysis (I will never forget my college statistics professor saying “The beauty of statistics is that you can make them say whatever you want.”).

Another severe limitation of this process is in the fact that CF physicians with direct clinical experience and intimate engagement with families faced with the challenges of CF were merely consulted for input, but were not an integral part of the evaluation process, formulary development or outcome assessment. Self-establishing ICER as a definitive expert on valuating patient lives and treatment worth in the absence of practical, clinical and empirically based experts in the disease state is yet another reason for disqualification.

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As was demonstrated with input from community organizations, and most likely from physicians, ICER chose what input was useful or not, and effectively manipulated data through contrived statistical formulas to achieve the desired outcome.

While I support intentions to achieve fair and reasonable pricing mechanisms, I do not support ICER's methodology as supportive of the patient population. There are several philosophical, societal and free market economic issues that I could extrapolate upon, yet I am confident that ICER will once again toss aside any feedback or response that is in objection of the reporting process or self-professed validity\* of the outcomes in this predetermined report.

Therefore, I will conserve my limited energy and time as I perform my chest physical therapy along with the enduring respiratory, physical and emotional health benefits of taking Trikafta. With the clearest lungs I have ever had, I profess my loudest expression of objection to the patient impact of this report.

If you do indeed hear this objection, which also represents the threat felt by the greater CF community, I ask you directly (not rhetorically) – What will ICER's response be when insurers tell me, my older brother, and thousands of others that Trikafta will no longer be covered because ICER's report constituted it as overpriced?

Will you simply wash your hands and say it is not your problem at that point?

Goliath forces of insurers and manufacturers are wrestling about high medication costs (which I support in a free market). However, the methodology of ICER threatens patient access to revolutionary, targeted and highly effective and is ethically wrong in leveraging patients as pawns who will ultimately pay the price in this systemic battle.

Again, I am sure that my input will be selectively discarded by ICER while pretending to actually listen. Please, prove me wrong by at least acknowledging in your next findings presentation that the community organizations and leaders in the CF community expressly object to ICER's methodology and the validity of these results.

On behalf of the Cystic Fibrosis Lifestyle Foundation, Board of Directors, and patients which we serve,



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\* In questioning the validity of this report, was the impact of likeliness to survive a pandemic presenting exponentially greater lethal threat to the lungs of those of us with cystic fibrosis a quantitative variable in the ICER report that supposedly considered all known cost factors of disease management?



*Submitted electronically to: [publiccomments@icer-review.org](mailto:publiccomments@icer-review.org)*

March 24, 2020

Dr. Steven Pearson  
Institute for Clinical and Economic Review  
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Dear Dr. Pearson,

On behalf of CFRI's Board of Directors, and the national cystic fibrosis community that we serve, I write to comment on the Institute for Clinical and Economic Review's (ICER's) draft evidence report regarding the comparative clinical effectiveness and value of elexacaftor/tezacaftor/ ivacaftor as a therapy for cystic fibrosis (CF). We are deeply opposed to the conclusions reached in the draft evidence report, and find the methodology of the analysis to be both unethical and flawed.

Cystic Fibrosis Research, Inc. (CFRI) is one of the largest nonprofit cystic fibrosis organizations in the country, whose mission is to fund research, provide education and personal support, and spread awareness of cystic fibrosis to those living with and affected by the disease. Our Board of Directors and staff include renowned CF clinicians and researchers, parents of children with CF, spouses of those with CF, and adults with CF. We know this disease intimately and work directly with members of the CF community from across the United States. As such, we receive broad input on the devastating impact of cystic fibrosis, as well as the unprecedented positive impact that CFTR modulators – specifically Trikafta – have had on the lives of many with this debilitating disease.

Cystic fibrosis remains a fatal disease. Last year, half the individuals with CF who died were under 30 years old. Those who battle CF face hours of respiratory therapy, countless pills, and often multiple injections, IVs, and hospitalizations. Every hospitalization is painful, isolating, frightening, and expensive. For those with advanced lung disease, the fear of a catastrophic hemoptysis or pneumothorax is ever present. Transplant offers hope for an extended life, but is fraught with its own tremendous risks, and is not a cure. The report grossly minimizes the extraordinary pain and suffering experienced by those with the disease.

Unethical Use of Quality Adjusted Life Year (QALY): There are many mutations of the CFTR gene that causes cystic fibrosis, and individuals with CF have extremely varied disease expression. The report does little to address the heterogeneous nature of the disease and its significance upon drug impact. Our impression is that to do so would make evident the many flaws related to the use of the Quality Adjusted Life Year (QALY) in your analysis. The utility weights used to determine an individual with CF's QALY, based on ppFEV1, is simplistic, and fails to address the complex impacts of the disease.

ICER's use of a cost-benefit analysis utilizing the Quality Adjusted Life Year and equal value of life-year gained negates the value of the report in its entirety. The use of QALY is a discriminatory methodology that will always penalize individuals with disabilities, and specifically those with incurable chronic diseases such as cystic fibrosis.

As you well know, Medicare is prohibited by law from using a QALY-based threshold to determine benefits and coverage. The use of QALY has been critiqued both in the United States and abroad. The Pioneer Institute, in its recent analysis of QALY and the Americans with Disabilities Act found that, "QALY would be extremely vulnerable to challenge under the ADA if it is utilized to determine treatments available to Medicaid patients because the use of QALYs has the potential to cause state governments to administer Medicaid to disabled persons in a discriminatory manner by providing them lesser benefits by prioritizing the achievement of "asymptomatic" status, rather than "medical effectiveness."

To place a numerical value on the lives of those with cystic fibrosis in order to determine drug pricing is unethical, and leads one to ponder others in history who have done the same with catastrophic impacts. We do not agree with your organization's claim that its use of QALY to determine drug price value is not inextricably related to placing a value on the lives of those most needing the drugs.

CFRI and its constituents were shocked by the following sentence in the report: "As an extreme scenario analysis, we evaluated Trikafta as a curative therapy and found that the cost-effectiveness ratio of lifetime therapy with Trikafta continued to far exceed commonly used cost-effectiveness thresholds even under the assumption that it maintained individuals with CF in normal health such that they never experienced any symptoms or complications of CF." Countless members of the CF community were alienated by that conclusion, which essentially informed those desperately in need of the therapy that they are not worth the cost.

Flawed Economic Analysis: We are very concerned by the economic analysis used in the report that appears to have multiple flaws leading to an overprediction of medication cost over time. Most notably, we question why you utilize static pricing to project a lifetime of use of Trikafta, without considering the landscape of the CF therapeutic pipeline. There are other companies in clinical trials with CFTR modulators. There is future potential for generics. In addition, there are numerous companies exploring genomic editing, and mRNA therapies. It is highly unlikely that Trikafta will remain the only option in the not-so-distant future. By assuming decades of use with static pricing, you have assigned a cost that is not based in reality.

We continue to be concerned that ICER fails to accurately assess the full array of medical costs associated with the multi-faceted management of the disease. Cystic fibrosis care runs in the hundreds of thousands of dollars per year per patient. ICER's analysis also fails to include the related loss of income caused by the disease – both for adults with CF and for the parents of children with cystic fibrosis. In addition to reduced medical costs due to reduced exacerbations, hospitalizations and transplantation, a therapy that potentially enables individuals with CF as well as CF caregivers to work has far broader financial implications.

Of course, we cannot put a price on the savings in the physical and emotional suffering experienced by those living with cystic fibrosis. CFTR modulators have transformed lives.

Trikafta has given many individuals with CF hope that they will have a better quality of life, and a longer life span. It would require far more than this imposed three-page limit to share the stories of success with Trikafta, including improved lung function, reduced dependence on insulin, reduced hospital stays, fewer exacerbations, improved weight gain, and improved mental health. You have heard from numerous patients and CF advocacy groups, but the life-changing impact of this therapy for many is not conveyed in your draft report.

CFRI and its constituents have deep concern that your report will give credence to state and private payers who seek to reduce costs by keeping vital therapies out of the hands of those who would benefit from them. Life with CF is a daily battle to slow the disease's progression. Prior to the arrival of CFTR-modulating therapies, the decline in lung function was inevitable, regardless of one's adherence to the time-consuming daily CF medical regimen. CFTR-modulating therapies – most notably Trikafta – have brought realistic hope that the downward course of the disease can be halted, and health improved. It would be a travesty should the draft Evidence Report be used to deny access to these medications by those who desperately need them.

Potential to Halt Innovation and Drug Development: Equally frightening to us is the reality that should your flawed analysis be embraced by payers to deny access to CFTR-modulator therapies, there will be a chilling effect on innovation in the biopharmaceutical industry. It is a tragedy that approximately 10% of those with cystic fibrosis are unable to benefit from these therapies due to their specific CFTR mutations. There are others with eligible mutations who cannot use Trikafta for a variety of reasons. ICER continues to disregard the unique challenges faced by the cystic fibrosis community and other rare disease groups to entice biotech companies to enter the rare disease realm. Our community is still suffering, and for those without new therapies, facing an early death is a horrific reality.

It is a challenge to incentivize research and drug development for those with CF. This report has the potential to provide payers with a justification to discontinue coverage for new and innovative therapies, with a cascade impact of suppressing research, and discouraging investment in new drug discovery and development. This would be catastrophic for the cystic fibrosis community, and has broad implications for other rare disease groups.

ICER's use of QALY, static pricing predictions, undercounting of CF healthcare costs, and failure to incorporate the impact of lost wages due to disability or providing care to a loved one leads to an assessment of drug pricing that is highly problematic and inaccurate. We strongly object to the flawed and unethical methodology used to evaluate this life-saving therapy, and as such, thoroughly reject the report's conclusions.

Sincerely,

A handwritten signature in blue ink, appearing to read 'Siri Vaeth', with a stylized flourish at the end.

Siri Vaeth, MSW  
CFRI Executive Director

P.S. In light of the extraordinary risks COVID-19 has upon the health of those with CF, Trikafta may play a key role in the survival of our community members.

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March 17, 2020

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Re: “Modulator Treatments for Cystic Fibrosis: Effectiveness and Value”  
(Draft Evidence Report of February 20, 2020)

Dear Dr. Pearson:

This letter responds, with gratitude, to the invitation of the Institute for Clinical and Economic Review (ICER) for public comment on the draft report entitled “Modulator Treatments for Cystic Fibrosis: Effectiveness and Value” (Draft Report) issued on February 20, 2020. I am writing on my own behalf and on behalf of my daughter Rose, who turned 18 in November of last year and is a scholar and future Olympian in dressage despite, or perhaps because of, being born with cystic fibrosis.<sup>1</sup>

Rose inherited the N1303K mutation (a Class II mutation, per Table 1.1 of the Draft Report) from me and the 621+1G>T mutation (a Class I “splice mutation” as that term is used in Table 1.1) from her mother. Thus, she is not eligible for any of the modulator treatments discussed in the Draft Report as developed by the investor-owned firm Vertex Pharmaceuticals.

I am happy to report that Rose is thriving as a CF patient, with a ppFEV<sub>1</sub> that typically overs at or near 100. However, maintaining that degree of health for Rose has typically required a high degree of vigilance, accurately characterized and labeled “treatment burden” at page 16 of the Draft Report, as well as one hospitalization per year for pulmonary exacerbation. Rose is eager to shed these burdens, as well as what the Draft Report describes at page 15 as the “psychosocial burden associated with living with a chronic, life-shortening illness.”

She knows, as do I, that as part of the ten percent of CF patients who are not eligible for modulator treatments, Rose will see her medical breakthrough in due course. But we also know that when the breakthrough comes, it will serve a small minority within an already-rare disease population. Thus, the same factors that drive the price of a modulator drug like Trikafta into the stratosphere (almost \$312,000 a year per patient, as noted at page 68 of the Draft Report) will almost certainly apply when the remaining ten percent get their miracle drug.

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<sup>1</sup> My daughter does not share my last name and thus, by identifying her here by first name I am not compromising her medical privacy, which she guards zealously and appropriately.

Moreover, we are keenly aware that much of the research and drug development work being undertaken on behalf of that ten percent by the Cystic Fibrosis Foundation (CFF) is funded by the \$3.3 billion payment received by the Foundation in 2014 in exchange for its share of future royalties from the modulator therapies discussed in the Draft Report. We salute the CFF for these fruits of its “venture philanthropy” initiative by which it co-invests, alongside pharmaceutical companies like Vertex, in future medical breakthroughs. But we also acknowledge that, as a result of this large payout to the CFF, we are morally implicated by the high cost of Trikafta and the other modulator treatments even though Rose is unlikely to benefit directly from them.

Although my interest in the Draft Report is driven by the primal parental energy that is characteristic of so many people I have met in the CF community, that interest is also informed by my professional life. I am an attorney who has, since 2016, served as the head of New Hampshire’s Office of the Consumer Advocate, the mission of which is to advocate on behalf of residential customers of public utilities.<sup>2</sup> Thus, much of my work is taken up with the analysis of the prices charged by monopoly providers of essential public services in the key network industries of electricity, natural gas, and water.

When we turn to investor-owned businesses to provide essential services, whether it’s the energy that heats and lights our homes or the drugs that extend lives and abate suffering, this reliance has, or ought to have, two key consequences. First, devoting private capital to these endeavors should yield innovation and quality improvement. Second, the public should not be exploited because profit must be reasonable and prices not excessive.

Vertex Pharmaceuticals has clearly succeeded with the first objective while acting in contempt the second. As noted at page 10 of the Draft Report, Vertex “declined to participate in the review process” despite having been invited to “submit relevant information on research, development, and manufacturing costs that may impact pricing of a drug.” From an investor perspective, return is linked to risk – which is why drugs like Kalydeco, Symdeco, and Trikafta *should* be expensive.

ICER should revise the Draft Report to explain and to acknowledge this reality of market economics, the better to hold Vertex accountable. The pharmaceutical company’s obduracy supports an inference that its modulator prices yield profits beyond even the lofty ones its investors should reasonably expect. But Vertex is not just failing to cooperate; it is supporting an ‘astroturf’ (i.e., fake grassroots) organization known as the Cystic Fibrosis Engagement Network that publicly condemns any use of *any* cost-benefit principles to evaluate the fairness of prices for modulators. *See, e.g.*, CFEN video presentation “What’s Wrong With ICER?,” complaining that “sometimes economists can have more control than your doctor about whether

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<sup>2</sup> These comments are provided exclusively in my personal capacity; my title and responsibilities as an official of state government are provided here for identification and contextual purposes only.



you get the medicine that treats your condition” and arguing that “doctors, not economists, should be the ones deciding which medicines patients get”).<sup>3</sup>

Both the authors and the readers of the Draft Report should know that not all Cystic Fibrosis Families condemn the use of cost-benefit analysis to evaluate from a demand-side perspective the propriety of charging \$312000 a year for a breakthrough medication – especially when the company that owns the medication refuses to supply any information that would support a supply-side evaluation of the price. The Draft Report should be clarified so as to explain forthrightly that when CF patients ask their neighbors (be they coworkers in the case of employer-provided health insurance or fellow taxpayers in the case of Medicaid) to share the financial burden of an ultra-expensive medication, this is not a matter of letting bean-counters (i.e., economists and statisticians) rather than doctors and other empathetic caregivers make treatment decisions. It is, rather, an acknowledgement that when society pays for a good, its value must be assessed from a societal perspective.

Overall, the Draft Report lacks clarity and therefore persuasiveness, particularly for a cystic fibrosis community that is understandably concerned that the ICER analysis could be used to deny CF patients access to modulator therapies. Although the early sections of the Draft Report do a good job of explaining cystic fibrosis and its consequences – thus confirming that ICER knows how to reduce a complicated scientific story to its essentials while writing with empathy – Chapter 5 of the Draft Report can be charitably described as inaccessible to those without advanced training in statistical analysis. This is profoundly regrettable given that Chapter 5 is the heart of the ICER analysis.

I am *not* suggesting that ICER should “dumb down” the Draft Report. I *am* suggesting that when the report’s key chapter is virtually impossible to understand for someone like the undersigned (who holds a bachelor’s degree, a masters degree, and a juris doctorate, and who has pursued a legal specialty that requires immersion in principles of finance, accounting, and engineering, and who has for the past 18 years of CF parenthood been studying the disease and its public policy implications) then ICER’s analysis of the modulator therapies is vulnerable to being dismissed and ridiculed by those who simply cannot understand what ICER is attempting to communicate. To the turgid analytical prose of Chapter 5 should be added introductory and concluding sections that explain this section’s analysis in summary fashion, using language sufficient to be understood at least by college educated non-mathematicians/statisticians.

In 2018, with much fanfare, ICER announced that it would supplement its reliance on cost per quality-adjusted life-year (QALY) with analysis of cost per Equal of Life Year Gained (evLYG). As the Cystic Fibrosis Foundation noted in its October 21, 2019 scoping comments, “QALYs do not account for patient-reported outcomes” and, thus, it is laudable that ICER “will acknowledge

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<sup>3</sup> Accessed on March 1, 2020 at [www.engagecf.org/resources/2019/11/6/whats-wrong-with-icer](http://www.engagecf.org/resources/2019/11/6/whats-wrong-with-icer). The “about” section of this web site discloses that CFEN is “a project of the [Alliance for Patient Access](http://AllianceforPatientAccess.org) (AfPA).” The list of AfPA funders, accessed on March 1, 2020 at [admin.allianceforpatientaccess.org/wp-content/uploads/2020/02/AfPADonorsJanuary2020-1.pdf](http://admin.allianceforpatientaccess.org/wp-content/uploads/2020/02/AfPADonorsJanuary2020-1.pdf) is a who’s who in the pharmaceutical industry and most assuredly includes Vertex.



such limitations under the framework for ultra-rare diseases and incorporate[] the [evLYG] as an additional effectiveness measure.” As ICER is surely aware, this is a muted form of similar criticism that ICER has received from other, more outspoken quarters of the CF community. *See, e.g.*, February 24, 2020 blog post of CF patient-advocate Gunnar Esaison entitled “How Do You Value Your Life With Cystic Fibrosis?” (in which Mr. Esaison, who uses Trikafta, concludes: “I can’t help but look at that [QALY] mortality function and laugh” and ridicules bioethics as not a “real profession”).<sup>4</sup>

How regrettable, then that ICER buries its analysis of evLYG in the Draft Reprt. Indeed, “evLYG” does not even appear in the list of abbreviations at pages vi-vii of the Draft Report.<sup>5</sup> There is no real discussion of evLYG in Chapter 5. It merely becomes clear (via review of Table 5.10 at page 76) that the modulator therapies under review become only slightly more cost-effective when the relevant metric is cost per evLYG rather than cost per QALY gained. It is almost as if ICER cannot bring itself to acknowledge that the evLYG is an important metric – a squeamishness that you *should* overcome, in my respectful opinion.

