

United States Senate
PERMANENT SUBCOMMITTEE ON INVESTIGATIONS
Committee on Homeland Security and Governmental Affairs

Rob Portman, Chairman
Tom Carper, Ranking Member

**COMBATTING THE OPIOID CRISIS:
THE PRICE INCREASE OF AN OPIOID
OVERDOSE REVERSAL DRUG AND THE COST
TO THE U.S. HEALTH CARE SYSTEM**

STAFF REPORT

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COMBATTING THE OPIOID CRISIS: THE PRICE INCREASE OF AN OPIOID OVERDOSE REVERSAL DRUG AND THE COST TO THE U.S. HEALTH CARE SYSTEM

EXECUTIVE SUMMARY

Over the last four years, the Subcommittee has conducted several extensive investigations on the opioid epidemic and the federal government’s response to the crisis. As part of that broader effort to examine the opioid crisis and its impact on the American people, the Subcommittee conducted a case study investigation into the cost of naloxone, the prescription drug used to revive individuals who overdose on opioids. This report documents the Subcommittee’s findings from that investigation, and specifically how one pharmaceutical company – kaleo, Inc. – exploited the opioid crisis by increasing the price of its naloxone drug EVZIO by more than 600 percent (from an initial price of \$575 per unit to \$3,750 and then \$4,100 eleven months later), resulting in more than \$142 million in charges to taxpayers in just the last four years.

Kaléo raised the price of EVZIO in February 2016 and launched its new distribution model planning to “[c]apitalize on the opportunity” of “opioid overdose at epidemic levels” and a “well established public health crisis.” As part of its new distribution model, the company’s sales force focused on ensuring doctor offices signed any necessary paperwork (called prior authorizations) for the EVZIO prescription to be filled and covered. This included paperwork indicating that EVZIO was medically necessary, which ensured the drug would be covered by government programs like Medicare and Medicaid for the Wholesale Acquisition Cost, less any patient copays, despite the fact that less costly alternatives exist.

* * * * *

The opioid crisis continues to grip our country. The Department of Health and Human Services’ 2018 National Survey on Drug Use and Health found that 11.4 million Americans misused opioids last year, while 2.1 million Americans suffered from opioid disorders. At the same time, the Centers for Disease Control and Prevention (“CDC”) found that 72,000 Americans died from drug overdoses in 2017 – more overdose deaths in just one year than the total number of American casualties during the entire Vietnam War. The majority of those overdose deaths—49,068 individuals or 68 percent—involved opioids.

The Impact of the Opioid Crisis. As opioid related deaths increase, so do the economic costs to the country. One recent study found the cost of the opioid crisis exceeded \$1 trillion from 2001 to 2017.¹ Opioid-related health care costs are also on the rise and estimated to be \$215.7 billion over the last 16 years.² This total includes the cost of emergency room visits, naloxone, and other indirect health costs associated with opioid abuse.³ As the death toll increased, so did the cost of one important drug that reversed the effect of an opioid overdose: “EVZIO” manufactured by the Richmond-based pharmaceutical company kaleo, Inc. (“kaléo”).

The crisis has hit the state of Ohio particularly hard. The Ohio Department of Health estimates that 4,854 individuals died in 2017 from drug overdoses; fentanyl caused 70 percent of those overdoses deaths. The financial burden on Ohio is staggering. An impact analysis of Lorain County, Ohio, with a population of 300,000, found that the opioid crisis cost the county nearly \$200 million in 2016.⁴ These costs spanned a broad spectrum, including lost wages (\$138.8 million); health care (\$42.9 million); criminal justice (\$7.2 million), child and family assistance (\$4.5 million); and treatment and prevention (\$5.4 million). Tragically, Lorain County has an opioid overdose rate that is 2.5 times higher than the national average.⁵

The opioid epidemic continues to enact a heavy toll in Delaware, as well. At least 39 Delawareans died in August of this year, the highest monthly death total since the epidemic began.⁶ This total is 1.5 times more than the previous high, which occurred just this past April.⁷ Overall, CDC data from 2015 and 2016 indicated that the increases in opioid-related deaths in Delaware are among the highest in the country. However, these death totals may not show the full extent of the problem given the increased use of naloxone to reverse opioid overdoses. Hospital records examined by the CDC show that total opioid overdoses in Delaware – including those reversed successfully through the administration of naloxone – increased at a higher rate than they did in any other state examined but one.⁸ In 2017, there were just over 2,700 documented naloxone administrations by first responders in the state.⁹ According to the Delaware Department of Justice, “Delaware’s opioid overdose death statistics would be substantially worse if not for

¹ Altarum, *Economic Toll of Opioid Crisis in U.S. Exceeded \$1 Trillion Since 2001* (Feb. 13, 2018), <https://altarum.org/news/economic-toll-opioid-crisis-us-exceeded-1-trillion-2001>.

² *Id.*

³ *Id.*

⁴ Altarum, *Community Assessment of the Opioid Crisis in Lorain County, Ohio* (Dec. 20, 2017), https://altarum.org/sites/default/files/uploaded-publication-files/Lorain-County-Community-Assessment_Executive-Summary.pdf.

⁵ *Id.*

⁶ DEL. DEP’T JUSTICE, ADDRESSING SUBSTANCE USE DISORDER IN DELAWARE: FOURTH ANNUAL UPDATE AND PLAN FOR FUTURE ACTION 1 (Oct. 10, 2018), <https://attorneygeneral.delaware.gov/wp-content/uploads/sites/50/2018/10/2018-DOJ-Opioid-Report.pdf>.

⁷ *Id.*

⁸ *Id.*

⁹ Email from Delaware Office of Emergency Medical Services to Subcommittee staff (Sept. 26, 2018).

the expanded use of naloxone.”¹⁰ Delaware states costs associated with the opioid crisis may number close to \$1.4 billion.¹¹

The FDA Approved Naloxone. The need to reverse opioid-related overdoses and save lives has never been more important. The Food and Drug Administration approved a drug called naloxone in 1971 to counteract the effects of an opioid overdose. Naloxone is administered three ways: (1) intravenously by a medical professional; (2) via an intranasal plunger delivered into one of the patient’s nostrils; or (3) via a needle injection into the patient’s muscle or fat. The more quickly an overdose victim receives naloxone, the more effective the drug is in countering the effects of the overdose.

While naloxone is available in generic form, two branded products exist for take-home use by untrained individuals in the case of an overdose: (1) Adapt’s nasal spray branded as “Narcan” and (2) kaléo’s auto-injector branded as “EVZIO.”

EVZIO is an auto-injector device that provides verbal instructions that talk the user through using EVZIO on an overdose victim. EVZIO went to market in July 2014 at \$575 per unit, which includes two auto-injectors and a training device. Since its introduction, kaléo has increased EVZIO’s price to \$750 in November of 2015; \$3,750 in February of 2016; and finally to its current cost of \$4,100 in January 2017 for an increased dosage of naloxone. Narcan is available at a cost of \$125, which also includes two doses.

Despite Advice to Price EVZIO Lower, Kaléo Set the Wholesale Acquisition Cost at \$575. In July 2014, kaléo took EVZIO to market with a Wholesale Acquisition Cost (“WAC”) of \$575. The WAC is the price of a drug prior to any discounts, rebates, or other price reductions the manufacturer agrees to with purchasers. Kaléo set the price at \$575 despite two drug-pricing consultants recommending an initial WAC between \$250 to \$300. In that price range, one consultant believed EVZIO could “own the naloxone market.” That consultant went on to work with Adapt to price Narcan at \$125 per unit. At that price, Narcan replaced EVZIO on at least two pharmacy benefit manager (“PBM”) formularies as the preferred take-home naloxone product.

¹⁰ DEL. DEP’T JUSTICE, ADDRESSING SUBSTANCE USE DISORDER IN DELAWARE: FOURTH ANNUAL UPDATE AND PLAN FOR FUTURE ACTION 1 (Oct. 10, 2018), <https://attorneygeneral.delaware.gov/wp-content/uploads/sites/50/2018/10/2018-DOJ-Opioid-Report.pdf>.

¹¹ Matthew P. Denn, *The Many Costs of Delaware’s Opioid Crisis*, DE BUS., May/June 2018, at 26 available at <http://www.dscc.com/delawarebusiness.html>; Brittany Horn, *What heroin costs Delaware – in lives and money*, DE ONLINE, Dec. 29, 2017, <https://www.delawareonline.com/story/news/local/heroinin Delaware/2017/11/29/what-heroin-opioids-cost-delaware/842267001/>.

Another study commissioned by kaléo about market access found that the medical industry responded favorably to EVZIO due to its life-saving potential, but had public health concerns about the drug regarding overuse and misuse. These concerns and the availability of a generic for \$16 would likely lead to health insurance plans requiring prior authorizations before a plan would approve a patient receiving EVZIO. Prior authorizations meant fewer patients filling prescriptions. Instead of heeding the advice of industry experts, kaléo took the drug to market at \$575. At that price, despite being a seemingly innovative product, EVZIO failed to develop a market.

Kaléo Hired Consultant Todd Smith. The traditional pharmaceutical distribution model through PBMs and health plans was not working for EVZIO. In an effort to circumvent the traditional pharmaceutical market and go directly to the patient, kaléo contacted consultant Todd Smith. Mr. Smith, and his partner Ben Bove, were known for taking drugs to market outside the traditional model of contracting with PBMs and insurance plans. The distribution model Mr. Smith used involved dramatically increasing the WAC of a drug – something he had a track-record for doing. For example, at Horizon Pharma, Mr. Smith raised the price of an arthritis medication called Duexis that combined ibuprofen and an acid reducer from \$140 for a bottle of 90 pills to \$2,400 a bottle in 2013. Mr. Smith’s new distribution model worked. Horizon earned \$290 million in revenue in 2014 following its implementation.

Kaléo worked with Mr. Smith to implement his model for EVZIO. Following a successful pilot program, kaléo put the new distribution model into effect and raised the price of EVZIO to \$3,750 in February 2016. Kaléo launched the new model planning to “[c]apitalize on the opportunity” of “[o]pioid overdose at epidemic levels” and “a well established public health crisis.”

Kaléo Increased the Price of EVZIO More Than 600 Percent Under New Distribution Model. As part of the new distribution model, the company’s sales force focused on ensuring physician offices signed any necessary paperwork or prior authorizations for the EVZIO prescription to be filled by the pharmacist and covered by a health plan. This included paperwork establishing that EVZIO was medically necessary, triggering coverage without first trying a cheaper option (called a “step edit”) for commercial plans and coverage by government programs like Medicare and Medicaid for the WAC, less any patient copays.

Kaléo asserted the model *expanded* access since a patient received EVZIO whether their insurance covered it or not. Kaléo self-insured prescriptions not covered by health plans giving the patient the EVZIO at no cost. For these patients, kaléo paid the cost of goods and any associated fees. The cost of a unit of EVZIO (two auto-injectors and a training device) amounted to roughly \$174, which included \$52 in manufacturing, \$29 in overhead, and \$93 in “obsolescence.” For commercial

patients with insurance coverage, kaléo paid any associated copays. Either way, the commercial patient received EVZIO for \$0.

The model relied on patients *with* insurance coverage to subsidize patients *without* coverage. Thus, the need to raise the price to \$3,750 and, eventually, 11 months later to \$4,100. Kaléo said insurance covers around 26 percent of EVZIO prescriptions for commercial patients and they give away the remaining 74 percent.

The Plan Worked. Kaléo saw a noticeable increase in the number of prescriptions filled. From July 2014 to June 2015, working through PBMs, only 4,769 prescriptions were filled. Following the implementation of the new distribution model and price increase to \$3,750, the company reported 66,327 prescriptions filled from February 2016 to January 2017. Overall, the fill rate for EVZIO went from 40 percent to up to 81 percent.

The distribution model also included kaléo ending its contracts with PBMs and health plans for both commercial and Medicare Part D drug coverage. This ended any administrative fees paid by kaléo, but also any rebates kaléo paid that reduced the cost of EVZIO. Kaléo also ended its participation in the Medicaid program on March 31, 2017. The effect of ending these contracts resulted in both Medicare and Medicaid paying more for EVZIO.

The Cost to Taxpayers under Medicare and Medicaid Skyrocketed. The sales for EVZIO in the first quarter of 2017 showed kaléo's dependency on government health care programs. While Medicare and Medicaid were only 24 percent of the units sold that quarter (2,522 units), the two programs were 75 percent of net sales (\$7.94 million). Commercial plans were 66 percent of units sold (7,127 units) with net sales of \$2.61 million. The Medicare program was paying an average of \$3,522 per EVZIO unit with Medicaid paying an average of \$2,412. At the same time, the commercial plans were only paying an average of \$367 per EVZIO. Government health care programs were subsidizing the broader distribution of EVZIO.

With kaléo's new distribution model in place, the cost to Medicare continued to skyrocket. Under the traditional pricing model in 2015, Medicare Part D paid \$1.9 million for 3,162 units of EVZIO—for an average of \$609 per unit. When kaléo switched to Mr. Smith's model in 2016, Medicare Part D paid \$37.6 million for 11,360 units of EVZIO—for an average of \$3,310 per unit. In 2017, the cost to the program for EVZIO rose to \$57.2 million for 14,861 units with an average cost of \$3,852 per unit. By taking EVZIO out of the traditional pharmaceutical market, kaléo capitalized on Medicare Part D's market-based design to control costs through competition. Despite Medicare paying over \$142 million for EVZIO since July 2014, kaléo has still not earned a profit in over four years of the drug being on the market.

While Kaléo ended its participation in Medicaid, the program continued to be charged for EVZIO, but outside the program's statutory savings mechanisms. Medicaid claims for EVZIO processed in 2018 by two of the country's biggest PBMs were on average above the WAC (\$4,368 for CVS and \$4,145 for Express Scripts). Kaléo stated it created its patient assistance program to replace its Medicaid participation, which provides EVZIO at no cost to qualifying patients.

Kaléo paid Mr. Smith's consulting firm over \$10.2 million for around two years of work to install this new distribution system. The rate was based on revenue generated by the new distribution model.

Kaléo's more than 600 percent price increase of EVZIO not only exploits a country in the middle of an opioid crisis, but also American taxpayers who fund government-run health care programs designed to be a safety net for our country's elderly and most vulnerable.

The Subcommittee's Past Investigations

This investigation continues the Subcommittee's examination of various facets of the opioid crisis. In the 114th Congress, the Subcommittee began its review of the crisis by examining the federal government's efforts to address opioid-related fraud and abuse in Medicare Part D. That program serves nearly 35 million senior citizens and seven million Social Security disability benefit recipients. In connection with that review, the Subcommittee also examined the anti-opioid abuse efforts of six of the nation's largest health insurance companies—both in their commercial insurance business and in their role as Medicare Part D plan sponsors. That investigation resulted in a bipartisan report titled *Combating the Opioid Epidemic: A Review of Anti-Abuse Efforts in Medicare and Private Health Insurance Systems*.

