COLORADO
Prescription Drug Affordability Board
Division of Insurance

# 2023 Affordability Review Summary Report: Trikafta

**December 15, 2023**

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# Executive Summary

## Affordability Review Summary Report Findings

Trikafta, first approved by the United States Food and Drug Administration in 2019 with an orphan drug designation, reduces symptoms and complications of cystic fibrosis for patients who have the F508del mutation of the CFTR gene. Cystic fibrosis is a rare, life-limiting, and multi-system disease. There is evidence that Trikafta provides significant clinical benefits to the nearly 90% of people with cystic fibrosis who are eligible for the drug. There are other therapeutic alternatives for the 10% of patients who are not eligible for Trikafta, though evidence suggests alternatives are not as effective and there are potential health equity implications regarding which patients are ineligible for Trikafta.

Well conducted studies show that Trikafta provides improvements in pulmonary function, reductions in pulmonary exacerbations, and improvements in overall health and perceived well being. While some studies question the clinical value of Trikafta relative to its price, patients, caregivers, clinicians, and researchers provided input about the life-transforming and cost-saving benefits of Trikafta. Their input included discussion of the marked reduction in pulmonary infections, drastically reduced need for hospitalizations and time off work, significant cost-savings from not having to pay for other CF-related medications, the ability to return to work or to school, ability to gain weight, marked improvement or reversal of CF complications such as diabetes and liver disease, being taken off the transplant list, and even being able to have children.

In passing Senate Bill 21-175, the legislature recognized the importance of both evaluating the effectiveness of a drug, as well as its cost to both consumers and the larger health care system in Colorado. Nearly half of insurance carriers who submit information to Colorado's All Payer Claims Database (APCD) reported that Trikafta was one of the top 15 prescription drugs that raised premiums for all covered lives. Trikafta has also appeared in other states' assessments of the costliest drugs and contributing to increases in insurance plan spending. In Colorado in 2022, Trikafta cost $234,439 per patient and in total over $108 million was spent on the drug. Data from the APCD reports that patients with commercial insurance coverage paid 3.59% of the total cost of Trikafta in 2022. In that year, the average annual out-of-pocket cost was nearly $9,000, though there was wide variation in average out-of-pocket costs, where 51% of individuals paid less than $50 a month, while some individuals paid as much as $22,700 per month.

While costs for Trikafta paid by both consumers and payers are notable, particular patients and caregivers told a more nuanced story regarding the journey someone with cystic fibrosis takes to access Trikafta. Patients reported receiving comprehensive cystic fibrosis-related care at one of two accredited cystic fibrosis care centers in Colorado, with some patients stating they and their families moved to Colorado specifically to receive treatment at these centers. Evidence was also gathered that average out-of-pocket costs may be lower than what is reported in the APCD due to patient assistance programs.

It is estimated that [redacted] of Vertex's national gross sales for Trikafta was spent on rebates, 340B discounts, manufacturer financial assistance programs, and other price concessions. Estimates of the exact amount of financial assistance provided per patient, including assistance provided by manufacturers, is unknown. While assistance programs are never guaranteed, cystic fibrosis patients in Colorado who utilized such programs provided a perspective that, to date, these programs are heavily relied upon to afford Trikafta. Several patients indicated that while not without its burdens, the Vertex patient assistance program for Trikafta is easier to navigate and access than many other patient assistance programs.

The following report and its appendices provide detailed evidence necessary for the Board's consideration of whether Trikafta is unaffordable to Coloradans.

## Board Deliberation and Vote Summary

After receiving and reviewing evidence in support of the affordability review components set forth in statute and rule, on December 8, 2023, the Colorado Prescription Drug Affordability Board (the Board) unanimously acknowledged there was sufficient evidence to proceed with deliberations for the Trikafta affordability review. The Board then deliberated whether the use of Trikafta was unaffordable for Colorado consumers.

After deliberations and hearing public comment from ten individuals, the Board voted 5-0 that the use of Trikafta consistent with the labeling approved by the FDA or with standard medical practice is ***not unaffordable*** for Colorado consumers. Several Board members emphasized their hope to hear from patients in the future if unaffordability problems develop, particularly due to patients' stated reliance on, and fragility of, patient assistance programs.

During deliberations, Board members noted that Trikafta is an extraordinarily expensive drug, but that patients and caregivers provided input that Trikafta is extremely beneficial and makes an enormous difference to cystic fibrosis patients.These same patients and caregivers, combined with claims data, provided evidence that the drug is not unaffordable to patients with cystic fibrosis at this time. Deliberation included discussion of:

- Trikafta's designation and approval as an orphan drug that is solely utilized to treat cystic fibrosis;
- Utilization statistics and increased utilization since Trikafta's approval;
- Insurance coverage types and health benefit plan design, including discussion that many patients utilizing Trikafta are covered by Medicaid or commercial insurance;
- Changes in patient out-of-pocket (OOP) amounts, including recent increases in co-insurance and a doubling of total patient OOP amounts from 2021-2022, and patient and caregiver input regarding the frequent use of patient assistance programs;
- Gross-to-net sales estimates and potential relationship to manufacturer assistance programs;
- Review of assessments that indicate Trikafta may not be cost effective, but input from patients, caregivers, and individuals with scientific and medical training provided insight into the significant health and financial benefits; and
- Concern that some carriers indicate that Trikafta is among the top 15 prescription drugs causing their health insurance premiums to rise.

To view the meeting recording in full, see:
https://us06web.zoom.us/rec/play/K0agi0kmVA9g022EFjO9DKVRBbDpBH7KycfrlQfUDF9PS1AU881bezxP7cUD8F3nfijzQa-I1d2BHb8.UtkQNMA5pTUD-5OQ?canPlayFromShare=true&from=my_recording&continueMode=true&componentName=rec-play&originRequestUrl=https%3A%2F%2Fus06web.zoom.us%2Frec%2Fshare%2FxIn9nB4CYc8FQJbbwHtsWbJ8QanKXYfRuKZmEivAkpBQQQbd9izNlHFIKkhYYG3X.WqECpHRlG4jMwqSr

# Summary Report Introduction

The Colorado Prescription Drug Affordability Board (the Board) was established in 2021 through the passage of Senate Bill 21-175. Governor Polis appointed five members to the Board in September 2021. Since then, the Board has appointed members to the 15-person Prescription Drug Affordability Advisory Council (the Advisory Council) and hosted a five-part learning series in spring 2022 to provide Board members, Advisory Council members, and interested stakeholders foundational knowledge necessary to implement a successful new prescription drug affordability program. The Board has also promulgated five rules to implement statutory requirements, and developed five policies to guide the program.

One of the Board's duties is to perform affordability reviews of prescription drugs as described in section 10-16-1406, C.R.S. This section outlines the Board's four steps in conducting affordability reviews:(1)

identification of eligible drugs, (2) selection of drugs for affordability reviews, (3) conducting affordability reviews on selected drugs, and (4) determining if use of the selected drugs are unaffordable for Colorado consumers.

The first step - identification of prescription drugs eligible for affordability reviews - was completed when the Board approved the final list of prescription drugs eligible for affordability reviews on June 9, 2023. The second step - selection of prescription drugs for affordability reviews - was completed when the Board selected five drugs for affordability reviews on August 4, 2023. This report has been prepared by Board staff to assist the Board in completing the third and fourth steps of the affordability review process for the prescription drug, Trikafta.

This report of the affordability review for Trikafta was conducted in accordance with 3 CCR 702-9, Part 3.1.E.6. Additionally, this report contains appendices with detailed information for each of the fifteen criteria the Board shall and may consider as a part of its affordability review, to the extent practicable.

# Report Structure

## About This Report

The main body of the Affordability Review Summary Report is divided into three profiles: a therapeutic and utilization profile; a cost and price profile; and an access to care profile. The profiles contain information from the fifteen statutory and regulatory components the Board considers as a part of an affordability review. The profiles were identified by Board members and Board staff as a way to present affordability review evidence in a commonsense manner. While these profiles incorporate all fifteen components the Board considers during affordability reviews, additional information is provided for each of the fifteen components in the appendices, with each component having an individual appendix. More information on the structure of each profile and the appendices is provided in the sections below.

While several components lend themselves to inclusion in only one profile, three components inform all profiles contained in the Summary Report. Those components, and information regarding the type and volume of feedback Board staff received, are summarized below:

- Input from patients and caregivers - Board staff gathered input from 32 patients and caregivers at two public meetings on September 27 and October 10. Additionally, 47 patients and caregivers completed surveys regarding the health and financial effects of Trikafta, and many of these patients and caregivers also attended the public meetings.
- Input from individuals with scientific and medical training - Board staff gathered input from eight individuals with scientific or medical training at one public meeting on September 27. Additionally, eight individuals with scientific & medical training completed surveys regarding the health and financial effects of Trikafta.
- Voluntarily submitted information - 41 patients, caregivers, and other entities submitted voluntary information. Vertex Pharmaceuticals Incorporated, the manufacturer of Trikafta, also voluntarily submitted information. Note: no assessment was conducted of accuracy of voluntarily submitted information or the extent to which the information applies to Coloradans.

The Summary Report and Appendices may contain proprietary, confidential, and trade-secret information. Such information is redacted in public reports.