Section 5.2 of the Draft Report makes clear that a key driver of CF treatment costs is are acute pulmonary exacerbations, defined as “those that involve treatment with IV antibiotics either in the hospital or with home treatment.” Draft Report at 59. This may be problematic to the extent avoided acute pulmonary exacerbations is a key benchmark. Over my 18 years as a CF parent, I have learned that the decision on whether to diagnose an acute pulmonary exacerbation is entirely subjective; a patient with a ppFEV<sub>1</sub> at or near 100, with no history of colonization by *Pseudomonas aeruginosa*, in the dead of winter, is at higher ‘risk’ of going on IV antibiotics than a patient in July who is itching to be outdoors, is used to living with *P. aeruginosa*, and has recently endured a similar inpatient stay. ICER should consider analyzing the cost of CF care, with or without modulators, on a cost-per unit of ppFEV<sub>1</sub> improvement basis even if, as the Draft Report suggests, these costs apparently vary depending on other factors. *See id.* (“disease management costs varied by level of ppFEV<sub>1</sub>”) and Draft Report at 51 (“the impact of an absolute increase of 5% in a patient with a baseline ppFEV<sub>1</sub> of 40% likely differs from that of a 5% increase in a patient with a baseline of 90%”).

The estimate in the Draft Report of the cost of best supportive care is rendered in frustratingly opaque fashion and does not comport with the lived experience of my family. According to page 69 of the Draft Report, the average annual cost of best supportive care in 2016 was \$77,163, which was “used to calibrate the best supportive care cost estimates prior to updating to 2019 dollars.” Table 5.6 on the following page suggests that for a patient younger than 18, the direct cost of CF care, for both “disease management” and pulmonary exacerbations, is \$81,271 in 2019 dollars. Please revise the Draft Report to include a lucid explanation of how the 2016 cost estimate was used to “calibrate” (if not determine) the 2019 estimates.

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<sup>4</sup> The cited blog post was found at [www.gunnaresaison.com](http://www.gunnaresaison.com) on February 24, 2020.

<sup>5</sup> This is titled “List of Acronyms Used in this Report,” which is incorrect. An acronym is an abbreviation that forms a word (e.g., NICE and PERT); all of the other abbreviations on the list (e.g., ppFEV<sub>1</sub> and CFFPR) are not acronyms.

According to reimbursement records provided by my family's health insurance provider (Anthem Blue Cross Blue Shield) and prescription drug plan (Express Scripts), in 2019 my daughter incurred \$140,767 in prescription costs last year and a comparable sum in healthcare costs. From our perspective, this was a routine CF year – one that included a single two-week inpatient stay to treat a pulmonary exacerbation. This suggests your estimate of the cost of best supportive care may be seriously in error, which bolsters the argument for a more rigorous and publicly disclosed analysis.

Finally, the Draft Report states that because Trikafta has an eligible patient population of greater than 10,000 individuals, the ICER “ultra-rare” framework did not apply and thus threshold prices were calculated only for cost-effectiveness thresholds less than \$200,000 per QALY. Draft Report at 55, 86. In the interest of analytical rigor and making the final report as persuasive as possible, ICER should analyze Trikafta under both the “ultra-rare” framework and its regular framework. At the very least, ICER should explain this arbitrary distinction between drugs that qualify for the ultra-rare framework and those that do not.

As ICER finalizes “Modulator Treatments for Cystic Fibrosis: Effectiveness and Value,” and as the California Technology Assessment Forum deliberates on the report, everyone involved should keep in mind that until pathologist Dorothy Hansine Andersen, M.D. first identified and named cystic fibrosis in 1938, this condition was just another mysterious reason babies died as infants. The astonishing medical progress Dr. Andersen touched off has not merely made it possible for people around the globe to live and to thrive with CF into adulthood and even senior citizenship – it has also, yes, required the expenditure of significant amounts of resources. This, to paraphrase Oliver Wendell Holmes, is the price of civilization.

The portion of that price presently attributable to Vertex Pharmaceuticals is almost certainly too high, but this cannot obscure the nobility and virtue of what this company's work, in concert with the CFF, has accomplished. As a CF family whose miracle medical breakthrough is still ahead of us, we hope the ICER process succeeds in making future breakthroughs more likely and more accessible to all who will benefit from them. It is imperative, and ICER should stress, that in no circumstances should any aspect of this process lead to therapies becoming unavailable to patients who will benefit from them.

Thank you for the opportunity to provide these comments. I commend ICER for seeking them and I hope you will consider adopting them, as well as others you will be receiving, in quest of producing a final report that drives the price of these life-changing modulator therapies to a more reasonable level.

Sincerely,

*/s/ D. Maurice Kreis*

D. Maurice (“Don”) Kreis  
CF Dad  
Concord, New Hampshire



March 25, 2020

*Submitted electronically to: [publiccomments@icer-review.org](mailto:publiccomments@icer-review.org)*

Dr. Steven D. Pearson  
Institute for Clinical and Economic Review  
Two Liberty Square, Ninth Floor  
Boston, MA 02109

*Re: Comments on the Draft Evidence Report titled: “Modulator Treatments for Cystic Fibrosis: Effectiveness and Value”*

Dear Dr. Pearson,

On behalf of Emily’s Entourage, I want to thank you for the opportunity to provide comments on the Institute for Clinical and Economic Review’s (ICER) *Draft Evidence Report*, “Modulator Treatments for Cystic Fibrosis: Effectiveness and Value.”

My name is Emily Kramer-Golinkoff. I am 35 years old with advanced stage Cystic Fibrosis (CF) and a co-founder of Emily’s Entourage (EE), a 501(c)3 that has raised millions of dollars to speed research and drug development for rare nonsense mutations of CF. As you know, CF is a rare, fatal genetic disease that affects a variety of organ systems, including the lungs and digestive system, with significant impact not only on patients but on caregivers as well.

We started EE because we saw the transformative advances underway for the vast majority of the CF community, but we realized that they would ultimately benefit roughly 90% of the CF community and those with nonsense mutations and other hard-to-treat mutations would be left behind. With two copies of a nonsense mutation, I fall in the unlucky 10% of the CF community without modulator therapies.

EE has serious concerns regarding the report for treatment of CF.

1. **Discriminatory methodology**

The QALY unfairly devalues the lives of those with disabilities, including fatal, incurable chronic illnesses like CF. The report fails to capture the complexities of CF and its varied clinical presentation and impact on patients’ and caregivers’ lives. Focusing on ppFEV1 provides an oversimplified, inaccurate view of the disease that does not reflect individuals’ live experience with CF.

In addition, use of the QALY to determine treatment coverage is prohibited by Medicare. For Medicaid, it would violate the Americans with Disability Act (ADA) by engaging in a

discriminatory process for evaluating coverage decisions and limiting access to life-saving treatments for disabled individuals, according to a recent analysis of QALY and the ADA by The Pioneer Institute.

2. **Flawed economic review**

ICER's economic review of Trikafta is flawed in a number of ways, which call into question its final results. First, the cost effectiveness calculations include the full list-price of Trikafta over a lifetime, which is not realistic on the basis of generic entry, new and improved drugs, and cures. When Trikafta goes off patent, the price will come down substantially. Without factoring in the price reduction with generic entry, the model is based on a full list-price that is time-limited and the cost projections are inaccurate.

In addition, the model unfairly penalizes Trikafta for extending life and attributes the consequent disease management costs to this therapy. If all costs are included in the model, then projected benefits should be too, including the projected productivity and impact of patients who are not getting sicker as well as alleviated caregiver burden and employment opportunities.

Finally, discounting health benefits devalues therapies like Trikafta that extend life by long periods of time. While achievement of long-term life extension is a benefit that should be celebrated, instead discounting health benefits systematically disadvantages therapies that treat chronic, genetic diseases like CF where the model starts at a young age.

3. **Stifling of innovation for remaining 10%**

EE represents those with CF nonsense mutations who do not benefit from the existing modulator therapies, a group in which I personally belong. Those of us in the outlying 10% still suffer from the same fatal, devastating disease that CF has always been. We continue to wait—with bated and fading breath—for advances that benefit our CFTR mutations. With a disease that advances despite our hardest efforts to delay it, it is a race against time for the outlying 10%.

The findings of the *Draft Evidence Report* will have a stifling effect on future innovation, disincentivizing companies from investing in therapeutic development for the final 10%. Stymying innovation for the final 10% will result in suffering and death, not to mention significant burden and loss of productivity among individuals with CF and caregivers.

In addition, the downstream effects of this report will not only result in reduced drug development for the final 10% of CF patients without modulators, but those effects will extend across all rare diseases. Individuals with rare diseases often represent the extremes of disease and innovation originally developed for these populations has the potential to scale far beyond the rare disease population, benefitting far larger swaths of the population, which is not accounted for in the ICER report.



The *Draft Evidence Report* fails to capture the lived experience of CF, the complex and highly varied ways it affects people with CF and caregivers, and the transformative, life-saving impact of these modulators, particularly Trikafta. In addition, the results are based on discriminatory methodology and a flawed economic analysis, and risk stifling biopharmaceutical innovation for the final 10% without modulator therapies and the larger rare disease population.

We sincerely appreciate your consideration of our concerns on behalf of the entire CF community and especially those in the final 10%. If EE can provide additional details or address these concerns in the final draft, please contact me at [emily@emilysentourage.org](mailto:emily@emilysentourage.org).

Sincerely,

Emily Kramer-Golinkoff, MBE  
Emily's Entourage Co-Founder



**Institute for  
Patient Access**

March 16, 2020

***Submitted electronically to:*** [publiccomments@icer-review.org](mailto:publiccomments@icer-review.org)

Steven D. Pearson, MD, President  
Institute for Clinical and Economic Review  
Two Liberty Square, Ninth Floor  
Boston, MA 02109

*Re: Comments on the Draft Evidence Report titled “Modulator Treatments for Cystic Fibrosis: Effectiveness and Value”*

Dear Dr. Pearson:

On behalf of the Institute for Patient Access, I thank you for the opportunity to provide comments regarding ICER’s draft evidence report, “Modulator Treatments for Cystic Fibrosis: Effectiveness and Value,” dated February 20, 2020.

### **About the Institute for Patient Access**

The Institute for Patient Access (IfPA) is a physician-led policy research organization dedicated to maintaining the primacy of the physician-patient relationship in the provision of quality health care. To further that mission, IfPA produces educational materials and programming designed to promote informed discussion about patient-centered care. IfPA was established in 2012 by the leadership of the Alliance for Patient Access, a national network of health care providers committed to shaping a patient-centered health care system. IfPA is a 501(c)(3) public charity nonprofit organization.

### **Draft Evidence Report Comments**

Cystic fibrosis affects 30,000 people in the United States. It is a progressive genetic disease that causes persistent lung infections and is associated with co-morbidities that include pancreatic insufficiency, sinus disease, pulmonary infection, asthma, diabetes, bronchiectasis and depression.<sup>1</sup> Cystic fibrosis patients experience increased hospitalization rates, life-threatening complications and a shortened lifespan – the median age of death for a person diagnosed with cystic fibrosis in the United States is 27 years.<sup>2</sup>

Managing the disease requires patients to endure a time-consuming regimen of medicines, chest physiotherapy and nebulizers. This daily regimen is not only costly, but also materially reduces

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<sup>1</sup> Hassan M, Bonafede MM, Limone B, Hodgkins P and Sawicki G (2016) “The Burden of Cystic Fibrosis: Pulmonary Exacerbations and Health Care Resource Utilization in a Commercially Insured Population in the United States” *Value in Health* 19.

<sup>2</sup> Becker CC, Clements K, Delong K, Harrow B, and O’Sullivan A (2011) “Economic Burden on Cystic Fibrosis in the U.S.: Costs of Care by Disease Severity and Age” *Value in Health* 14.

patients' quality of life and their school or workplace productivity. The same is true for caregivers. Medicines that are both efficacious and well tolerated will reduce these costs and, consequently, are highly valued by the patient community.

As noted in the draft evidence report, two classes of modulator drugs treat cystic fibrosis: potentiators and CFTR correctors. Ivacaftor is the only potentiator drug available. Lumacaftor, tezacaftor, and elexacaftor fall into the CFTR corrector class. The efficacy of the two classes of drugs generally increases when they are used in combination. As highlighted in the report, the FDA has approved three combination therapies. The most recent is also the only triple combination medicine, elexacaftor/ivacaftor/tezacaftor. The draft evidence report evaluates this triple-combination therapy and also updates past reviews of the three prior therapies.

IfPA has serious concerns, however, that the estimated cost-effectiveness results are inaccurate. The report applies a flawed and inapplicable methodology that significantly undervalues the benefits patients receive from these therapies, particularly triple-combination therapy.

*Evidence Ratings Fail to Account for the Triple-Combination Therapy's Originality and the Fact that Cystic Fibrosis Is a Rare Disease*

ICER's evidence ratings are not objective measures. Rather, the ratings reflect researchers' judgement regarding two attributes: (1) the estimated clinical benefit of the drug; and, (2) how certain the researchers are of the drug's clinical benefit. The scores are, consequently, ICER researchers' subjective assessment of the existing evidence.

In this case, the draft evidence report acknowledges that, based on the evidence, all of the combination drugs under consideration improved patient outcomes. The report also notes that the adverse side effects from the medicines were mild and uncommon. It is reasonable to conclude that efficacious medicines with minimal side effects should be rated highly. Yet the draft evidence report instead assigns triple-combination therapy a B+ and C++ evidence rating for two of the comparisons.

The report justifies these subjective ratings by noting, several times, that there are insufficient published randomized trials or observational data for triple-combination therapy in the relevant populations. In short, the available data is encouraging, but relatively little of that data is available at this point. As ICER surely realizes, there is limited data about triple-combination therapy because cystic fibrosis is a rare disease and because the drug was approved by the FDA only as of October 2019. The draft evidence report's low assessment of triple-combination therapy, therefore, essentially penalizes the treatment for being a new orphan drug that treats a rare disease.

Triple-combination therapy was granted orphan drug status by the FDA's Office of Orphan Products Development to encourage the development of treatments for cystic fibrosis. By failing to acknowledge the reality of new orphan drugs, the draft evidence report undermines the important goals of the orphan drug program. ICER's subjective assessment is particularly troubling because a low evidence rating could suggest that the drug is less effective. Not only is there no evidence to justify such a supposition, there is ample reason to expect that triple-combination therapy will provide a significant benefit to many cystic fibrosis patients. In sum, the low evidence rating is inappropriate and could unjustifiably reduce patients' access to triple-combination therapy.

### *The Draft Evidence Report Fails to Account for the Benefits of Expanding the Treatable Population*

Treating cystic fibrosis is challenging because the disease is caused by thousands of different rearrangements in a person's genetic code. Due to this complexity, the available combination therapies before triple-combination therapy, which were all major treatment advancements, could treat only a minority of patients. Lumacaftor/ivacaftor, for example, benefits only about 40% of patients.<sup>3</sup>

Triple-combination therapy, according to the FDA, expands the treatable population to approximately 90% of cystic fibrosis patients.<sup>4</sup> There is tremendous value in this advance. The FDA, in its October 21, 2019 press release affirmed that triple-combination therapy makes:

...a novel treatment available to most cystic fibrosis patients, including adolescents, who previously had no options and giving others in the cystic fibrosis community access to an additional effective therapy,” said acting FDA Commissioner Ned Sharpless, M.D. “In the past few years, we have seen remarkable breakthroughs in therapies to treat cystic fibrosis and improve patients’ quality of life, yet many subgroups of cystic fibrosis patients did not have approved treatment options. ***That’s why we used all available programs, including Priority Review, Fast Track, Breakthrough Therapy, and orphan drug designation, to help advance today’s approval in the most efficient manner possible***, while also adhering to our high standards. (emphasis added)

The FDA used “all available programs” to expedite triple-combination therapy’s approval for a reason. Expanding the share of patients with an effective treatment to 90% of the population is a significant benefit. The draft evidence report fails to demonstrate that the analysis considered these benefits when evaluating triple-combination therapy, which is particularly concerning with respect to the cost-effectiveness models. Without accounting for the expansion of patients who now have an effective treatment, the cost-effectiveness models are, by design, undervaluing triple-combination therapy.

### *The Long-term Cost Effectiveness Model Ignores Unquantifiable Benefits*

Medications that more effectively manage a disease create both quantifiable and unquantifiable benefits for patients. The methodology behind the long-term cost effectiveness models focus mostly on the quantifiable benefits. The unquantifiable benefits are, to a large extent, excluded from the analysis. Excluding these benefits biases the results toward undervaluing the medicines – the larger the number of unquantifiable benefits excluded, the more the results are undervalued.

The draft evidence report acknowledges this problem by stating that “economic models such as the ones used in this analysis cannot capture the full range of quality-of-life effects associated with

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<sup>3</sup> See Cystic Fibrosis News Today: <https://cysticfibrosisnewstoday.com/2018/09/24/vertex-and-treating-cf-costs-can-unsettle-but-vertex-remains-close-to-community-interview-series/>.