During the current 115th Congress, the Subcommittee expanded its review of the opioid crisis by investigating how illicit opioids like fentanyl were shipped into the United States from China through international mail. The Subcommittee held an initial oversight hearing on May 25, 2017, titled *Stopping the Shipment of Synthetic Opioids: Oversight of U.S. Strategy to Combat Illicit Drugs*, at which representatives from the Postal Service, the Postal Service Office of Inspector General, the State Department, Customs and Border Protection, and UPS testified. Eight months later, on January 25, 2018, the Subcommittee held a second hearing and issued a bipartisan report titled: *Combating the Opioid Crisis: Exploiting Vulnerabilities in International Mail*. On October 24, 2018, the president signed into law the *Synthetic Trafficking & Overdose Prevention Act* (or "STOP Act"), legislation designed to assist law enforcement to identify and stop fentanyl being shipped into the United States.

Next, the Subcommittee turned to the rising cost of the opioid antagonist naloxone, a prescription medication used as an emergency treatment to counteract overdoses by blocking opioids' effects on the brain. The Subcommittee has specifically focused its investigation on the initial pricing and subsequent price increases of EVZIO, a branded naloxone auto-injector produced by kaléo.

As part of its investigation, the Subcommittee reviewed more than 170,000 documents and conducted over 20 interviews, including interviews with individuals from kaléo, Express Scripts, CVS Caremark, the Centers for Medicare & Medicaid Services, the Department of Veterans Affairs, and the Department of Defense. The Subcommittee also interviewed individuals from consulting companies that advised kaléo on pricing issues, including D2 Consulting and Insight Strategy Advisors. All entities and individuals complied with the Subcommittee's requests for information, documents, and interviews.

Findings of Fact and Recommendations

Findings of Fact

- (1) **Two industry experts suggested kaléo price EVZIO between \$250 and \$300 and offer discounts and rebates.** Dean Erhardt of D2 Consulting suggested EVZIO should have a wholesale acquisition cost (“WAC”) of \$300 per unit (two auto-injectors). At that price, he believed EVZIO could “own the market.” Mr. Erhardt went on to help Adapt Pharma price its naloxone nasal spray, Narcan, at \$125, which resulted in Narcan replacing EVZIO on at least two PBM formularies as the preferred naloxone product. Another industry expert, Insight Strategy Advisors (“ISA”), recommended a list price of \$250 per unit.
- (2) **A study on market access at a \$575 WAC raised concerns about prior authorizations due to public health issues and the availability of a generic option.** Kaléo commissioned another study by ISA on how the market would react to a \$575 WAC. That ISA study found that public health concerns and a cheaper generic alternative (\$16) would likely lead to prior authorizations before a patient could receive EVZIO. Prior authorizations meant fewer prescriptions would be filled. Despite these findings, kaléo took EVZIO to market with a WAC of \$575.
- (3) **Kaléo contracted with PBMs, which control the majority of prescription drug sales, to distribute EVZIO.** Even though kaléo contracted with several PBMs (including CVS and Express Scripts) and had a seemingly innovative product, kaléo failed to generate sales. Kaléo stated this was due to plans requiring prior authorizations before filling the prescription or the patient failing at a cheaper alternative therapy (called a “step edit”) before being eligible for EVZIO.
- (4) **Kaléo hired consultants Todd Smith and Ben Bove, who implemented a new distribution model that included raising the price of EVZIO to \$3,750, and 11 months later to \$4,100.** Messrs. Smith and Bove previously executed this pricing model at Horizon Pharma where they raised the price of a bottle of arthritis medication from \$140 to \$2,482. They did the same at Novum Pharma raising the price of a skin gel from \$189 to \$7,968. The distribution model employed a sales force charged with encouraging prescribers to route prescriptions through specialty pharmacies, which handle any prior authorization paperwork for insurance coverage, including paperwork establishing that the drug is medically necessary. A prior authorization triggers coverage without a step edit for commercial plans, but also for government programs like Medicare and Medicaid.

- (5) **Following the price increase, CVS and Express Scripts both excluded EVZIO from formularies, which meant client insurance plans no longer covered the drug.** Both PBMs went on to end contracts with kaléo for commercial coverage. This meant kaléo no longer paid administrative fees or rebates to the PBMs. Around the same time, Adapt Pharma introduced Narcan at \$125 per unit (two doses), which became the preferred naloxone drug by the two PBMs.
- (6) **The new distribution model worked.** EVZIO fill rates jumped from 39 percent to up to as much as 81 percent.
- (7) **While kaléo said its new model focused on commercially covered patients, the majority of its initial revenues were from Medicare and Medicaid.** For example, in the first quarter of 2017, Medicare and Medicaid were only 24 percent of units sold (2,522 units), but 75 percent of net sales (\$7.94 million). Commercial plans were 66 percent of units sold (7,127 units) and 25 percent of net sales (\$2.61 million). Medicare paid an average of \$3,522 per unit; Medicaid paid \$2,412; and commercial plans paid \$367.
- (8) **The cost of EVZIO to the Medicare program increased exponentially.** The program paid increasing amounts for EVZIO totaling \$142,259,003 since July 2014:

Estimated Amounts Charged to Medicare for EVZIO

Year	Units Sold	Total Paid	Rebates	Total Cost to Part D	Average Cost per Unit
2014*	266	\$149,931	\$1,329	\$148,602	\$558
2015	3,162	\$2,012,388	\$84,611	\$1,927,777	\$609
2016	11,360	\$40,709,738	\$3,097,845	\$37,611,893	\$3,310
2017	14,861	\$60,615,963	\$3,369,131	\$57,246,832	\$3,852
2018**	13,509	\$45,846,395	\$522,496	\$45,323,899	\$3,355

*July 2014 to December 2014

**January to August 2018

- (9) **Kaléo ended its participation in the Medicaid program on March 31, 2017, but the program continued to be charged the full WAC for EVZIO.** The average cost per unit for Medicaid claims processed by CVS in 2018 was \$4,368 and \$4,069 by Express Scripts. Kaléo stated it created its patient assistance program to replace its Medicaid participation, which provides EVZIO at no cost to qualifying patients.

- (10) **PBMs passed varying amounts of savings through fees and rebates to their clients.** PBMs charge fees and negotiate rebates with drug manufacturers to reduce the cost of a drug sold through the PBM to its health insurance clients. CVS collected \$22,691,084.19 in administrative fees and rebates from Kaléo for EVZIO and passed 90 percent (or \$20,305,541) to its clients. Express Scripts passed clients 70 percent of the fees and rebates it collected for EVZIO in 2014 and 80 percent in 2015. However, following the EVZIO price increase in 2016, it passed only 15 percent of fees and rebates to its commercial clients for EVZIO. Express Scripts stated this was due to its “Inflation Protection Program” that protected clients from rising brand inflation. Express Scripts passed 88 percent of fees and rebates in 2014 through its Medicare Part D contract with Kaléo, 70 percent in 2015, and 69 percent in 2016.
- (11) **Kaléo paid Mr. Smith and his partner Mr. Bove over \$10.2 million for about two years of work.** This amount included \$5.6 million to terminate the consulting contract early. The pay rate was based on revenue generated by their distribution model for EVZIO. The two men were compensated through their consulting firm Underhill Pharma LLC.

Recommendations

- (1) **The Centers for Medicare & Medicaid Services (“CMS”) should review its policies governing physician use of medical necessity formulary exceptions for Medicare Part D.** Kaléo’s new distribution model relied on prescribers signing paperwork indicating EVZIO was medically necessary for their patients, ensuring that the drug would be covered by Medicare despite its high cost. While it is important for Medicare Part D patients to receive the treatments their physicians believe is best for them, CMS should review the use of medical necessity formulary exceptions to prevent companies from inappropriately influencing prescribing.
- (2) **Congress should mandate a three-day limit on opioid prescriptions.** A study by the Centers for Disease Control and Prevention (“CDC”) noted that long-term opioid abuse often begins with the treatment for acute pain. The study found that the chances of chronic use of opioids rose rapidly after the third day of use. The CDC recommendations noted that long-term opioid abuse often begins with opioid treatment for acute pain in as little as three days. Limiting and initial opioid prescription will ensure that patients get better care and will be less likely to become dependent on opioids. Less dependency would lead to fewer overdoses requiring naloxone. Opioids prescribed for

chronic pain or for end of life care would be exempted from this requirement.

- (3) Congress should require all states to utilize prescription monitoring programs (“PDMPs”) for opioids and other dangerous drugs that are authorized to freely share data among states.** PDMPs are statewide databases containing prescriber and patient prescription data on opioids and other select drugs commonly abused. Medical professionals and law enforcement use the database to identify individuals with patterns of behavior indicative of abuse or prescribers engaging in illegal activities. Both Ohio and Delaware have PDMPs in place.
- (4) Congress should require CMS to improve transparency regarding the total amount spent for drugs purchased by government health care programs.** Prescription drug manufacturers and PBMs negotiate confidential rebates and discounts for drugs listed on PBMs’ formularies. While the CMS drug spending dashboard for Medicare and Medicaid increased transparency into drug costs for the two programs, it is inaccurate because it does not include information on rebates and discounts.
- (5) Congress should allocate funding for research to develop innovative, more potent opioid overdose reversal drugs and non-opioid pain relief drugs.** Research breakthroughs in these areas could lead to cheaper alternatives to drugs like EVZIO that are easier to use than generic naloxone alternatives, and also pain treatment approaches that are less likely to lead to abuse, dependency, and overdose.
- (6) Congress should allocate funding for state and local governments to train members of the public on the use of generic and brand name naloxone products.**
- (7) States should consider changing laws to authorize and train emergency medical technicians and other first responders to administer naloxone.** Given how effective naloxone can be in reversing opioid overdoses and preventing overdose deaths, states should expand first-responders’ ability to administer naloxone and other life-saving drugs, such as epinephrine, which is used to treat allergic reactions. For example, Delaware has already taken this action.

I. BACKGROUND

The United States is in the midst of an opioid epidemic. The Department of Health and Human Services' Substance Abuse and Mental Health Services Administration's ("SAMHSA") 2018 National Survey on Drug Use and Health found 11.4 million Americans over the age of 12 misused opioids in 2017. The same study found 2.1 million Americans have opioid disorders defined as a "clinically significant impairment" due to opioid use.¹² According to preliminary estimates from the Centers for Disease Control and Prevention ("CDC"), drug overdoses killed about 72,000 Americans in 2017.¹³ Approximately 49,068 of those deaths—or 68 percent—involved opioids.¹⁴

Given the severity of the opioid epidemic and its prominence as a matter of national concern, efforts to combat the issue have been, and will continue to be, of significant interest to the Subcommittee and to federal, state, and local lawmakers. As part of its ongoing commitment to investigating a wide range of opioid-related issues, the Subcommittee launched an investigation into the pricing of naloxone to shed light on the drug pricing process, the market forces that influence that process, and the resulting effects on patient costs, patient access, and federal spending.

A. The Opioid Epidemic

Opioids and opiates are a class of drugs that interact with opioid receptors on brain cells to reduce users' perception of pain and increase feelings of pleasure.¹⁵ The classification includes some illegal drugs, like heroin, and some controlled, legal pain medications.¹⁶ Some—known as "opiates"—are naturally derived from the poppy plant, such as morphine, codeine, and heroin.¹⁷ Others, called "opioids," like fentanyl, are made synthetically in a lab to mirror the

¹² *Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health*, SUBSTANCE ABUSE AND MENTAL HEALTH SERVICES ADMIN., HHS Publication No. SMA 18-5068, NSDUH Series H53 (2018), <https://www.samhsa.gov/data/report/2017-nsduh-annual-national-report>.

¹³ *Provisional Drug Overdose Death Counts*, CENTERS FOR DISEASE CONTROL AND PREVENTION, NAT'L CTR. FOR HEALTH STAT., (Sept. 12, 2018), <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>. According to the CDC, these national provisional counts "are often incomplete and causes of death may be pending investigation...resulting in an underestimate relative to final counts." *Id.*

¹⁴ *Id.*

¹⁵ Carrie Krieger, Phar.D., *What Are Opioids and Why Are They Dangerous?*, MAYO CLINIC (Mar. 21, 2018), <https://www.mayoclinic.org/diseases-conditions/prescription-drug-abuse/expert-answers/what-are-opioids/faq-20381270>.

¹⁶ "Opiates" or "Opioids" — *What's the Difference?*, OR. ALCOHOL & DRUG POL'Y COMM'N, <https://www.oregon.gov/adpc/Pages/Opiate-vs.-Opioid.aspx> (last visited Sept. 27, 2018).

¹⁷ *Id.*

chemical structure of natural opiates.¹⁸ Still others are called “semi-synthetic opioids,” which are derived in part from opium and codeine. These include oxycodone, hydrocodone, hydromorphone, oxymorphone, and buprenorphine.¹⁹ In common parlance, however, many use “opioid” to refer to all opiates and opioids,²⁰ and the Subcommittee will do so throughout this report.

Opioid addiction affects people from all backgrounds, ages, and ethnicities, and the opioid crisis has spread throughout all areas of the country, including rural areas, suburbs, and large cities.²¹ The Subcommittee previously provided a detailed overview of the epidemic in its January 2018 staff report *Combating the Opioid Crisis: Exploiting Vulnerabilities in International Mail* and provides updates below to statistics and trends referenced in its prior report.²²

1. Deaths from Opioid Overdoses

According to provisional estimates from the CDC, approximately 72,000 Americans died from drug overdoses in 2017—almost a 10 percent increase from 2016.²³ Of those about 72,000 drug overdose deaths, 68 percent (or 49,068) were related to opioids.²⁴

The CDC attributes the rise in overdose deaths to synthetic opioids and “predominantly fentanyl,” an extremely potent synthetic opioid.²⁵ Deaths related to synthetic opioids, such as fentanyl and its analogs, increased dramatically. These were associated with nearly 30,000 lethal overdoses—about 60 percent of all opioid deaths in 2017—reflecting an increase of about 11 percent over the last five years. The CDC’s most recent provisional statistics indicate that deaths from heroin, prescription opioids, and methadone declined in the last year.²⁶

¹⁸ *Id.*

¹⁹ *Novel Synthetic Opioid Terminology*, UNIV. OF MD. FOR SUBSTANCE ABUSE RES., <https://ndews.umd.edu/resources/novel-synthetic-opioid-terminology> (last visited Sept. 27, 2018).

²⁰ *Opiates/Opioids*, NAT’L ALL. OF ADVOCATES FOR BUPRENORPHINE TREATMENT, https://www.naabt.org/education/opiates_opioids.cfm (last visited Oct. 22, 2018).

²¹ U.S. CTRS. FOR DISEASE CONTROL AND PREVENTION, U.S. DEP’T OF HEALTH AND HUMAN SERVS., *DRUG OVERDOSE DEATHS IN THE UNITED STATES* (Dec. 2017), <https://www.cdc.gov/nchs/data/databriefs/db294.pdf>.

²² STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, 115TH CONG., *COMBATING THE OPIOID CRISIS: EXPLOITING VULNERABILITIES IN INTERNATIONAL MAIL* (Comm. print. 2018).

²³ *Overdose Death Rates*, NAT’L INST. ON DRUG ABUSE, <https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates> (last updated Aug. 2018).

²⁴ *Id.*

²⁵ *Id.*

²⁶ *Provisional Drug Overdose Death Counts*, CTRS. FOR DISEASE CONTROL AND PREVENTION, NAT’L CTR. FOR HEALTH STAT. (Sept. 12, 2018), <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>.

