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If Trikafta Isn't Good Enough for ICER, What Drug Is?

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Last week ICER released a report **concluding** that Vertex's groundbreaking triple-combination cystic fibrosis (CF) drug, **Trikafta, is too expensive** for the value it provides to patients.

By all scientific and clinical standards—including ICER's own—**Trikafta**, a novel combination of a CFTR potentiator and two correctors, is a transformative drug. It compensates for a mutation present in 90% of all CF patients, turning a disease that has long been a death sentence into a manageable chronic condition. Following stellar Phase 3 data, the FDA approved Trikafta **five months ahead of schedule**. The patient, physician, and research communities exploded in exuberance when it was approved. NIH director Francis Collins, who helped discover the CFTR gene in 1989, **whipped out his guitar and sang on stage** in celebration.

ICER awarded Trikafta an "A" – its highest grade – for "certainty that Trikafta provides a substantial net health benefit over standard of care." However, the magnitude of this achievement did not translate to a favorable review on price. Trikafta is priced comparably to similar drugs for rare conditions, at just under $24,000 per month in the US. And that's a list price – insurance plans and Medicaid pay a lower but undisclosed net price, so after typical discounts and rebates (~15%), Trikafta's net price is likely closer to $20,000 per month.

Once a patient starts on the drug, they have to stay on it to manage their disease. That's not unusual for small molecule drugs or injectable biologics. But Trikafta works better for CF than most drugs work for their respective rare diseases. Even so, **in ICER's words**: "Despite [Vertex's CF drugs] being transformative therapies, the prices set by the manufacturer – costing many millions of dollars over the lifetime of an average patient – are out of proportion to their substantial benefits."

This assessment caused an outcry among patients and foundations. They argued that the drug is a life-changer, and that ICER's analysis didn't include important variables that matter to patients. In a sentence that shocked CF families, **ICER argued** that even if Trikafta were able to generate a *total functional cure* such that patients never experienced any complications related

to their disease, the drug would still not be worth paying for at the price set by Vertex:

> "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***." (emphasis added)

The callousness of this response aside, it isn't that a drug—or even a cure—can never be overpriced. That's conceivable, especially in the absence of any competition. But ICER tries to make the point that Trikafta is overpriced while leaving a lot of math on the table that does not suit its argument.

It's worth exploring those overlooked variables and the societal norms that underlie value-based pricing analyses, which CF patients have cited in their defense of this vital medicine. It's especially important to take this broader view considering how those norms might change following the COVID-19 pandemic. Let's explore more accurate ways to model cost-effectiveness so that we don't risk talking ourselves out of inventing what we really need.

Drug costs are mortgages, not rents

Healthcare costs in the United States are on the rise and will continue to increase. This is because paying for the time and expertise of trained medical professionals, keeping hospitals and clinics clean and operational, and maintaining the huge administrative burden of our medical system is expensive and will remain so. These costs are like an ever-rising rent that we as a society will always have to pay.

But **drug costs are mortgages, not rents**. Drugs are the only element of the healthcare system that not only pay for themselves but save our system money in the long run. How? They go generic. After a new drug enjoys a finite branded period, patents expire, competitors enter the market, prices drop by 85-90%, and that advancement belongs to society as a low-priced generic forever. By law, Trikafta will go this route one day, too, most likely within about 15 years from its launch, as nearly all small-molecule drugs do. Vertex's monopoly is temporary, not permanent, by design.

But ICER's methodology does not take into account the fact that any drug will go generic. Instead, they model the drug's launch price as its price each year for the entire lifespan of each patient, wildly overestimating its total lifetime cost.

For the sake of argument, let's assume an average CF patient starts taking Trikafta at age 10 and gets the patented drug for 15 years. If the patient remains in steady health, as would reasonably be assumed based on the drug's profile, that 25-year-old patient in the year 2035 can expect many more years of healthy living on this drug at a less expensive generic price, not today's premium branded one. ICER isn't unaware of this flaw; rather, they expressly refuse to address it.