<sup>4</sup> (2019) “FDA approves new breakthrough therapy for cystic fibrosis. Treatment approved for approximately 90% of patients with cystic fibrosis, many of whom had no approved therapeutic options” *FDA Press Release*, October 21; <https://www.fda.gov/news-events/press-announcements/fda-approves-new-breakthrough-therapy-cystic-fibrosis>.



the disease, or the improvements in quality of life experienced by CF patients taking CFTR modulator therapy.”

Quality-of-life measures are difficult, but important, to quantify. Cystic fibrosis patients generally rate their quality of life as low,<sup>5</sup> and they highly value medicines that can reduce their daily burdens and increase their quality of life – even small improvements to their quality of life are valued highly. Since the economic models fail to capture these important unquantifiable benefits, the long-term cost-effectiveness calculation significantly undervalues the benefit these treatments offer patients.

### *The QALY Methodology Is Inappropriate for Rare Diseases*

According to the draft evidence report, “the primary health outcome was quality-adjusted life years (QALYs) but we also report life expectancy in life years (LYs), equal value life years gained (evLYGs) and the lifetime number of acute pulmonary exacerbations.” While reporting on other factors is a positive development, the “primary health outcome” drives the conclusions drawn from the report. QALYs have well-documented weaknesses, particularly for rare diseases, that make this methodology inappropriate for evaluating the cost effectiveness of cystic fibrosis medications.

As evidence of these weaknesses, a recent report by the Pioneer Institute argues that the use of QALYs may violate several legal provisions of the Americans with Disability Act (ADA). In the study, the authors argue that:

QALY would be extremely vulnerable to challenge under the ADA if it is utilized to determine treatments available to Medicaid patients because the use of QALYs has the potential to cause state governments to administer Medicaid to disabled persons in a discriminatory manner by providing them lesser benefits by prioritizing the achievement of “asymptomatic” status, rather than “medical effectiveness.” This outcome, which would have a disparate impact on individuals with both physical and mental disabilities, would be a clear violation of the ADA.<sup>6</sup>

In addition to the concerns that the use of QALY methodology violates the ADA, there is also concern that QALY methodology discriminates against people with rare diseases.<sup>7</sup> Rare diseases, by definition, have limited clinical trial data. These data limitations bias the results toward undervaluing the medicines and inject an excessive amount of uncertainty regarding the accuracy of the QALY estimates. Consequently, QALYs are particularly inappropriate for determining the value of cystic fibrosis treatments.

Another relevant concern about QALY methodology underscores why it is inappropriate for evaluating cystic fibrosis treatments. People living with cystic fibrosis have severely restricted lung function that reduces their endurance. Patients have indicated that clinically small

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<sup>5</sup> Uchmanowicz I, Jankowska-Polańska B, Rosińczuk J, Wleklik M (2015) “Health-related quality of life of patients suffering from cystic fibrosis” *Adv Clin Exp Med*. Jan-Feb; 24(1):147-52; <https://www.ncbi.nlm.nih.gov/pubmed/25923099>

<sup>6</sup> McKenna J and Smith W (2020) “The Legality of QALY under the ADA” *Pioneer Institute*, February; <https://pioneerinstitute.org/featured/new-report-legal-analysis-suggests-icers-quality-adjusted-life-years-methodology-violates-the-americans-with-disabilities-act/>.

<sup>7</sup> Pearson I, Rothwell B, Olaye A, and Knight C (2018) “Economic Modeling Considerations for Rare Diseases” *Value in Health* 21: 515-524.

improvements in their lung function can meaningfully improve their quality of life. QALYs, however, are designed to undervalue improvements that may be clinically small, even if they are meaningful for patients in everyday life.

Beyond these foundational problems with QALY methodology, the draft evidence report also inconsistently applies the QALY methodology by using a lower range for the cost-effectiveness threshold for triple-combination therapy (\$50,000-\$200,000 per QALY) than for two other therapies evaluated (\$50,000-\$500,000 per QALY). There is no sound justification for using a different cost-effectiveness threshold across medicines that treat the same patient population.

## **Conclusion**

Cystic fibrosis is a devastating disease that severely restricts patients' quality of life and is associated with a shorter lifespan. The economic costs for managing cystic fibrosis are high. According to the American Thoracic Society, the average cost of care for cystic fibrosis was \$48,000 in 2006. A good deal of these costs are costs associated with hospitalization.

These are the average costs, however, and the burden for patients diagnosed with severe cystic fibrosis can be much higher. According to a 2011 study, the annual costs for patients with mild disease severity are \$30,000, but the annual costs incurred by patients who are diagnosed with severe cystic fibrosis are much higher – \$215,000.<sup>8</sup> Younger patients diagnosed with severe cystic fibrosis incur even higher annual costs. Patients aged 10 to 14 with severe cystic fibrosis were estimated to be as high as \$343,900.<sup>9</sup>

Prior to the approval of triple-combination therapy, most patients living with cystic fibrosis did not have access to an effective treatment. Now, widely effective triple-combination therapy has generated tremendous excitement and hope in the patient community. It is critical that ICER acknowledge the value that a broadly effective treatment offers to patients.

Based on the concerns raised above, IfPA is concerned that the draft evidence report significantly undervalues these cystic fibrosis medications, particularly triple-combination therapy. If IfPA can provide further detail or aid the Institute for Clinical and Economic Review in incorporating any of the above recommendations into its final draft, please contact us at 202-499-4114.

Sincerely,



Brian Kennedy  
Executive Director

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<sup>8</sup> Becker CC, Clements K, DeLong K, Harrow B, and O'Sullivan A (2011) "Economic Burden on Cystic Fibrosis in the U.S.: Costs of Care by Disease Severity and Age" *Value in Health* 14.

<sup>9</sup> Ibid.

March 18, 2020

Dr. Steven D. Pearson  
President  
Institute for Clinical and Economic Review  
Two Liberty Square, Ninth Floor  
Boston, MA 02109

Dear Dr. Pearson,

The Partnership to Improve Patient Care (PIPC) is writing to comment on the Institute for Clinical and Economic Review's (ICER) draft evidence report regarding treatments for Cystic Fibrosis (CF). CF is a rare and chronic genetic disease which causes persistent lung infections and limits the ability for people to breathe over time. Living with and managing cystic fibrosis can be physically, emotionally, and financially taxing for both patients and their caregivers. For this reason, it is imperative that ICER take a comprehensive approach when evaluating new treatments so that all aspects of value and quality of life improvements are considered during the assessment process.

**The QALY is an inappropriate tool to measure the value of treatments for cystic fibrosis.**

As PIPC has previously stated, the QALY is both a discriminatory metric and a poor measure of health benefits for health care interventions. This is particularly true with respect to a disease such as CF, as patients experience significant disabling effects over time.

We have noted in the past that the QALY disserves those with chronic and disabling conditions, as it is fundamentally designed to undervalue what may be deemed clinically small improvements. The ability of novel treatments to bring improvements through increased efficacy or the reduction of side effects, regardless of whether they are perceived as clinically significant, can substantially improve quality of life for patients with CF. This is particularly applicable to CF patients in regard to lung function. Even small improvements in lung function can increase a CF patient's endurance and ability to participate in day-to-day activities, such as attending work or school. The QALY undervalues these improvements and thus does not paint an accurate picture of the value of these treatments to patients.

The use of this limited metric also presents an incredibly narrow view to measure CF progression over time. ICER's model only measures the treatments' effects on lung function, weight, and acute pulmonary exacerbations, when we know there are many other outcomes that matter to patients with CF. There are tools and data available to capture a more robust picture of disease progression and quality of life for CF patients. If ICER's goal is truly to capture the value of these treatments, it should not use the EQ-5D as the patient-reported outcome tool for this assessment. The quality of life of patients with CF is better measured with the Cystic Fibrosis Questionnaire – Revised (CFQ-R), which assesses 13 domains relevant to patients living with

CF, compared to a mere five domains associated with the EQ-5D. Most importantly, given that QOL in the ICER model is linked directly to a measure of lung function, studies have shown both considerable variance in quality of life across stages and severity of disease, but also across the many aspects of QOL that the disease affects beyond lung function, in particular nutrition,<sup>1</sup> depression<sup>2</sup> and anxiety.<sup>3</sup> It is imperative that ICER utilize the CFQ-R or other disease-specific instruments when assessing these treatments. Furthermore, ICER should ensure that *all* outcomes are mapped back to the QALY.

**We have concerns about ICER's willingness to prioritize financial savings over patient life and well-being.**

PIPC has consistently voiced our discomfort with the use of the QALY in measuring health outcomes as it devalues health gains for the disabled, chronically ill, and elderly. We would like to go a step further regarding ICER's CF report and make the point that not only is the QALY discriminatory, it does not accurately represent society's values in relation to health care. ICER's use of the metric is callous and out of touch with the goal of bringing better health to individuals, which should *always* be the primary function of the health care system.

ICER's CF report makes the incredibly concerning assessment that **even if Trikafta were found to be curative, it would still not be cost-effective**. In saying this, ICER makes clear that it is very willing to put a price on a human life, which is devastating to the patient community, and which we believe would be incredibly troubling to society writ large. We do not disagree that prices should be set in a reasonable manner and that we should be having a robust discussion about what that looks like in an era of disease-modifying and curative therapies. We also feel that finances being prioritized over a patient's life is an inappropriate starting place for this conversation.

The purpose of innovation in health care is to treat and cure patients. From an ethical standpoint, society chooses to spend resources on those that need them most. Studies have shown that when asked to quantify their preferences for providing care to different patients, people will frequently choose to allocate resources to those who are most in need of help.<sup>4</sup> CF is a horrific disease that drastically shortens lives. Taking the societal view spelled out above, we should be prioritizing access to care for those who are chronically ill, not limiting it.

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<sup>1</sup> Sawicki GS, Rasouliyan L, McMullen AH, Wagener JS, McColley SA, Pasta DJ, Quittner AL. Longitudinal assessment of health-related quality of life in an observational cohort of patients with cystic fibrosis. *Pediatric pulmonology*. 2011 Jan;46(1):36-44.

<sup>2</sup> Knudsen KB, Pressler T, Mortensen LH, Jarden M, Skov M, Quittner AL, Katzenstein T, Boisen KA. Associations between adherence, depressive symptoms and health-related quality of life in young adults with cystic fibrosis. *SpringerPlus*. 2016 Dec;5(1):1-8.

<sup>3</sup> Bregnballe V, Thastum M, Lund LD, Hansen CR, Preissler T, Schiøtz PO. Validation of the Danish version of the revised cystic fibrosis quality of life questionnaire in adolescents and adults (CFQ-R14+). *Journal of Cystic Fibrosis*. 2008 Nov 1;7(6):531-6.

<sup>4</sup> McKie J, Richardson J. Social preferences for prioritizing the treatment of severely ill patients: the relevance of severity, expected benefit, past health and lifetime health. *Health Policy*. 2017 Aug 1;121(8):913-22.

### **Societal and economic benefits should be included in ICER's cost-effectiveness model.**

The financial burden of CF is very high, both in direct medical costs and indirect costs, such as lost productivity and caregiving costs. Annual medical costs alone incurred by adult patients with severe CF can run upwards of \$200,000 whereas younger patients with severe CF can incur even higher OOP costs.<sup>5</sup> Direct medical costs do not even begin to capture the full financial burden of this disease. CF requires consistent care and caregiving, which places a huge emotional and financial burden on families. Very frequently when a child is diagnosed with CF, one parent will need to leave the workforce and become a full-time caregiver. CF patients also are very easily prone to infections and frequently require special accommodations in schooling and work. Several studies have shown that some of the largest costs of CF come from direct non-health care costs and indirect costs attributable to productivity losses.<sup>6</sup> If ICER's goal is to truly capture the value of these treatments from a societal perspective, these costs must be included in the base case.

### **ICER fails to capture heterogeneity of the patient population.**

CF is a complex disease with considerable heterogeneity in both its severity and the degree to which therapies are effective. If ICER's aim is to produce actionable and accurate data for policymakers, then this heterogeneity must be incorporated in the model.

Unfortunately, the ranges of the sensitivity analysis are the only tool within the report to convey the impact of this patient diversity, and ICER's choices for input ranges around its sensitivity analysis are unjustifiably narrow. The range for sensitivity in the analysis are just 0.002 – 0.005. This is an incredibly small variance given the choice for the base case is already very shallow.

Additionally, given the heterogeneity, even within subgroups of CF patients, we believe it would be more appropriate to produce ranges, rather than means, for cost-effectiveness for a disease as diverse as CF. Averages are not consensus; they are just poor proxies for highly heterogeneous outcomes.

### **ICER's decision not to model with dynamic pricing leads to consistently flawed assessments.**

ICER claims that it chooses not to incorporate the fact that drug prices change over time, as it would lead to a layer of uncertainty. However, it also states that numerous recently published models measuring the cost-effectiveness of cystic fibrosis drugs have indeed used dynamic pricing, suggesting ICER is willing to deviate from conventional methodologies often accepted by researchers and value assessors.

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<sup>5</sup> Becker CC, Clements K, Delong K, Harrow B, and O'Sullivan A (2011) "Economic Burden on Cystic Fibrosis in the U.S.: Costs of Care by Disease Severity and Age" *Value in Health* 14.

<sup>6</sup> Angelis, Aris et al. "Social and economic costs and health-related quality of life in non-institutionalised patients with cystic fibrosis in the United Kingdom." *BMC health services research* vol. 15 428. 28 Sep. 2015, doi:10.1186/s12913-015-1061-3

The relevance of dynamic pricing is heightened in conditions where consequences accrue over an extended period of time. CF is an obvious example of this. In fact, the ICER model assumes treatment continues for up to fifty years. This is in stark contrast to many other interventions which are either evaluated over a short time period, or for which the consequences of intervention only accrue over a short period of time.

Using static pricing in this context misunderstands how health care spending as well as uptake and integration of new technologies into health systems work. Uptake of new technologies does not happen overnight and does not begin at 100 percent utilization but rather happens slowly over time. When providing data for value attribution of a new technology within a living, evolving health system, the dynamic understanding of value is far more relevant than the static version. This point was made very clearly by Harvard researcher David Grabowski in a 2012 study of statins.<sup>7</sup>

Numerous studies have shown that using static prices in cost-effectiveness models make little sense when developing lifetime models.<sup>8,9,10</sup> While it is not impossible, it is highly unlikely that the price of these drugs will be the same in ten or twenty years, let alone fifty. The price pattern for the vast majority of drugs is that of significant decline following 5-7 years of relative stability and on average results in prices close to 10-20% of launch price after ten years.<sup>11</sup> This means that over the course of fifty years, relying on the launch price for the entire lifespan of each patient will likely overestimate costs between 300% and 400%.

We know ICER's reports have an impact on payer decisions and ultimately patient access. With that responsibility it is imperative ICER make every attempt to present accurate and unbiased information. Relying on static pricing runs counter to ICER's intention of painting a complete value picture.

## Conclusion

ICER needs to reconsider its use of the QALY and model construction to ensure it is capturing an accurate picture of the value of treatments to patients. We are also very disturbed by ICER's statement that a drug for a devastating disease, even if curative, may not be worth the cost. We

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<sup>7</sup> Grabowski DC, Lakdawalla DN, Goldman DP, Eber M, Liu LZ, Abdelgawad T, Kuznik A, Chernew ME, Philipson T. The large social value resulting from use of statins warrants steps to improve adherence and broaden treatment. *Health Affairs*. 2012 Oct 1;31(10):2276-85.

<sup>8</sup> Garrison Jr LP, Mansley EC, Abbott III TA, Bresnahan BW, Hay JW, Smeeding J. Good Research Practices for Measuring Drug Costs in Cost-Effectiveness Analyses: A Societal Perspective: The ISPOR Drug Cost Task Force Report—Part II. *Value in Health*. 2010 Jan;13(1):8-13.

<sup>9</sup> Healy P, Pugatch M. Capturing value: Why dynamic efficiency should be considered in the pricing and reimbursement of medicines. Stockholm: Stockholm Network. 2012.

<sup>10</sup> Vondeling GT, Cao Q, Postma MJ, Rozenbaum MH. The impact of patent expiry on drug prices: a systematic literature review. *Applied health economics and health policy*. 2018 Oct 1;16(5):653-60.

<sup>11</sup> Lichtenberg, F. R., & Duflos, G. (2009). The effect of patent expiration on US drug prices, marketing, and utilization by the public. Manhattan Institute for Policy Research.

disagree, as do the patients and families impacted by your analysis, that ICER should have the authority to determine the value of a patient with cystic fibrosis.

Sincerely,



Tony Coelho  
Chairman  
Partnership to Improve Patient Care

March 25, 2020

Steven D. Pearson, M.D.  
President, Institute for Clinical and Economic Review  
2 Liberty Square  
Boston, MA 02109

Dr. Pearson,

My name is Juliana Keeping, and my son Eli is 7-years old. Eli was diagnosed with cystic fibrosis at two weeks old and has two copies of the DF508 mutation, our illness community's most common version of this genetic, life-shortening illness.

I'm writing in response to the draft evidence report released February 20, 2020 called, "Modulator Treatments for Cystic Fibrosis: Effectiveness and Value," on behalf of myself and son.

Eli takes Symdeko, one of the four CFTR modulators discussed in your report. When Trikafta, the newest modulator, becomes available for children, I will switch Eli to this drug, which costs almost \$312,000 per year.

In addition to Symdeko, each day, Eli takes handfuls of pills and completes multiple breathing treatments to stay as healthy as he can, including a current regimen of vitamins and supplements, digestive enzymes, antibiotics, an antacid, the CF-specific breathing treatment Pulmozyme, plus albuterol and saline. An hour of physical therapy on a shaking vest helps keep his lungs healthy, with a new addition of sessions breathing into an Oscillating Positive Expiratory Pressure (OPEP), a device that we began to use this month.