2. Economic Toll of the Opioid Crisis

The opioid epidemic is not only claiming lives, it is also wreaking financial havoc on communities forced to devote an unsustainable amount of resources to combat it on a daily basis.²⁷ Individuals, businesses, and governments are bearing the costs of the opioid crisis—individuals in the form of lost wages; businesses in lost productivity and higher health care costs; and federal, state and local governments in lost tax revenue and additional spending on health care, social services, education, and criminal justice.²⁸

According to one study, the annual cost of the opioid epidemic in the United States grew from \$29.1 billion in 2001 to about \$115 billion in 2017.²⁹ The study also estimates that between 2001 and 2017, opioid-related health care costs were \$215.7 billion, a figure that includes emergency room visits, use of ambulances and naloxone, and indirect health care costs due to the increased risk of other diseases.³⁰

The financial burden is particularly crippling to small communities, such as Lorain County, a suburb west of Cleveland, Ohio, with a population of 300,000 and an opioid overdose rate 2.5 times the national average.³¹ An impact analysis of the burden on Lorain County found that the opioid crisis cost the county nearly \$200 million in 2016 alone, and revealed that comparatively little was being spent on treatment and prevention efforts that could curb these substantial losses.³²

3. Prescription Opioids

Doctors prescribe opioids to treat moderate to severe pain.³³ Commonly prescribed opioids include oxycodone, hydrocodone, morphine, and methadone.³⁴ Opioids are subject to misuse. This includes taking them through different

²⁷ *Press Release*, U.S. Drug Enf't Admin., DEA Warning to Police and Public: Fentanyl Exposure Kills (June 10, 2016), <https://www.dea.gov/press-releases/2016/06/10/dea-warning-police-and-public-fentanyl-exposure-kills>.

²⁸ *Economic Toll of Opioid Crisis in U.S. Exceeded \$1 Trillion Since 2001*, ALTARUM (Feb. 13, 2018), <https://altarum.org/about/news-and-events/economic-toll-of-opioid-crisis-in-u-s-exceeded-1-trillion-since-2001>.

²⁹ *Id.*

³⁰ *Id.*

³¹ *Addressing the Opioid Crisis in Ohio*, ALTARUM (Feb. 12, 2018), <https://altarum.org/publications/addressing-the-opioid-crisis-in-ohio>.

³² *Id.*

³³ ERIN BAGALMAN & ADA S. CORNELL, CONG. RESEARCH SERV., IF10741, NALOXONE FOR OPIOID OVERDOSE: REGULATION AND POLICY OPTIONS (2017); U.S. CTRS. FOR DISEASE CONTROL AND PREVENTION, U.S. DEP'T OF HEALTH AND HUMAN SERVS., OPIOID OVERDOSE: OPIOID DRUGS, <https://www.cdc.gov/drugoverdose/opioids/index.html> (last updated Aug. 24, 2017).

³⁴ *Opioid Overdose: Opioid Drugs*, U.S. CTRS. FOR DISEASE CONTROL AND PREVENTION, U.S. DEP'T OF HEALTH AND HUMAN SERVS., <https://www.cdc.gov/drugoverdose/opioids/index.html> (last updated Aug. 24, 2017).

methods than prescribed, such as crushing a pill so that it can be injected or snorted or taking a larger quantity than prescribed.³⁵ As opioids can be diverted through resale or theft to illicit markets, they may also be misused by individuals who take the drugs without a prescription.³⁶ Misuse can lead to addiction, overdose, and death.³⁷ Moreover, even regular use, as prescribed by a doctor, can lead to dependence.³⁸ A 2017 CDC study found that “the chances of chronic use begin to increase after the third day [opioids are] supplied and rise rapidly thereafter.”³⁹ It continued “treatment of acute pain with opioids should be for the shortest durations possible.”⁴⁰

4. The Rise of Illicit Opioids

Trends involving prescription opioid use, misuse, and addiction are intertwined with illegal markets for opioids.⁴¹ According to the National Institute on Drug Abuse, past misuse of prescription opioids is one of the strongest risk factors for starting heroin or other illicit opioid use.⁴²

Traditionally, markets for illegal opioids were primarily limited to heroin, but have been expanding to encompass additional substances, most recently to legal, but controlled, synthetic opioids such as fentanyl and its analogs (e.g., acetyl fentanyl, ocfentanil, carfentanil).⁴³ These types of drugs can also be manufactured illegally. Illegal synthetic opioids can be shipped into the United States from

³⁵ *Drugs of Abuse: Opioids*, NAT’L INSTIT. ON DRUG ABUSE, <https://www.drugabuse.gov/drugs-abuse/opioids> (last updated Jan. 17, 2018)); M.R. Lofwall, D.E. Moody, W.B. Fang, P.A. Nuzzo & S.L. Walsh, *Pharmacokinetics of intranasal Crushed OxyContin and Intravenous Oxycodone in Nondependent Prescription Opioid Abusers*, 52(4) J. CLIN. PHARMACOL. 600 (2012), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4006196/>.

³⁶ LISA N. SACCO, JONATHAN H. DUFF & AMANDA K. SARATA, CONG. RESEARCH SERV., R42593, PRESCRIPTION DRUG MONITORING PROGRAMS 2 (May 24, 2018).

³⁷ *Drugs of Abuse: Opioids*, NAT’L INSTIT. ON DRUG ABUSE, <https://www.drugabuse.gov/drugs-abuse/opioids> (last updated Jan. 17, 2018).

³⁸ *Opioid Overdose: Prescription Opioids*. U.S. CTRS. FOR DISEASE CONTROL AND PREVENTION, U.S. DEP’T OF HEALTH AND HUMAN SERVS., <https://www.cdc.gov/drugoverdose/opioids/prescribed.html> (last updated Aug. 29, 2017).

³⁹ ANUJ SHAH, ET AL, *Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use – United States, 2006-2015*, U.S. CTRS. FOR DISEASE CONTROL AND PREVENTION, U.S. DEP’T OF HEALTH AND HUMAN SERVS., (March 17, 2017) <https://www.cdc.gov/mmwr/volumes/66/wr/mm6610a1.htm>.

⁴⁰ *Id.*

⁴¹ *Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use*, NAT’L ACAD. OF SCI. (July 13, 2017), <https://www.ncbi.nlm.nih.gov/books/NBK458661/>.

⁴² *Prescription Opioid Use is a Risk Factor for Heroin Use*, NAT’L INSTIT. ON DRUG ABUSE, <https://www.drugabuse.gov/publications/research-reports/relationship-between-prescription-drug-heroin-abuse/prescription-opioid-use-risk-factor-heroin-use> (last updated January 2018).

⁴³ *Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use*, NAT’L ACAD. OF SCI. (July 13, 2017), <https://www.ncbi.nlm.nih.gov/books/NBK458661/>.

abroad to drug trafficking organizations or individual users, who may combine them with other illegal drugs such as cocaine and heroin, or use them to manufacture counterfeit pills that look like prescription opioid medications.⁴⁴

i. Heroin

Heroin is a synthetic derivate of the opium plant that can produce intense feelings of euphoria. Its use by humans traces to 1874, when it was synthesized from morphine and subsequently marketed as a medication.⁴⁵ Heroin is a Schedule I narcotic regulated by the Drug Enforcement Administration (“DEA”) because it has no currently accepted medical use and a high potential for abuse. It is illegal to distribute, purchase, or use for non-medical research purposes.⁴⁶

The use of heroin has been increasing in recent years among men and women, most age groups, and all income levels.⁴⁷ Some of the greatest increases have occurred in demographic groups with historically low rates of heroin use, including women, privately insured individuals, and people with higher incomes.⁴⁸ Approximately four out of five new heroin users started out misusing prescription painkillers.⁴⁹

Though the number of Americans dying from heroin overdoses continues to rise, the most recent numbers from SAMHSA’s 2018 National Survey on Drug Use and Health reflect that the number of new heroin users in 2017 has dropped by about 50 percent.⁵⁰ Even though fewer people may in fact be initiating use of heroin, the drug has become increasingly fatal as illegal drug manufacturers have begun lacing it with fentanyl and other synthetic opioids, as discussed in more detail below. These synthetic opioids are incredibly potent and inexpensive. In

⁴⁴ *Id.*

⁴⁵ *Id.*

⁴⁶ *Drug Fact Sheet: Heroin*, U.S. DRUG ENF’T ADMIN., https://www.dea.gov/sites/default/files/sites/getsmartaboutdrugs.com/files/publications/DoA_2017Ed_Updated_6.16.17.pdf#page=42 (last updated June 16, 2017).

⁴⁷ *Opioid Overdose: Heroin Overdose Data*, U.S. CTRS. FOR DISEASE CONTROL AND PREVENTION, U.S. DEP’T OF HEALTH AND HUMAN SERVS., <https://www.cdc.gov/drugoverdose/data/heroin.html> (last updated Jan. 26, 2017).

⁴⁸ *Today’s Heroin Epidemic*, U.S. CTRS. FOR DISEASE CONTROL AND PREVENTION, U.S. DEP’T OF HEALTH AND HUMAN SERVS., <https://www.cdc.gov/vitalsigns/heroin/index.html> (last updated July 7, 2015).

⁴⁹ *Opioid Addiction 2016 Facts & Figures*, AMERICAN SOCIETY OF ADDICTION MEDICINE, <https://www.asam.org/docs/default-source/advocacy/opioid-addiction-disease-facts-figures.pdf>.

⁵⁰ *Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health*, SUBSTANCE ABUSE AND MENTAL HEALTH SERVICES ADMIN., HHS Publication No. SMA 18-5068, NSDUH Series H53 (2018), <https://www.samhsa.gov/data/report/2017-nsduh-annual-national-report>.

other words, the increase in fatal heroin overdoses is not due to more people starting to use heroin, but may be attributed to heroin becoming more dangerous.⁵¹

ii. Fentanyl and Other Illicit Synthetic Opioids

Synthetic opioids are a class of drugs designed to provide pain relief by mimicking naturally occurring opioids such as codeine and morphine.⁵² Synthetic opioids, such as fentanyl and tramadol, tend to be highly potent. Only a small amount of the drug is required to produce a given effect.⁵³ Fentanyl is 50 times more potent than heroin and 100 times stronger than morphine.⁵⁴ As with other opioids, synthetic opioids affect the portion of the central nervous system that controls breathing, and can cause death by slowing or stopping respiratory function.⁵⁵ The CDC estimates that of the 72,000 overdose-related deaths in 2017, synthetic opioids caused 30,000.⁵⁶

Pharmaceutical companies legally manufacture synthetic opioids, and doctors may prescribe them for pain management.⁵⁷ Legal prescription drugs, however, are not driving the increase in synthetic opioid deaths. Illicitly manufactured drugs (mostly fentanyl) distributed through the black market are largely to blame for the rapid rise in overdose deaths.⁵⁸ Because fentanyl is cheap and relatively easy to make, it is easy to mix small doses of the substance with other illicit drugs such as heroin, marijuana, and cocaine, making those drugs even more potent and dangerous.⁵⁹ Many counterfeit prescription pills—illicitly manufactured to look like drugs such as oxycodone—also contain fentanyl as a key ingredient.⁶⁰

⁵¹ R.A. Rudd, N. Aleshire, J.E. Zibbell & R.M. Gladden, *Increases in drug and opioid overdose deaths—United States, 2000–2014*, MORBIDITY AND MORTALITY WKLY. REP., 64(50) (Jan. 1, 2016), <https://doi.org/10.1111/ajt.13776>.

⁵² *Synthetic Opioid Overdose Data*, U.S. CTRS. FOR DISEASE CONTROL AND PREVENTION, U.S. DEP'T OF HEALTH AND HUMAN SERVS., <https://www.cdc.gov/drugoverdose/data/fentanyl.html> (last updated Dec. 16, 2016).

⁵³ *Id.*

⁵⁴ *What is Fentanyl?*, NAT'L INSTIT. ON DRUG ABUSE, U.S. DEP'T OF HEALTH AND HUMAN SERVS., <https://www.drugabuse.gov/publications/drugfacts/fentanyl> (last updated June 2016).

⁵⁵ *Id.*

⁵⁶ *Provisional Drug Overdose Death Counts*, U.S. CTRS. FOR DISEASE CONTROL AND PREVENTION, NAT'L CTR. FOR HEALTH STAT., (Sept. 12, 2018), <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>.

⁵⁷ *What is Fentanyl?*, NAT'L INSTIT. ON DRUG ABUSE, U.S. DEP'T OF HEALTH AND HUMAN SERVS., <https://www.drugabuse.gov/publications/drugfacts/fentanyl> (last updated June 2016); *Fentanyl*, U.S. NAT'L LIBRARY OF MED., <https://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0000728/> (last visited Sept. 4, 2018).

⁵⁸ *Synthetic Opioid Overdose Data*, U.S. CTRS. FOR DISEASE CONTROL AND PREVENTION, U.S. DEP'T OF HEALTH AND HUMAN SERVS., <https://www.cdc.gov/drugoverdose/data/fentanyl.html> (last updated Dec. 16, 2016).

⁵⁹ *Id.*

⁶⁰ U.S. DRUG ENF'T ADMIN., U.S. DEP'T OF JUSTICE, DEA-DCT-DIB-021-16, COUNTERFEIT PRESCRIPTION PILLS CONTAINING FENTANYLS: A GLOBAL THREAT (July 2016),

B. The Role of Naloxone

Naloxone is a drug used to counter the effects of opioid overdose.⁶¹ As the number of overdose deaths continues to climb, the market for and availability of naloxone medications have become increasingly important. Naloxone is used as an immediate treatment in emergency settings and is also used in combination with other drugs for long-term medication assisted treatment. This report focuses on naloxone products intended for emergency use.

Opioid overdoses can cause death by depressing a user's respiratory function.⁶² Naloxone can reverse the depression of respiratory function, as well as sedation and low blood pressure, allowing the overdose victim to resume normal breathing.⁶³ The medical community regards naloxone as a highly effective and frequently life-saving treatment.⁶⁴ Naloxone is most effective when administered immediately.⁶⁵ It is considered a safe medication as clinical studies show that it does not produce tolerance or psychological dependence.⁶⁶

1. Development and FDA Approval of Naloxone

Naloxone was developed and patented in the 1960s as a novel opioid antagonist with fewer side effects than its predecessors. In 1971, the Food and Drug Administration ("FDA") approved naloxone for treating opioid overdoses by intravenous ("IV") or intramuscular ("IM") injection, with IV being the recommended route.⁶⁷ The rapid rise in prescription painkiller and heroin overdoses spurred practitioners to seek ways other than IV injection to administer

https://content.govdelivery.com/attachments/USDOJDEA/2016/07/22/file_attachments/590360/fentanyl%2Bpills%2Breport.pdf.

⁶¹ *Opioid Overdose Reversal with Naloxone (Narcan, Evzio)*, NAT'L INSTIT. OF HEALTH, <https://www.drugabuse.gov/related-topics/opioid-overdose-reversal-naloxone-narcan-evzio> (last updated Apr. 2018).

⁶² Catherine J. Jolley, James Bell, Gerrard F. Rafferty & John Strang, *Understanding Heroin Overdose: A Study of the Acute Respiratory Depressant Effects of Injected Pharmaceutical Heroin*, PLOS ONE 10, 11 (Oct. 23, 2015), <https://doi.org/10.1371/journal.pone.0140995>.