## Therapeutic and Utilization Profile

The Therapeutic and Utilization Profile includes information about Trikafta's clinical efficacy and the people who use it. This section provides information regarding Trikafta's indication, utilizer profile, health equity impact, and therapeutic alternatives. Affordability review components present in this profile include information from Appendices B, G, H, I, J, and L.

## Price and Cost Profile

The Price and Cost Profile includes information on what different entities on the prescription drug supply chain charge for Trikafta, as well as what different entities pay for Trikafta. This profile also contains information on Trikafta's financial effects on health, medical, and social service costs. Affordability review components present in this profile include information from Appendices A, B, D, E, H, I, J, K, and O.

## Access to Care Profile

The Access to Care Profile examines potential access to care concerns related to Trikafta and whether there is evidence that the causes of access to care concerns may be related to Trikafta's price or cost. This profile includes an examination of potential relationships of changes between utilization, price, and costs as well as information on safety net providers, utilization management requirements, and health benefit plan design. Affordability review components present in this profile include information from Appendices A, B, C, E, F, H, I, J, K, M, and N.

## Appendices

This report contains an appendix for each of the fifteen components the Board is to consider as a part of affordability reviews, as well as a last appendix, Appendix P - Data Sources and Limitations. Descriptions of the appendices related to the fifteen affordability review components are outlined below.

**Table A**

*Appendices and Relevant Statutory, Rule, and Policy Guidance for Affordability Review Components*

| Component Name | Component Details |
|---|---|
| **Appendix A:** Current WAC & Change in WAC | The Board shall consider the wholesale acquisition cost of the drug. C.R.S. § 10-16-1406(4)(a). |
| **Appendix B:** Therapeutic Alternatives | The Board shall consider the cost and availability of therapeutic alternatives to the prescription drug in the state. C.R.S. § 10-16-1406(4)(b). |
| **Appendix C:** Price Effect on Access | The Board shall consider the effect of the price on Colorado consumers' access to the prescription drug. C.R.S. § 10-16-1406(4)(c). |
| **Appendix D:** Relative Financial Effects | The Board shall consider the relative financial effects on health, medical, or social services costs, as the effects can be quantified and compared to baseline effects of existing therapeutic alternatives to the prescription drug. C.R.S. § 10-16-1406(4)(d). |
| **Appendix E:** Patient Copayment & Other Cost Sharing | The Board shall consider the patient copayment or other cost sharing of the drug. C.R.S. § 10-16-1406(4)(e). |
| **Appendix F:** Safety Net Providers | The Board shall consider the impact on safety net providers if the prescription drug is available through section 340B of the federal "Public Health Service Act", Pub.L. 78-410. C.R.S. § 10-16-1406(4)(f). |
| **Appendix G:** | The Board shall consider orphan drug status. C.R.S. § 10-16-1406(4)(g). |

| Component Name | Component Details |
|---|---|
| Orphan Drug Status | |
| **Appendix H:** Patients & Caregivers | The Board shall consider input from patients and caregivers affected by the condition or disease that is treated by the prescription drug that is under review by the Board. C.R.S. § 10-16-1406(4)(h)(I). |
| **Appendix I:** Individuals with Scientific & Medical Training | The Board shall consider input from individuals who possess scientific or medical training with respect to a condition or disease treated by the prescription drug that is under review by the Board. C.R.S. § 10-16-1406(4)(h)(II). |
| **Appendix J:** Voluntarily Submitted Information | The Board shall consider any other information that a manufacturer, carrier, pharmacy benefit management firm, or other entity chooses to provide. C.R.S. § 10-16-1406(4)(i). |
| **Appendix K:** Rebates, Discounts, and Price Concessions | The Board may consider estimated manufacturer net-sales or net-cost amounts (including rebates, discounts, and price concessions) for the prescription drug and therapeutic alternatives; and<br>The Board may consider manufacturer financial assistance the manufacturer provides to pharmacies, providers, consumers, and other entities. C.R.S. § 10-16-1406(4)(j); 3 CCR 702-9, Part 3.1.E.2.j.i. |
| **Appendix L:** Health Equity | The Board will consider whether the pricing of the prescription drug results in or has contributed to health inequities in priority populations. C.R.S. § 10-16-1406(4)(j); 3 CCR 702-9, Part 3.1.E.2.j.ii. |
| **Appendix M:** Information from HCPF | The Board shall consider information from the Department of Health Care Policy and Financing, including additional analyses HCPF conducts relevant to the prescription drug or therapeutic alternative under review; and/or information regarding safety net providers participating in the 340B, including information to assist with gathering input to assess the impact to safety net providers for a prescription drug under review that is available through Section 340B of the Federal "Public Health Service Act", Pub. L. 78-410. C.R.S. § 10-16-1406(4)(j); 3 CCR 702-9, Part 3.1.E.2.j.iii. |
| **Appendix N:** Non-Adherence & Utilization Management | The Board may use information regarding non-adherence to the prescription drug, as well as information related to utilization management restrictions placed on the prescription drug. C.R.S. § 10-16-1406(4)(j); 3 CCR 702-9, 3.1.E.2.j.iv. |
| **Appendix O:** Pricing Information | The Board may consider any documents and information relating to the manufacturer's selection of the introductory price or price increase of the prescription drug, including documents and information relating to: (a) Life-cycle management; (b) The average cost of the prescription drug in the state; (c) Market competition and context; (d) Projected revenue; (e) The estimated cost-effectiveness of the prescription drug; and (f) Off-label usage of the prescription drug. C.R.S. § 10-16-1406(6).<br>The Board may access pricing information for prescription drugs by: (I) accessing publicly available pricing information from a state to which manufacturers report pricing information; (II) accessing available pricing information from the all-payer health claims database and from state entities; and (III) accessing information that is available from other countries. C.R.S. § 10-16-1406(7)(a). |

# Trikafta Therapeutic and Utilization Profile

The Therapeutic and Utilization Profile includes information about Trikafta's clinical efficacy and the people who use it. This section provides information regarding Trikafta's indication, utilizer profile, health equity impact, and therapeutic alternatives.

## Indication

Trikafta has one FDA-approved indication for treatment: cystic fibrosis. The National Institute of Health's (NIH) Genetic and Rare Diseases (GARD) Information Center describes cystic fibrosis, commonly referred to as "CF", as a genetic disorder that causes mucus to build up and damage organs in the body, particularly the lungs and pancreas.[1] GARD outlines that over time, mucus buildup and infections can lead to permanent lung damage, including the formation of scar tissue (fibrosis) and cysts in the lungs. Cystic fibrosis is caused by genetic changes in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

More than 2,500 different mutations in the CFTR gene have been described, with the most common CFTR mutation being F508del.[2] Trikafta is a fixed-dose combination of 3 molecules: ivacaftor, a CFTR potentiator, tezacaftor, and elexacaftor (both CFTR correctors). Trikafta was first approved by the FDA in 2019 for the treatment of cystic fibrosis and is currently approved for patients aged two years and older who have at least one F508del mutation in the CFTR gene or a mutation in the CFTR gene that is responsive based on in vitro data.[3] If the patient's genotype is unknown, an FDA-cleared cystic fibrosis mutation test should be used to confirm the presence of at least one F508del mutation or a mutation that is responsive based on in vitro data.

Individuals with scientific or medical training stated in public meetings and in surveys that Trikafta is rarely prescribed off label due to the broad population for which the drug is approved. Trikafta is indicated for nearly 90% of patients with cystic fibrosis based on their CFTR genotype. Though Trikafta has not been studied or FDA-approved for use during pregnancy, two individuals with scientific or medical training said that Trikafta is often continued for people with cystic fibrosis who are pregnant due to the rapid decline in health when a patient stops a drug suddenly. One individual indicated that on rare occurrences, Trikafta is continued in pregnant people who are carriers of infants with cystic fibrosis to prevent the need for immediate surgery for cystic fibrosis-caused bowel obstruction in their infants. See Appendix I for more information.

Trikafta is classified by the World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) classification system as "other respiratory system products".[4] The medical guidelines for cystic fibrosis are Cystic Fibrosis Foundation Pulmonary Guidelines. Use of Cystic Fibrosis Transmembrane Conductance Regulator Modulator Therapy in Patients with Cystic Fibrosis.[5]

The FDA considers cystic fibrosis to be a rare disease, since it affects fewer than 200,000 people in the United States. It is estimated that in 2020, there were close to 40,000 children and adults living with cystic fibrosis in the United States.[6] The FDA granted Trikafta orphan drug designation and approval in August 2018. See Appendix G for more information on Trikafta's orphan drug designation .

Common symptoms and complications of cystic fibrosis include:[7]

- Respiratory - Recurrent pulmonary and sinus infections often requiring hospitalization and which can eventually lead to the development of pulmonary fibrosis and the need for lung transplantation
- Pancreatic - Scarring of the pancreas leading to both decreased production of pancreatic digestive enzymes which causes malabsorption and weight loss and decreased production of insulin which causes diabetes.