The cystic fibrosis community is excited about Trikafta, which studies show increased the amount of air patients could expel from their lungs in one second by an average of 14%<sup>1</sup>. Anecdotes from our clinic and wider disease community are even more encouraging, and give me hope that one day my son will be able to breathe like me, and to outlive me, with this drug.

Eli is among the fortunate 90 percent<sup>2</sup> of people living with CF for whom Trikafta can make a difference, meaning 10 percent of the estimated 100,000<sup>3</sup> people in the world living with CF have no modulator. My family remains dedicated to finding a comparable treatment, and a cure,

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<sup>1</sup> <https://www.statnews.com/2019/10/21/new-vertex-cystic-fibrosis-drug-approved-extending-treatments-to-90-of-patients/>

<sup>2</sup> <https://www.statnews.com/2019/10/21/new-vertex-cystic-fibrosis-drug-approved-extending-treatments-to-90-of-patients/>

<sup>3</sup> <https://www.cysticfibrosis.org.uk/what-is-cystic-fibrosis/faqs>



for every person with CF — including those with the rarest of the rare mutations, which is why we continue to fundraise for research, as our community has for decades.

But if an into-the-stratosphere \$312,000 per year is accepted as a price tag for a drug that treats the vast majority of individuals with this rare disease, what would an acceptable price be for a drug that treats the remaining 10 percent? It's a question that should give us pause.

Drugmakers like Vertex are taking advantage of patients like my son by pricing drugs based not on what makes a fair and reasonable return for their investment, but what they can get away with.

And, while more people with cystic fibrosis are living longer, a change we've long fought for, it means patients need incredibly expensive drugs, longer.

Today, Americans with cystic fibrosis are being forced off of the Vertex drugs they fundraised to create<sup>4</sup>, because they cannot afford them. If our community and our country continue to fail to address alarming prices set by monopoly drug makers, more people with CF will suffer under crushing prices, with promising medication priced cruelly out of reach.

Our reality is this: My son could just as easily become a victim of unrestrained drug pricing as he could his disease. The writing is on the wall.

### **Value-Based Pricing and ICER Process**

Today, prescription drugs are priced without regard to the value they deliver to patients. Instead, corporations price their drugs based on maximizing profits. Value-based pricing for prescription drugs holds great promise as a framework that can move us away from pricing based only on the market power of drug corporations. Instead, we believe value should be the starting point for negotiations with government, employers, insurers, and other payers.

The work of the Institute for Clinical and Economic Review (ICER) can be foundational to the creation of a new system to ensure that patients have access to drugs they need and that those drugs are accessible, affordable, and fairly priced. I applaud ICER for its work and for its inclusive and responsive process which engages patients and their families, listens to concerns, and takes into account our real world experience.

### **Limitations of ICER Framework**

The ICER value analysis is just one input that should be considered in arriving at the appropriate price for a new drug therapy. ICER does not address societal and ethical issues that are of utmost importance for the health and well-being of patients and our nation.

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<sup>4</sup> <https://www.bloomberg.com/news/features/2015-07-07/this-medical-charity-made-3-3-billion-from-a-single-pill>

ICER does not consider the role of the patient community, taxpayers and government in the invention of new drugs. Because ICER does not consider appropriate returns for the drug manufacturer, it cannot take into account societal investment which reduces risk for manufacturers and should therefore reduce return to the company commercializing the drug.

ICER does not consider what is an appropriate price based on the investment to develop, produce, and distribute a drug. Given limited societal funds and necessary trade-offs when scarce resources are directed to unwarranted profits, this is an element that should be taken into account when arriving at a price.

### **The Prices of Trikafta, Orkambi, Symdeko, and Kalydeco Are Simply Too High**

Trikafta costs \$311,741 per year; Symdeko, \$292,200 per year; Orkambi, \$272,623 per year; and Kalydeco, \$311,704 per year.

**Table 5.5. Drug Cost Inputs**

Intervention	WAC per Day* <sup>116</sup>	Annual Drug Cost
Kalydeco	\$853.40	\$311,704
Orkambi	\$746.40	\$272,623
Symdeko	\$800.00	\$292,200
Trikafta	\$853.50	\$311,741

\*WAC as of December 2, 2019

†Costs for dosing for ages 2-5

Since long before the ICER analysis, I have believed that the prices of modulators are too high<sup>5</sup>, with no data-based justification ever offered from the drug manufacturer as to why.

While invited to do so, Vertex refused to offer research, development, and manufacturing data in ICER's latest review process<sup>6</sup>.

The price of the community's modulators have been criticized since Kalydeco's introduction in 2012, when it became one of the most expensive pills in American medicine<sup>7</sup>.

<sup>5</sup> [https://www.change.org/p/vertex-pharmaceuticals-jeffrey-m-leiden-stop-price-gouging-our-charity-funded-drugs?use\\_react=false](https://www.change.org/p/vertex-pharmaceuticals-jeffrey-m-leiden-stop-price-gouging-our-charity-funded-drugs?use_react=false)

<sup>6</sup> Tice JA, Kuntz KM, Wherry K, Chapman R, Seidner M, Pearson SD, Rind DM. Modulator Treatments for Cystic Fibrosis: Effectiveness and Value; Draft Evidence Report. Institute for Clinical and Economic Review, February 20, 2020. <https://icerreview.org/material/cystic-fibrosis-2-draft-evidence-report>, pg. 10.

<sup>7</sup> <https://www.medpagetoday.com/pulmonology/cysticfibrosis/42018>

ICER's 2018 report found that the price of the modulator drugs "would need to be reduced by about half to be considered cost effective." The latest draft report doesn't quarrel with that conclusion, and neither do we.

The 2020 draft report states a 65 percent to 66 percent discount would be necessary for Trikafta to be cost effective, and I don't disagree<sup>8</sup>. My reasons for concluding the prices are too high are different from—and yet complement—the ICER analysis.

All told, we as patients must stand guard against unjustifiable price gouging wherever it arises.

### **The Role of CFF Community Charitable Giving and Taxpayers**

Taxpayers and charitable donations<sup>9</sup> paid for the foundational science behind leading to the discovery of the first CFTR modulator, Kalydeco. The funding came from donations through the Cystic Fibrosis Foundation (CFF), which were tax deductible, and from the National Institutes of Health (NIH). Vertex bought the patents to cystic fibrosis drugs like Kalydeco for a payment of \$3.3 billion<sup>10</sup> and agreed to pay royalties to the Cystic Fibrosis Foundation.

One argument for high prices is that investors must be compensated for the high risk involved in doing the basic scientific research and clinical trials to bring a drug to market. Without that incentive, pharmaceutical manufacturers say, new life-saving treatments will not be invented and made available to people who need them.

But in the case of all CFTR modulator drugs, the CF community and taxpayers took the early, critical risk by investing money into the research<sup>11</sup>, and Vertex moved to acquire the IP only after the treatments were shown to be viable. In fact, the New York Times reported,<sup>12</sup> "Cystic fibrosis was not a priority, and Vertex officials have said the program might have been dropped if the foundation had not been paying for it." Thus, Vertex cannot lay claim to a return adjusted for high risk.

### **Vertex Is Continuing to Exploit Its Monopoly To Gouge Patients and Payers**

Vertex claims it needs to charge these prices to "continue to invest" in new drugs.

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<sup>8</sup> Igle JA, Kuntz KM, Wherry K, Chapman R, Seidner M, Pearson SD, Rind DM. Modulator Treatments for Cystic Fibrosis: Effectiveness and Value; Draft Evidence Report. Institute for Clinical and Economic Review, February 20, 2020. <https://icerreview.org/material/cystic-fibrosis-2-draft-evidence-report>, p. 87.

<sup>9</sup> <https://www.medpagetoday.com/pulmonology/cysticfibrosis/42018>

<sup>10</sup> <https://www.wsj.com/articles/cystic-fibrosis-foundation-sells-drugs-rights-for-3-3-billion-1416414300>

<sup>11</sup> <https://www.nytimes.com/2012/02/01/business/fda-approves-cystic-fibrosis-drug.html>

<sup>12</sup> <https://www.nytimes.com/2014/11/19/business/for-cystic-fibrosis-foundation-venture-yields-windfall-in-hope-and-cash.html>

Yet Vertex has, since 2018, relied on a tax bonanza to repurchase hundreds of millions of dollars its own shares<sup>13</sup>, money that could have been used to lower drug prices. So far, its stock buybacks total more than a half billion, with another \$464 million in stock repurchases authorized<sup>14</sup>.

Leaders have bragged about having billions of cash on hand<sup>15</sup>.

Vertex's behavior is consistent with findings published in the Journal of the American Medical Association<sup>16</sup> that "[t]here is no evidence of an association between research and development costs and prices; rather, prescription drugs are priced in the United States primarily on the basis of what the market will bear." Truer words could not be spoken about Vertex pricing for these drugs.

### **Vertex Executives Have a History of Ethically Challenged Behavior**

In 2012, Vertex reported positive clinical trial results for a combination of Kalydeco and another drug<sup>17</sup>, leading to an increase in its stock price. At least half a dozen Vertex executives took advantage of the inflated stock price to cash in \$100 million in stock options before revealing the true trial data three weeks later, which were less positive.

In response, Sen. Chuck Grassley (R-Iowa) wrote a letter to the U.S. Securities and Exchange Commission asserting Vertex executives appeared to have taken advantage of the situation, "knowing the overstated clinical trial results would eventually be made public and cause the stock price to drop," the Milwaukee Journal Sentinel reported<sup>18</sup>. "The letter said the stock sales were troubling for industry investors and the federal government, which pays billions of dollars a year for drugs through Medicaid and Medicare."

Former Vertex CEO Jeffrey Leiden himself has made a killing at the expense of patients and other payers. His compensation has been condemned by groups like the corporate governance watchdog, Institutional Shareholder Services (ISS), which has called a \$48.5 million paycheck

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<sup>13</sup> <https://www.axios.com/big-pharma-stock-buybacks-research-123f10f1-79d0-44be-a515-a6603fbcfd9a.html>

<sup>14</sup>

[https://docs.google.com/spreadsheets/d/1aBqL9ZbQwOXxsILbm\\_066wSgp0pY1Gok3nON1nE9AWY/edit#gid=0](https://docs.google.com/spreadsheets/d/1aBqL9ZbQwOXxsILbm_066wSgp0pY1Gok3nON1nE9AWY/edit#gid=0)

<sup>15</sup> <https://www.fool.com/investing/2018/03/15/7-things-vertex-pharmaceuticals-ceo-just-said-that.aspx>

<sup>16</sup> <https://www.ncbi.nlm.nih.gov/pubmed/27552619>

<sup>17</sup> <http://archive.jsonline.com/watchdog/watchdogreports/charitys-investment-a-prescription-for-profits-for-drug-maker-p79tfc9-208027961.html/>

<sup>18</sup> <http://archive.jsonline.com/watchdog/watchdogreports/charitys-investment-a-prescription-for-profits-for-drug-maker-p79tfc9-208027961.html/>

“excessive” and not based on rigorous performance metrics<sup>19</sup>. In a recent year, Mr. Leiden’s compensation was \$78.5 million<sup>20</sup>.

## **Patients Can’t Afford These Drugs**

In the United States, patients with insurance are being slammed with high out-of-pocket costs or being forced to stop working in order to qualify for government assistance and gain access to Trikafta, Symdeko, Orkambi, and Kalydeco. Due to high drug prices, patients are forced to patch together grant funding to cover costs, funding that can evaporate without notice.

I recently spoke to Robert Davis, a 50-year-old living with cystic fibrosis who has experienced a health crisis due to unaffordable Vertex medications. For the last three years, Robert has taken Kalydeco or Symdeko. Because CFTR modulators have not stopped the need for other pricey CF medications, Robert has owed more than \$17,500 for his medications. He can rely on patient assistance programs to cover some of the cost, but it’s never enough. The list prices are too high. So in August 2018, Robert began rationing his medication, taking one pill instead of two. Within weeks, he experienced breathlessness more severe than what he was used to and over the ensuing days, he felt a gurgle in his lungs. It was a familiar warning, followed shortly by coughing up palmsful of blood, a terrifying complication to CF called hemoptysis. He drove himself to the doctor and was admitted to the hospital for a week while being treated with antibiotics before being sent home for another week of IV antibiotics to recover.

Lora Moser, another adult with cystic fibrosis, was suddenly denied her grant funding when her husband got a new job — his new wages rose just \$650 outside of the program’s wage requirements. Denied the \$15,000 that helped pay for her medication costs, she stopped taking her most important medications, fell into a deep depression, and was hospitalized after she lost lung function. Lora’s grant was restored after she began speaking out in multiple media reports, but, she shared with me that, each year, “I’m a nervous wreck. My life is in pharma’s hands. They literally hold my ability to access the drugs in their hands.”

The scenarios created by our drug costs are dangerous for people with cystic fibrosis like Robert, Lora, and my son, Eli.

But the problems don’t end at simply being able to afford these medications.

Cystic fibrosis patients who have encountered sudden insurance changes have been sued for the cost of their drugs. Patients on Medicaid caught in legal battles over drug costs in states like Arkansas have experienced sharp downturns in health<sup>21</sup>. As ICER’s latest draft report notes, some major insurers have created restrictive criteria in some cases, forcing patients of children

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<sup>19</sup> [https://www.bizjournals.com/boston/blog/mass\\_roundup/2015/05/vertex-ceos-45-8m-pay-package-called-out-as.html](https://www.bizjournals.com/boston/blog/mass_roundup/2015/05/vertex-ceos-45-8m-pay-package-called-out-as.html)

<sup>20</sup> <https://www.axios.com/newsletters/axios-vitals-9a0834d4-db8a-4dde-8620-0637dc704fe3.html?chunk=0>

<sup>21</sup> <https://www.wsj.com/articles/arkansas-reaches-settlement-in-cystic-fibrosis-drug-suit-1423162197>

with cystic fibrosis and adults with CF to spend hours of precious time engaged in onerous appeals processes.<sup>22</sup>

Of course we are being forced to fight for coverage; the drugs were priced far too high from the start. And only the drug maker sets the price.

## **Conclusion**

Trikafta's price should be lowered. Orkambi, Kalydeco, and Symdeko are priced too high according to ICER's analysis. Vertex's profitability and executive compensation merely confirm that fact looking at the issue through another lens. Vertex does not deserve a high risk adjusted price as philanthropy and taxpayer-funded research lowered the risk for the company dramatically. Vertex could use its tax windfall to lower drug prices, but it is instead paying executives and buying back stock. It can easily lower the price to come in line with ICER's findings.

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<sup>22</sup> Tice JA, Kuntz KM, Wherry K, Chapman R, Seidner M, Pearson SD, Rind DM. Modulator Treatments for Cystic Fibrosis: Effectiveness and Value; Draft Evidence Report. Institute for Clinical and Economic Review, February 20, 2020. <https://icerreview.org/material/cystic-fibrosis-2-draft-evidence-report>, p. 17-22.

950 W Sierra Madre Ave, Apt 607  
Azusa, CA 91702

February 24, 2020

Institute for Clinical and Economic Review  
Two Liberty Square, Ninth Floor  
Boston, MA 02109

**To:** Jeffrey A. Tice, MD [Lead Author]  
**From:** Ryan A. Mincer [CF Patient on Trikafta]

I am writing to you in regards to your recently released draft report titled: Treatments for Cystic Fibrosis: Effectiveness and Value [dated 02/20/20]. I recently came across your report and reviewed its conclusions, which prompted me to write to you in protest. I am a patient with Cystic Fibrosis, who has been on Trikafta for about 4 months now; the drug called Trikafta has been nothing short of a miracle in my life. While Vertex Pharmaceuticals has been very clear to not refer to this drug as a “cure” – my personal experience is that it *\*should\** be referred to as a “cure-like therapy.” Before I started Trikafta, my lung function was at an FEV1 of 28% and my doctor was just about to refer me to the lung transplant clinic for an initial evaluation at UCLA Medical Center. I was at an all-time low emotionally, my health was deteriorating, I was sick all the time, my shortness of breath was debilitating, I was hopeless, I had just transitioned onto Long-Term Disability, and people in my immediate circle described me as looking like a cancer patient. Today, I am at 50% lung function, have a fully time job, my weight is up 20lbs, I have what feels like zero mucous in my lungs, I have amazing energy, and I am thriving in life. I have not felt this good in over a decade. My co-workers and boss all describe me as looking and acting like a new person. They comment about how I never cough anymore. And more importantly, I feel like a new person; I feel alive.

My concern about your report is that it will inadvertently take all of that away from me and many other people in the CF community who I care very deeply about. I understand that you represent a non-profit which is attempting to compile an unbiased perspective on cost-effectiveness by analyzing costs and benefits using historical models. I have no doubt that you achieved this goal and have produced quite an impressive analysis based on the data available to you. I also have no doubt that the individuals that analyzed and synthesized the data did so in a manner that was above-board, ethical, and exemplary. While I have not consumed ALL of the information in this impressive report (though I intend to eventually), as someone who has both Cystic Fibrosis and a Bachelor of Arts in Economics from UC San Diego, I have (as you can imagine) a great deal of respect for what you are attempting to do – and it is certainly an analysis that can and should be done to maximize patient outcomes. Relying solely on anecdotal evidence cannot and should not be the standard in any report such as this. Anecdotal evidence must surely be incorporated, but in a way that is quantitative and useful for decision-making. However, the language that you choose to utilize in this report can and will have a tremendous impact on the people that read it and take actions based on its findings. Even publishing this initial draft will likely get the attention of insurance companies to the detriment of Cystic Fibrosis patients.