⁶³ Rachel Rzasal Lynn & JL Galinkin, *Naloxone Dosage for Opioid Reversal: Current Evidence and Clinical Implications*, 9 THERAPEUTIC ADVANCES IN DRUG SAFETY 63 (Jan. 2018), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5753997/>.

⁶⁴ *Id.*

⁶⁵ *Naloxone hydrochloride- Drug Label Information*, NAT'L INSTIT. OF HEALTH, <http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=76f7eee1-d524-43a4-a868-ffa9f29638a6>.

⁶⁶ Daniel Kim, Kevin S. Irwin & Kaveh Khoshnood, *Expanded Access to Naloxone: Options for Critical Response to the Epidemic of Opioid Overdose Mortality*, 99 AM. J. PUB. HEALTH 402 (2009).

⁶⁷ *Naloxone*, AM. CHEMICAL SOC'Y, <https://www.acs.org/content/acs/en/molecule-of-the-week/archive/n/naloxone.html>; *Naloxone for Treatment of Opioid Overdose*, INSYS DEVELOPMENT COMPANY, INC. (Oct. 5, 2016),

naloxone quickly and safely under non-hospital conditions, such as IM or intranasal (“IN”) delivery.⁶⁸

The amount of time between an overdose and the administration of naloxone is critical to a patient’s survival. Since 1996, community-based programs have been distributing take-home naloxone kits to the public that people without formal medical training can quickly use in an emergency.⁶⁹ The results of these programs have been positive. According to the CDC, non-medical personnel reversed more than 26,000 opioid overdoses between 1996 and 2014.⁷⁰

The CDC encourages the targeted distribution of take-home naloxone kits to individuals who are most likely to experience or witness an overdose, including people who use opioids, and first responders.⁷¹ Most states and the District of Columbia have implemented non-patient-specific prescription models for naloxone, such as standing orders that allow local pharmacies to dispense the drug to patients without a prescription from a health care provider.⁷² The Surgeon General has even urged anyone with a friend or family member who uses opioids for treatment of chronic pain to obtain naloxone and learn how to administer it.⁷³

2. Naloxone Administration

Naloxone can be administered in three ways. First, medical professionals or other trained individuals can administer IV delivery of naloxone,⁷⁴ which takes effect in approximately one to two minutes.⁷⁵ Although effective, this requires expertise and training—to be able to draw the naloxone up from a vial and then inject it with a needle and syringe. Due to vein damage, it can be difficult to

⁶⁸ *Id.*

⁶⁹ *Community-Based Opioid Overdose Prevention Programs Providing Naloxone — United States, 2010*, 61 MORBIDITY & MORTALITY WKLY. REP. (Feb. 17, 2012),

⁷⁰ Eliza Wheeler et al., *Opioid Overdose Prevention Programs Providing Naloxone to Laypersons — United States, 2014*, 64 MORBIDITY & MORTALITY WKLY. REP. 631 (June 19, 2015), <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6423a2.htm>.

⁷¹ JENNIFER J. CARROLL, TRACI C. GREEN & RITA K. NOONAN, U.S. CTRS. FOR DISEASE CONTROL AND PREVENTION, U.S. DEP’T OF HEALTH AND HUMAN SERVS., EVIDENCE-BASED STRATEGIES FOR PREVENTING OPIOID OVERDOSE: WHAT’S WORKING IN THE UNITED STATES 8–9 (2018), <https://www.cdc.gov/drugoverdose/pdf/pubs/2018-evidence-based-strategies.pdf>.

⁷² *Preventing the Consequences of Opioid Overdose: Understanding Naloxone Access Laws*, SUBSTANCE ABUSE AND MENTAL HEALTH SERVS. ADMIN., <https://www.samhsa.gov/capt/sites/default/files/resources/naloxone-access-laws-tool.pdf> (last updated January 20, 2018).

⁷³ *Surgeon General’s Advisory on Naloxone and Opioid Overdose*, U.S. DEP’T OF HEALTH & HUM. SERVS., <https://www.surgeongeneral.gov/priorities/opioid-overdose-prevention/naloxone-advisory.html> (last visited Sept. 28, 2018).

⁷⁴ Shawn E. Fellows, Alexander J. Coppola & Mona A. Ghandi, *Comparative Methods of Naloxone Administration: A Narrative Review*, 13 J. OPIOID MGMT. 253, 254 (2017).

⁷⁵ Mark A. Merlin et al., *Intranasal Naloxone Delivery is an Alternative to Intravenous Naloxone for Opioid Overdoses*, 28 AM. J. EMERGENCY MED. 296, 297 (2010),

deliver naloxone via IV to chronic drug users, particularly in emergency situations.⁷⁶

Second, medical and non-medical professionals can administer naloxone via IN.⁷⁷ The person treating the overdose victim administers the drug by peeling back a protective package to remove the device, and then placing and holding the tip of the nozzle in either nostril of the patient and pressing the plunger on the device firmly to release the dose into the patient's nose.⁷⁸

Third, medical and non-medical professionals can administer naloxone via IM delivery.⁷⁹ Like IV delivery, this method uses a needle to deliver the drug, but does not involve continuous infusion into a patient's vein. The person administering the drug to the patient via IM delivery injects the dose directly into a patient's muscle or fat.⁸⁰ Naloxone can be administered via IM delivery by using a syringe or an auto-injector device such as EVZIO.⁸¹ When compared with IV administration of naloxone in a medical facility, IN and IM delivery methods appear to be similarly effective with the potential for less significant side effects, such as injection site pain or infection.⁸²

3. Naloxone Brand Names

Naloxone is available under two brand names: (1) EVZIO, as an auto-injector manufactured by kaleo, Inc.; and, (2) Narcan, as a nasal spray manufactured by Adapt Pharma. Both are described below.

i. Kaleo, Inc.'s EVZIO

In April 2014, the FDA approved kaléo's EVZIO device—the first naloxone treatment specifically designed for non-medical bystanders to use in the event of

⁷⁶ K. Wanger, L. Brough, I. Macmillan, J. Goulding, I. MacPhail & JM. Christenson, *Intravenous vs Subcutaneous Naloxone for Out-Of-Hospital Management of Presumed Opioid Overdose*, 5 ACAD. EMERGING MED. 29 (1998), <https://www.ncbi.nlm.nih.gov/pubmed/9562190>.

⁷⁷ Christina R. Lewis, Hoa T. Vo & Marc Fishman, *Intranasal naloxone and related strategies for opioid overdose intervention by nonmedical personnel: a review*, 8 SUBSTANCE ABUSE REHABIL. 79–95 (Oct. 11, 2017), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5644601/>.

⁷⁸ *Key Steps to Administering Narcan Nasal Spray*, NARCAN, <https://www.narcan.com/patients/how-to-use-narcan/> (last visited Oct. 22, 2018).

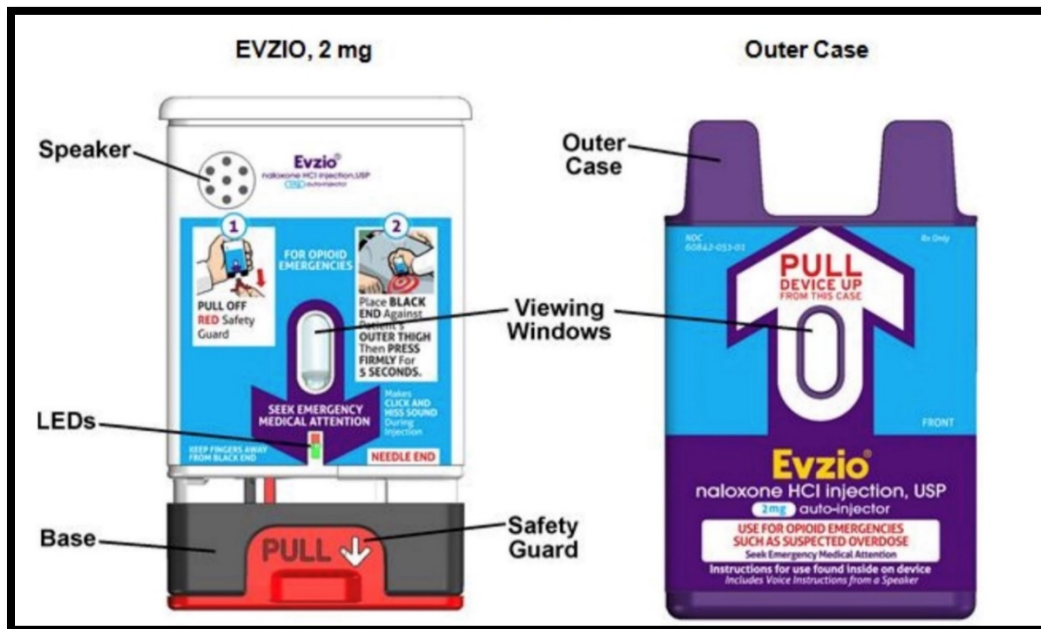
⁷⁹ K. Wanger, L. Brough, I. Macmillan, J. Goulding, I. MacPhail & JM. Christenson, *Intravenous vs Subcutaneous Naloxone for Out-Of-Hospital Management of Presumed Opioid Overdose*, 5 ACAD. EMERGING MED. 294 (1998), <https://www.ncbi.nlm.nih.gov/pubmed/9562190>.

⁸⁰ *Naloxone Injection*, VHA PHARMACY BENEFITS MANAGEMENT SERVICES (July 2014), https://www.pbm.va.gov/PBM/clinicalguidance/abbreviatedreviews/Naloxone_Autoinjector_EVZIO_Abbreviated_Review_revised_2014_07_16.docx.

⁸¹ *Id.*

⁸² Shawn E. Fellows, Alexander J. Coppola & Mona A. Ghandi, *Comparing Methods of Naloxone Administration: A Narrative Review*, 13 J. OPIOID MGMT. 253, 259 (2017).

an opioid overdose.⁸³ EVZIO is a handheld auto-injector—a small rectangular box that can fit in a pocket. It is a battery-operated, single-use device that comes pre-filled with naloxone and does not require assembly before it is used on a patient.⁸⁴



EVZIO contains a speaker that provides voice instructions to guide the administrator through each step of the injection. Once an administrator removes the outer case, he or she presses the device against the patient’s outer thigh, and at that point, the device automatically inserts the needle into the patient’s muscle or skin, delivers the naloxone, and retracts the needle fully back into its “housing.”⁸⁵ EVZIO can be injected through clothing if necessary.

In October 2016, the FDA approved – and kaléo later launched in January 2017 – a new version of EVZIO that delivers 2.0 mg of naloxone, five times the dose administered by the original device (0.4mg). Kaléo stated it created the new version with the increased dosage because of the growing numbers of opioid overdoses caused by highly potent synthetic opioids, as well as reports of an

⁸³ *Drug Approval Package: EVZIO (Naloxone hydrochloride) Injection*, U.S. FOOD & DRUG ADMIN, https://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/205787Orig1s000TOC.cfm (last visited Sept. 28, 2018).

⁸⁴ *Naloxone Injection*, VHA PHARMACY BENEFITS MANAGEMENT SERVICES (July 2014), https://www.pbm.va.gov/PBM/clinicalguidance/abbreviatedreviews/Naloxone_Autoinjector_EVZIO_Abbreviated_Review_revised_2014_07_16.docx.

⁸⁵ *NDC 60842-051 EVZIO: Naloxone Hydrochloride*, NAT’L DRUG CODES LIST, <https://ndclist.com/ndc/60842-051> (last visited Sept. 28, 2018).

increasing percentage of patients who required multiple doses of naloxone at the initial lower dosage.⁸⁶

ii. Adapt Pharma's Narcan

The FDA approved the first needle-free version of naloxone in November 2015.⁸⁷ Narcan, manufactured by Adapt Pharma, is a naloxone nasal spray developed for use in a non-medical setting.⁸⁸ The device does not require any assembly and is sprayed into the nostril of someone who has overdosed.⁸⁹ Narcan was developed through a collaboration between Adapt and the National Institute on Drug Abuse. The FDA gave the product fast-track designation and priority review due to its ready-to-use formulation that could be used in communities and homes where the majority of overdose-related deaths occur.⁹⁰



Narcan has been commercially available since February 2016 in a 4.0 mg dosage.⁹¹ In January 2017, the FDA approved Narcan nasal spray in a 2.0 mg formulation.⁹²

iii. Generic Naloxone

FDA-approved generic naloxone products for emergency treatment of opioid overdose are currently only available in injectable form.⁹³ Certain generic

⁸⁶ Rachael Rzasa Lynn & JL Galinkin, *Naloxone Dosage for Opioid Reversal: Current Evidence and Clinical Implications*, 9 THERAPEUTIC ADVANCES DRUG SAFETY 63, 63–64 (2017), <http://journals.sagepub.com/doi/pdf/10.1177/2042098617744161>.

⁸⁷ NARCAN® (naloxone HCl) Nasal Spray 2mg Approved by U.S. Food and Drug Administration (FDA), ADAPT Pharma (Jan. 25, 2017), http://adaptpharma.com/adapt_press_release/january-25-2017-narcan-nasal-spray-2mg-approved-by-us-food-and-drug-administration/.

⁸⁸ NARCAN, <https://www.narcan.com/> (last visited Aug. 3, 2018).

⁸⁹ Abigail Abrams, *The Surgeon General Says More People Should Carry Naloxone, the Opioid Antidote. Here's Where to Get It and How Much It Costs*, TIME (Apr. 5, 2018), <http://time.com/5229870/naloxone-surgeon-general-cost-where-buy/>.

⁹⁰ Meg Snyder, *New Route of Administration for Opioid Overdose Antidote*, R&D MAG. (June 29, 2016), <https://www.rdmag.com/article/2016/06/new-route-administration-opioid-overdose-antidote>.

⁹¹ NARCAN® (naloxone HCl) Nasal Spray 2mg Approved by U.S. Food and Drug Administration (FDA), ADAPT Pharma (Jan. 25, 2017), http://adaptpharma.com/adapt_press_release/january-25-2017-narcan-nasal-spray-2mg-approved-by-us-food-and-drug-administration/.

⁹² *Id.*

⁹³ *Opioid Overdose Reversal with Naloxone (Narcan, Evzio)*, NAT'L INSTIT. OF HEALTH, <https://www.drugabuse.gov/related-topics/opioid-overdose-reversal-naloxone-narcan-evzio> (last updated Apr. 2018).

injectable products, however, are available with an atomizer for intranasal use, which is considered an “off-label” use.⁹⁴ These off-label kits contain both a syringe and an atomizer and require assembly at the time of use.⁹⁵

Five manufacturers have FDA approval for 0.4 mg naloxone per milliliter dose injections: Hospira Inc.; Mylan; West-Ward; Somerset Therapeutics; and Akorn.⁹⁶ Only one company, International Medication Systems, Ltd., manufactures 1 mg per milliliter injections, which is the dose used off-label as a nasal spray.⁹⁷ These 1 mg units currently cost \$330 for a pack of ten, or about \$16.50 per milliliter, following a 95 percent price increase in September 2014.⁹⁸

Several competing nasal naloxone products are in late stages of development or regulatory review at this time, so the landscape of approved generic products is expected to evolve over the next few years.⁹⁹

C. The Commercial Health Care Market in the United States

Americans spend about \$1,100 per person per year on prescription drugs.¹⁰⁰ According to the Centers for Medicare & Medicaid Services (“CMS”), Americans spent nearly \$330 billion on prescription drugs in 2016.¹⁰¹ CMS estimates that patients’ out-of-pocket spending for prescription drugs in 2017 was just over 13 percent.¹⁰²

⁹⁴ Christa R Lewis, Hoa T Vo & Marc Fishman, *Intranasal Naloxone and Related Strategies for Opioid Overdose Intervention by Nonmedical Personnel: A Review*, 8 SUBSTANCE ABUSE & REHABILITATION 79 (2017), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5644601/>.

