# Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators: Current and Future Utilization and Spend Among 15 Million Commercial Lives

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## Background

- Cystic fibrosis (CF) is a homozygous, autosomal recessive genetic disorder resulting from genetic mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. CF affects 30,000 people in the United States and 70,000 worldwide.[1]
- Kalydeco® (ivacaftor), Orkambi® (lumacaftor/ivacaftor), and Symdeko® (tezacaftor/ivacaftor) are CFTR modulators currently approved for use in patients with specific CFTR mutations. FDA approval was based on lung function improvement (FEV,% predicted) and little is known about mortality benefit. **Table 1** provides a summary of the currently approved modulator indications, approval dates, and eligible patient populations for each agent.[2–4]
- In 2018, the Institute for Clinical and Economic Review (ICER) determined the modulator class "represent[s] a low long-term value for money, due in large part to their high costs." CFTR modulators have an average annual wholesale acquisition cost (WAC) of $290,000 and cost between $840,000 and $975,000 per quality-adjusted life year (QALY) gained.[5]
- Since May 2017, pharmacy spend has increased following approval of additional indications for existing products. Pharmacy spend continued increasing in 2018 after launch of the new modulator, tezacaftor/ivacaftor. Added indications are anticipated throughout 2019.[1]
- Little is known about real-world utilization, spend, and discontinuation rates.

## Objectives

- Examine current CF prevalence and modulator trends in utilization and spend.
- Describe new start, switch, and modulator discontinuation rates over a six-month follow-up.
- Forecast future modulator spend among commercially insured members

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## Methods

- Integrated pharmacy and medical claims data among 15 million commercial members were queried between May 2017 and April 2018 to identify:
  - Members with two or more ICD-10 codes (E84.xx) in any field at least 30 days apart
  - Members with a modulator pharmacy claim
- A member's first modulator claim between May 2017 and April 2018 was their index date and determined their index drug.
- Members were required to be continuously enrolled six months before (pre-period) and six months after (post-period) their index date.
- New modulator starts were members that did not have any modulator claim in the pre-period.
- A modulator switch was defined as a change from one modulator to another in the post-period.
- Modulator discontinuation was defined as greater than a 45-day gap in drug supply for any modulator in the post-period.
- Total paid per member per month (PMPM) for each modulator and the modulator class was trended from January 2015 through November 2018 using a compound annual growth rate (CAGR) calculation.
- PMPM was calculated as total paid (plan plus member) modulator pharmacy costs each month divided by monthly membership.
- The 2019 modulator PMPM forecast assumptions:
  1. Tezacaftor/ivacaftor is currently approved for ages 12 and older and should receive approval in early 2019 for ages 6–11 homozygous for the F508del mutation or who have a mutation that responds to tezacaftor/ivacaftor.
  2. Increased tezacaftor/ivacaftor utilization could come from lumacaftor/ivacaftor switchers or new starts.
  3. February 2018 launch of tezacaftor/ivacaftor.
  4. The forecast used a WAC of $290,000 annually and assumes members are 100 percent adherent to therapy for 12 months.
  5. Three levels of modulator utilization were forecasted among mutation-eligible members:
     a. Minimal increase, 60 percent
     b. Moderate increase, 80 percent
     c. Maximum utilization, 100 percent

## Results

- Among approximately 15 million commercial members, 2,147 members were identified as having CF for a prevalence of 14.3 per 100,000.
- An estimated 60 percent of CF members, 1,288 of 2,147 are mutation eligible and could receive a modulator based on the Cystic Fibrosis Foundation estimation.[6]
- 695 members in our commercial data had a modulator claim resulting in the current treatment rate at 54 percent among those eligible (695 of the estimated 1,288 eligible). Our finding is consistent with the Cystic Fibrosis Foundation registry data from 2017 showing 59 – 63 percent of eligible modulator members were receiving modulator therapy.[6]