Trikafta is an extremely expensive drug. There is no way of sugar-coating its \$311,000 annual cost. But as a patient, I want to tell you that I believe that this medication is worth every penny. If I had \$311,000 of disposable income (which I certainly do not), I would absolutely

spend every penny of it on this medication. That is why I am imploring you to reconsider how you couch your findings. For example, as part of your conclusions, you stated the following:

*"We found that CFTR modulator therapies plus best supportive care substantially improve patient health outcomes compared to best supportive care. **Because of the high cost of these drugs, however, the cost of CFTR modulator therapies exceed commonly used cost-effectiveness thresholds.** For ultra-rare diseases, decision-makers often give special considerations that lead to coverage and funding decisions at higher willingness-to-pay thresholds. We evaluated thresholds up to \$500,000 per QALY for Kalydeco and Symdeko with total eligible populations below 10,000 and **still found that drug prices would need to be reduced by about 35% to 51% to be considered cost effective at this threshold.**"*

If I am a health insurance company reading this draft report, my initial thought is going to be: "why are we paying for our covered patient (Ryan Mincer) to take this drug if it's not cost-effective?" That's a very dangerous and slippery slope that honestly scares me. I am scared of someday being denied this medication by my insurance company. I am scared of once again slipping into physical deterioration. I am scared that this report may inadvertently cause CF patients like myself to lose our precious quality-of-life or possibly even our lives because the numbers say that this drug is not cost-effective.

In writing this letter, I implore you to make two changes to your report:

1. Immediately recall and unpublish (remove from the internet) your \*draft\* report. Publishing your extensive research alongside these incendiary conclusions has the ability to turn heads to the detriment of, and discrimination against, patients with Cystic Fibrosis.
2. Change the way that you word your study conclusion so that you place a greater emphasis on quantitative quality-of-life data. The efficacy numbers for this drug speak for themselves. Trikafta is a good drug, an effective drug, and a relatively safe drug. I hope you can agree that quantitative quality-of-life data is an important and significant indicator of whether a drug is truly "cost-effective."

Thank you for taking the time to consider my position on your report; I am grateful that I have the opportunity to voice my concern.

Sincerely,

Ryan Anthony Mincer  
Azusa, CA 91702  
ryanmincer@gmail.com



# UNIVERSITY OF MINNESOTA

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Dr S D Pearson  
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Two Liberty Square, 9<sup>th</sup> Floor  
BOSTON MA 02109

18 March 2020

*Submitted via Email*

[Publiccomments@icer-review.org](mailto:Publiccomments@icer-review.org)

Dear Dr Pearson

## PUBLIC COMMENTS ON CYSTIC FIBROSIS EVIDENCE REPORT: MODELING AND EQ-5D-3L

As a professional health economist, with some 40 years experience, I have been concerned for some time with evidence standards and the lack of the standards of normal science in ICER modeled value frameworks. This applies more broadly to health technology assessment practices as advocated by groups such as ISPOR. I have published a number of commentaries on the lack of standards of normal science in the ICER value frameworks in the University of Minnesota journal *INNOVATIONS in Pharmacy* over the past 4 years<sup>1</sup>. My latest commentary considers your proposed 2020-2023 VAF<sup>2</sup>. In addition, I have just published a commentary on your draft evidence report on cystic fibrosis<sup>3</sup>. This should be considered alongside the questions I have below.

Please find attached a list of questions that I and colleagues at the University of Minnesota have in regard to the modeling of imaginary worlds to support value claims in respect of cystic fibrosis. I would appreciate your responses to the questions raised in respect of the cystic fibrosis evidence report. We would appreciate a response to each question. In previous of our public comments your responses have been vague and, in my and my colleagues view, have been misleading. I would encourage you to respond directly to the question and not make reference to 'agreed standards'. As you will no doubt agree, meeting the standards of normal science for claims that are credible, evaluable and replicable is the foundation for the discovery of new facts; not the acceptance of assumption driven imaginary worlds which recycle 'known' facts.

A particular concern is the assumption by those developing cost per QALY lifetime models that the EQ-5D has ratio measurement properties. It does not even have interval properties. The EQ-5D has only ordinal properties, it is a manifest scale, and should not be used to construct QALYs. If your staff are unaware of measurement properties for instruments in the social sciences for non-physical attributes, I would be pleased to explain this to them. Unfortunately, apart from the lack of scientific merit in constructing lifetime imaginary models, the misapplication of the EQ-5D -3L utilities means that your reference case model collapses. We note that Drummond et al in the last edition of their textbook maintain that the EQ-5D-3L has interval properties <sup>4</sup>. This is incorrect; their arguments are confused (I believe that they meant to assume ratio properties). I suggest the following references may assist you in exploring this question <sup>5 6 7 8 9</sup>. The issue is that the EQ-5D-3L was not designed to have interval properties. If you want to attempt to demonstrate it has (*ex post facto*) then you need to show that it has these properties for each disease state application (unidimensionality) for the target population.

I have, with the assistance of colleagues, prepared a detailed response list to your responses to our public comments on sickle cell disease. These are posted on the web at <file:///C:/Users/Paul/Downloads/Working%20Paper%20No.%205%20March%202020.pdf>

I note that your response to public comments are not released until the release of your final evidence report. As there has been some interest by colleagues, companies and others in the merits or otherwise of the ICER reference case VAF, these questions, as they are in the public domain, will be distributed. I am sure that they will be an issue at your cystic fibrosis review meeting.

Would you please acknowledge receipt of these questions.

Sincerely

Paul C Langley Ph.D.  
Adjunct Professor  
College of Pharmacy  
University of Minnesota  
Minneapolis MN  
Director  
Maimon Research LLC  
Tucson AZ 85750  
Tel: (520) 577 0436  
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**ICER: LONG TERM COST EFFECTIVENESS OF INTERVENTIONS FOR CYSTIC FIBROSIS: KALYDECO (IVACAFTOR); OKAMBI (LUMACAFTOR/IVACAFTOR); SYMDEKO (TEZACAFTOR); TRIKAFTA (ELEXACAFTOR/TEZACAFTOR/IVACAFTOR)**

**PUBLIC COMMENT QUESTIONS: VALUE ASSESMENT FRAMEWORK  
PLEASE RESPOND TO EACH QUESTION**

1.Fundamental Measurement (1)	<p>It appears that many people building simulated imaginary lifetime models (e.g., ICER Value Assessment Framework) believe that it is appropriate to consider the EQ-5D-3L (used in the cystic fibrosis model) as having ratio properties (i.e., a true zero). As this is incorrect would you explain why you persist? If you are unsure of the meaning of measurement scales, a full description of their mathematical properties is included in <a href="file:///C:/Users/Paul/Downloads/Working%20Paper%20No.%205%20March%202020.pdf">file:///C:/Users/Paul/Downloads/Working%20Paper%20No.%205%20March%202020.pdf</a></p> <p>You might also refer to the Bond and Cox reference on Rasch measurement theory.</p>
2.Fundamental Measurement (2)	<p>It has been recognized for almost 20 years that the EQ-5D-3L utilities are an ordinal manifest score as the basis for creating their utilities are responses on an ordinal scale for five symptom with three response levels for each symptom. If ICER believes this is not the case, in continuing to use the EQ-5D-3L, could ICER explain why they take this view? If you are unaware of this literature please consider the references below by Grimby et al, Tennant et al, McKenna et al (2 papers)</p>
3.Fundamental Measurement (3)	<p>If ICER rejects the notion of the EQ-5D-3L as an ordinal manifest score, could ICER demonstrate that, if we consider the interval measurement scale, that the EQ-5D-3L for the cystic fibrosis population has invariance of comparisons? Could ICER discuss this in the context of floor and ceiling effects? Is the utility difference between 0.4 and 0.45 equal to that between 0.8 and 0.85?</p>
4.Fundamental Measurement (4)	<p>If ICER accepts that the EQ-5D-3L has interval properties and moves to ratio properties, can ICER demonstrate that the EQ-5D-3L has a 'true zero'? How would ICER reconcile this to the fact that with the EQ-5D-3L preference algorithm the lowest utility value allowed is -0.59? Would ICER agree that this invalidates the notion of a 'true zero'.</p>
5.Fundamental Measurement (5)	<p>If ICER continues to apply the EQ-5D-3L in its models does the acceptance of the EQ-5D-3L with no 'true zero', i.e., a scale that allows (given distance from zero) multiplication and division, mean ICER accepts negative QALYs?</p>
5.Fundamental Measurement (6)	<p>If ICER accepts the existence of negative QALYs for a disease</p>

	state (i.e., EQ-5D-3L score < 1.0)) how does the ICER VAF factor this into lifetime QALYs?
6. QALYs (1)	ICER recognizes that the application of its value assessment framework rests on a belief that it is possible to create, within an imaginary lifetime model, claims expressed in terms of incremental costs per QALY for comparator products. If this is the case, how does ICER justify the creation of QALYs when it is demonstrably true that the EQ-5D-03L utilities fail to have ratio properties? In other words, you cannot multiply time spent in a disease state by an EQ-5D-3L score.
7.QALYs (2)	Given ICER's choice of utilities for constructing QALYs, could ICER demonstrate from one or more empirical assessments that the EQ-5D-3L has ratio fundamental measurement properties for the target cystic fibrosis hypothetical population in its reference case modeling?
8. Unidimensionality	It is accepted in the social sciences and indeed in the physical sciences that measurement scales should have the property of unidimensionality. That is, the focus should be on one attribute at a time. The EQ-5D-3L would appear to fail this standard in combining a number of health attributes into a single score? Would ICER agree or would ICER subscribe to the view that the EQ-5D-3L has demonstrable unidimensional properties? If so, could ICER demonstrate this for the target patient population?
9.Assumptions (1)	If ICER cannot demonstrate that the EQ-5D-3L has ratio properties (let alone latent measurement properties) how can ICER persevere with its value assessment framework and recommendations for pricing and affordability? If the EQ-5D-3L algorithm allows for negative utilities (which it does) then this is conclusive that there is no 'true zero' and the notion of a QALY collapses because multiplication is disallowed.
10.Assumptions (2)	Is ICER prepared to argue that while the EQ-5D-3L fails the standards of fundamental measurement, this is immaterial in its construction of imaginary value assessment frameworks as they are only driven by assumption anyway?
11.Claims (1)	Is the reference case imaginary lifetime model intended to generate credible, evaluable and replicable claims for cost-effectiveness? If not, why not?
12.Claims (2)	How much credibility should be attached to the ICER model when it is only one of many that could create imaginary claims in cystic fibrosis for the products assessed? What sets the ICER model apart from others?
13.Claims (3)	In the 2018 ISPOR task force report on health Economics (Neumann et al, <i>Value Health</i> 2018;21:119-25) it is determined that economic evaluations are intended, not to test hypotheses, but to inform decision makers of the approximate value of interventions in terms of imaginary

	incremental cost-per-QALYs gained. Does ICER subscribe to this view? How approximate is the modeled information in cystic fibrosis?
13.Claims (4)	In respect of 12 (above) how would ICER define the 'approximate value' of its cystic fibrosis modeling for incremental cost-per-QALY gains? How is this to be distinguished from 'approximate disinformation'?
14. Claims (5)	Where different utilities and model structures are presented in cystic fibrosis lifetime modeled claims, how would ICER propose that their modeled 'approximate information' is more 'approximate' than other modeled claims for 'approximate information'?
15.Unidimensionality	Could ICER detail whether or not the EQ-5D-3L, as a health related quality of life measure, has a latent unidimensional construct? If not, how are we to characterize the 'construct' (if any) that supports this instrument?
16.Rasch Measurement	It has been recognized since the 1960s (and in in health technology assessment since the 1990s) that if we are to capture the patient voice in therapy assessments we require a needs based QoL instrument to capture therapy impacts with interval measurement properties. Why has ICER continued to apply generic measures of HRQoL defended by what many see as a bogus population perspective argument? Could ICER provide their case for non-patient centric HRQoL measures?
17.Thresholds	In the modeled case for cystic fibrosis ICER makes there is a clear case, based on fundamental measurement, to reject the modeled cost-per-QALY claims? Given ICERs persistence with this flawed methodology, why should we take these threshold cost-per-QALY claims and pricing recommendations seriously? How does ICER defend these recommendations?
18. Imaginary Claims	Apart from the fatal measurement assumptions, ICER asks us to believe that is possible (even with the problematic EQ-5D-3L manifest score) that the claims for a range of outcome measures should be taken seriously? Is there any intent on ICER's behalf that these claims should meet the standards of normal science for credibility, evaluation and replication?

## REFERENCES

<sup>1</sup> <https://pubs.lib.umn.edu/index.php/innovations/section/view/formularyevaluations>

<sup>2</sup>Langley PC. Nonsense on Stilts – Part 1: The ICER 2020-2023 Value Assessment Framework for Constructing Imaginary Worlds. *InovPharm*. 2020;11(1):No. 12  
<https://pubs.lib.umn.edu/index.php/innovations/article/view/2444>

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<sup>3</sup> Langley P. More Unnecessary Imaginary Worlds – Part 3: Cystic Fibrosis and the Institute for Clinical and Economic Review's Draft Evidence Report. *InovPharm*.2020;11(1): No 15  
<https://pubs.lib.umn.edu/index.php/innovations/article/view/3056>

<sup>4</sup> Drummond M, Sculpher M, Claxton K et al. Methods for the Economic Evaluation of Health Care Programmes. 4<sup>th</sup> Ed. New York: Oxford University Press, 2015

<sup>5</sup> Bond T, Fox C. Applying the Rasch Model. 3<sup>rd</sup> Ed. New York: Routledge, 2015

<sup>6</sup> Grimby G, Tennant A, Tesio L. The use of raw scores from ordinal scales. Time to end malpractice. *J Rehabil Med*. 2012;44:97-98

<sup>7</sup> Tennant A, McKenna S, Hagell P. Application of Rasch analysis in the development and application of quality of life instruments. *Value Health*. 2004;7(! Suppl 1):S22-S26

<sup>8</sup> McKenna S, Heaney A, Wilburn J et al. Measurement of patient reported outcomes 1: The search for the Holy Grail. *J Med Econ*. 2019;22(6):516-522

<sup>9</sup> McKenna S, Heaney A, Wilburn J. Measurement of patient reported outcomes 2: Are current measures failing us? *J Med Econ*. 2019;22(6):S23-30

I have been on Trikafta for four months. I'm 36 years old and was diagnosed with CF at 15 months old. My life has changed significantly since being on Trikafta. Before Trikafta I was consistently sick and always on meds. I have a wife and two children and for the past few years, I've felt doomed to die before 40.

Since being on Trikafta, I feel 150% better. My lung function is up, I can take a deep breath (for the first time in 5 years), my energy level is amazing and I haven't been on any meds since starting. In fact, I've discontinued 4 other maintenance medications since being on Trikafta.

I haven't had any side effects and I'm excited about growing old with my family!

**Scott Bell** | CEO

*Where Companies Come to Grow!*



Steven D. Pearson, MD, President  
Institute for Clinical and Economic Review  
Two Liberty Square, Ninth Floor  
Boston, MA 02109

March 24, 2020

RE: Comments on the draft evidence report titled: “Modulator Treatments for Cystic Fibrosis: Effectiveness and Value”

Dear Dr. Pearson:

I am writing in regards to your company’s recent draft report which evaluates the cost effectiveness and value of CFTR modulator meds like Trikafta. **I thoroughly disagree** with your conclusion that Trikafta does not offer enough value, and is not worth paying for. I feel it is incredibly dangerous and irresponsible to conclude so. I hope you will **consider real, firsthand accounts** from people living with CF and the CF Community, and factor them into your currently one-sided report.

I have been living with Cystic Fibrosis for 26 years. My lungs have rapidly deteriorated in recent years. I had to quit my job, move back home and put my life on hold – that is until I started Trikafta. Thanks to Trikafta I am the healthiest I have ever been in my life. Trikafta has reversed my diabetes progression, dramatically increased my lung function and allowed me to return to work and actively contribute to our economy once again. In short – these meds which you don’t find enough value in have saved my life – you can’t put a simple score on that.

While these modulator meds may be costly in the short-term, long-term cost savings will be huge. As people with CF progress towards end-stage, costs rise astronomically. Between needing an organ transplant, spending months at a time on ivs in the hospital and needing additional care and meds for many spin-off diseases (diabetes, heart disease, sinus disease etc.), Cystic Fibrosis is most expensive to manage the further along it has been allowed to progress. With modulator meds like Trikafta, patients with CF will have much slower disease progression – many needing LESS meds, LESS hospital stays, LESS specialty doctors and LESS need for a double lung transplant.

With modulator meds like Trikafta we have the potential to transform a fatal disease into a manageable condition, and yet your report still advocates for “best supportive care” instead – the “supportive care” that we were all rapidly dying on before we had access to these modulator meds. Your advocacy for "best supportive care" over most effective care, is disturbing and unethical. How low have we fallen to advocate for cost savings over human life?



In short, the CFTR modulator meds have many long-term benefits and cost savings that vastly outweigh your concern over the current price point. I do not feel you have factored any of this into your report.

I hope you thoroughly reconsider your report and conclusion, and adjust your findings based on more well-rounded input and evidence. It's incredibly damaging to release a report like this without thoroughly demonstrating both sides.

Thank you for your time,

Colleen Black

To Whom It May Concern:

March 12, 2020

I am writing as a concerned citizen regarding ICER's CFTR Modulator Draft Evidence Report. I am the parent of a person with Cystic Fibrosis. We have waited 30 years for such a drug regimen as Trikafta. The results are unquestionable. My daughter is now testing as a normal person on her sweat chloride tests after only 4 weeks on this drug. After spending a lifetime of trying to survive the complications of this dreaded disease, she now has hope. We have hope for our daughter, and for all those like her, who've never dreamed of having a healthy and functionally normal life. CF patients spend every day with the uncertainty of what life will hold for them. Most of us dream of what we will do with our lives...what we will "be", who we will fall in love with, what our children will be like, and if we will get to travel, or if we will be able retire at some point. Cystic Fibrosis takes all of that dreaming away.