⁹⁵ *Id.*

⁹⁶ E-mail from Nat’l Library of Med., Nat’l Inst. of Health, to Subcommittee Staff (Oct. 2, 2018, 3:05 p.m. EST).

⁹⁷ *Id.*

⁹⁸ Meg Tirrell, *As Opioid Epidemic Worsens, the Cost of Waking Up from an Overdose Soars*, CNBC (Jan. 4, 2017), <https://www.cnbc.com/2017/01/04/as-opioid-epidemic-worsens-the-cost-of-waking-up-from-an-overdose-soars.html>.

⁹⁹ Christa R Lewis, Hoa T Vo & Marc Fishman, *Intranasal Naloxone and Related Strategies for Opioid Overdose Intervention by Nonmedical Personnel: A Review*, 8 SUBSTANCE ABUSE & REHABILITATION 79 (2017), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5644601/>.

¹⁰⁰ *Pharmaceutical Spending*, ORGANISATION FOR ECONOMIC CO-OPERATION & DEVELOPMENT <https://data.oecd.org/healthres/pharmaceutical-spending.htm> (last visited Sept. 28, 2018).

¹⁰¹ CTRS. FOR MEDICARE AND MEDICAID SERVS., NHE FACT SHEET 2016, CMS.GOV WEBSITE, <https://www.cms.gov/research-statistics-data-and-systems/statistics-trends-and-reports/nationalhealthexpenddata/nhe-fact-sheet.html>, (last visited November 6, 2018).

¹⁰² CTRS. FOR MEDICARE AND MEDICAID SERVS., “National Health Expenditure Projections 2017-2026,” Table 11, <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/NationalHealthAccountsProjected.html>, (last visited November 6, 2018).

1. Patient Assistance Programs and Coupons

U.S. drug manufacturers fund a variety of programs to help consumers defray the cost of prescription drugs. This assistance includes drug discount coupons, free drugs, and cost-sharing payments for individuals with low incomes or high medical expenses. Drug manufacturers and independent charities also dispense billions of dollars in assistance annually through nonprofit patient assistance programs (“PAPs”).¹⁰³

Drug manufacturers state this assistance reflects a commitment to facilitating access to medications for patients in need.¹⁰⁴ There is evidence that coupons and other assistance programs do help consumers save money and make it easier for patients to continue their course of treatment, particularly when that treatment involves high-cost specialty drugs.¹⁰⁵

The Department of Health and Human Services Office of Inspector General has also found, however, that these programs can be used to bolster sales and drug prices, and can increase costs for government and commercial health payers.¹⁰⁶ For example, a discount coupon may reduce the amount an insured consumer pays out of pocket, but it generally does not reduce the price an insurer or government program is charged for the drug.¹⁰⁷ Cost-sharing assistance offered through certain PAPs yields similar results.¹⁰⁸ Generally, increased use of coupons and PAPs may also increase costs for beneficiaries in health care plans if a payer decided to raise premiums, deductibles, or cost sharing to offset some of the expenses of higher drug utilization.¹⁰⁹

2. Pharmacy Benefit Managers

Pharmacy benefit managers (“PBMs”) are third-party intermediaries that process prescription transactions, negotiate drug discounts, and determine what pharmacies and drugs will be included in a health plan’s benefits.¹¹⁰ Pharmaceutical companies set the advertised price of a drug, known as the list price. PBMs are able to “aggregate the buying power of health plans and employer

¹⁰³ SUZANNE M. KIRCHOFF, CONG. RESEARCH SERV., R44264, PRESCRIPTION DRUG DISCOUNT COUPONS AND PATIENT ASSISTANCE PROGRAMS (PAPs) 9 (2017).

¹⁰⁴ *Id.*

¹⁰⁵ *Id.* at 1.

¹⁰⁶ U.S. DEP’T OF HEALTH & HUM. SERVS. OFF. OF INSPECTOR GEN’L, SPECIAL ADVISORY BULLETIN: PHARMACEUTICAL MANUFACTURER COPAYMENT COUPONS 3 (Sept. 2014), https://oig.hhs.gov/fraud/docs/alertsandbulletins/2014/SAB_Copayment_Coupons.pdf.

¹⁰⁷ SUZANNE M. KIRCHOFF, CONG. RESEARCH SERV., R44264, PRESCRIPTION DRUG DISCOUNT COUPONS AND PATIENT ASSISTANCE PROGRAMS (PAPs) 2 (2017).

¹⁰⁸ *Id.*

¹⁰⁹ *Id.* at 1-2.

¹¹⁰ Thomas Gryta, *What is a Pharmacy Benefit Manager?*, WALL ST. J., (July 21, 2011), <https://www.wsj.com/articles/SB10001424053111903554904576460322664055328>.

groups” and in turn can use that as leverage to negotiate with pharmacies and drug manufacturers to secure discounts below the list price, as well as rebates.¹¹¹

PBMs are able to charge administrative fees to drug manufacturers in exchange for managing the health plan drug formularies, or lists of covered drugs, and other programs.¹¹² PBMs can also receive a negotiated percentage of drug rebates, and depending on the contract, may be paid by drug companies to carry its drug exclusively on a health plan formulary.¹¹³ The diagram below provides additional details concerning the PBM’s distribution and reimbursement process.¹¹⁴

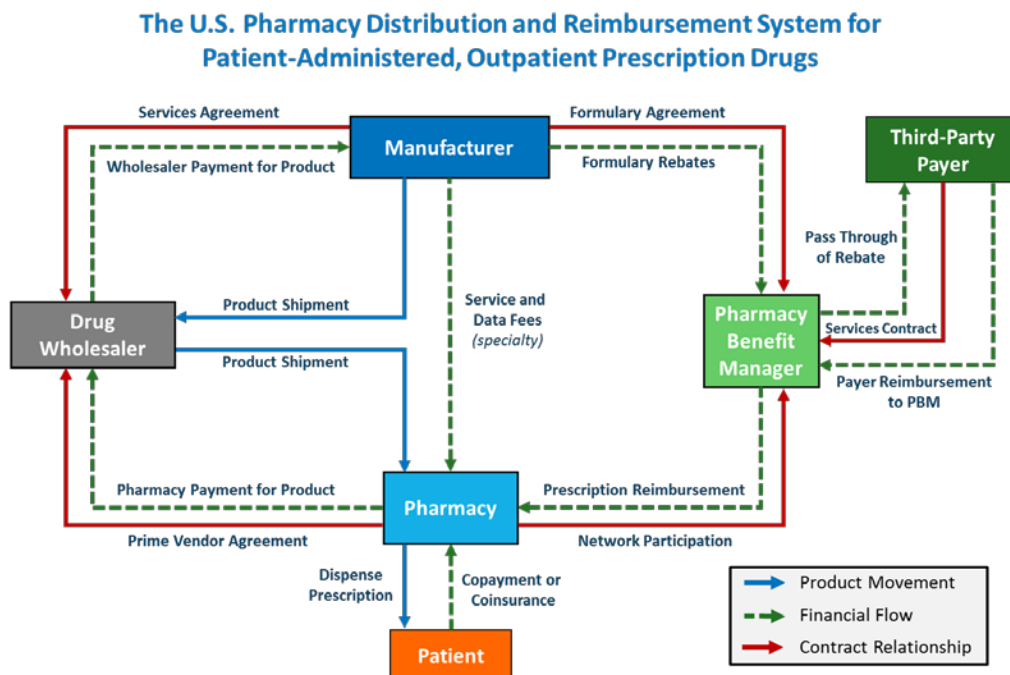


Chart illustrates flows for patient-administered, outpatient drugs. Please note that this chart is illustrative. It is not intended to be a complete representation of every type of financial, product flow, or contractual relationship in the marketplace.
 Source: Fein, Adam. J., *The 2016 Economic Report on Retail, Mail and Specialty Pharmacies*, Drug Channels Institute, January 2016.
 (Available at http://drugchannelsinstitute.com/products/industry_report/pharmacy/)

PBMs generally state they pass most of the rebates and fees they receive from drug manufacturers onto the health plans and subsequently to patients,

¹¹¹ Wayne Winegarden, Ph.D., *The Economic Cost of Pharmacy Benefit Managers: A Review of the Literature*, PACIFIC RESEARCH INSTITUTE 3 (May 2017), https://www.pacificresearch.org/wp-content/uploads/2017/06/PBM_Lit_Final.pdf.

¹¹² Jessica Wapner, *Understanding the Hidden Villain of Big Pharma: Pharmacy Benefit Managers*, NEWSWEEK (Mar. 17, 2017), <http://www.newsweek.com/big-pharma-villain-pbm-569980>.

¹¹³ *Id.*

¹¹⁴ Drug Channels, *Follow the Dollar: The U.S. Pharmacy Distribution and Reimbursement System* (Feb. 23, 2016), <https://www.drugchannels.net/2016/02/follow-dollar-us-pharmacy-distribution.html>.

which they say lower health care costs.¹¹⁵ However, depending on the contract, PBMs may not be required to share information about these rebates and fees with plan sponsors.¹¹⁶ According to a March 2017 *Bloomberg* article, “in the U.S., \$15 of every \$100 spent on brand-name drugs goes to middlemen...[and] the largest share, about \$8, goes to [pharmacy] benefit managers.”¹¹⁷

Over the past decade, several PBMs merged. Now, the largest three PBMs (CVS Caremark, Express Scripts, and OptumRx—a subsidiary of the insurer UnitedHealth Group) control about 85 percent of the market.¹¹⁸ These three companies collect more than \$200 billion per year to manage prescription services for insurance carriers covering 180 million Americans and government programs serving about 110 million more.¹¹⁹

3. Federal Government Funded Health Care Programs

The federal government plays a substantial role in the prescription drug market. That role has grown even more important over the past decade due to the implementation of Medicare Part D and the expansion of Medicaid eligibility through the Patient Protection and Affordable Care Act of 2010 (“ACA”).¹²⁰ National, state, and local government spending accounts for approximately 44.1 percent of total U.S. retail prescription drug spending, as compared to 25 percent in 2005, the year before Medicare Part D was fully implemented.¹²¹

Government-sponsored drug benefits are not governed by a single system; rather, they are spread out among the various agencies and departments that direct each of the various federal health insurance programs.¹²² There is no single federal procurement system for purchasing pharmaceuticals, so each program

¹¹⁵ Michael Hiltzik, *How ‘price-cutting’ middlemen are making crucial drugs vastly more expensive*, L.A. TIMES (June 9, 2017), <http://www.latimes.com/business/hiltzik/la-fi-hiltzik-pbm-drugs-20170611-story.html>.

¹¹⁶ Wayne Winegarden, Ph.D., *The Economic Cost of Pharmacy Benefit Managers: A Review of the Literature*, PAC. RES. INST. 5 (May 2017), https://www.pacificresearch.org/wp-content/uploads/2017/06/PBM_Lit_Final.pdf.

¹¹⁷ Neil Weinberg & Robert Langreth, *Drug Costs Too High? Fire the Middleman*, BLOOMBERG BUSINESSWEEK. (Mar. 3, 2017), www.bloomberg.com/news/articles/2017-03-03/drug-costs-too-high-fire-the-middleman.

¹¹⁸ THE COUNCIL OF ECON. ADVISERS, REFORMING BIOPHARMACEUTICAL PRICING AT HOME AND ABROAD 10 (Feb. 2018), <https://www.whitehouse.gov/wp-content/uploads/2017/11/CEA-Rx-White-Paper-Final2.pdf>

¹¹⁹ Michael Hiltzik, *How ‘price-cutting’ middlemen are making crucial drugs vastly more expensive*, L.A. TIMES (June 9, 2017), <http://www.latimes.com/business/hiltzik/la-fi-hiltzik-pbm-drugs-20170611-story.html>.

¹²⁰ SUZANNE M. KIRCHOFF, JUDITH A. JOHNSON & SUSAN THAUL, CONG. RESEARCH SERV., R44832, FREQUENTLY ASKED QUESTIONS ABOUT PRESCRIPTION DRUG PRICING AND POLICY 13 (2018).

¹²¹ *Id.*

¹²² *Id.* at 14.

negotiates its own prices and rebates.¹²³ The resulting differences can be quite drastic. For example, in 2012, Medicaid received rebates equivalent to 47 percent of total expenditures, while Medicare Part D received a far lower rate of 15 percent.¹²⁴ With no required uniformity, each program contains varying incentive and procurement structures that influence their relationships with the pharmaceutical industry. As a result, each agency faces unique challenges in responding to the opioid epidemic, and drug manufacturers may have varying success in having their drugs covered by federal programs.

i. Medicare Part D

Medicare provides health insurance coverage for individuals who are age 65 and older and those with permanent disabilities.¹²⁵ The program will serve an estimated 60 million individuals in 2018.¹²⁶ Medicare has four components, Parts A through D, each of which addresses a different aspect of health care.¹²⁷ Part D provides prescription drug benefits. Given the significant number of Medicare Part D enrollees prescribed opioids, it plays a substantial role in opioid-related policy—including naloxone pricing.

Part D is a voluntary prescription drug benefit created pursuant to the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (“MMA”).¹²⁸ As of July 2018, 44.2 million individuals were enrolled in Part D plans.¹²⁹ Part D relies on private prescription drug plans to provide coverage for certain drugs. Individuals that choose to participate in Medicare Part D acquire coverage through a private insurer that contracts with Medicare, referred to as “plan sponsors.”¹³⁰ For Medicare to pay for a drug, Part D must cover it through inclusion on the plan sponsor’s formulary and the drug must be approved by the FDA.¹³¹ Formularies are lists of prescription drugs covered by the insurance plan. As such, a plan sponsor may choose to cover some drugs, but exclude coverage for other drugs.¹³²

¹²³ *Id.*

¹²⁴ U.S. DEP’T OF HEALTH & HUM. SERVS. OFF. OF INSPECTOR GEN., MEDICAID REBATES FOR BRAND-NAME DRUGS EXCEEDED PART D REBATES BY A SUBSTANTIAL MARGIN 6 (Apr. 2015), <https://oig.hhs.gov/oei/reports/oei-03-13-00650.pdf>.

¹²⁵ SUZANNE M. KIRCHHOFF & JOHNATHAN H. DUFF, CONG. RESEARCH SERV., IF10875, MEDICARE COVERAGE OF OPIOID ADDICTION TREATMENT SERVICES (2018).

¹²⁶ *Id.*

¹²⁷ PATRICIA A. DAVIS, CONG. RESEARCH SERV., R40082, MEDICARE: PART B PREMIUMS 1 (2018).