[1] https://rarediseases.info.nih.gov/diseases/6233/cystic-fibrosis
[2] https://hopkinscf.org/knowledge/cftr/
[3] Section 12 of the FDA label has a list of CFTR gene mutations responsive to Trikafta.
[4] https://www.whocc.no/atc_ddd_index/?code=R07AX&showdescription=no
[5] https://pubmed.ncbi.nlm.nih.gov/29342367/ . Note: Trikafta was not included in the medical professional guidelines, as it was not approved when the guidelines were published in March 2018.
[6] https://www.cysticfibrosisjournal.com/article/S1569-1993(23)00061-9/fulltext#:~:text=The%20prevalence%20of%20CF%20in,under%2015%20years%20of%20age
[7] https://rarediseases.info.nih.gov/diseases/6233/cystic-fibrosis

- Hepatic - Cystic fibrosis-related liver disease can lead to cirrhosis and end stage liver disease with all its complications.

## Utilizer Profile

Trikafta's utilization has increased since the FDA approved the drug in 2019. According to Colorado's All Payer Claims Database (APCD) 461 individuals utilized Trikafta in 2022. Additionally, data from the APCD indicates that patients who utilize Trikafta are most commonly insured through Medicaid, followed closely by commercial insurance, with a significantly smaller number of patients covered by Medicare Advantage plans. Trikafta's utilization statistics are provided below.[8] APCD utilization estimates can be viewed as low estimates, since data for some self-insured commercial insurance plans (ERISA) and Medicare FFS enrollees, as well as uninsured individuals, is not included. See Appendix P for more information.

A separate data source that collects information on the health status of people with cystic fibrosis is the Cystic Fibrosis Foundation Patient Registry. This data source contains information from patients who receive care in a CF Foundation-accredited care center and agree to participate in the registry. This information is used to create care guidelines, assist care teams, and study cystic fibrosis treatments, outcomes, and design clinical trials. The CFF Patient Registry estimates there are over 700 Coloradans living with CF. See Appendix J for more information. Affordability reviews focus on patients living in Colorado to the extent practicable; data is typically noted when it is beyond Colorado.

**Table B**

*Trikafta Utilization Statistics*

| Utilization Statistic | 2019 | 2020 | 2021 | 2022 |
|---|---|---|---|---|
| Patient Count | 139 | 317 | 457 | 461 |
| Mean Age | 28.2 | 26.2 | 26.3 | 26.3 |

Table B shows the number and average age of patients taking Trikafta from 2019 -2022.

[8]Utilization information in this section is from the Colorado All Payer Claims Database (APCD). APCD data limitations are outlined in Appendix P.

**Figure A**

*Trikafta Monthly Utilization by Payer Type*

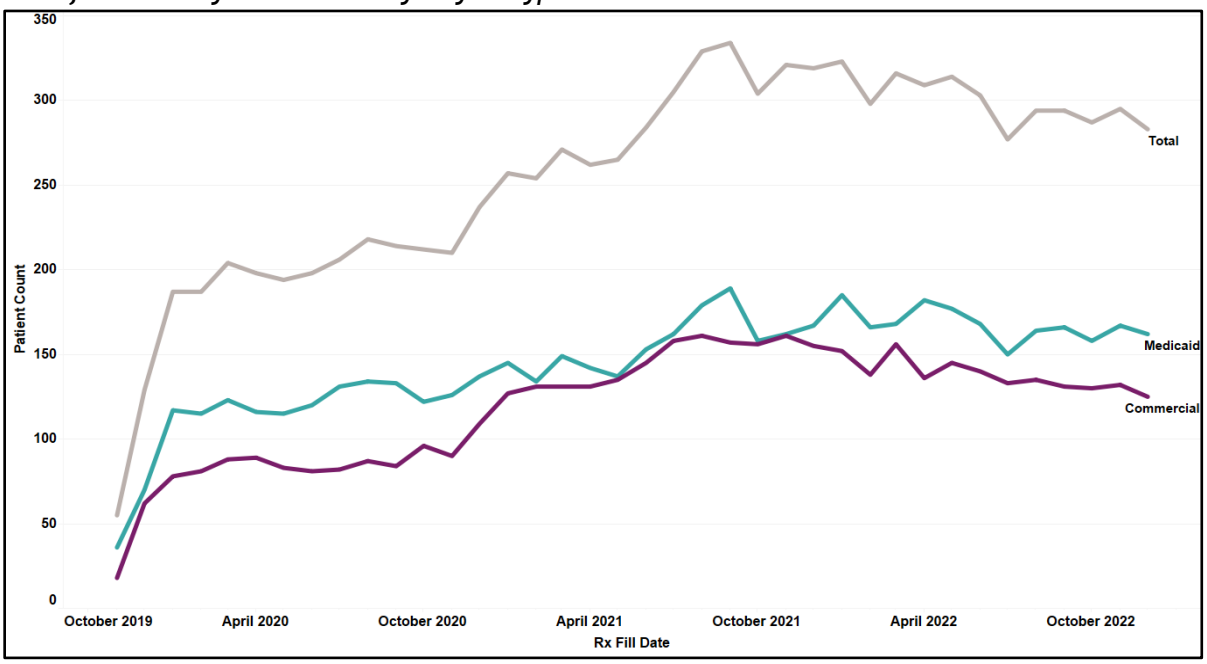


Figure A[9] shows the number of patients who filled a prescription for Trikafta each month between October 2019 and December 2022, where the gray line represents the total number of patients, the teal line shows the number of Medicaid patients and the purple line shows the number of commercially insured patients.

**Figure B**

*Insurance Information*

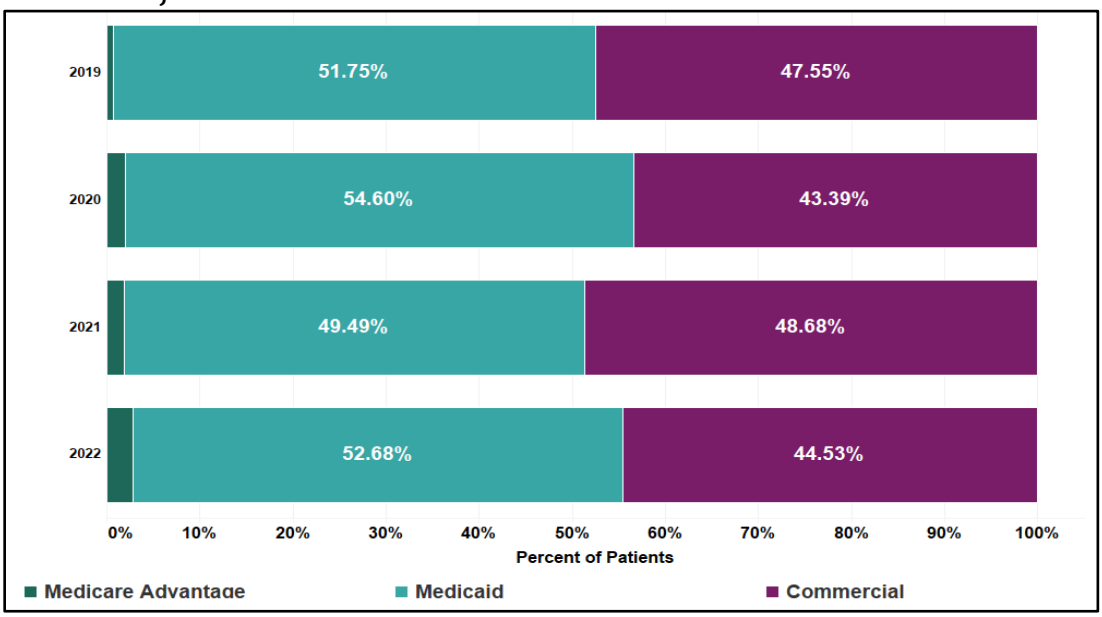


Figure B shows Trikafta payer mix percentages from 2019-2022. This figure shows the percent of patients by payer type and year where green represents patients with Medicare Advantage plans, Teal represents patients with Medicaid, and purple represents patients with commercial insurance.

[9] Medicare Advantage utilization not shown as there were fewer than 12 utilizers in all months of review.

## Health Equity Impact

Obtaining prescription drug-specific information regarding health equity can be a complex task. There is evidence that priority populations[10] experience health inequity associated with their use of medications, which causes an increased risk of adverse outcomes including mortality, morbidity burden, quality of life deficit, and patient safety issues.[11] Further, there may be condition- or disease-specific studies that investigate health inequities, but there are not always studies that investigate the impacts of a specific prescription drug. However, in the case of Trikafta, there is both data regarding cystic fibrosis generally and Trikafta specifically, summarized below.

The Cystic Fibrosis Foundation estimates that approximately 15% of people in the US living with cystic fibrosis identify as racially or ethnically diverse.[11] Research shows that people of color with cystic fibrosis, particularly people who are Black and Hispanic, experience unique challenges and often have negative experiences that can lead to poorer outcomes such as delayed diagnosis and first evaluations, engagement barriers, fewer approvals for transplants, disparate health outcomes, and low representation in clinical trials.[12] One study found that patients with cystic fibrosis from minority groups are less likely to be eligible for CFTR modulators. Of the 10% of individuals with cystic fibrosis that do not have a medication that treats the underlying cause of cystic fibrosis, approximately 33% of patients in this group are from historically medically underserved and minority communities.[12] Because people with cystic fibrosis who are racial and ethnic minorities have increased disease severity and earlier mortality, this can further contribute to health disparities.[13] See Appendix L for more information.