### Figure 1

- 457 out of 695 (66 percent) members with a modulator claim were continuously enrolled six months pre and post their index date.
  - Modulator index drug for these 457 members was:
    - 123 (26.9 percent) ivacaftor
    - 304 (66.5 percent) lumacaftor/ivacaftor
    - 30 (6.6 percent) tezacaftor/ivacaftor
  - 145 of the 457 (31.7 percent) current utilizers were identified as new starts. All members with a tezacaftor/ivacaftor index claim were new starts.
  - Five of the 457 (1.1 percent) current utilizers switched from their index drug to a different modulator during six-month follow-up.
  - During the six-month follow-up period, 65 of the 457 (14.2 percent) current utilizers discontinued their index drug. Ivacaftor had the highest discontinuation rate at 17.9 percent.

### Figure 2

- Total paid PMPM for all modulators increased twelve-fold from $0.08 in January 2015 to $0.96 in November 2018 with a CAGR of 88.5 percent.
  - Ivacaftor PMPM from January 2015 to June 2015 was stable at $0.10. After new indications were added in 2017, the ivacaftor PMPM steadily increased to a maximum of $0.24 in June 2018.
  - Lumacaftor/ivacaftor PMPM from July 2015 to May 2017 was stable at $0.33 with an increase in the latter half of 2017 to a maximum of $0.47 in August 2017. PMPM for lumacaftor/ivacaftor decreased following tezacaftor/ivacaftor launch in February 2018.
  - Tezacaftor/ivacaftor PMPM increased steadily following launch to $0.43 in November 2018.

### Figure 3

- Assuming minimal increase in utilization to 60 percent of mutation-eligible members receiving modulator therapy, the PMPM is forecasted to reach $1.21 by December 2019.
- Assuming moderate increase to 80 percent of mutation-eligible members receiving modulator therapy, the PMPM is forecasted to reach $1.66 by December 2019.
- Assuming maximum utilization of 100 percent of mutation-eligible members receiving modulator therapy, the PMPM is forecasted to reach $2.07 by December 2019.

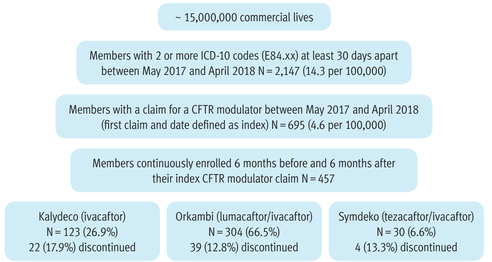
## Limitations

- Administrative medical and pharmacy claims have the potential to be miscoded and include assumptions of members' actual drug use and diagnoses.
- The data used in the study was limited to a commercial population and results are not generalizable to Medicare or Medicaid populations.
- Tezacaftor/ivacaftor was approved in February 2018 limiting the analysis to 30 tezacaftor/ivacaftor members. As a result, modulator utilizers with index dates greater than six months prior to February 2018 would not be identified as switches even if they started on tezacaftor/ivacaftor.
- Several different methods for determining discontinuation exist. This analysis used a 45-day gap to describe discontinuation rates and other methods would generate different results. Our data showed 99 percent of claims had a 30-day supply or less, which strengthens our use of a 45-day gap.
- Our forecast made assumptions about future CF prevalence, new start rate, and CFTR modulator expenditures.

**Table 1.** Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulator Summary Information

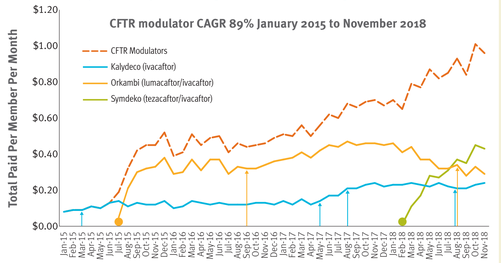
| Agent [approval] | Kalydeco® (ivacaftor) [Jan. 31, 2012] | Orkambi® (lumacaftor/ivacaftor) [July 2, 2015] | Symdeko® (tezacaftor/ivacaftor) [Feb. 12, 2018] |
|---|---|---|---|
| **Indication** | Twelve months and older who have one mutation that is responsive to ivacaftor | Two years and older homozygous for the F508del mutation | Twelve years and older homozygous for the F508del mutation or who have at least one mutation that is responsive to tezacaftor/ivacaftor |
| **Mutation-eligible patients[6]** | 14% | 36% | 27% |
| **Annual wholesale acquisition cost as of February 2019** | $307,238 (one 4.5% price increase in January 2013) | $268,963 (one 5% price increase in July 2017) | $288,000 (no price increases) |
| **Annual price to achieve $50,000 to $150,000 per quality-adjusted life year gained[5]** | ~$58,000 – $86,000 | ~$56,000 – $80,000 | ~$56,000 – $82,000 |