¹²⁸ SUZANNE M. KIRCHHOFF, CONG. RESEARCH SERV., R40611, MEDICARE PART D PRESCRIPTION DRUG BENEFIT 1 (2018).

¹²⁹ *Id.*

¹³⁰ *Id.*

¹³¹ *Id.*

¹³² *Id.*

For prescription drugs not covered by a plan sponsor’s formulary, the plan sponsor must maintain procedures for the beneficiary to receive an off-formulary drug.¹³³ The plan sponsor “must grant an exception whenever it determines that the drug is medically necessary, consistent with the physician’s or other prescriber’s statement.”¹³⁴ The statement of medical necessity by the prescriber must include: (1) an explanation for why the drugs on the plan’s formulary would not be as effective as the non-formulary drug and (2) an explanation for why any step therapies would be ineffective or “likely to cause an adverse reaction or other harm” to the beneficiary.¹³⁵ When evaluating the formulary exception request for medical necessity, “[a] supporting statement provided by a physician or other prescriber is entitled to great weight....”¹³⁶

In 2016, one-third of all Part D beneficiaries (at that time, 14.4 million out of 43.6 million) received prescription opioids.¹³⁷ These 14.4 million enrollees received 79.4 million opioid prescriptions, 80 percent of which were for Schedule II or III controlled substances, which the FDA recognizes as having higher potential for abuse.¹³⁸

ii. Medicaid

Medicaid is a federal-state entitlement program that provides health insurance coverage for low-income individuals.¹³⁹ Along with Medicare, it was created by the Social Security Amendments of 1965. It empowers states to create their own administrative structures, standards for eligibility, payment policies, and benefit packages, while complying with broad federal guidelines.¹⁴⁰ While it is not mandatory for states to participate in the program, all have chosen to do so.¹⁴¹

Federal and state governments fund Medicaid. The federal government reimburses the states for a percentage of the costs paid to health care providers and managed care plans.¹⁴² The Affordable Care Act expanded the program by

¹³³ 42 C.F.R. § 423.578.

¹³⁴ *Id.*

¹³⁵ *Id.*

¹³⁶ Medicare Part D Prescription Drug Benefit Manual, Ch. 18, *Part D Enrollee Grievances, Coverage Determinations, and Appeals*, pgs. 39-40 (May 12, 2014).

¹³⁷ U.S. DEP’T OF HEALTH & HUMAN SERVICES OFFICE OF INSPECTOR GEN’L, OPIOIDS IN MEDICARE PART D: CONCERNS ABOUT EXTREME USE AND QUESTIONABLE PRESCRIBING 2 (July 2017), <https://oig.hhs.gov/oei/reports/oei-02-17-00250.pdf>.

¹³⁸ *Id.*

¹³⁹ CLIFF BINDER, CONG. RESEARCH SERV., R43778, MEDICAID PRESCRIPTION DRUG PRICING AND POLICY 1 (2014).

¹⁴⁰ *Medicaid 101*, MEDICAID & CHIP PAYMENT & ACCESS COMM’N, <https://www.macpac.gov/medicaid-101/> (last visited Sept. 14, 2018).

¹⁴¹ ALISON MITCHELL, CONG. RESEARCH SERV., R43357, MEDICAID: AN OVERVIEW 1 (2015).

¹⁴² U.S. DEP’T OF HEALTH & HUMAN SERS, 2016 ACTUARIAL REPORT ON THE FINANCIAL OUTLOOK FOR MEDICAID 3 (2016), <https://www.medicaid.gov/medicaid/finance/downloads/medicaid-actuarial-report-2016.pdf>.

increasing eligibility for Medicaid programs.¹⁴³ In June 2018, nearly 73.4 million individuals were enrolled in Medicaid and the Children’s Health Insurance Program, a program affiliated with Medicaid that provides health coverage to eligible children.¹⁴⁴

Medicaid covers a significant portion of the opioid-addicted population in the United States. In 2016, the Kaiser Family Foundation found that Medicaid covered 38 percent of nonelderly adults with an opioid addiction.¹⁴⁵ Forty-three percent of those individuals received addiction treatment through Medicaid, which is almost double the percentage of those receiving treatment with private insurance (21 percent) and those receiving treatment with no insurance (23 percent).¹⁴⁶ Given the number of its enrollees who are addicted to opioids or receiving addiction treatment, Medicaid policies play a key role in the opioid epidemic.

iii. The Department of Veterans Affairs

The Veterans Health Administration (“VHA”) under the Department of Veterans Affairs (“VA”) operates the largest integrated health care delivery system in the country.¹⁴⁷ It serves more than 9 million enrolled veterans at 1,243 health care facilities and has an annual budget of approximately \$68 billion.¹⁴⁸

The VHA operates under a different model than Medicare and Medicaid, as it owns a majority of its health care delivery sites and directly employs health care

¹⁴³ *Id.* at 13.

¹⁴⁴ *June 2018 Medicaid & CHIP Enrollment Data Highlights*, CENTERS FOR MEDICARE & MEDICAID SERVS, <https://www.medicaid.gov/medicaid/program-information/medicaid-and-chip-enrollment-data/report-highlights/index.html> (last visited Sept. 14, 2018).

¹⁴⁵ Julia Zur & Jennifer Tolbert, *The Opioid Epidemic and Medicaid’s Role in Facilitating Access to Treatment*, KAISER FAM. FOUND. (Apr. 2018), <https://www.kff.org/medicaid/issue-brief/the-opioid-epidemic-and-medicoids-role-in-facilitating-access-to-treatment/>; see also RESULTS FROM THE 2016 NATIONAL SURVEY ON DRUG USE AND HEALTH: DETAILED TABLES, SUBSTANCE ABUSE AND MENTAL HEALTH SERVS ADMIN (Sept. 2017), <https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2016/NSDUH-DetTabs-2016.pdf>. States are not required to cover outpatient prescription drugs under their Medicaid programs, but many do because drugs are seen as less costly than inpatient medical care. CLIFF BINDER, CONG. RESEARCH SERV., R43778, MEDICAID PRESCRIPTION DRUG PRICING AND POLICY 8 (2014).

¹⁴⁶ *The Opioid Epidemic and Medicaid’s Role in Facilitating Access to Treatment*, KAISER FAM. FOUND. (Apr. 2018), <https://www.kff.org/medicaid/issue-brief/the-opioid-epidemic-and-medicoids-role-in-facilitating-access-to-treatment/>; see also RESULTS FROM THE 2016 NATIONAL SURVEY ON DRUG USE AND HEALTH: DETAILED TABLES, SUBSTANCE ABUSE AND MENTAL HEALTH SERVS ADMIN (Sept. 2017), <https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2016/NSDUH-DetTabs-2016.pdf>.

¹⁴⁷ SIDATH VIRANGA PANANGALA, CONG. RESEARCH SERV., R42747, HEALTH CARE FOR VETERANS: ANSWERS TO FREQUENTLY ASKED QUESTIONS 1 (2016).

¹⁴⁸ *About VHA*, U.S. DEP’T OF VETERANS AFF., <https://www.va.gov/health/aboutVHA.asp> (last visited Sept. 14, 2018).

professionals to provide services to its veteran patients.¹⁴⁹ Unlike other types of insurance plans, VA health care does not use coinsurances, deductibles, or premiums.¹⁵⁰ Veterans can obtain prescriptions from VA health care providers or VA-authorized providers and can receive their medicine through a mail order pharmacy or from a VA medical facility pharmacy.¹⁵¹ Veterans receive most medications for free and are only required to make copays for medicines prescribed for non-service connected issues.¹⁵²

Patients treated in the VA health care system play a significant part in the opioid epidemic. Chronic pain affects half of veterans using the VA, complicated by high rates of psychiatric issues such as substance use disorder and post-traumatic stress disorder.¹⁵³ According to a 2011 study of the VA system, VHA patients are twice as likely to die from accidental overdose as non-veterans.¹⁵⁴

iv. The Department of Defense and TRICARE

The Department of Defense (“DOD”) operates its own health care delivery system, which serves approximately 9.4 million active duty and retired U.S. military personnel and dependents.¹⁵⁵ Beneficiaries can obtain services from DOD-operated and staffed military treatment facilities (which are typically located on or near a U.S. military base) or through care from civilian providers purchased through an insurance-like program called TRICARE.¹⁵⁶ TRICARE services account for about 60 percent of the total cost of care delivered through the DOD’s health system.¹⁵⁷

Under TRICARE, enrollees are charged a copay for both brand-name and generic drugs through retail network pharmacies or mail delivery services, but can

¹⁴⁹ SIDATH VIRANGA PANANGALA, CONG. RESEARCH SERV., R42747, HEALTH CARE FOR VETERANS: ANSWERS TO FREQUENTLY ASKED QUESTIONS 1 (2016).

¹⁵⁰ *Id.*

¹⁵¹ *Pharmacy Service*, BENEFITS <https://www.benefits.gov/benefits/benefit-details/305> (last visited Sept. 27, 2018).

¹⁵² *Medication Copayments: Facts You Should Know*, DEP’T OF VETERANS AFF. (Aug. 2016), https://www.va.gov/HEALTHBENEFITS/resources/publications/IB10-971_medication_copayment_brochure.pdf.

¹⁵³ Walid F. Gellad, Chester B. Good & David J. Shulkin, *Addressing the Opioid Epidemic in the United States: Lessons From the Department of Veterans Affairs*, 177 JAMA INTERN MED. 611 (2017), <https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2608540>.

¹⁵⁴ AS Bohnert, MA Ilgen, S Galea, JF McCarthy & FC Blow, *Accidental Poisoning Mortality Among Patients in the Department of Veterans Affairs Health System*, 49 MED CARE 393 (Apr. 2011).

¹⁵⁵ BRYCE H. P. MENDEZ, CONG. RESEARCH SERV., IF75700, DEFENSE PRIMER: MILITARY HEALTH SYSTEM (APR. 20, 2018), <https://fas.org/sgp/crs/natsec/IF10530.pdf>.

¹⁵⁶ BRYCE H. P. MENDEZ, CONG. RESEARCH SERV., IF10951, SUBSTANCE ABUSE PREVENTION, TREATMENT, AND RESEARCH EFFORTS IN THE MILITARY (Aug. 2018).

¹⁵⁷ *Id.*

receive some drugs free of charge at military pharmacies.¹⁵⁸ In 2017 alone, the military health system, which includes TRICARE, filled 119 million prescriptions.¹⁵⁹

In August 2018, DOD acknowledged that service members are prescribed opioids at a higher rate than the wider U.S. population.¹⁶⁰ But, service members have a much lower opioid death rate of 2.7 deaths per 100,000 compared to that of the general population—10.4 deaths per 100,000.¹⁶¹ The incidence rate for dependence or abuse among service members has declined by 38 percent between 2012 and 2016.¹⁶² DOD requires that all service members receive substance abuse education and provides substance-abuse treatment options to all beneficiaries of the military health system.¹⁶³

¹⁵⁸ *TRICARE Pharmacy Program Overview*, DEFENSE HEALTH AGENCY (Feb. 2018), https://tricare.mil/-/media/Files/TRICARE/Publications/BrochuresFlyers/Pharmacy_Overview.ashx?la=en&hash=E9F6D3759CF437D203A41AC3ADBAC407BA964849F8B5449D580CE80F69C5060B.

¹⁵⁹ *Facts and Figures*, DEFENSE HEALTH AGENCY, <https://tricare.mil/About/Facts> (last visited Sept. 14, 2018).

¹⁶⁰ BRYCE H. P. MENDEZ, CONG. RESEARCH SERV., IF10951, SUBSTANCE ABUSE PREVENTION, TREATMENT, AND RESEARCH EFFORTS IN THE MILITARY (Aug. 2018).

¹⁶¹ BRYCE H. P. MENDEZ, CONG. RESEARCH SERV., IF10951, SUBSTANCE ABUSE PREVENTION, TREATMENT, AND RESEARCH EFFORTS IN THE MILITARY (Aug. 2018).

¹⁶² *Id.*

¹⁶³ *Id.*

II. KALÉO DEVELOPED THE FIRST TAKE-HOME NALOXONE AUTO-INJECTOR FOR OPIOID OVERDOSE

Kaleo, Inc. (“kaléo” or “the Company”) is a specialty pharmaceutical company headquartered in Richmond, Virginia.¹⁶⁴ Twin brothers Eric and Evan Edwards co-founded the company in 2004 as Intelliject, LLC.¹⁶⁵ The Company later changed its name to kaleo, Inc. in December 2013.¹⁶⁶ This section discusses kaléo’s development of EVZIO and the company’s initial pricing as it took the drug to market.

A. Kaléo Developed an Auto-injector for Naloxone and Branded the Product as “EVZIO”

Kaléo developed EVZIO, a naloxone hydrochloride auto-injector used for the emergency treatment of opioid overdose.¹⁶⁷ The drug temporarily reverses the effects of an opioid overdose, including respiratory and central nervous system depression.¹⁶⁸ EVZIO uses a recorded audio message to guide an individual through the injection process. Kaléo received FDA approval for EVZIO in April 2014 and commercially launched the product in July 2014.¹⁶⁹ The original EVZIO carried a naloxone dosage of 0.4 mg, but in January 2017, kaléo increased the dosage to 2.0 mg with the launch of its “EVZIO 2.0” product.¹⁷⁰ Kaléo said the increased dosage was in response to reports that it was taking multiple EVZIO injections to revive patients overdosing on more powerful opioids, such as fentanyl.¹⁷¹ While the only difference between the original EVZIO and EVZIO 2.0 is the dosage of naloxone, the FDA considers EVZIO 2.0 an entirely different product.¹⁷² Kaléo launched EVZIO in 2014 at a wholesale acquisition cost (“WAC”) of \$575. The WAC is the manufacturer’s list price to wholesalers or direct purchasers; it does not include any discounts, rebates, or other reductions in

¹⁶⁴ KALEO-PSI-00045868-00045932.

¹⁶⁵ KALEO-PSI-00052980-00053005.

¹⁶⁶ KALEO-PSI-00045868-00045932.

¹⁶⁷ EVZIO.com, *Prescriber Information*, https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=5f8e8d17-a72f-406d-a736-48e61620f9d8&type=display#s_ppi.

¹⁶⁸ *Id.*

¹⁶⁹ Food and Drug Administration, *FDA approves hand-held auto-injector to reverse opioid overdose* (Apr. 3, 2014), <http://wayback.archive-it.org/7993/20170112032835/http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm391465.htm>.

¹⁷⁰ Letter from Sharon Hertz, Director, Division of Anesthesia, Analgesia, and Addiction Products, Office of Drug Evaluation II, Center for Drug Evaluation and Research, Food and Drug Administration to Glen Kelly, Director Regulatory Affairs, kaleo, Inc. (Oct. 19, 2016), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2016/209862Orig1s000ltr.pdf.

¹⁷¹ Interview of Matthew Simmons, Vice President of Finance and Analytics at kaléo (May 16, 2018).

¹⁷² *Id.*

price.¹⁷³ Today, kaléo sells EVZIO 2.0 at a WAC of \$4,100 per unit, which includes two auto-injectors and a training device.