We strongly object to valuing a person's life based upon the cost. We love people, young and old. We value all people, with all of their imperfections. We value those who are disabled, mentally or physically. We even value those who can't "give back".

The beauty of being an American is that we are taught to dream. We don't accept the status quo. We race to find answers and cures, so that people have a better life. This is our culture. This is who we are. To divert from that thinking process is be un-American. I understand economics very well. I understand that these treatments and therapies cost much. If we base our value upon evidence reports, such as ICER's, we are essentially shutting down the value of discovery for all of our future. There is absolutely no reason to search for or develop cures for diseases. Essentially, this report and others like convey that survival of the fittest is what is important...letting those who are weaker die off, so that society can be rid of the burden of them. Society won't have to look at them any longer. However, because of the world we live in, I can guarantee you that eventually all of us will become weak and sick and will need help. The lack of value for people's lives will catch up, and there will be no care to cure anybody. Please remember what we value in this country, and that is to value the lives of our fellow man/woman.

We object to ICER's Quality Adjusted Life Year numeric value of people, as payers may use this report to justify denial of coverage for these therapies.

Sincerely, Marie C. Caulkins

March 4, 2020

Dear ICER

I am writing regarding your review of CFTR modulators cost-effectiveness and clinical value for Cystic Fibrosis patients. My daughter, Elizabeth, is almost 4 year old and has Cystic Fibrosis. She was fortunate to be among the first to receive one of these modulators (Ivacaftor) at an early age, just after her 1<sup>st</sup> birthday. The benefits of this treatment were immediate and continue to be profound. On the 3<sup>rd</sup> day she was on the drug I went into her bedroom to check on her and was terrified to hear silence. She always had a noisy nasally sound to her breathing. We referred to her as her brothers noise machine at night. That evening I was certain she had stopped breathing but when I rushed to her crib I started to cry as I realized she was fine and the modulator was working. Her breathing has been normal ever since. She has also not been hospitalized or had any respiratory exasperation since.

While respiratory health is always a primary fear with CF, growth and development are also significant concerns because of the excess mucus in the digestive system. Elizabeth's height and weight have continued to climb and we recently discovered that while she had been seriously pancreatic insufficient she has had full pancreatic recovery. She no longer needs enzymes to digest her food. Her most recent Dr visit put her weight in the 73<sup>rd</sup> percentile and height in the 93<sup>rd</sup> percentile.

This miracle drug has not only given us these tremendous health benefits it has allowed us to return to an almost normal family life. We no longer have to live in fear of the common cold. We no longer have to skip pre-school programs that include lunch but don't have instructors authorized to administer medication. We can leave our daughter with friends or a babysitters without a training session on how to administer her enzymes if she has a glass of milk or a snack. We no longer have to worry about taking weeks off of work while she is hospitalized. We no longer have to find time for extra nebulizer and physical therapy sessions to combat infections. She goes to school, rides her bike, plays with her friends, loves to dance, she grows out of her sparkly dress but refuses to get rid of it because its so beautiful, and participates in all that life has to offer. When you ask her what she is going to be when she grows up she say "a Mom". Before starting this modulator that reply would have been heartbreakingly unlikely. Now it is a real possibility. What is the price tag for that kind of gift?

Elizabeth continues to adhere to her twice-daily vest therapies and multiple nebulizer treatments to reduce the risk of any respiratory infections, which last about 30 minutes each session. This dictates the schedule of our entire family. A simple request by our kids to go camping last summer required extra planning to ensure we could have access to electricity to run her vest and nebulizer. Studies are underway now to see if it is safe to reduce these treatments. While we are glad to comply with the therapy schedule to ensure her good health the time constraints are significant and harder to manage as Elizabeth gets older. They are anticipating that this treatment burden will be reduced as a

result of these modulators which will allow for a much more normal life for Elizabeth and the rest of our family.

Thank you for your consideration,

Christy Clow

I am 36 years old. I have one DeltaF508 gene & one unidentifiable gene. I started taking trikafta in November of 2019. My life has changed drastically for the better! I finally feel like a normal person. I can breathe out without wheezing. I can be out in the cold without having coughing fits. I can laugh again without going into coughing fits. I can take in a huge deep breath. I can sleep in without waking up having coughing fits every morning. I literally don't cough anymore. My lung function has improved 10% I've been able to gain weight and keep it on. I don't know what I would do without this medication. It is the closest thing to a cure. I have not had any side effects. It is truly a miracle!

Ashley

To whom it may concern,

I have been taking Trikafta for 2 months and I can honestly say it is a miracle drug. To have lived my entire life, 54 years, with a disease that is a death sentence and in a matter of days your life does a 100% turn around is unbelievable. There are no words that can express what it feels like to be able to breathe easily and not feel consistently short of breaths. I cannot imagine my life without this medication and having to go back to those very sick days. Everyday I am in amazement on how my life has changed in such a short period of time. Thank you Vertex for saving my life.

Dr. Maria Valdes-Dominguez

## Vertex triple therapy review

My daughter is a 13-year-old with Cystic Fibrosis. She began Trikafta three months ago. Her lung function went from 70% to 100% in only three short weeks. She is up at least 11 pounds. She hasn't gained a total of 11 pounds in years, and now she's gained it in only months. She went from being sick and coughing her whole life and not gaining weight, to being like she doesn't even have the disease. Although the disease is still present, the symptoms of the disease are not. This slows and/or stops progression. It has been life changing. The medication is necessary for all cystic fibrosis patients who have the genetic makeup to use it. It is life changing. Please consider passing these statements along from a cystic fibrosis mother, who will not give up on her kids!

February 26, 2020

Institute for Clinical and Economic Review (ICER)  
2 Liberty Square, 9<sup>th</sup> Floor  
Boston, MA 02109

Dear Sir or Madame,

We are the parents of a beautiful baby girl who suffers the debilitating and life-altering effects of cystic fibrosis (CF). Our daughter is barely three months old and has already undergone three complicated and life-threatening surgeries, resulting in her spending nearly half of her life in the neonatal intensive care unit.

As responsible and loving parents, we want to convey the following points regarding ICER's Draft Evidence Report assessing the comparative clinical effectiveness and value of treatments for cystic fibrosis:

- 1) Quality-Adjusted Life Years (QALY) calculations should not be used to justify/deny coverage or restrict a doctor's power to prescribe medication to a patient with a chronic disease, including CF.
- 2) Denying CFTR modulators to CF patients simply based on a cost-effectiveness argument fails to consider that these patients will eventually require recurring hospitalizations (as our daughter has experienced), painful and costly medical procedures (as our daughter has undergone), and disability income assistance (which we hope to avoid in the future).
- 3) Using a discriminatory and narrow-minded cost-effectiveness model prevents access to breakthrough medications that not only improve the lives of current patients but also discourages future innovations that could lead to a cure for CF.

We hope you take into account similar messages from CF patients, parents with children who suffer from CF, non-profits, research institutes, and medical professionals.

Sincerely,  
Daniel and Andrea Freiman  
Miami, FL



Good morning,

I am a parent of an 18 year old CFer and wanted to provide our input of the new CFTR Modulator Trikafta.

My daughter Makenzie has both copies of the Delta f508 gene defect and began taking Trikafta in November. She had just been hospitalized from October 16-31 due to the typical CF exacerbation causing low lung function. When she went into the hospital on the 16th her FEV1 was 52% (down from 59% just a month prior), when she was discharged on October 31 her FEV1 was only 53%.

As soon as she started taking Trikafta we noticed change immediately. After only two days of the medication Makenzie started coughing up mucus nonstop, she lost her voice for a full week due to the coughing but it was only temporary. After the cough settled down the most incredible change is she started getting an appetite. For the first time she was starving for every meal and had to take snacks to school just to make it between meal times.

A month after taking Trikafta her lung function improved by 14% to 67%. The highest we have seen in years. At her most recent check-up in February her lung function remained the same which was actually surprising to her because she feels better than ever and even said she hardly feels like she has CF anymore.

We are very grateful for the new drug as we have been seeing a steady decline and at times discussed the possibility lung transplant but we don't feel like we'll be going down that road anytime soon thanks to Trikafta.

Sara

No one says it more effectively than this user of the drug who's life is so vastly improved.

<https://amayasora2992.livejournal.com/223743.html>

You need to withdraw this farce of a report and wait five years until more data exists, then, if it works just say so and let people keep getting it.

Honestly,

Deidre Hammon  
Senior Advocate  
CSD Children's Advocacy Project

February 21, 2020

## Patient and Family participation in ICER review regarding cystic fibrosis modulators

My six year old daughter, Penny, has cystic fibrosis. Cystic fibrosis (CF) is a genetic, life limiting disease that primarily affects the respiratory and digestive systems. When Penny was three weeks old, we were told she had a life expectancy of 38 years old.

Currently, Penny does an hour of treatments per day - when she is healthy. She does two or more hours a day when she is sick. Penny started taking medications at 3 weeks old and by 8 months old she was swallowing pills. At her peak she was taking more than 25 pills a day to keep her body working the way it should. When she was 2 the FDA approved a lifesaving medication called Kalydeco for her age group and because of this drug she is down to three pills a day. This is a true miracle for our family and has made caring for her much easier. With the medication, Penny is now able to gain weight, her lung function has improved, and her pancreatic function has been restored. Because of Kalydeco Penny hasn't had a hospital stay since she was 4 months old, which is uncommon for cystic fibrosis patients.

From a purely business point of view, Kalydeco has saved our insurance hundreds of thousands to millions of dollars in hospital stays, doctor and specialist visits, medications, and therapies. Kalydeco has eliminated her need for multiple daily medications. She has not been on antibiotics for over a year which also translates to not having had as many sick visits to the doctor and specialists. She has not had any hospital stays since beginning Kalydeco.

By the numbers, Penny's pulmonary function test is at 122%. Her pancreatic function is <500 and prior to Kalydeco it was 18. Her BMI is up to 51% when prior to Kalydeco, she was hovering around 10%.

Kalydeco and eventually Trikafta will allow our daughter to live her life. It will let her be a contributing member of society. No one will know what those with CF allowed to live their lives to their full potential will be able to do.

While I know the cost of modulators are astronomical, please revise your recommendation in the affirmative for CF modulators.

I am a 39 year old woman living with Cystic Fibrosis. I was diagnosed at 1 year old back in 1981. Back then, my mother was told that I would not live to be an adult. You can imagine, if you try, the ramifications this would have on any parent. Hearing that your baby would be lucky to live to be 5 years old. This disease devastated my mother. She never left my side and cared for me the best she could. I turned out to be one of the lucky ones, many of my friends growing up weren't as fortunate.

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> If you take a moment you can also try to imagine what it would be like for your entire childhood, wondering when you might be next to go. Knowing, because all of the people that have cared for you your whole life keep telling you, that you will never "grow up." The ramifications for me were huge. I didn't try to take care of myself, I felt there was no point. After all, I had many friends that took care of themselves, and they also died far too young. I didn't worry about my education or dream of my future career or college. I lived in the moment and I tried as hard as I could to ignore this horrible disease. Every few months or so I would be reminded at a clinic visit or a hospital admission for 14 days worth of needles, IV's, antibiotics and breathing treatments 4 times a day. Don't get me wrong, I had made many friends at the hospital among staff and patients alike and I made the best of it. It doesn't change the fact that I had needles poked into me everyday for 14 days straight, because the harsh antibiotics would literally burn through my little veins causing them to infiltrate. This would cause huge painful lumps under my skin where the fluid was. It would take multiple sticks to place a new IV and this happened everyday. I would cry and scream, I would hide under the bed and lock myself in the bathroom. Again, this wasn't only happening to me, imagine being a parent and having to see your child go through this, and knowing how much it hurt them, and at the same time knowing that was what it took to keep them alive.

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> I obviously made it through all of that and I am stronger for it. Eventually I stopped believing that I would die any day now. Better treatments had come along and I was doing pretty good. Then, in 2016 I contracted a new bacteria in my lungs on top of my normal colonization of antibiotic resistant pseudomonas. The 2 new bacteria were called micro bacterium abcessus and micro bacterium avium. These new bugs proved extremely hard to treat and detrimental to my health and lung function. Before these new infections my lung function held pretty steady around 54% of normal. After these infections my lung function would not come out of the 30's. No matter how hard I tried, and try I did. I was on 2 types of oral antibiotics and 2-4 types of iv antibiotics, along with 2 types of inhaled antibiotics and steroids - for 18 months! Read that again please. The impact this infection had reached everyone and everywhere in my life. I couldn't work, my relationships suffered because I was miserable. My family worried about me. I was in the hospital 5 times for 10-22 days at a time. I needed supplemental oxygen 24/7.

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> So you may be wondering, what changed? In 2017 I was lucky enough to start Symdeko on compassionate use, because I had rapidly lost so much of my LF. After starting symdeko my rapid, steady LF decline stopped! I was able to clear my micro bacterium infections. I felt much more like myself again. I got off of 24/7 oxygen, I didn't go inpatient to the hospital for 12 months!!! I wasn't able to regain much LF but I was able to hold steady at 38-40% and I was happy because my quality of life was a hundred times better than the entire year prior. In 2018 something spectacular happened. I was asked to join the triple therapy drug trial (Trikafta). When I started the study I was given placebo, which was Symdeko only, instead of Trikafta. I know this now, because nothing changed (bad or good). However 6 weeks later I was rolled into the open label study and actually given the triple therapy. Well, that I noticed! About 6 hours after my very first dose I started to cough. I coughed up about a Dixie cup worth of sputum every few hours for 2 days straight!!! This drug was completely clearing my airways of all that thick, sticky disgusting, bacteria breeding mucus. After being on the drug for 2 weeks my LF increased to 44, then 46 and now it is 48%. I was also able to gain weight, and for the first time in my entire life I am at a healthy weight. After 38 years of malabsorption and being under weight, I achieved a normal body weight after about 3 months on Trikafta. That may not be huge to you, but I am old as far as CF patients

go. I have had 39 years of lung damage from constant infections and blocked airways and inflammation. And even still this drug has changed my life 1000% for the better!!! I feel more like myself. I am active. I do yoga, I can walk my dogs. I can laugh without a 5 minute coughing attack after. I can grocery shop without needing a 2 hour nap after. I can wash my hair without getting short of breath (yeah that used to happen). I will be turning 40 in April and I never thought I'd get here. In 2016 I didn't think I'd make it to 37. Thanks to Vertex I did. With all that being said this drug can completely change the trajectory of someone's life with CF. I just imagine all the kids 12 and up starting this medication and feeling "normal", them not getting sick and hospitalized every few months and missing school. Them having hope for the future. Knowing full well that they should plan for the future because it's coming! The ability to exercise and play sports and strengthen their lungs and keep them strong.

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> Most people with CF eventually colonize pseudomonas. This bacteria is deadly. Trikafta can change that! This medication thins the sputum in our lungs to an incredible degree. Making it possible to cough out and keep our airways clear. It makes our cells function at a "normal" level. Meaning sweat test results can be within normal limits. This medication can completely change the trajectory of this disease. It is not a cure, but it is the closest thing that I've seen in my lifetime. I want to see the children with CF live more normal lives. I want them to hope for the future. I want them to avoid being colonized with these deadly resistant strains of bacteria.

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> Please think about the young people with CF and about their families. Imagine if you or someone you care about had to go through all of this to have mediocre health and a promise to die young. Now imagine that there are 3 pills that you can take and all of that changes. Would it be worth it?

I have been on this drugs since the beginning of its clinical trials in cf patients with heterozygous mutations. It has exponentially increased my quality of life.

Before Trikafta- I coughed throughout the day, people always thought I had a cold. I coughed throughout the night worse than throughout the day and struggled to get quality sleep. I had to buy an adjustable frame for my bed so I could sleep more upright to minimize coughing spells at night. Mentally I had very serious fears and anxiety about my health deteriorating despite excellent therapy compliance, daily exercise and doing everything in my power to stay as healthy as I could. My exercise tolerance allowed me to alternate jogging and walking for maybe 30 minutes or so. I coughed up a significant amount of mucus daily and felt like I could do my treatments many times per day and still have mucus stuck in my lungs.

After Trikafta- Zero cough during the day. Zero cough at night. No need to ever put my bed in an upright position to sleep well throughout the night. Mentally I am happier than ever and able to make serious plans for my future with no fear or anxiety. My exercise tolerance within the first week or two of taking the drug blew my mind- I was able to job without walking or stopping for 45 minutes, something I've never been able to do before. I continue to do all my therapies daily, but I barely cough up anything any more. I never feel congested any more.

As far as side effects, I have tolerated Trikafta very well. My only side effect is some cystic acne- sometimes it's worse than other times- it seems to flare up and calm down with no rhyme or reason, but I will take the acne in exchange for feeling healthy again.

This medication has been truly life altering for me. I feel as though this drug has added many years to my life and much confidence in my future. It is the best thing that has ever happened to me. It's not a cure for CF, but it is a miracle drug!