During the selection of eligible prescription drugs for affordability reviews, the Board reviewed a Social Vulnerability Index Score (SVI) for all eligible prescription drugs. The SVI score represents the percent of individuals who use Trikafta who live in a county with a score above the Colorado average score. Individuals residing in counties with SVI scores higher than the statewide average may be more vulnerable to adverse outcomes due to social conditions in their county. The SVI score measurement is not meant to be a comprehensive assessment of Trikafta and health equity. Rather, it is meant to be a contextual snapshot to better understand if the typical patient who uses Trikafta lives in a county that has a higher vulnerability to adverse outcomes due to social conditions than the average Colorado county.

In 2022, 55.53% of patients taking Trikafta lived in a county with a higher SVI score than the statewide average. This means that patients taking Trikafta have a slightly higher likelihood of living in a county with higher vulnerability to adverse outcomes due to social conditions than the average Coloradan. See Appendix L for more information.

[10] The Board's adopted definition of priority populations is: people experiencing homelessness; people involved with the criminal justice system; black people, indigenous people, and people of color; American Indians and Alaska natives; veterans; people who are lesbian, gay, bisexual, transgender, queer, or questioning; people of disproportionately affected sexual orientations, gender identities, or sex assigned at birth; people who have AIDS or HIV; older adults; children and families; and people with disabilities, including people who are deaf and hard of hearing, people who are blind and deafblind, people with brain injuries, people with intellectual and developmental disabilities, people with other co-occurring disabilities; and other populations as deemed appropriate by the Prescription Drug Affordability Board. 3 CCR 702-9, 1.1.C.
[11] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10037618/#:~:text=In%20comparison%20to%20the%20general,16%2C17%2C18%5D.
[12] https://www.cff.org/about-us/addressing-health-inequities-cystic-fibrosis-community
[13] https://onlinelibrary.wiley.com/doi/abs/10.1002/ppul.25285

**Figure C**
*Colorado SVI Scores for Trikafta Patients*

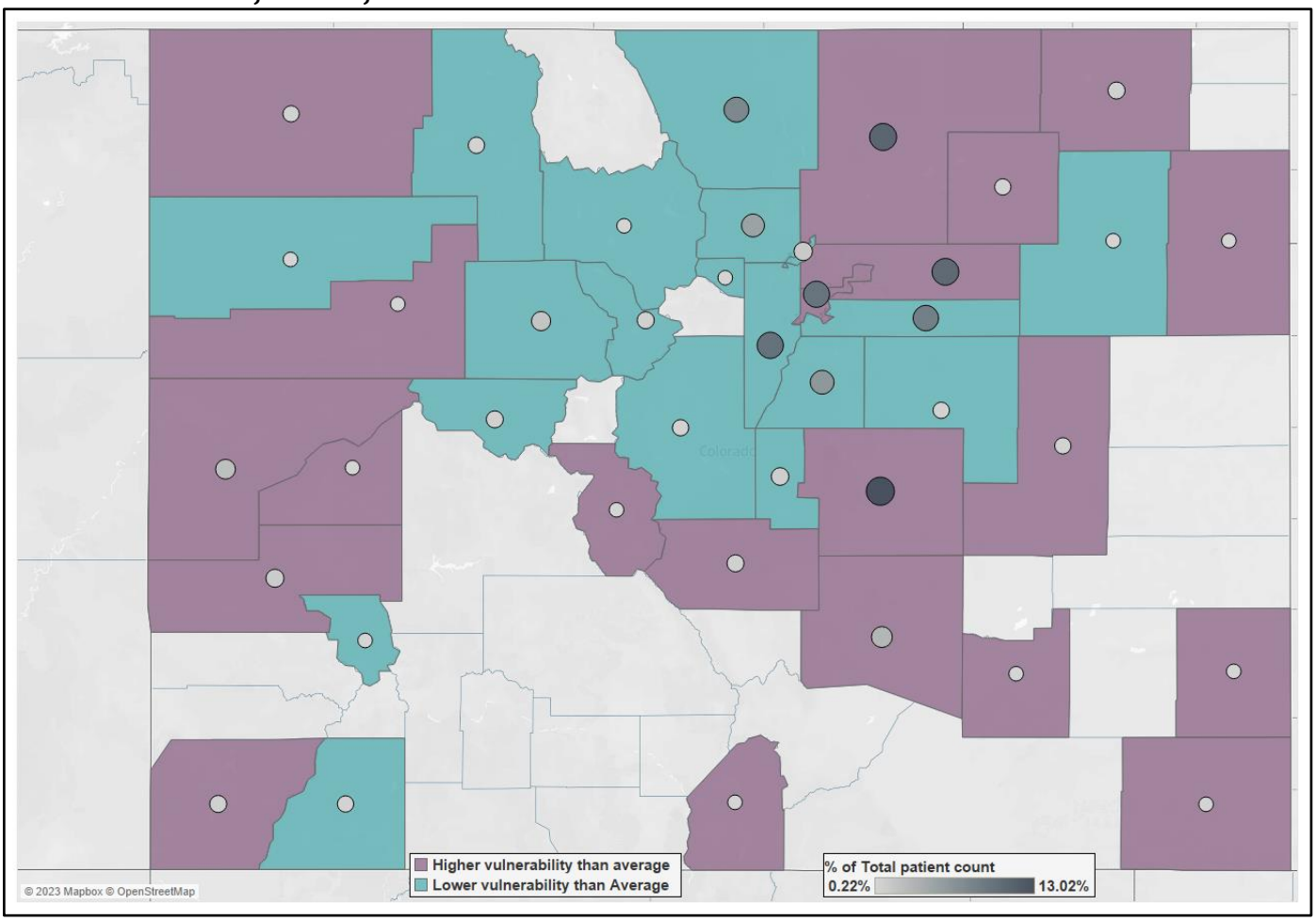


Figure C shows a map of utilizers of Trikafta in 2022 where a purple county represents higher vulnerability counties and a teal county represents a lower vulnerability county. The dots represent the portion of Trikafta utilizers that live in that county, the size and color of the dot represents the portion of utilizers in that county where a larger, darker dot represents more utilizers than a smaller, lighter dot.

Board staff received robust patient and caregiver input through an online survey aimed at gathering information regarding the health and financial effects of Trikafta. Survey participants could voluntarily provide information regarding whether they were a member of a priority population. Forty-four of the forty-seven respondents identified they were members of a priority population, with the vast majority identifying as an individual with a disability.

## Therapeutic Alternatives

The Board adopted a definition of therapeutic alternatives as prescription drugs in the same pharmacological or therapeutic class that have been shown through peer-reviewed studies to have similar therapeutic effects, safety profile, and expected outcome when administered to patients in a therapeutically equivalent dose or prescription drugs recommended as consistent with standard medical practice by medical professional association guidelines (3 CCR 702-9, Part 1.1.C). For the purposes of this affordability review, therapeutic alternatives were identified through the review of medical professional association guidelines. The resulting in-class therapeutic alternatives are summarized in Table C below.

**Table C**
*Trikafta Therapeutic Alternatives Details*

| Non-proprietary name | Brand Name | Mechanism of Action | FDA Approval Date |
|---|---|---|---|
| ivacaftor | Kalydeco | CFTR Modulator | 1/31/2012 |
| lumacaftor/ivacaftor | Orkambi | CFTR Modulator | 7/2/2015 |
| tezacaftor/ivacaftor | Symdeko | CFTR Modulator | 2/12/2018 |

Table C shows details of Trikafta's therapeutic alternatives and FDA approval dates.

While medical professional association guidelines list three prescription drugs that qualify as therapeutic alternatives to Trikafta, the Board and Board staff compiled evidence that Trikafta should be treated as a prescription drug that satisfies an unmet need and that in practice, Trikafta's therapeutic alternatives are inferior to Trikafta for patients for which Trikafta is indicated. Evidence came from four sources:

- Input from patients & caregivers - Many patients and caregivers who engaged in the affordability review process reported that Trikafta was a life-changing drug.
- Input from individuals with scientific & medical training - Many clinicians and researchers who engaged in the affordability review process reported that Trikafta has many short-term clinical benefits and the potential of promising long-term benefits.
- Voluntarily submitted information - Entities from across the prescription drug supply chain and care continuum voluntarily submitted information that Trikafta is a breakthrough therapy for cystic fibrosis.
- Clinical-effectiveness evidence - Evidence compiled for Appendix D regarding clinical effectiveness indicates Trikafta is clinically superior to therapeutic alternatives for some patients with cystic fibrosis.

Given the emerging evidence considered for affordability reviews, during the October 27, 2023 Board meeting, the Board agreed with a Board staff recommendation to not weigh information related to Trikafta's therapeutic alternatives heavily in the affordability review. As a result, this affordability review summary report contains some information on therapeutic alternatives, but does not provide in-depth analyses related to therapeutic alternatives for some sections of this report.

# Trikafta Price and Cost Profile

The Price and Cost Profile includes information on what different entities on the prescription drug supply chain charge for Trikafta, as well as what different entities pay for Trikafta. This profile also contains information on Trikafta's financial effects on health, medical, and social service costs.