When called out on this point multiple times by CF patients and foundations, **ICER punts**:

"As is consistent with best practices at international HTA agencies and with the great preponderance of academic work in health economics, ICER's cost-effectiveness analyses do not routinely make estimates of price changes across comparator treatments linked to patent and exclusivity time horizons, especially given the unpredictability of these changes in the US health care market."

Yet the fact that a small molecule drug like Trikafta will go generic is one of the few predictable things about healthcare. One can model the possibility that some patent gamesmanship may result in a few years' delay of a generic launch (inappropriate though it may be), but when modeling value on the scale of decades, these uncertainties hardly alter the fact that Trikafta's genericization is inevitable. ICER argues that uncertainty in the timing of genericization and whether the price will drop by 80%, 85%, or 90% precludes modeling it at all. This is a disingenuous strategy, to say the least, and ignores a simple modeling assumption that can and should be factored in.

Economists who have modeled the impact of genericization have pointed out that doing so reveals a drug to be **two- to three-fold more cost-effective** than misrepresenting its mortgage cost as rent. Payers, regulators, and the biotech community should spurn ICER's analyses if they continue to neglect drugs' core value proposition. At this point, continuing to refuse to account for genericization is tantamount to perpetuating disinformation.

COVID-19 expands our de nition of value

What would it be worth to you to know that if you contracted COVID-19, there would be a safe, effective treatment to get you back on your feet?

What would that peace of mind do for you when deciding whether to allow family members to go back to work or school?

What would such reassurance do for the global economy?

The COVID-19 pandemic illustrates that another vital benefit that drugs provide (and value-based pricing analyses fail to capture) is peace of mind: the freedom to act, plan, and work without the threat of a disease hijacking your life.

The mother of a CF patient captures this intangible benefit in her exchange with ICER:

CF Mother: *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.*

ICER: *We modeled Trikafta as a cure and it still did not meet societal norms for cost relative to benefit.*

What ICER dismisses is that "societal norms for cost relative to benefit" are ours to set. ICER's "societal norms" reflect the norms of its own staff, and certainly the publicly stated sensibilities of its major backer, billionaire **John Arnold**. But they do not represent those of the majority of Americans, who view healthcare as a human right. America excels in nurturing the kind of innovation that advances its goals. It is within our country's means and abilities to improve our health and that of the world.

With the capabilities of biomedical innovation now on display and the world calling for more COVID-19 investment from all of society's pockets – government, insurance, non-profit, and private sector – the pockets that everyone acknowledges we must not reach into are those of patients. Patients need affordable drugs, and America can make that possible not just *for most*, as it does now, but *for all* with proper insurance reform. That means ensuring that all Americans are insured and minimizing barriers to access for essential medications (i.e. by reducing out-of-pocket costs). Then we can collectively incentivize and fuel innovation to solve our unmet needs. We can do that by paying branded prices that, while seemingly high per patient, are finite and, in the long run, represent better value than continuing to suffer from the diseases that plague us.

Right now in the US, because of Trikafta, about 30,000 patients have a new, hopeful outlook on life. Every one of them is surrounded by family members that can now worry less about managing the disease and start thinking more about pursuing their own dreams. There is substantial human potential that can be unleashed whenever a powerful new drug like Trikafta comes along.

Until we achieve insurance reform for everyone, we can put some patches in place to pay for this advance. The COVID-19 pandemic has already shown us that this is doable: for example, by **capping insulin copayments at $35** for everyone regardless of insurance status and offering **many medicines for low fixed costs** to tens of millions of the uninsured. If drugmakers and insurers can do this for patients now, they can do it in the future.

It's time we recognize that value can't be captured by a single organization's formula – especially one with the gall to insist a launch price lasts forever and that disregards the value of curing a devastating disease for ourselves and future generations. It's hard to think of a societal norm more American than investing towards an accomplishment as immense as conquering CF, taking pride as a nation in getting the job done, and celebrating the heroes who did it.

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