Sincerely,

Kym

To whom it may Concern,

I am a mother of a sweet, loving son that was cursed with Cystic Fibrosis. Colby is 18 years old and a senior in high school. His health has been in my opinion good for a cf warrior. He loves sports. He started basketball and baseball at 3 years old. Over the years he focused on baseball. He loves the sport and gives it his all. However, over the years his health has weighed him down some. Conditioning, practices, games, several late nights after away games followed by an hour of CF treatments, have taken a toll. It wasn't until about six weeks ago when he started taking Trikafta that he began having the stamina to make it through entire practice sessions. Not only has Colby seen a difference, teachers, classmates, friends, and family members that were unaware of the new medicine have noticed the difference. To compare Trikafta to Orkambi and Symdeco (which we have tried both), is not close to a fair comparison. Those medications made little to no difference in my sons health. We just had his first check up since starting Trikafta. His BMI has been stuck around 25-30 percentile for years, however, he is now in the 46 percentile. Although this is outstanding for a CF patient, that isn't even a tip of the iceberg for what Trikafta has done for him. His lung function increased 12% after 5-6 weeks of this miracle drug. My son's PFT was 101%, a number we have not seen often or in a long while, and to be honest didn't know if we'd ever see again. Please imagine your child receiving a treatment that absolutely changed their present condition, their outlook on life, their future plans, and just how they feel daily, only to hear it isn't a cost effective option. Do you put a dollar amount on your children, spouses, or any loved ones health? My son has went from coughing until vomiting daily to clearing his throat maybe 3 times a week. He can actually breathe and take deep breaths now!! Have you ever ran a mile and then regained your breath only by breathing through a straw? I didn't think so. This is how CF patients feel on a daily basis without activity, UNTIL TRIKAFTA!! We just overcame flu with temps up to 104.8, lying in bed for 4 days, barely drinking and barely eating. Colby lost 7 pounds through this round of the flu and still had the BMI and lung function increase. The fact that we didn't end up missing 2-3 weeks of his senior year due to an admittance to the hospital as a result of the flu was simply a miracle. That miracle has a name, it's TRIKAFTA. Please realize the importance of this medication in all families impacted by Cystic Fibrosis before you decide if this drug is cost effective.

Thank You for your time.  
Lori Lear

Dear Sir or Madam,

I understand your organization is reviewing the efficacy and cost of Orkambi, Symdeco and Trikafta. My 35-year old daughter has CF and has benefitted from each of these medications, with the benefit growing as each was introduced.

I do understand why cost is being reviewed, as these medicines have been expensive, but I sincerely hope you are looking at the long-term likely impact of what all this research will bring to 90% of patients with CF. Each modulator was an improvement over the first, and I cannot begin to describe the wonderful results my daughter and thousands of other CF patients are seeing with Trikafta.

Orkambi was a start, that was not tolerated well by some patients but for those who got a benefit, the change was real. To gain weight, to be able to breath just a bit more easily is a BIG deal with this disease. The scientists also used what they learned from Orkambi to develop Symdeco. My daughter found Symdeco did make a difference for her, whereas she did not experience very much change with Orkambi.

For Katie, who was 33 when she started Symdeco she had just come off 2 years of significantly declining health. Symdeco helped to stop the slide. With a progressive disease, stopping the slide is as important as improvement. I know scientists want to know how many FEV percentage points were gained. But when a 33-34 year old with CF can stop declining at 50% lung function, that is a WIN! She has not been hospitalized in two years. How much money does that save? Probably more than the cost of the medicine.

Finally, in November of 2019 she started Trikafta. After just one week, Katie could work out in the gym without having a coughing fit. She "didn't feel her lungs any more." Imagine living every day of your life as if you were in the final days of bronchitis. Then all of a sudden, the bronchitis is over. You can take a deep breath. Her 5 year old son once again has a Mom who can go for a hike. She can play with him more often and more vigorously. And she can catch the cold he brings home from kindergarten without being admitted to the hospital.

The long-term impacts of these drugs are yet to be seen. For the 12-year olds who just started Trikafta the impact will be lungs that never develop the scar tissue my daughter has. Young men who will not be sterile. A young woman who can become pregnant without IVF or other medical assistance. Patients who won't develop CF-Related diabetes. Fewer antibiotics, fewer nebulized medications. This is not a cure, but it is pretty darn close. Please understand the "math" on Trikafta is far from done.

Finally, I had a conversation with a CF physician yesterday and I asked him how much this is changing his world. He said, "we only have 3 adult CF patients in the hospital today. Normally, we'd have around 12 at this time of year. And none of the patients in the hospital are on Trikafta." We need medicine like Trikafta for ALL CF patients. We do not need this gain to be taken away or undermined by an agency that is only looking at out-of-pocket expense. We have to look at the full picture of the human health, happiness and hope these medicines have brought to patients and families across the country.

Thank you for your consideration.

Eileen McConville  
Hampstead, NC



To whom it may concern. My name is John McDermott. I am 59 years old and have Cystic Fibrosis (CF) which was diagnosed at 6 months of age. On 12/4/2019 I started on Trikafta. Within two weeks I stopped coughing up copious amounts of phlegm every day. Imagine coughing up phlegm every day of your life for almost 59 years and then suddenly you stop all because of one medication in pill form.

In January of 2020 I developed a cold. For the last twenty years a simple cold for me resulted in a CF exacerbation requiring hospitalization and IV antibiotics for two to three weeks. The cold I developed in January of 2020 went away in 12 days without the need for antibiotics or the hospital. I credit Trikafta for this hospital avoidance.

Often I review my health insurance explanation of benefit forms. A typical hospitalization for me would usually cost (the amount paid not billed) in excess of sixty thousand dollars. During this time I would be unable to work costing me gross income of ten thousand dollars.

I have been on other CFTR modulators (Orkambi then Symdeko) since February of 2017. Over this time period my need for NPH insulin has decreased 50%. My lung function (FEV 1) has increased from 46% of predicted to 60% of predicted. I feel better and am able to work more.

Trikafta for me is life changing. It is also life changing for most of the CF patient population. My only complaint is that it was not available for me until I reached age 59. Thank you for considering my comments.

I am a 27 year old woman living with cystic fibrosis (cf). As a child, I thought this was no big deal- I still had friendships, hobbies (dancing, reading and nature related especially), and what I felt was a fairly normal life despite daily treatments and having to learn to take dozens of pills a day while my peers still struggled to down a liquid cough syrup. I even went to school and entered high school despite being told at the age of 10 I would be lucky to maintain that or even reach the age of 30. I largely blew off most of that and believed none of that would truly reach me.

Things began to change around 10th grade. For the first time since childhood, I found myself seriously ill and hospitalized. I was suddenly truly confronted with my own mortality in a way most teenagers avoid. I began to be the “weird sick kid” at school, I missed classes due to illness, and I became severely depressed. Over the remaining years of high school, I found myself isolated and with little hope of graduating after so many absences. And it was a struggle- despite note after note from my clinic, my high school made little effort to accommodate my needs and I barely received a diploma despite making up missed work. I was left fearing the same would happen in college and wondering if it was even possible to attempt it. New protein modulators began to appear on the market, promising hope—but none of them were approved for my geno type.

Fast forward a few years. The yearly hospital stays increased to 2 or 3, but I was still able to work and attend college online. But, rapidly, my exacerbations increased to the point I was forced to quit my job in order to focus on school- both at once was too much. At first it went ok, but it wasn’t long before I began experiencing the same problems I had in high school- too many absences from hospitalization. University’s say they will accommodate people with disabilities (certified), but the truth is those of us with invisible chronic illnesses often face a different reality.

By the age of 25-26 I was admitted roughly every 2 months for 2-3 weeks of antibiotics. School soon became an impossibility, and I became isolated again.

Cut to age 27: a new protein modulator, Trikafta, was approved early by the FDA- and I actually qualified for this one. My pulmonologists were eager to start me on it and at the very least stem, if not improve, my lung function decline.

I was hesitant at first—I had heard of a litany of unpleasant side effects caused by trikafta—but, as I began to despair of ever reaching some sense of normalcy again, I knew I had to try it.

Within a month, I had started trikafta. The first week or so was unpleasant as promised, but not drastically different than any other exacerbation I’d weathered. My biggest fear was of the trikafta failing to improve anything.

But just about 10 days after starting, I realized something: for the first time in memory, I had gone several hours without coughing. I began to have increased stamina; the dog walks that normally exhausted me after just 5 min were increasing to 10, 15, 20 min walks. Within a month, I was exercising in the gym for 45 min most days of the week. My partner mentioned I wasn’t even coughing at night while supine- I was actually sleeping. The trademark cough I’d had all my life (often used by friends and family to locate me in stores) was barely present, and sounded like a small clearing of the throat. The real shock came at my 3 month trikafta follow up: my pft’s, which had been hovering at 67% post hospital, upper 30s and low 40s while admitted, had increased to 85%.

I began to think of the future, to plan my wedding in earnest, to live. I realized school could once again be an option and even completed—one day I would work in my chosen field with a degree and contribute to society in a meaningful way.

To say trikafta is important to those with cf is a drastic understatement. Trikafta is life-changing and necessary for life. It is the difference between a life of solitude and decline, watching others live as we wither and wish. Even those who cannot qualify for trikafta at last have a real hope of finally having a drug developed which encompasses ALL variants of cf. For those who are compassionate, it is obvious to recommend loss of insurance coverage for this drug would be utmost cruelty. For those concerned with pure financial value of life, this is the best path to allow those with cf to spend less time hospitalized (which equals less cost) and the utilization of newly healthy individuals in the work force or as volunteers for various societal needs.

In the end, ask yourselves, would you place a number on the worth of your loved ones? Wouldn't you pay it?

Sincerely,

Rochel

To whom it may concern, This drug has saved my life. I went from coughing everyday to having no cough and eliminating a lot of mucus out of my body. This means less pain; less stomach pain, more controlled blood glucose levels, less coughing nonstop. This medicine has also given me hope about being able to have children as well as many other Women with CF.

Now with the CoronaVirus this medicine that has helped get rid of excess mucus in my lungs, if I were to get this virus god forbid but my chances are better than if I were not on Trikafta.

The side effects I had were only short lived and the positive of this medicine outweighs the few side effects I had. Everyone's body reacts differently to this medicine and if they don't like the side effects than they shouldn't take it. The money that is going towards this medicine should not be stopped because some people have bad side effects. Our lives are important and this medicine shouldn't be taken from us. It has given me hope, happiness, and less pain. Please continue with CFTR modulators.

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♥-Maddie-



March 24, 2020

Emily A. Schaller  
Rock CF Foundation  
2990 W. Grand Blvd, STE M21  
Detroit, MI 48202

*Re: Comments on the Draft Evidence Report titled: "Modulator Treatments for Cystic Fibrosis: Effectiveness and Value"*

To whom it may concern:

I am writing to share my experience of living with cystic fibrosis and how the modulator treatments have immensely improved my life. As you are aware, ivacaftor was the first medication available to target the underlying cause of cystic fibrosis, and I've been lucky enough to have been on it since the Phase 3 clinical trial. Ivacaftor has been groundbreaking scientifically, but even more so clinically. Since the approval of ivacaftor three other modulators have been approved to treat the majority of those living with cystic fibrosis.

When I was diagnosed with cystic fibrosis in 1983, I was 18 months old. Upon diagnosis my parents were told that I might not live long enough to graduate from high school. At the time there were minimal treatments available for CF. Aside from the few pills I had to take, my parents had to perform manual chest percussion therapy several times a day to help me clear the mucus from my lungs. This mucus is what traps bacteria and causes recurring lung infections.

To ICER Review Board:

I have heard that the review of Trikafta is showing how the pros are not outweighing the financial cost. I disagree with this stance. Therefore, I would like to submit my personal experience on this life changing medication for your consideration.

I on Week 5 of Trikafta. The impact it has already made on my Cystic Fibrosis related symptoms are outstanding!

1) Hitherto, I was unable to sleep laying down. Laying flat was too difficult to breath so slept propped up with several pillows. By Day 3 on this miracle drug I was able to sleep completely flat. It has been YEARS since I could do that!

2) When I first wake up in the mornings I was unable to take anything more than shallow breaths, coupled with tremendous coughing as too much phelm had built up in my upper airways during the night. Within ONE WEEK of Trikafta I have since been able to take a complete, full, deep breath right after waking up, before starting any chest physiotherapy, without ANY coughing. Zero coughing.

3) I have not had ANY negative symptoms from taking Trikafta that I know others have experienced. I have an increased appetite, more positive outlook on daily life and the future. This has given me a new lease on life!! To say I am happy is an understatement. I am excited about the future, no longer scared of it.

4) On Wednesday was my one month follow up with my CF Clinic. Just prior to get the Rx for Trikafta, my FEV1 was 60%. One month later, my FEV1 was 74%! A 14 percent increase in 30 days! Unbelievable results.

I have waited my entire life for a drug to be this effective in minimizing and even stopping some of the worst symptoms of Cystic Fibrosis.

The extremely positive emotional, mental, and physical changes I have experienced in the last month showed me how vital it is for everyone with Cystic Fibrosis to have access to Trikafta.

“Basic human rights” is a popular, sometimes overused, catch phrase right now. But this drug has given me the very basic human right - the ability to BREATHE! I absolutely NEED to stay on this drug, as well as the tens of thousands of others just like me in America today.

Please reconsider your stance of the cost effectiveness of this lifesaving drug.

Thank you for your time.

Sincerely,

Sarah Syme

Lancaster, CA, USA

Throughout my three decades of life I have seen CF treatments evolve from vitamins and enzymes to aid with digestion and growth, to treatments that help control the respiratory disease. Today we have four treatments available that target the underlying cause of CF. This is significant for the cystic fibrosis community because we are seeing vast improvements in health which is leading to less costly hospitalizations, surgeries and treatments.

The personal improvements that I have seen with my health have been an increase in lung function from the mid 50's to the 80's. Chronic lung infections that would land me in the hospital several times a year have been reduced to once every two or three years. This is because the thick mucus in my lungs has been vastly reduced. My weight has stabilized, my chronic sinusitis has disappeared, and my quality of life is on par with those in my age group.

Before ivacaftor I was living on Social Security and Disability and uncertain about not only my health, but also my financial stability. Because of the life changing outcomes I've experienced from ivacaftor, I now work full time for the Rock CF Foundation, a non profit that I founded in 2007 to heighten public awareness about cystic fibrosis and empower others with CF to lead a healthier positive life. In 2015 I purchased my own home, and have since set up a retirement fund. I've run three full marathons and over a dozen half marathons. All of this possible because of ivacaftor.

While what I am sharing with you is awesome, it has felt quite conflicting to be excited about my experiences sometimes. Ivacaftor only treats 4-8% of the CF population which is roughly 1,200 people. In 2019 things changed when Trikafta was approved by the FDA. Because of the tireless work of Vertex and the CF community this treatment will benefit roughly 90% of my friends in the CF community, and future generations of cystic fibrosis patients. I am now witnessing my friend experience results like mine and there is nothing in the world that should stop anyone from receiving these treatments and rewriting the story of cystic fibrosis.

Sincerely,

Emily A. Schaller

February 24, 2020

Institute for Clinical and Economic Review

RE: Modulator Treatments for Cystic Fibrosis

To Whom It May Concern,

I am writing in response to your drafted analysis of CFTR protein modulator treatments for cystic fibrosis patients. I am a 19-year-old female with cystic fibrosis (deltaF508), currently studying biology, microbiology, and chemistry and the University of North Carolina. I propose that your drafted analysis of CFTR modulators is reductive and insufficiently considers the change in quality of life and mental health experienced by patients undergoing this treatment.

I began TRIKAFTA (elexacaftor/tezacaftor/ivacaftor) on November 21, 2019, after approximately one year of taking SYMDECO (tezacaftor/ivacaftor). Six days prior to beginning treatment with TRIKAFTA, my FEV1 was 82%. On December 6, 2019 (approximately two weeks after beginning TRIKAFTA), my FEV1 was 120% - a 38% increase in FEV1 over two weeks. In addition, I regularly cultured 3+ *B. cepacia* before beginning treatment with TRIKAFTA. I have not cultured *B. cepacia* at all since beginning treatment with TRIKAFTA.

While these numbers are incredible and reflective of a pivotal transition in my life, they do not provide the whole picture. But I am beginning to doubt the feasibility of quantifying the “whole picture” of this treatment. Where my entire life has changed, words fail me wholly. I have been trying, since the day I started TRIKAFTA, to quantify my experience. I don’t think that I will ever be able to fully convey the weight of the change that this medication has made in my life. Instead, I can only provide snapshots of my life with TRIKAFTA: turning around in the PFT lab to see my best friend, who has attended every monthly CF clinic with me for years, in tears. The doctor that has been treating me for years saying, “Wow. Your whole future is ahead of you, huh?” for the first time. Laughing without coughing. Climbing stairs on my own. Sleeping through the night without my lungs filling with blood and waking me up. Having enough oxygen to sing in the shower for the first time. Holding a conversation without getting out of breath. Planning for a future that is suddenly not a pipe dream. Can you imagine? Nineteen years of putting your life on hold for hospital visits and treatments, fervently trying to fit a whole lifetime worth of happiness, love, and hope into twenty-odd years? And then, suddenly, thinking past tomorrow for the first time in your life. Are there even words – let alone numbers – that appropriately convey that weight?

I implore you to consider: are numbers all that matter? Can the value of human life be simplified to lung function? Inherent in the determination that TRIKAFTA is “overpriced” is the argument that my life is overpriced. I can’t tell you with any degree of certainty that I am worth more than the price tag on this medication because I don’t know how much my life is worth. I haven’t lived it yet. But I am desperate for a chance to try.

Anna Rogers



Hello,

My name is Julia Ruggirello and I am a cystic fibrosis patient. Over the last year I have been fortunate to be on a new Vertex CF modulator, Trikafta. I have spent many years participating in medical studies to enhance the health of those living with CF. In 2015-2016 I participated in the Vertex study for Symdeko. I felt incredible while taking this medication and it was due to different clinical research that my gene type was not selected to be a fit for this medication. I enrolled in another CF modulator study which would soon to become Trikafta in November 2018. I participated in the phase II trials of this drug and due to no variations in lung function and how I was feeling I knew I had the placebo. On April 8, 2019 I began taking Trikafta. Over the next several weeks I began seeing positive trends in my lung function. I could breathe deeper, I wasn't coughing, I had more energy. This drug single handedly changed my life.

In 124 days I get to marry the love of my life. It has been over 20 weeks since I have been hospitalized. To me, these are the numbers that matter.