**Table D**

*Trikafta's 2022 Price & Cost per Person Statistics*

| Price & Cost Per Person Statistics | Amount |
|---|---|
| Average WAC per Course of Treatment per Person[14] | [redacted] |
| Average Paid per Person | $234,439 |
| APPY - Plan Paid | $228,044 |
| APPY - Out-of-Pocket[15] | $8,907 |

Table D shows statistics on Trikafta's price and cost per person in 2022.

**Table E**

Trikafta's 2022 Statewide Price & Cost Statistics

| Statewide Price and Cost Statistics | Amount |
|---|---|
| Total Paid Amount | $108,076,387 |
| Total Plan Paid[16] | $105,128,165 |
| Total Medicaid Paid | $46,810,964 |
| Total Patient Paid | $2,121,439 |
| Gross-to-net Estimates | [redacted] |

Table E shows statistics on Trikafta's price and cost throughout Colorado in 2022.

The current WAC for Trikafta is [redacted] per tablet as of October 12, 2023, with the most recent update to the WAC on January 1, 2022. The initial WAC was [redacted] on October 21, 2019.[17] This is a 4.90% increase from 2019 to 2023; this increase is lower than the pace of inflation during the same timeframe. The average course of treatment is [redacted] tablets per patient per year, making the current WAC per course of treatment [redacted].[18] See Appendices A and O for more information.

In April 2023, the FDA approved the use of Trikafta for children ages two to five years who have at least one F508del mutation in the CFTR gene or a mutation in the FTR gene that is responsive based on in vitro data.[19] This newly approved dosage comes in oral granules and has a current WAC of [redacted] per packet: there have

[14] Course of treatment is calculated based on utilization not FDA labeling recommended doses. For course of treatment methodology please see June 9th, 2023 PDAB Board staff memo: https://drive.google.com/file/d/16BFOEB-LMiulmYzhKhxeGjvbFoh88cTs/view?usp=sharing

[15] Medicaid copayments are $0-$3 for each prescription fill, as a result, Medicaid out of pocket paid amounts are removed from all averages in the data presented below, however, it is included in the statewide totals when reviewing the total amount patients paid. Medicaid copay information: https://www.healthfirstcolorado.com/copay/

[16] Total Plan Paid represents the amount paid by a patient's primary insurance coverage, even though secondary coverage may have paid an amount. Secondary insurance coverage paid amounts are generally captured in Total Paid Amounts.

[17] AnalySource Data

[18] Course of Treatment methodology outlined in Board Staff Memo from June 6, 2023: https://drive.google.com/drive/folders/1vVX6hoy4njlrhhlkBylMQZBscVxK9jyT

[19] https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/217660s000lbl.pdf

been no changes in WAC since approval. As this is a newly approved indication, there is no utilization data in the APCD and the course of treatment was not calculated.

Pursuant to section 10-16-1405, C.R.S., carriers and pharmacy benefit managers submit data about the highest cost prescription drugs to the APCD, including the fifteen prescription drugs that caused the greatest increase to the carrier's premiums. Nine of the nineteen carriers who submitted data reported Trikafta in the top fifteen drugs that caused the greatest increase to premiums, seven of these submitters reported Trikafta in the top five drugs that caused the greatest increase to premiums. Additionally, prescription drug transparency data from other states indicates Trikafta is among the costliest drugs in the state (Maine, Oregon), highest year-over-year cost increases (Maine), and top drugs with greatest increases in plan spending (Oregon). See Appendix O for more pricing information.

## Out-of-Pocket Estimates

Patient copayment and other cost sharing depends on many factors, including: a patient's insurance coverage, how much has already been contributed to out-of-pocket maximum amounts in a benefit year, and whether the patient receives other assistance to pay for their portion of prescription drug. The APCD provides data on the patient portion of the claim paid for the drug, but does not contain any information on assistance programs. Patients and caregivers provided input regarding their experiences with assistance programs through public meetings, surveys, and voluntarily submitted information. See Appendix H for more information.

The average annual out-of-pocket cost per person per year for individuals with commercial insurance or Medicare Advantage plans is $8,906.67. There was wide variation in monthly average out-of-pocket costs, where 50.941% of individuals paid a total amount between $0-$50, though some individuals paid as much as $22,700-$22,750.[20] Figure D outlines the monthly out-of-pocket amounts for commercially insured individuals by type of out-of-pocket expense. See Appendix E for more details.

[20] For the vast majority of patients covered by Medicaid, patient prescription drug copayments are between $0-$3 for each prescription drug fill and most individuals with Medicaid coverage do not have deductibles or coinsurance. See Appendix E for more information.

**Figure D**

*Trikafta's Monthly Out-of-Pocket Amounts for Commercially Insured Individuals by Type of Out-of-Pocket Expense from 2019-2022*

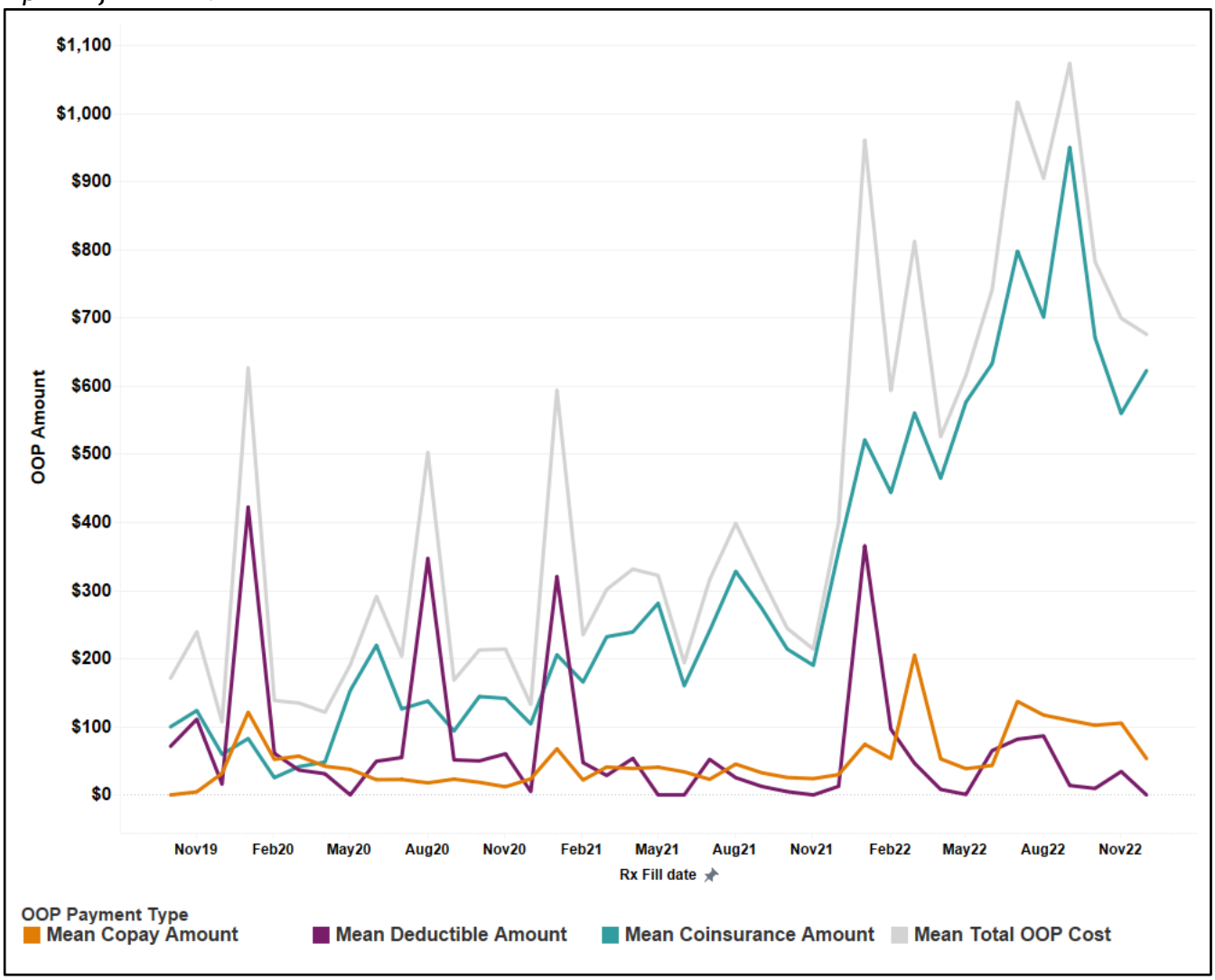


Figure D shows this graph shows the average out-of-pocket amount for commercially insured patients where the orange line shows the monthly average copayment amount, the purple line shows the monthly average deductible amount, the teal line shows the monthly average coinsurance amount, and the gray line shows the total out-of-pocket amount. There are distinct increases in the average deductible amounts in each January and in August of 2020, which is most likely representative of new plan years and individuals contributing more towards their deductibles before they are met. The average monthly coinsurance amount has been increasing with a peak in September 2022 at an average of $951.

Another snapshot of out-of-pocket costs for individuals with commercial insurance and Medicare Advantage is summarized below.