B. Kaléo Set the Initial Price of EVZIO at \$575

Kaléo launched EVZIO in July 2014 at a WAC of \$575.¹⁷⁴ Kaléo’s Pricing Committee set EVZIO’s starting WAC. The Pricing Committee is comprised of senior employees across the company’s legal, finance, and commercial departments.¹⁷⁵ Dan Hackman, the current Vice President of Patient Access & Affordability Strategy at kaléo, told the Subcommittee that all of kaléo’s pricing decisions are made by the Pricing Committee, “with the blessing of Spencer [Williamson],” the Chief Executive Officer (“CEO”).¹⁷⁶

Kaléo’s Pricing Committee considered numerous factors to help determine EVZIO’s starting WAC. Mr. Williamson explained the factors kaléo considered in a white paper titled “*How we came up with the price for EVZIO.*”¹⁷⁷ He pointed to high research and development costs, FDA approval costs, educational and awareness costs, distribution channel considerations, insurance coverage and accessibility, and the estimated value to patients as factors that influenced the price.¹⁷⁸

Research and Development. Mr. Williamson wrote in the white paper, “First, pharmaceutical research and development is expensive.”¹⁷⁹ An internal spreadsheet showed the cost of development, testing, FDA approval, equipment cost, and “all costs before launch” for EVZIO totaled \$47,569,000.¹⁸⁰ Kaléo conducted numerous studies to demonstrate the effectiveness of proper drug delivery and the ability for the product to operate in non-medically supervised settings, including studies to optimize ease of patient use, tests to ensure product functionality in a variety of environments and under numerous adverse conditions, and tests to ensure EVZIO could be injected through clothing.¹⁸¹ In his explanation for the cost of EVZIO, Mr. Williamson asserted there were over 150

¹⁷³ CLIFF BINDER, CONG. RESEARCH SERV., R43778, MEDICAID PRESCRIPTION DRUG PRICING AND POLICY 60 (2014).

¹⁷⁴ *Id.*

¹⁷⁵ Interview of Matthew Simmons, Vice President of Finance and Analytics at kaléo (May 16, 2018).

¹⁷⁶ Mr. Hackman previously served as the Chief Commercial Officer of kaléo from September 2015 to February 2017. Interview of Dan Hackman, Vice President of Patient Access at kaléo (July 26, 2018).

¹⁷⁷ KALEO-PSI-00060650-00060655.

¹⁷⁸ *Id.*

¹⁷⁹ *Id.*

¹⁸⁰ KALEO-PSI-00082648.

¹⁸¹ KALEO-PSI-00060650-00060652.

mandatory product validation tests as part of the FDA approval process, including tests related to ensuring EVZIO could be injected through clothing.¹⁸²

Educational Costs. The white paper also highlighted that kaléo considered costs associated with educating physicians, patients, families, and caregivers on the product, including promotional materials, awareness campaigns, support for non-profit organizations, personnel including medical science liaisons and pharmaceutical sales representatives, and educational programs, when setting the WAC.¹⁸³ In the spreadsheet cited above, kaléo listed the cost of education and awareness after launch from July 2014 to October 2015 at \$31,632,000.¹⁸⁴

Distribution Channels. In his white paper, Mr. Williamson explained that pharmaceutical companies must enter into contracts with wholesalers, distributors, pharmacies, and PBMs, all of which involve separate contracts and negotiations. Mr. Williamson said that kaléo “completed market research to determine what price would encourage payers to cover EVZIO broadly and keep the out-of-pocket costs for patients to a minimum.”¹⁸⁵ As part of its initial distribution strategy, kaléo signed contracts with several PBMs and health plans, including Express Scripts, Inc., Caremark PCS Health, LLC, Kaiser Permanente, Highmark, Inc., and Aetna.¹⁸⁶

Value to Patients. Mr. Williamson’s white paper also emphasized EVZIO’s inherent value to patients as part of his explanation for its high price. He explained that EVZIO was “specifically designed, developed and intended for administration by caregivers and family members in the out-of-hospital setting.”¹⁸⁷ Mr. Williamson acknowledged that naloxone has been available since 1971 in vials and glass syringes at a relatively low cost: roughly \$3 for a simple syringe dose.¹⁸⁸ He argued that these cheaper, manual naloxone administration systems required significant training to operate and were at a high risk for breakage or misuse.¹⁸⁹ Thus, those options were ill suited for use by a layperson without medical supervision.¹⁹⁰ Kaléo’s EVZIO, by contrast, was specially designed for non-medical users and required little to no training.¹⁹¹

¹⁸² *Id.*

¹⁸³ *Id.*

¹⁸⁴ KALEO-PSI-00082648.

¹⁸⁵ KALEO-PSI-00060650-00060655; Interview of Matthew Simmons, Vice President of Finance and Analytics at kaléo (May 16, 2018).

¹⁸⁶ KALEO-PSI-00077978; KALEO-PSI-00078000-00078006; KALEO-PSI-0006526; KALEO-PSI-00062460-00062480; KALEO-PSI-00062503-00062524; KALEO-PSI-00062481-00062502.

¹⁸⁷ KALEO-PSI-00060650-00060655.

¹⁸⁸ *Id.*

¹⁸⁹ *Id.*

¹⁹⁰ *Id.*

¹⁹¹ *Id.*

Mr. Hackman explained to the Subcommittee that “a study showed that untrained people trying to use a generic naloxone kit failed 100 percent of the time.”¹⁹² Kaléo found that the trained home user still failed 49 percent of the time.¹⁹³ In contrast, with EVZIO the untrained home user was successful 94 percent of the time. With training, that success rate was 100 percent, according to combined study results.¹⁹⁴

Health Care Cost of the Crisis. Mr. Williamson also argued in his white paper that EVZIO’s WAC was cost-effective at \$575 in light of the economic burden of opioid overdoses in the United States.¹⁹⁵ He asserted the cost of EVZIO was justified, given high direct and indirect costs including emergency medical costs, inpatient costs, absenteeism, and lost future earnings due to mortality.¹⁹⁶ He based this assertion on a 2013 study conducted by Dr. Phillip Coffin titled “*Cost-effectiveness of distributing naloxone for Heroin-Overdose Reversal*,” which found that a single naloxone kit remained cost-effective as long as it was priced below \$4,480.¹⁹⁷ Mr. Williamson wrote,

Our research demonstrated we could justify the wholesale acquisition cost of EVZIO in the thousands of dollars, especially given the fact that the shelf life of the product lasts up to 2 years. However, with the goal of broad insurance coverage and accessibility in-mind, the wholesale acquisition cost of EVZIO containing two auto-injectors and a trainer for practice will be \$575.00.¹⁹⁸

Matthew Simmons, kaléo’s Vice President of Finance and Analytics, told the Subcommittee that kaléo “considered how much we could save the health care system by stopping people from showing up to the hospital in a bad state” and that kaléo “looked at pharmacoeconomic studies” to help determine what EVZIO was worth to the entire health care system.¹⁹⁹

Kaléo also considered other factors in determining the initial WAC for EVZIO. These included:

¹⁹² KALEO-PSI-0153900-0153928; Subcommittee staff briefing with kaléo (Sept. 7, 2018).

¹⁹³ Subcommittee staff briefing with kaléo (Sept. 7, 2018).

¹⁹⁴ *Id.*

¹⁹⁵ KALEO-PSI-00060650-00060655.

¹⁹⁶ *Id.*

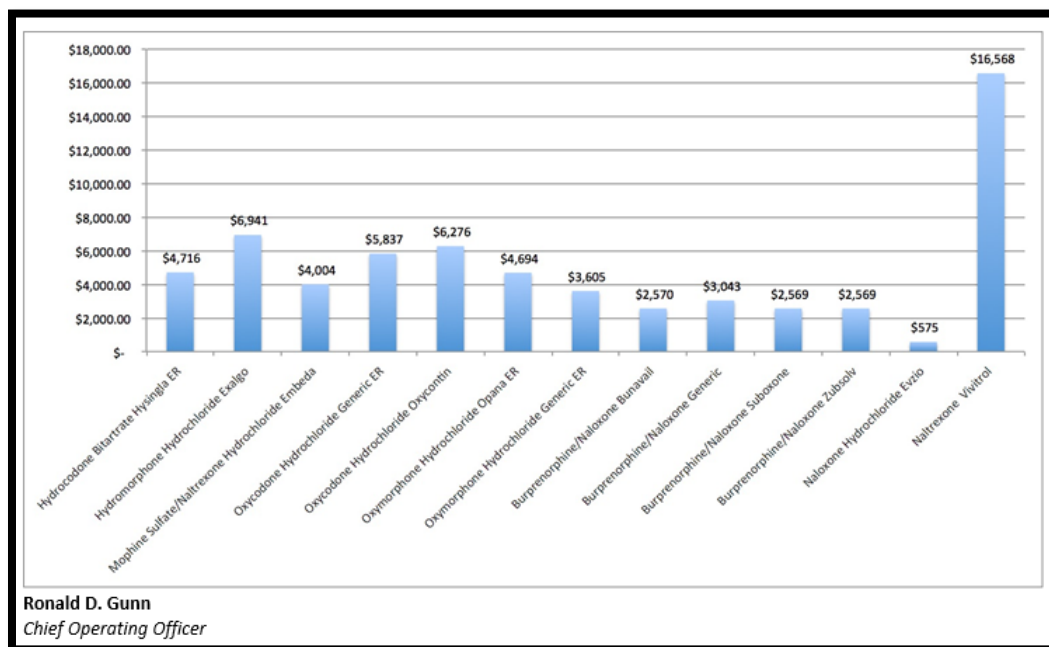
¹⁹⁷ *Id.*; Phillip O. Coffin, MD, & Sean D. Sullivan, PhD, Cost-Effectiveness of Distributing Naloxone to Heroin Users for Lay Overdose Reversal, 158 ANNALS INTERNAL MED. 1,5 (2013), <https://pdfs.semanticscholar.org/b256/437b20256f9763ca0224bbc012916aff8087.pdf>.

¹⁹⁸ KALEO-PSI-00060650-00060655.

¹⁹⁹ Interview of Matthew Simmons, Vice President of Finance and Analytics at kaléo (May 16, 2018).

EVZIO is Taken on a Limited basis and has a Limited Shelf Life. Kaléo designed EVZIO to counteract the effects of an opioid overdose. Mr. Simmons explained EVZIO was a “special case,” because it is not a medicine that people take on a recurring basis.²⁰⁰ Rather, “the drug is designed to be like a home security system, where you hope you never have to use it.”²⁰¹ Mr. Simmons said the product is good for a limited amount of time, generally 24 months, which kaléo also factored into EVZIO’s WAC.²⁰²

The Cost of Opioid Antagonists. Mr. Simmons also said that, because EVZIO was the first FDA-approved product in its class, it was challenging for kaléo to use existing drugs as a benchmark price for EVZIO. In an email on October 29, 2015, Ronald Gunn, kaléo’s Chief Operating Officer, circulated a “snapshot of the annual WAC for select abuse deterrent opioids and drugs used to treat opioid use disorder compared to [EVZIO].”²⁰³ The email and chart compared the cost of EVZIO to other opioid antagonists:²⁰⁴



Profitability. Mr. Simmons also said that profitability was a consideration when setting the initial price at \$575. Mr. Simmons said, “[n]ormally you start with a gross price, and then back out all the discounts and deductions, distribution

²⁰⁰ *Id.*

²⁰¹ *Id.*

²⁰² *Id.*

²⁰³ KALEO-PSI-00027405-00027406.

²⁰⁴ *Id.*

fees, wholesale fees, rebates to different customer bases, and patient assistance.”²⁰⁵ Mr. Simmons explained that when kaléo did the math and considered how many units of EVZIO they thought they could sell, and calculated how much it was going to cost kaléo to make, they determined that \$575 would be a sustainable price.²⁰⁶ Each unit of EVZIO (two auto-injectors and a training device) costs the company \$174.39 to produce. This amount includes \$52.24 in manufacturing costs, \$29.15 in manufacturing overhead costs, and \$93 in “obsolescence.”²⁰⁷

C. Kaléo Commissioned Outside Pricing Studies for EVZIO

Messrs. Simmons and Kris Ford, kaléo’s Vice President of Corporate Strategy and Business Development, both highlighted that in part because EVZIO was the first product kaléo would launch on its own, the company utilized outside advisors to help determine the initial pricing of EVZIO.²⁰⁸

1. Two Pricing Consultants Advised Kaléo to Price EVZIO around \$300 and Offer Additional Discounts

*Insight Strategy Advisors.*²⁰⁹ In 2011, kaléo engaged Insight Strategy Advisors (“ISA”) to “obtain a high-level understanding of pricing for their [] product being developed for Opioid Overdose.”²¹⁰ ISA designed an analysis based on kaléo’s request and scope that included eight payers “of various size and plan type combinations to insure a mix of ‘price sensitivities.’”²¹¹ These payers included PBMs, national and regional plans, as well as one Medicare plan.²¹² When questioned about a take-home auto-injector with voice instructions “payers saw the value of the talking device to elucidate instructions, they were adamant that voice guidance was not justification for a price premium.”²¹³

As part of the study, ISA also questioned payers about coverage, including at what price the payer would no longer cover the drug.²¹⁴ Payers suggested that at a

²⁰⁵ Interview of Matthew Simmons, Vice President of Finance and Analytics at kaléo (May 16, 2018).

²⁰⁶ *Id.*

²⁰⁷ KALEO-PSI-00153956.

²⁰⁸ Interview of Matthew Simmons, Vice President of Finance and Analytics at kaléo (May 16, 2018); Interview of Kris Ford, Vice President of Corporate Strategy and Business Development at kaléo (June 28, 2018).

²⁰⁹ Insight Strategy Advisors was founded in 2002 and focuses on issues facing the life sciences industry, including market access strategy, pricing and contracting, and distribution. It is a subsidiary of Precision Value & Health.

²¹⁰ At the time of the engagement, kaleo was named “Intelliject” and the proposed name for EVZIO was “resCUE.” ISA0000001-0000033.

²¹¹ *Id.*

²¹² *Id.*

²¹³ *Id.*

²¹⁴ *Id.*

price of \$300 access to coverage “turns more restrictive” and \$500 was the price that “some payers move [the drug] to ‘not covered.’”²¹⁵ Based on its findings, ISA recommended a “list price strategy” focused “on achieving broad Tier 2 via catering to payer list price sensitivities.”²¹⁶ Using this strategy, ISA recommended a list price in the range of \$225-\$275.²¹⁷ The final pricing recommendation stated, “ISA conservatively recommends pricing each [auto-injector] device at \$125 for a combined, double dose cost of \$250.”²¹⁸

D2 Consulting. Another consulting firm, D2 Consulting (“D2”), advised kaléo on how to price EVZIO.²¹⁹ Kaléo retained D2, in part, to assist with negotiating and entering into contracts with payers and PBMs.²²⁰ Kaléo worked mainly with Dean Erhardt, the co-founder and President of D2. Mr. Erhardt worked with kaléo to help the company launch EVZIO and continued to assist the company for a year post-launch until the contract concluded.²²¹ In October 2013, Mr. Erhardt organized a strategy meeting with approximately a dozen insurance representatives in the marketplace to provide an overview of pre-market research, discuss EVZIO, and solicit feedback on its viability.²²²

Mr. Erhardt advised kaléo that if it priced EVZIO at \$300-\$350 with a 15-20 percent discount it would “own the [naloxone] market.”²²³ Mr. Erhardt put together a managed care advisory board, which gave kaléo positive feedback regarding EVZIO’s functionality, given that it was the first injection product on the market.²²⁴ The advisory board was concerned, however, about the price of EVZIO at \$700 or more, which would result in patients paying more.²²⁵

Mr. Erhardt stated kaléo ended its contract with D2 because kaléo went in another strategic direction other than recommended by D2.²²⁶ Kaléo maintained it ended its contract with D2 because it hired an internal team to perform the work it hired D2 to perform. D2 went on to work with Adapt on its naloxone product, Narcan. Kaléo’s eventual price increases made Narcan much more attractive,

²¹⁵ *Id.*

²¹⁶ *Id.*

²¹⁷ *Id.*

²¹⁸ *Id.*

²¹⁹ D2 is a consulting firm that specializes in commercialization for pharma with a focus on small company distribution and reimbursement. Interview with Dean Erhardt, D2 Consulting (Aug. 16, 2018).