Per the recent ICER report was written to essentially do a cost-analysis of the newly approved FDA drug, Trikafta. I began Trikafta 48 weeks ago and my life has significantly changed. The recent report was disappointing for those lucky enough to access this drug. The report laid out that these new CF-modulator are simply not cost-effective. The implications of this report are far-reaching, as insurance companies utilize these reports to determine medication coverage.

People often ask why I work so much (at any given time I work 3-4 jobs). To be quite frank, it is because I never want to be a burden to those I love. I fear daily for the derailing of my health and without Trikafta that was where I was headed. Over the last ten years, my lung function continued to be inconsistent and trended in decreasing patterns. Before Trikafta I often fluctuated between 49-53% lung function. The bacteria that I grow in my lungs began to stop responding to antibiotic treatment. Coughing up pure blood was nearly a daily occurrence. I have been working with the anticipation that I only had a few "strong" years left where I could continue to provide for myself independently.

It is with Trikafta that these fears are subsided. I wake up each morning no longer wheezing and coughing. I wake up energized, ready to take on the 3 or 4 jobs I need to tend to that day. I wake up counting my infinite blessings. It is because of the CF modulator drugs I am able to think of marriage, family, career advances. Trikafta gave me 70% lung function and a life to continue to look forward to.

To the hardworking folks at ICER, while I understand you're only doing your job, it is these numbers, the ones that can be counted and the ones that can't, this is what matters most.

Hello,

Cystic fibrosis is a rare disease that kills MANY babies, children, and young adults. It robs people of happiness, and robs parents (like me) of knowing that their babies will be safe and have a healthy, happy life. My three month old, Alivia was diagnosed at seven days old and it was the most heartbreaking day of my life. Knowing that she will struggle just absolutely killed me. Trikafta has been a huge blessing for many of those with C.F. They have regained their life and cystic fibrosis is no longer in charge. They have HOPE for a future. For your company to start this cruel, cruel argument that it is "not worth it" because the cost outweighs the benefits is absolutely sickening. I cannot believe that there are monsters in this country that would choose to deny a human of a chance at getting better. Makes me worried for my daughters future. I cant sleep most nights as it is, now to worry that she and I will have to deal with more bad because people CHOOSE to be that way is downright wrong. We didnt get to CHOOSE that she has this lifelong chronic illness. It is terrible that the research done; all the time, dedication and effort, is being ridiculed by people because of the cost. Please have a change of heart and stop fighting this miracle drug. Let babies have a fighting chance to live happier, healthier lives without the thought that they will pass and be robbed of a life worth living. It would be different if your children or loved ones had this condition so why dont you put yourself in our shoes.

A very heartbroken first time mother,

Sabrina

My daughter started on Trikafta in Dec 2019. At that time her FEV1 was in the upper 40s after finishing a recent hospitalization and IV antibiotics in November. The 3 years prior to starting the Trikafta she was hospitalized every 2 to 3 months. She diligently followed her doctor's advice regarding medications, nebulizer treatments and airway clearance, but each year her health continued to worsen. This made it impossible for her to work, continue college classes, exercise and generally lead the life a woman in her 20s would expect to live. She frequently was so exhausted, short of breath and coughing that even doing basic housework or going to the grocery store was a challenge. Since starting Trikafta her FEV1 is in the 80s. She has not been hospitalized or needed any antibiotics either IV or oral since starting Trikafta. This medication has given her her life back. She continues to take her medications, do airway clearance and nebulizer treatments. She is going back to college, looking at getting a part-time job and is exercising everyday. She is stronger than she has been in years. This medication has been amazing, truly in the category of the miracle I have prayed for since she was diagnosed with CF.

Sincerely,

Sandra Zakroff, MD

Insurance companies should support this drug! All lives matter!

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Since July 30, 2018 the day of my daughter 3 day blood transfusion appointment day at a local hospital here in Orlando Florida, now 2 years later not 1 doctor, staff, or no experts has been able to give me/us an explanation of what happened to my 16 year old baby. Where she ended up on Life-support for almost 2 years now w/ a tracheostomy & feeding tube. As of today, as you are reading this! My daughter received a blood transfusion & shortly afterwards she started feeling weird, dizzy, throwing up & confused with a high fever of 104.+. The hospital staff never reached out to me to alarm me of the fever after I requested for them to contact me if there were any issues. When I called on August 2, 2018 at 9am to see if her discharged orders were ready, the person on the other end of the call asked was mom. I said yes, who else would it be?. She replied that my daughter had a fever all night & was on her way to PICU!! Not one doctor, nurse, surgeon nor staff has been able to answer what happened to my baby. She was removed from her regular room (where she received the blood transfusion) after 9am on 8/02/18. I got to the hospital at 9:45am. We never saw her as we waited, in the PICU waiting room on the 5th floor for hours!! Once, I demand to see my daughter after the night shift change (around 9pm) she was hook up on all kinds of tubes, life-threatening , life-changing & on a ventilator with high pressures. Her lungs was severely damaged, heart destroyed, kidneys damaged, stroke & etc medical conditions!!! So much more to add not enough time. Our story definitely needs to be heard all over the world!! Not to mention, our landlord sold the property where we live from under us. Unbelievable life-changing situation & family definitely gas shown that they really don't give a damn. Pray for us!!!

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My son, has been on Trikafta for 4 months. He has gained 8 pounds and his PFTs are up 20%. There is no denying the effectiveness of this drug.

The worry, of course, is the long term effect. Taking all of his other treatments away, to lessen the cost of treatment, is unconscionable at best. Without knowing how long Trikafta is going to work, it would be insane to recommend the cessation of his other medical protocols. Please take a wait and see approach based on scientific evidence rather than the dollar amount associated with it.

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My 31 year old son with C.F. Has been on trikafta for the past 3 months. This has been a miracle drug for him he no longer coughs at all , has gained weight and feels so much healthier!

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To whom ever it may concern,

I am writing this letter to let you know how important these modulator drugs are for our children! I am a mother of a CF warrior and my daughter is currently on Orkambi. Since being on this drug her health has been better than we could have hoped. She is now gaining weight at a normal rate and thriving! She has been able to stay out of the hospital since being on it. We are waiting for Trikafta to be approved for her age group and look forward to the even better effects that it will have. It is the closest thing we have at this point to a cure and is having life saving effects for those with CF! These drugs literally add years to their lives and better quality of life! Please make these drugs available for everyone who is in need of them by keeping the price affordable. Children should not be denied these medications because of their cost!

Thank you

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My significant other is one of the many individuals living with Cystic Fibrosis. He will be 27 years old in May and is now the healthiest he has ever been in his life because of the new CFTR modulator Trikafta. I have had the pleasure of watching his health go from draatically declining to healthier than even myself. He is now able to do more than he ever could before. He says he can finally feel what "normal" feels like. He doesn't struggle to breathe. He rarely coughs. His whole world is completely changed. This medication is truly a miracle. I am a first hand witness of what it can do for the CF population. Everyone with Cystic Fibrosis that is eligible to take this medication deserves to be able to afford it and have access to it. This could add so many tomorrows for so many people. Please do not take that away from my significant other or any other Cystic Fibrosis fighter.

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Within 1 week of my son being on Trikafta his lung functions greatly improved. His first hospital visit he was 11 years old and had only 2 more tune ups. He got pandorahea in April 2019 and had 3 hospital visits in 2019. He started Trikafta in January...

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Please help us lower cost of drugs . The trikafta I am on now is life saving . We need support Cystic Fibrosis is too expensive . I'm 29 years old with cystic fibrosis .

I want to live as long as humanly possible . Just help support the cf community and don't take away any of our life saving drugs .

We need them to function like a normal person . Feel free to email me back .

We are counting on you ICER.

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Hello! My 18 year old daughter started Trikafta on November 25, 2019. She took her first dose and within hours was coughing up mucus. This from a girl who does not cough or ever produce sputum. Let me mention that she had been at the doctor on November 13th and was being seen again in 3 weeks to see if lung function improved or they were going to admit her over her Christmas break from college. She is only able to take a modified dose due to being on Itraconazole for aspergillus. So Val to her doses.... she then took her second dose on November 28th and her 3rd dose on December 2nd. On December 4th she went to her appointment. At her 11/13 visit her 25/75 small airways which give her the most trouble were at 66% and her FEV1 was 88%. In just that short amount of time with just 3 doses of Trikafta on her 12/4 visit she blew 25/75 - 118% and FEV1 - 110%. We have never had small airways this high and haven't seen FEV1 at 100% in years!! This is an astonishing miraculous increase of 52% and 22%. These numbers have stayed up at her next appointment her 25/75 was 111% and FEV1 was 107%. This all with no other side effects. Thank you for reading my daughters experience with this LIFESAVING medication. Please try to put yourselves or your families in our position as cf parents and patients. Thank you

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My name is Ashley. I have cystic fibrosis and I am 33 years old. I have 3 children and I just recently started Trikafta in December. This medicine has drastically changed my life! Over the past 5 years my lung function has dropped quite a bit from high 50's- low 40's. It's a scary number change when you have cf. I was short of breath suddenly with no relief, I would cough suddenly when just stepping outside when it was cold. I couldn't laugh without coughing, and definitely wasn't feeling energetic. As soon as I started this medicine I can breathe again! I have told people I actually have to teach myself to breathe because I'm not used to taking in a breath. I am not coughing at all! Which is amazing. I have gained 7 pounds so far and I just feel different.

If your wanting to get on these websites and base the drug effectiveness on what other CF patients are saying it would really hurt more people that the drug is actually working for. If you go on ANY cf page, you will see mostly complaints. Yes, I know this disease sucks.. I get it and I get that some are worse than others but a lot of cf patients just complain about anything they can. It can be very negative which is why I try to stay off of those Facebook pages. I joined Trikafta just to see what was happening with this drug. What i can see is a wide range of symptoms. Some complain more than others about the same things, like rash, itchy eyes, stomach pains etc. what they aren't doing is trying to find personal relief for these things. They just expect to take a medicine that is going into your body and changing the genetic mutations, without symptoms. Some of us have a lot of damage so I compare it to a cf chemo of some sort. We just have to get through the healing process and it won't always be right away. There are ways to fix certain symptoms but these people just get on to complain before actually trying to fix it first. The only downside is how expensive this medicine is. Otherwise don't rely on reading these peoples comments because if it doesn't work for certain cf individuals then their doctors should be able to decide to take them off or not. But I think more cf patients have good outcomes on this and a lot you won't even see on fb!

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To whom it may concern,

Hello my name is Briana. I am 33 years old, about to be 34 and I just started Trikafta. I am 14 days in. This medication has been life changing already! Before I couldn't walk any major distance without having to stop to take a break. My lungs hurt almost every. Now I was able to go out and walk around for a couple hours and I didn't need a break! My lungs no longer hurt. I used to wake up in the middle of the night coughing, since starting Trikafta I can actually get 8 hours of sleep. That hasn't happened in years. The side effects were pretty miserable the first 5 days. But they went away. Day 6 I sat there amazed because I didn't hurt. The side effects do not outweigh the benefits. I haven't had my dr appointment since starting Trikafta but I already see and feel the difference. This really is a miracle drug. Don't take this away from us. I want my 10 year old to know what it's like to have a mom that can play with her, go swiping her, or hiking. I want her to have her mom in her life. With us medication I will get to watch her grow and watch her make those important milestones in life. Everyone deserves better. Everyone deserves the right to know what "normal" feels like. We deserve to be apart of our families lives. I never head weight gain issues, but I know many that have and do. Since starting this medication they are finally able to gain weight. I always had lung issues more than anything else. I am no longer coughing up dark green chunks of mucus. Sorry I know that is gross but that was my life before this medication. That was many of our lives. We finally have hope. Real hope. To finally experience life. To laugh, play, and enjoy life without the constant coughing, wheezing, shortness of breath, and pain. Don't take that away from us. Don't take that away from our kids and our families. I am so looking forward to continuing this medication. The side effects go away and the benefits are so wonderful and amazing. This medication is truly life changing. And we deserve a life. Thank you for your time.

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Dear Reviewers,

Trikafta is saving lives. It is transforming lives. This is the first real breakthrough medication for Cystic Fibrosis. Please don't decide that this population should go back to suffering and dying because Trikafta is expensive. Give these people a chance at a real life for the first time.

Thank you.

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So you made the decision that the drug Trikafta was too expensive to cover. That the value of it wasn't worth the expense. Have you yourself lived with Cystic Fibrosis? Have you watched a loved one suffer from Cystic Fibrosis? Have you watched a loved one suffer from any chronic progressive medical condition? Have you ever wished and hoped there was SOMETHING, ANYTHING that could slow or stop disease progression so they would have more HEALTHY time with you? That their QUALITY of life would FINALLY be some of the BEST it could be? That's what Trikafta is doing. I'm not sure how you can put a price tag on the value of a life. When our children can finally breath a normal breath. When the idea of a cold doesn't send you into fear of a hospitalization. When all the meds that they have taken to this point in their life to give them a basic baseline of healthy but you know it'll never be enough in the long run start to fail and then comes the fear of losing them. Then comes hospitalization after hospitalization. Maybe IF they are lucky a transplant. And that transplant MIGHT give them 5 years but probably not. All of that insurance covers. All of it. And then something amazing comes out. Something that may prevent them from ever having to face death at 10, 15, 20. And it all is in the hands of people WHO HAVE NEVER lived with this damn disease. And those people tell us that hey guess what, you're life has a price tag. And it's too high for the insurance companies. You're life, the life of your child isn't worth quality any more. It's worth X amount of dollars. And that's too much. People how are the smartest, brightest, most amazing people you will ever met now can't afford to love if your decision stands to not approve Trikafta. Can you look your child in the eyes and tell them, "sorry I feel your life isn't worth the price tag?" Can you look your spouse, mother/father, best friend in the eye and say "we value our bottom dollar more than your life"? If you can then I feel sorry for you. Sorry for the hatred and greed in your heart. If you cannot do that then stop telling us that we have to tell our family members there's a price tag on their head and it's too expensive. Don't make me tell my kids that there are people out there that they've never met feel that feel should suffer and die at a young age because the medicine that could and will give them a real chance at a "normal" life is just too expensive for insurance to cover.

Be the change. Be better than this. Be a human with a heart.

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Please don't take our trikafta away . I am living with cystic fibrosis not dying from it , Because of trikafta ! If you take it away everyone with Cystic Fibrosis will die .  
I am working full time and I'm a value to my company all because I am staying out the hospital . Please have a heart and keep letting us thrive with trikafta and other future drugs . The cure is in reach . We need more medication to help us live and thrive longer .

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Please consider the difference this medication will make in the life's of so many children and young adults. Please remember how expensive having a child with a chronic illness can be and make sure to not let the insurance companies deny this life changing medication for my Grandchild and the thousands like him.

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I am writing on behalf of two very special people in my life who both have Cystic Fibrosis. These two beautiful little kids deserve every chance at a normal life. I am pleading that you please reverse your stance on Trikafta. This treatment could be life altering for many others with CF. Thank you.

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Please reverse your review on the drug Trikafta. This medication finally gives those living with Cystic Fibrosis a fighting chance at a normal long and healthy life. Please do not encourage insurance companies not to support it. This is a matter of life and death. Please allow them to live.

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To Whom It May Concern,

I am a Certified Anesthesia Technician who spent many years working at Children's Hospital Colorado. I was witness to several patients who spent their last days fighting for every breath. Waiting for a chance at life and hoping that a donor would be found so they could potentially be saved. But essentially they were drowning slowly. Their only hope was the death of another. Rarely did new lungs actually come. Not only did I witness the above, but I have also prayed daily that I would never have to see my nephew and niece struggle to tell their parents "I love you" because they don't have enough air in their lungs to push the words out. You see, 21 years ago my sister gave birth to a beautiful baby boy. He was diagnosed with Cystic Fibrosis within a couple of days of his birth. Not long after, my niece also received the same diagnosis. As a family, we all studied CF and the consistent reminder that there is no cure was always on our minds. We just always kept HOPE in our hearts. Hope that if a cure couldn't be found that there would at least be a treatment that could improve quality and hopefully quantity of life. Finally those prayers came true. For the first time there is a drug on the market that could and is showing benefits. CF patients are able to BREATHE! I don't know what it is like to not be able to fill my lungs with air. A CF patient doesn't know what it is like to fill their lungs with air. But as fast as we are giving CF patients a chance to discover what taking a deep breath is like...that chance is threatened. I think of cancer patients. There are so many variations of chemotherapy that can be given to provide a patient with a chance to live. It is just a chance. But we give them that chance. If one med doesn't work, another is tried. But the key is they have a CHANCE to see if it will work. CF patients also deserve a chance. They have all lived their entire lives with a terminal illness. Don't they deserve to have a CHANCE as well? If life quality can improve, then the potential to reduce expensive hospital stays and possibly even reduce the needs for costly transplants and anti rejection drugs is real. Please encourage insurance companies to provide support of using Trikafta<sup>TM</sup> and similar medications for their customers. Keep HOPE alive for kids and young adults so that for a piece of their lives they can live as normal of life as possible for someone with a terminal illness. In the medical world, we should always look ahead with hope because often times hope is what keeps us fighting. Give the HOPE. Please.

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To Whomever it May Concern,

It has been brought to my understand that you are reviewing the critical medication Trikafta, and deciding whether it's patients are worthy enough to afford it. Cystic Fibrosis effects so many people around the world, and those living with it have been hopeful for a cure. No, there is still not one, but now we have a drug to improve the quality of life, expand life expectancy, and give more hope to the people living with CF and their families that this disease does not have to rule their lives.

It makes sense that insurance does not want to cover such a large price tag, but just like other medications, require a PA from the physician to make sure the med is being prescribed correctly. It is unlawful to deny a patient their life changing medication because you don't like the price of it. That is why insurance is provided for the public; it is made it be used. If this med is not covered, it will impact thousands of people who have already gotten to live while taking this medicine, forcing them to go back to life without air.

Thank you.

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