**Figure 1.** Cystic Fibrosis Diagnosis and Prevalence and Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulator Use Among 15 Million Commercial Lives




Modulator discontinuation was defined as greater than a 45-day gap in drug supply for any modulator in the post-period.

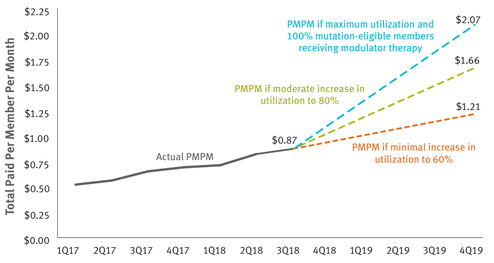
**Figure 2.** Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulator Trends in Utilization and Spend January 2015 through November 2018 Among 15 Million Commercial Lives




Compound annual growth rate (CAGR) = ((0.96/0.08) exponential (1/3.9 years))-1

Dots represent new product launch and arrows represent new indication approval

**Figure 3.** Current and Forecasted Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulator Total Paid Per Member Per Month (PMPM)




The Cystic Fibrosis Foundation estimates that 60 percent of CF patients are eligible to receive a CFTR modulator.[6] Out of 2,147 members with CF, 1,288 would be eligible to receive a CFTR modulator. The current treatment rate among 1,288 candidates was 54 percent (695) among 15 million commercially insured members.

## Conclusions

- Integrated medical and pharmacy data provided the opportunity to determine CF prevalence, utilization rate and forecast for this large commercial population.
  - CF prevalence was rare at 14 per 100,000 which is consistent with the Cystic Fibrosis Foundation.
  - The CFTR modulator treatment rate was 54 percent, also consistent with the Cystic Fibrosis Foundation who reports ~60 percent treatment rate among CF mutation-eligible patients.
- Since 2015, new CFTR modulators and additional indications has resulted in a dramatic twelve-fold PMPM increase from $0.08 to $0.96, with a CAGR of 89 percent. We forecast a potential doubling of CFTR modulator spend if 100 percent mutation-eligible members are treated. The increased costs could result in increased premiums.
- Based on the ICER conclusion of CFTR modulators representing a low long-term value at the annual $290,000 cost, health insurers should continue focusing efforts to determine best management opportunities and value-based contracting.

## References

1. Cystic Fibrosis Foundation. About Cystic Fibrosis. Available at: https://www.cff.org/What-is-CF/About-Cystic-Fibrosis/. Accessed July 20, 2018.
2. Kalydeco [package insert]. Boston, MA: Vertex Pharmaceuticals, Inc.; July 2017.
3. Orkambi [package insert]. Boston, MA: Vertex Pharmaceuticals, Inc.; January 2018.
4. Symdeko [package insert]. Boston, MA: Vertex Pharmaceuticals, Inc.; February 2018.
5. Modulator Treatments for Cystic Fibrosis: Effectiveness and Value. ICER Evidence Report. Institute for Clinical and Economic Review, June 2018.
6. Cystic Fibrosis Foundation. 2017 Cystic Fibrosis Foundation Patient Registry Highlights. Available at: https://www.cff.org/Research/Researcher-Resources/Patient-Registry/2017-Patient-Registry-Annual-Data-Report.pdf. Accessed July 20, 2018.