**Table F**

*Monthly Average Out-of-Pocket Amounts for Commercial Coverage in 2022*

| Average Out-of-Pocket Cost | Commercial |
|---|---|
| Average Out-of-Pocket Cost | $784 |
| Average Deductible Amount | $67 |
| Average Coinsurance Amount | $625 |
| Average Copayment Amount | $91 |
| Average days supply | 29.2 |

Table F shows Trikafta's 2022 average monthly out-of-pocket expenditure for individuals who are commercially insured.

In 2022, in an average month, an individual with commercial insurance paid a total of $784, $67 went towards their deductible, $625 was in coinsurance, and their copayment was $91, on average this was for 29.2 days of Trikafta. These averages are calculated based on claims from the APCD, which does not include information about assistance programs that individuals might use when filling their prescriptions.

Vertex Pharmaceuticals Incorporated provided information on Vertex GPS: Guidance & Patient Support, which is available to eligible patients who need additional help and provides free medicine to patients who do not have insurance and meet certain eligibility criteria.[21] Board staff heard in public meetings that as many as 75% of patients rely on some form of patient assistance program and utilize these assistance programs to purchase Trikafta for less than $50 per month. Thirty of the forty-seven patients and caregivers surveyed indicated that they use manufacturer assistance to help pay for Trikafta, the majority of which used patient support programs provided by Vertex. See Appendices H, I, J, and K for more information.

## Rebates, Discounts, and Price Concessions Estimates

The gross-to-net sales estimate is a proprietary estimate where SSR Health estimates all price concessions the manufacturer gives, including rebates, 340B discounts, assistance programs, and other price concessions provided by manufacturers compared to gross sales to get a percentage estimate of all discounts.[22] The gross-to-net sales estimate was [redacted] in the last quarter of 2019, which increased to [redacted] in the second quarter of 2023. See Appendix K for more information.

## Trikafta's Health and Financial Effects

One component of affordability reviews is an assessment of the relative financial effects on health, medical, or social service costs, as the effects can be quantified and compared to baseline effects of existing therapeutic alternatives to the prescription drug. Information regarding Trikafta's relative financial effects on health, medical, or social service costs is summarized here from literature reviews (Appendix D), input from patients and caregivers (Appendix H), input from individuals with scientific and medical training

[21] https://drive.google.com/file/d/1Te0uSno7bob1sV7e1SY9ZzhXG2JDMQGR/view?usp=drive_link
[22] All gross-to-net estimates are provided on a four quarter moving average.

(Appendix I), and voluntarily submitted information (Appendix J). These summaries are structured to focus first on Trikafta's health effects, followed by financial effects.

### Trikafta's Health Effects

The FDA label provides information on Trikafta's impact on:

- **Change in ppFEV1**[23] (percent predicted forced expiratory volume in 1 second): PpFEV is a measure of lung function by measuring how much air a person can exhale in a forced breath in one second. Trikafta provided an increase in lung function v. placebo.
- **Number of pulmonary exacerbations:** There is no widely accepted definition of pulmonary exacerbation, but it generally means an increase in respiratory symptoms like cough, sputum production, and shortness of breath accompanied by an acute decrease in lung function. The number of pulmonary exacerbations significantly decreased for people taking Trikafta.
- **Change in sweat chloride**: Sweat chloride is the amount of salt in a person's sweat. Trikafa provided a decrease in sweat chloride.
- **Change in body mass index:** Body mass index (BMI) is a measure of a person's weight in relation to their height. Trikafta resulted in an increase in patients' BMI
- **Change in CFQ-R respiratory domain score**: The Cystic Fibrosis Questionnaire-Revised (CFQ-R) is a quality of life measure for children, adolescents, and adults with CF.[24] It is scored on a scale of 1-100, with higher scores indicating better health-related quality of life. Trikafta resulted in a 20% increase in CFQ-R Scores.

Vertex Pharmaceuticals Incorporated cited a poster presented at the 2021 Academy of Managed Care Pharmacy NEXUS Conference stating "as younger patients initiate treatment, validated modeling indicates that treatment with Trikafta is predicted to extend survival in patients with cystic fibrosis ages six years and older by 24-37 years of age".[25]

Patients and caregivers reported in public meetings and surveys that Trikafta provides significant health benefits. Patients and caregivers reported Trikafta had the following health effects:

- Pulmonary disease impact - patients and caregivers described that taking Trikafta resulted in: increased lung function, with patients moving from a high level of oxygen dependency to no oxygen requirement. Some patients reported no longer needing to be on a lung transplant list because of Trikafta.
- Gastrointestinal Issues and Nutrition - patients and caregivers reported improved nutrition absorption and digestion, sustained weight gain, and general reduction in gastrointestinal issues.
- Cystic fibrosis-related diabetes - some patients and caregivers provided input that Trikafta reduced their need for daily insulin injections to manage cystic fibrosis-related diabetes.
- Other medications - patients and caregivers reported significantly reduced medication burden, with decreased need for antibiotics, prescription steroids, and other high risk-medications.
- Psychosocial impact - Mental and emotional benefits such as increased energy, a happier disposition and ability to laugh, living a full life, meeting life milestones of marriage, going to college, having children, and looking forward to the future. Ability to participate in physical activity, work a full time job, and support a family.

[23] https://www.atsjournals.org/doi/pdf/10.1513/AnnalsATS.201707-539OT#:~:text=Definition%20of%20abbreviations%3A%20N%2FA,expiratory%20volume%20in%201%20second
[24] https://qol.thoracic.org/sections/instruments/ae/pages/cfq-cfq-r.html
[25] See Appendix J for more information and citation.

See Appendix H and J for more information from patients and caregivers, including audio recordings from two public stakeholder meetings, patient and caregiver survey results, and voluntarily submitted information from patients and caregivers.

Individuals with scientific and medical training also reported in a public meeting and surveys that Trikafta provides significant health benefits. Health benefits outlined by these individuals included:

- Trikafta is very effective in treating patients two and older with P508del genotypes in whom previous CFTR modulator regimens were ineffective
- Trikafta has shown sustained improvements in lung function, reduced frequency of hospitalizations, increased BMI, and lower prevalence of positive bacterial cultures.
- Population level changes: decreased all-cause mortality rate by more than 50%; decrease in rate of first lung transplant.
- Trikafta impacts the psychosocial health of cystic fibrosis patients. Examples of improved psychosocial health included:
    - Improved outlook and hope for the future; an example used to support this was an increase in the number of cystic fibrosis patients having children, and
    - Ability to attend school and/or enter the workforce
- Trikafta is a treatment that may impact other multi-organ system diseases caused by or related to cystic fibrosis. Examples mentioned included:
    - Cystic fibrosis-related diabetes – there are real-world studies indicating teenagers who take Trikafta are less likely to develop cystic fibrosis-related diabetes, and
    - Liver disease – some cystic fibrosis patients develop liver disease and may require a liver transplant; Trikafta has the potential to impact the development of liver disease in cystic fibrosis patients.

See Appendix I and J for more information from individuals with scientific and medical training, including an audio recording from one public stakeholder meeting, individuals with scientific and medical training results, and voluntarily submitted information from individuals with scientific and medical training.

In addition to gathering information from patients, caregivers, and individuals with scientific and medical training, Board staff conducted literature reviews to compile evidence of the clinical effectiveness of Trikafta. To do this, Board staff examined studies conducted by Health Technology Assessment (HTAs) organizations. HTA organizations, often found within or supporting governmental agencies in other countries, provide evaluations of both clinical and cost effectiveness of prescription drugs. HTAs can provide consistent and thorough assessments of a prescription drug' clinical effectiveness. A summary of these organizations, the country where they are found, and their conclusions regarding the clinical effectiveness of Trikafta are outlined in the table below. Similar to other data points, this information indicates Trikafta has significant clinical effectiveness for patients for whom Trikafta is indicated.

**Table G**

*Trikafta Health Effectiveness Analyses by HTA organizations*

| Institute or Organization (Country) | Summary of Health Effects Findings[26] |
|---|---|
| ICER (United States) | From Modulator Treatments for Cystic Fibrosis: Effectiveness and Value - Final Evidence Report and Meeting Summary published September 2020:<br><br>*Trikafta for Patients who are Homozygous for the F508del Mutation* - We therefore assign a rating of "superior" (A) to the comparative clinical effectiveness of Trikafta in this population, both versus best supportive care and versus Symdeko. |

[26] Information in this table are direct quotes from studies referenced in Appendix D.

| Institute or Organization (Country) | Summary of Health Effects Findings[26] |
|---|---|
| | *Trikafta for Patients who are Heterozygous for the f508del Mutation and a Residual Function Mutation* - Thus, we judge that Trikafta will be at least as effective as Symdeko versus best supportive care (B+). Using similar logic, we judge that we have moderate certainty that Trikafta has a comparable, small, or substantial net health benefit compared with Symdeko, with high certainty of at least a comparable net health benefit (C++).<br><br>*Trikafta for Patients who are Heterozygous for the f508del Mutation With a Minimal Function Mutation* - Thus, we have high certainty Trikafta provides a substantial (moderate-large) net health benefit relative to best supportive care. We therefore assign a rating of "superior" (A) to the comparative clinical effectiveness of Trikafta in this population. |
| CADTH (Canada) | From CADTH - Reimbursement Review - Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor - Clinical Review, Pharmacoeconomic Review, Stakeholder Input published September 2022:<br><br>For patients 6 to 11 years of age, a 24-week, double-blind, placebo-controlled RCT (Study 116; N = 121) and a pivotal, single-arm, open-label trial (Study 106B; N = 66) demonstrated that treatment with ELX-TEZ-IVA resulted in clinically meaningful improvements in lung function (increase in ppFEV1 ), nutritional status (increase in BMI z scores), and HRQoL (increase in CFQ-R respiratory domain scores) and CF biomarkers (reduction in sweat chloride). In addition, AE data suggested that ELX-TEZ-IVA reduced the occurrence of pulmonary exacerbations in pediatric patients.<br><br>For patients 12 years and older, a 24-week, placebo-controlled RCT (Study 102; N = 403) conducted in patients with an F/MF genotype demonstrated that, compared with placebo, 24 weeks of treatment with ELX-TEZ-IVA was associated with statistically significant and clinically meaningful improvements in lung function (increase in ppFEV1 ), nutritional status (increase in BMI), HRQoL (increase in CFQ-R respiratory domain scores), CF biomarkers (reduction in sweat chloride), and a reduced rate of pulmonary exacerbations, including events that required IV antibiotics and/or hospitalization to manage. |
| IQWiG (Germany) | From Commission No. A22-15, A22-21 Extract published May 2022:<br>In summary, this results in a hint of considerable added benefit of ivacaftor/tezacaftor/elexacaftor + ivacaftor versus the ACT of BSC for CF patients 6 to 11 years who are heterozygous for the F508del mutation in the CFTR gene and have an MF mutation. |
| NCHI (Netherlands) | From GVS advice elexacaftor/tezacaftor/ivacaftor in combination with ivacaftor published April 2021:<br><br>*Integral weighting package criteria (p.3)* - This is an effective treatment. Not only do patients have fewer symptoms and therefore a better quality of life; they also use less inflammatory inhibitors, they are less often hospitalized, they are less likely to undergo a lung transplant, and they are better able to participate in the fabric of society and in the labour market. |

Table G shows a summary of health effects findings from HTA organizations. See Appendix D for more information and citations.

## Trikafta's Financial Effects

Understanding a prescription drug's financial effects on health, medical, and social service costs as compared to therapeutic alternatives can be a complex task. HTA organizations conduct evaluations of the effects and impacts of a prescription drug, which may address the direct, intended consequences as well as their indirect, unintended consequences. Though nearly all HTA organizations take into account patient, caregiver, and provider perspectives when determining a prescription drug's cost effectiveness, Board staff were able to gather direct input from those groups on Trikafta's financial effects on health, medical, and social service costs.

Patients, caregivers, and individuals with scientific and medical training were asked in public meetings and in surveys to share any additional information about how Trikafta affects them financially. At a high level, participants and respondents shared the following experiences:

- Reduces health care costs, including costs for doctors, procedures, and regular hospitalizations
- Reduces or eliminates need for other prescriptions such as antibiotics and prescription steroids.
- Transportation and costs for doctor visits.
- Reduces the need for regular assistance from caregivers to live daily life.
- Allows them to work and make a living.
- Reduces sick days and absence from work.
- Reduces time monitoring and maintaining health, leading to increased work performance and earning potential.

See Appendix H (input from patients and caregivers), Appendix I (input from individuals with scientific and medical training), and Appendix J (voluntarily submitted information) for more detail.

Similar to Table G above, Board staff conducted literature reviews to compile evidence of the cost effectiveness of Trikafta. A summary of these organizations, the country where they are found, and their conclusions regarding the clinical effectiveness of Trikafta are outlined in the table below. Of note, the three HTA organizations below determined that, even acknowledging the significant clinical effectiveness of Trikafta, a substantial discount of Trikafta's list price in the corresponding country would be required to make Trikafta cost effective. See Appendix D for more information.

**Table H**

*Trikafta Cost Effectiveness Analyses by HTA organizations*

| Institute or Organization (Country) | Summary of Financial Effects Findings[27] |
|---|---|
| ICER (United States)[28] | From Evidence Report on Treatments for Cystic Fibrosis published April 2020:<br><br>ICER's recommended health-benefit price benchmark (HBPB) for Trikafta is $67,900-$85,500 per year, which would require at least a 73% discount off the treatment's current list price. |
| CADTH (Canada)[29] | From CADTH Reimbursement Recommendation - Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor - Recommendation published July 2022:<br>The price of Trikafta that was submitted to CADTH needs to be reduced by at least 90% for the treatment to be considered cost-effective at a $50,000 per quality-adjusted lifeyear threshold. |
| NCHI (Netherlands)[30] | From GVS advice elexacaftor/tezacaftor/ivacaftor in combination with ivacaftor published April 2021:<br><br>For patients with the homozygous F508del mutation, the price of the triple therapy in combination with ivacaftor monopreparation must decrease by 75% to fall within the reference value of €50,000 per QALY.<br><br>In the case of the heterozygous subgroup, there is a deterministic ICER of €283,991/QALY. For this indication, the price should decrease by about 70% to fall below the reference value of €80,000 per QALY. |

Table H shows a summary of financial effects findings (see Appendix D for more information). Note that IQWiG (Germany) did not conduct a cost-effectiveness analysis.

[27]All cost-effectiveness studies in Table H utilize a cost per quality-adjusted life year (QALY) or similar measure. The Board may consider these studies as a part of affordability reviews, but may not use QALY analyses in determining an upper payment limit or other appropriate costs of Trikafta.

[28]https://icer.org/news-insights/press-releases/cf_evidence_report_2020/

[29]https://www.cadth.ca/sites/default/files/DRR/2022/SR0710%20Trikafta%20-%20CADTH%20Final%20Rec-meta.pdf

[30]https://english.zorginstituutnederland.nl/publications/reports/2021/04/29/gvs-advice-elexacaftor-tezacaftor-ivacaftor-kaftrio-in-combination-with-ivacaftor-kalydeco

# Trikafta Access to Care Profile

The Access to Care Profile examines potential access to care concerns related to Trikafta and whether there is evidence that the causes of access to care concerns may be related to Trikafta's price or cost. This profile includes an examination of potential relationships of changes between utilization, price, and costs as well as information on safety net providers, utilization management requirements, and health benefit plan design.

## Price Effect on Access

Trikafta's WAC has increased one time since it was approved by the FDA in 2019: on January 1, 2022 with an increase of 4.9%. See Appendix A for more details. From 2019-2022 APCD data shows fluctuations in average monthly patient out-of-pocket costs, with a general decrease in average monthly out-of-pocket costs from Trikafta's approval through September 2021, followed by a general increase in average monthly out-of-pocket costs. Meanwhile, APCD data shows monthly increases in average utilization of Trikafta, though there was a general flattening in utilization that began in September 2022. While increases in out-of-pocket costs for Trikafta may have impacted utilization, there are other reasons utilization may have flattened that cannot be found in APCD data. Utilization may have changed due to patients switching to other types of insurance or moving out of state. Patients and caregivers provided anecdotal input that Trikafta allowed many patients with cystic fibrosis to enter the workforce, and employer-sponsored health plans are less likely to report utilization data via claims reporting to the APDC.

**Figure E**

*Changes in Trikafta Average Monthly OOP Cost, Patient Count, and WAC from October 2019-December 2022*

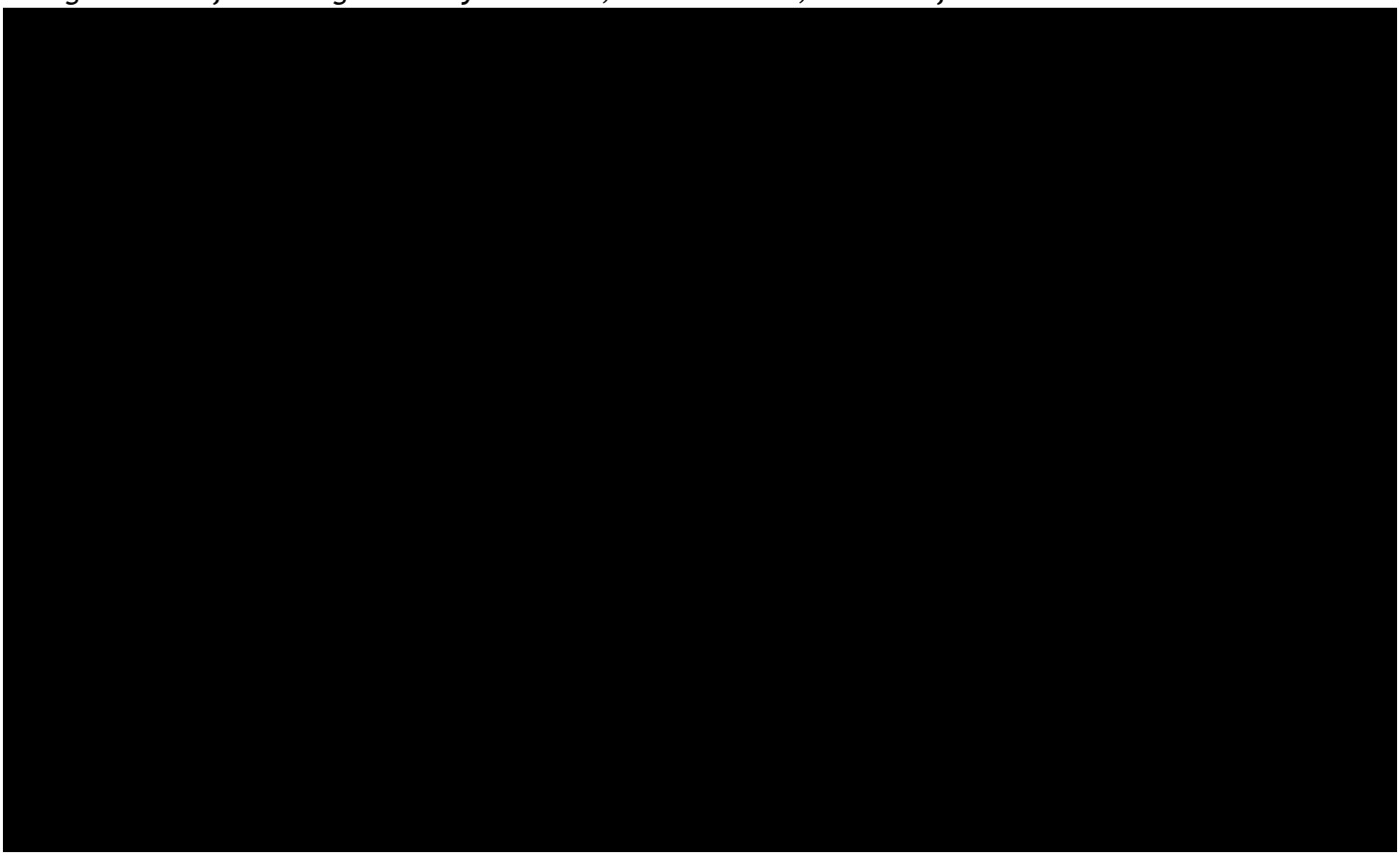

Figure E shows the per unit WAC price effective each month (green line), the number of patients who filled a prescription for Trikafta each month (blue line), and the 12 month moving average of monthly out-of-

pocket cost (yellow line).[31] Out-of-pocket costs are shown as a moving average to smooth the changes in monthly out-of-pocket costs due to benefit plan design (i.e. higher out-of-pocket costs prior to a deductible being met). See Appendix C for more information. As previously mentioned, out-of-pocket cost estimates are impacted by health benefit plan design, which affects when in the plan year a patient may pay more for a prescription drug. For example, a patient's cost sharing for prescription drugs might be higher during the beginning of their plan year and then drop significantly after the patient has met their deductible amount. See Appendix E for more information.

Additionally, patients and caregivers provided input that many patients use manufacturer, foundation, or non-profit patient assistance programs to help purchase Trikafta and that resulting out-of-pocket costs were between $0-50 per month. Utilization information, coupled with anecdotal evidence from patients and caregivers, suggest that patients with cystic fibrosis do not currently face access barriers to Trikafta because of Trikafta's price, due in part to assistance programs. It is worth noting that assistance programs are not guaranteed, and some patients, caregivers, and providers provided input that it takes time to understand how to navigate assistance programs. See Appendix K for more information. Anecdotally, information was provided via the patient and caregiver survey that, of the 47 patients and caregivers surveyed, eight participants indicated that cost impacted their access to Trikafta and three respondents indicated that they skipped or stretched doses of the drug to save money. See Appendix H, Appendix I, and Appendix N for more information.

**Table I**

*Annual Utilization and Expenditures*

| | 2019 | 2020 | 2021 | 2022 |
|---|---|---|---|---|
| **Patient Count** | 139 | 317 | 457 | 461 |
| **Total Paid** | $8,406,890 | $74,194,155 | $107,221,341 | $108,076,387 |
| **Average Paid Per Person** | $60,481 | $234,051 | $234,620 | $234,439 |
| **Total Patient Paid** | $44,120 | $495,071 | $1,142,330 | $2,121,439 |
| **Average OOP Cost** | $579 | $3,123 | $4,616 | $8,907 |
| **WAC per Unit** | [redacted] | [redacted] | [redacted] | [redacted] |

Table I shows the year over year increases in the number of patients using Trikafta, the total amount paid for Trikafta, the average paid per person, the total amount that patients paid, and the average amount that each patient paid.

While out-of-pocket costs are increasing in Figure C-1 and Table C-1, patients overwhelmingly indicated that they do not have issues paying out-of-pocket costs, in part due to assistance programs. See Appendices C, E, and H for more information. From 2021 to 2022 there was a 4.9% increase in the WAC, and while there was only a 0.80% increase in total expenditures, the total patient paid amount increased to over $2.1 million, an 85.71% increase from 2021 to 2022. Input provided indicated this increase in total patient paid amount was

[31] Figure E does not contain any information about therapeutic alternatives since the Board agreed with a Board staff recommendation on Oct. 27, 2023 to not heavily weigh data related to Trikafta's therapeutic alternatives.

not felt directly by patients, which could be due to increases in assistance programs. While there is no way to know for sure what portion of Vertex's gross sales was spent by the company on assistance programs, over the same time period there was an increase at the national level in gross-to-net sales percentage from [redacted]

It is unclear how assistance programs, including manufacturer financial assistance programs, should be relied upon, since there are no national or state laws requiring manufacturers offer such assistance, nor is there clear, public guidance on patient eligibility for assistance programs. There is also a lack of transparency and uniform data regarding how many patients qualify for copayment assistance who are covered by insurance with copayment accumulator programs, how many patients qualify for copayment assistance who are covered by insurance without copayment accumulator programs, nor how many patients reach annual copayment assistance maximum amounts. See Appendix K for more information.

## Safety Net Providers, Utilization Management Requirements, and Health Benefit Plan Design

Patients, caregivers, and clinicians provided input that treatment for cystic fibrosis generally is often received at a cystic fibrosis care center. CF Care Centers are located at teaching and community hospitals and offer comprehensive, high-quality care as funded and accredited by the Cystic Fibrosis Foundation.[32] Individuals with scientific and medical training also provided input that the two CF Care Centers in Colorado are safety net hospitals and participate as covered entities in the federal 340B Drug Pricing Program administered by the U.S. Health Resources & Services Administration (HRSA). These individuals also provided input that Trikafta is typically dispensed at specialty pharmacies, which are generally considered to be pharmacies that focus on high-cost medication therapy for patients with complex conditions.[33] No safety net providers volunteered information regarding Trikafta's utilization in a safety net setting, nor the nature of 340B discount for Trikafta. See Appendices F, I, and M for more information.

Though it is difficult to precisely know if there are uninsured patients in Colorado with cystic fibrosis, the Cystic Fibrosis Foundation's Patient Registry estimates that nationally in 2022 fewer than 1% of people with cystic fibrosis are uninsured.[34] Additionally, all 47 patients and caregivers who completed surveys identified at least one type of insurance coverage. See Appendices H and N for more information.While patients and caregivers did not provide input raising concerns with accessing providers or specialty pharmacies, patients provided feedback that utilization management requirements impacted access.

Of the 47 patients and caregivers who completed surveys, 29 said their insurance plan requires prior approval to fill the prescription, 15 said their insurance plan limits the supply of the drug, four worried that the cost of the prescription will raise their premium, and one said their insurance required them to try a medication they had previously failed. Two patients stated in public meetings that copayment accumulators are one utilization management practice that is most concerning to people with cystic fibrosis. One participant experienced issues with Medicare and Tricare related to not allowing copayment assistance. In this situation, the patients reach out to grant programs to help pay for their medication. One participant stated that occasionally insurance companies have asked for prior authorization that include a request for failure of other therapies and added that such requests add burden and stress on patients with cystic fibrosis beyond those already caused by their life-threatening disease. See Appendix H for more information. Individuals with scientific or medical training largely said that they had not encountered issues with utilization management. See Appendix I for more information.

Utilization management requirements, along with prescription drug formularies, are meant to encourage the use of medically appropriate and cost-effective drug-related products that meet the needs of patient

[32] https://www.cff.org/managing-cf/care-centers
[33] https://www.pharmacist.com/Practice/Patient-Care-Services/Specialty
[34] https://www.cff.org/medical-professionals/patient-registry

populations.[35] To better understand health benefit plan design coverage and formulary structure, data was accessed by Colorado Division of Insurance (DOI) staff for the affordability review. Data pulled was for carriers in the individual and small group markets for which DOI receives annual rate filings. As such, this data does not describe the entire insurance market in Colorado, but can shed valuable information on benefit plan design and out-of-pocket costs.

Of the ten carriers that submitted filings, five cover Trikafta. Each of the ten carriers offer many health benefit plans, with 46 Individual Plans and 96 Small Group Plans providing coverage for Trikafta. In general, the carriers place Trikafta on the highest prescription drug formulary tier, which means a higher portion of Trikafta is paid by patients, as compared to prescriptions drugs on lower tiers, until the maximum out-of-pocket is met. See Appendix E for more information.

[35] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10398227/#:~:text=The%20intent%20of%20a%20formulary,the%20needs%20of%20patient%20populations.