²²⁰ Kaléo asserted it did not retain D2 to advise on pricing matters. Letter from Michael Bopp, attorney for kaléo to Subcommittee staff (Nov. 9, 2018).

²²¹ Interview with Dean Erhardt, D2 Consulting (Aug. 16, 2018).

²²² *Id.*

²²³ *Id.*

²²⁴ *Id.*

²²⁵ *Id.*

²²⁶ *Id.*

according to Mr. Erhardt.²²⁷ Mr. Erhardt explained to the Subcommittee that he and D2 worked with over 250 drug manufacturers.²²⁸ Of those, kaléo is the only company that raised the price of a drug instead of lowering the price to make it more marketable and affordable.²²⁹

2. Kaléo Commissioned a Study for Pricing EVZIO at \$575

Kaléo again hired ISA in early 2014 to assess how health care payers would respond to EVZIO priced at \$575.²³⁰ ISA conducted a “Pricing Validation” study in February 2014, which sought feedback on kaléo’s anticipated EVZIO price of \$575 from six pharmacy directors that “represented 69 [million] lives across national, PBM, and regional plans and covering commercial, Medicare and managed Medicaid.”²³¹ ISA also designed this study to be within kaléo’s acceptable scope and budget to obtain feedback from payers.²³²

ISA’s study found that “[p]ayers were extremely positive in regards to [EVZIO], mainly because it was quick delivery of an efficacious product for overdose,” but that payers had concerns that included “public health issues (such as overuse of [EVZIO] for those that continually overdose) and misuse of [EVZIO].”²³³ ISA also concluded “[v]ery few payers would manage the product without quantity limits and/or a prior authorization.”²³⁴

On EVZIO’s application, ISA found “[p]ayers recognize that [EVZIO] is a potentially life-saving product, and want to provide access for their patient populations – but that is tempered by concerns around appropriate use.”²³⁵ Harry G. Schiavi, President and CEO of ISA, stated the health care payers involved in the analysis were concerned about appropriate use of EVZIO.²³⁶ One anonymized “regional plan” interviewed by ISA for the price validation study noted:

On one hand it is a great product ... But at the same time, the concern is that well, it is a very quick antidote so if you are a drug abuser or opioid abuse, heroin addict or OxyContin or whatever opioids, then this is their insurance policy.²³⁷

²²⁷ *Id.*

²²⁸ *Id.*

²²⁹ *Id.*

²³⁰ KALEO-PSI-00059727-00059730; KALEO-PSI-00059695-00059726.

²³¹ KALEO-PSI-00059727-00059730.

²³² Subcommittee staff briefing with Insight Strategy Advisors (Oct. 29, 2018).

²³³ KALEO-PSI-00059695-00059726.

²³⁴ *Id.*

²³⁵ *Id.*

²³⁶ Subcommittee staff briefing with Insight Strategy Advisors (Oct. 29, 2018).

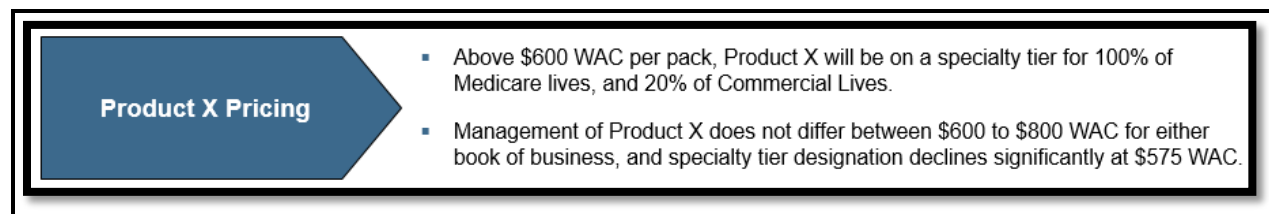
²³⁷ KALEO-PSI-00059695-00059726.

Payers involved in the analysis identified the delivery system as a positive aspect of EVZIO, but cited public health and opioid dependence concerns as a disadvantage.²³⁸ For example, one “regional plan” noted:

I would prefer these people are followed by healthcare professionals who can then potentially help them through their addiction because I just think that is the right thing to do for these patients.²³⁹

Given the public health concerns about appropriate use, “five [out of six] payers stated there will always be a prior authorization and/or quantity limits in place because of concerns around appropriate use.”²⁴⁰

ISA found that “[a]bove \$600 WAC per pack, [EVZIO] will be on a specialty tier for 100% of Medicare lives, and 20% of Commercial lives” in this study sample, but that “specialty tier designation declines significantly at a \$575 WAC.”²⁴¹ If EVZIO was placed on a specialty tier, then the copay by the patient would likely increase or trigger co-insurance, which would decrease the likelihood of the prescription being filled.²⁴²



Product X Pricing

- Above \$600 WAC per pack, Product X will be on a specialty tier for 100% of Medicare lives, and 20% of Commercial Lives.
- Management of Product X does not differ between \$600 to \$800 WAC for either book of business, and specialty tier designation declines significantly at \$575 WAC.

While ISA predicted the \$575 WAC would keep EVZIO from specialty tier designation, most payers viewed EVZIO as a “non-preferred branded product due to the availability of generic naloxone.”²⁴³ In fact, ISA estimated that 60 percent of the lives covered by the participating payers would not have preferred access due to concerns about around misuse and appropriate utilization.²⁴⁴ For Medicare patients, 91.6 percent of the lives covered by the participating payers would require a prior authorization and a quantity limit before the patient received an EVZIO.²⁴⁵

Overall, ISA determined “[r]egardless of price, payers are reluctant to provide [EVZIO] as a preferred product due to appropriate use concerns.”²⁴⁶ As such, a “regional plan” stated: “It would be hard to prefer – I mean if a generic

²³⁸ *Id.*

²³⁹ *Id.*

²⁴⁰ *Id.*

²⁴¹ *Id.*

²⁴² *Id.*

²⁴³ *Id.*

²⁴⁴ *Id.*

²⁴⁵ *Id.*

²⁴⁶ *Id.*

product is available at \$16 per vial, I mean how much of a rebate do you have to give?”²⁴⁷ A PBM commented: “This is not a chronic illness where we try to encourage utilization ... this is not a class we want to encourage utilization in – it would never be preferred.”²⁴⁸ Regarding the price of EVZIO, ISA found:

- Payers recognize that [EVZIO] is a potentially life-saving product, and want to provide access for their patient populations – but that is tempered by concerns about appropriate use.
- This research validates that at \$575 WAC, for 100% of Commercial lives and 98% of Medicare lives, [EVZIO] will be available as a non-preferred branded product [based on participating payers].
- [EVZIO] will likely never have quantity limits taken off, though half the plans would consider relaxing a prior authorization after at least a year of experience with [EVZIO].
- [EVZIO] will not have preferred access for 60% of the covered lives in this research, due to concerns around misuse and appropriate utilization.²⁴⁹

The ISA study also noted, and Mr. Schiavi confirmed, that kaléo needed to be able to identify for payers the target physician and patient population for EVZIO.²⁵⁰ ISA also suggested that kaléo “be prepared to discuss the public health issue of opioid misuse and overdose, because it is difficult for payers to differentiate between the two.”²⁵¹ It was clear from ISA’s analysis that kaléo was going to have to deal with prior authorizations before a patient could receive an EVZIO.²⁵² Mr. Schiavi stated that it was going to be difficult for kaléo to develop a market for EVZIO given the response of the payers that participated in the study.²⁵³

Neil Hughes, kaléo’s Chief Commercial Officer at the time, summarized his key takeaways from ISA’s “pricing validation work” in an email to Sharon Clarke and Mr. Williamson of kaléo.²⁵⁴ Mr. Hughes believed that ISA’s work “strongly supported” kaléo’s “target price point of \$575,” and that pricing EVZIO higher would lead to an unfavorable result of EVZIO being placed on the “Specialty Tier,” which has higher patient co-insurance.²⁵⁵ Mr. Hughes wrote:

Their overall reaction to the product and making it available to opioid patients was positive. Our target price point of \$575 WAC seemed

²⁴⁷ *Id.*

²⁴⁸ *Id.*

²⁴⁹ *Id.*

²⁵⁰ *Id.*; Subcommittee staff briefing with Insight Strategy Advisors (Oct. 29, 2018).

²⁵¹ KALEO-PSI-00059695-00059726.

²⁵² *Id.*; Subcommittee staff briefing with Insight Strategy Advisors (Oct. 29, 2018).

²⁵³ *Id.*

²⁵⁴ KALEO-PSI-00059727-00059730.

²⁵⁵ *Id.*

strongly supported by the results...at \$600 WAC 20% of commercial and 50% of Medicare lives would flip to Specialty Tier with patient co-insurance at between 20%-50% of WAC.²⁵⁶

Mr. Hughes also highlighted that there would be “broad use” of prior authorizations, but that they would not be as challenging as the prior authorizations kaléo’s other drug, AUVI-Q, had faced.²⁵⁷ Mr. Hughes wrote:

It does look as if there will be broad use of [prior authorizations] – not as an attempt to create a break to uptake, but rather to ensure appropriate patients use it. These will not be challenging [prior authorizations] (like being blind to get AUVI-Q!) but will still require prescribing [doctors]/clinics to do some paperwork, so the better prepared our field force can be to support this, the better off we will be.²⁵⁸

Mr. Hughes also said, of the prior authorizations, that he

[G]ot the impression that the goal was not to be elaborate (and thus effectively create a “hassle-factor” as a brake to uptake), but to ensure appropriate usage. That might vary from checking [that] patient has an Opioid Rx, to a plan wanting to confirm a particular additional risk factor.²⁵⁹

He continued “[t]he intent is NOT to create a huge hassle for the potential patient (ISA were at great pains to say that, ‘the payers want their patients to have access to this product’); but it could unintentionally create some inertia among patients that needs to be overcome.”²⁶⁰

D. Kaléo Contracted with Pharmacy Benefit Managers to Sell EVZIO

In order to make EVZIO available to patients, kaléo signed contracts with pharmacy benefit managers (“PBMs”) and health plans. Kaléo signed contracts with two of the largest PBMs: Express Scripts and CVS Caremark. Express Scripts is one of the largest PBMs in the United States and manages drug benefits for over 80 million lives. CVS has more than 94 million PBM members. Contracting with these two PBMs gave kaléo access to a number of commercial and Medicare Part D health insurance plans. Those contracts are explained in more detail below.

²⁵⁶ *Id.*

²⁵⁷ *Id.*

²⁵⁸ *Id.*

²⁵⁹ *Id.*

²⁶⁰ *Id.*

1. Express Scripts

One of the largest PBMs in the United States is Express Scripts, headquartered in St. Louis, Missouri.²⁶¹ Express Scripts offers a wide range of services to its 3,000 clients, including “network pharmacy claims processing, home delivery pharmacy care, specialty pharmacy care, benefit-design consultation, drug utilization review, formulary management, and medical and drug data analysis services.”²⁶² The company reported \$100.6 billion in revenue for 2017,²⁶³ and ranked 25th on the list of Fortune 500 companies in the United States.²⁶⁴ Overall, Express Scripts handles pharmacy benefits for around 83 million members.²⁶⁵ In March 2018, Express Scripts announced Cigna would purchase the company in a \$67 billion cash and stock transaction. The companies expect the transaction to close by the end of 2018.²⁶⁶

Kaléo signed two contracts with Express Scripts for formulary management of EVZIO: (1) an agreement for commercial plans known as “Preferred Savings Grid Rebate Program Agreement” and (2) a “Medicare Part D Rebate Program Agreement.”

Preferred Savings Grid Rebate Program Agreement for Commercial Health Plans. The Preferred Savings Grid Rebate Program Agreement (the “Rebate Savings Agreement”) between Express Scripts and kaléo went into effect on October 1, 2014.²⁶⁷ The Rebate Savings Agreement provided Express Scripts would receive 4.375 percent in administrative fees for each unit of EVZIO sold.²⁶⁸ In exchange for these administrative fees, Express Scripts performed certain services, such as:

- “[G]eneral maintenance, administration, and oversight of [distributing EVZIO to Express Script members] as necessary to provide an efficient means for [kaléo] to offer competitive pricing for its Products applicable to utilization across a broad market sector of Plans;”
- Negotiating and contracting with [Express Script] Clients; and

²⁶¹ Corporate Overview, EXPRESS SCRIPTS (2018), <http://lab.express-scripts.com/about/~media/de38e32f2ce24587be9ff3613420125e.ashx>.

²⁶² *Id.*

²⁶³ *Id.*

²⁶⁴ Express Scripts Holding, FORTUNE, <http://fortune.com/fortune500/express-scripts-holding/> (last visited Oct. 9, 2018).

²⁶⁵ Corporate Overview, EXPRESS SCRIPTS (2018), <http://lab.express-scripts.com/about/~media/de38e32f2ce24587be9ff3613420125e.ashx>.

²⁶⁶ 2017 Annual Report, EXPRESS SCRIPTS 1 (2018), <https://expressscriptsholdingco.gcs-web.com/static-files/76a9c03e-2e6b-4f6b-80de-fe80d4ebc826>.

²⁶⁷ KALEO-PSI-0153760-0153789.

²⁶⁸ *Id.*

- “[A]llocating and distributing Rebates and distributing supporting reports to participating Plans or Clients, in accordance with applicable terms of the agreement between [Express Scripts], or its Affiliates and the Client[.]”²⁶⁹

The Rebate Savings Agreement also required kaléo to pay Express Scripts five percent of the wholesale acquisition cost in the form of a rebate.²⁷⁰ The contract designated EVZIO to an “unspecified competitive product category,” which meant that there were no other competitors in its group trying to gain access to the Express Scripts formulary.²⁷¹

The Rebate Savings Agreement also provided that Express Scripts would receive a “price protection rebate” of 10 percent.²⁷² Express Scripts explained to the Subcommittee this meant that if the drug manufacturer increased the price of the drug more than 10 percent in any given year, the manufacturer paid any additional cost to Express Scripts. For example, if the drug manufacturer increased the price of the drug 12 percent in one year, the manufacturer paid the additional 2 percent to Express Scripts.²⁷³

Effective January 1, 2015, Express Scripts and kaléo agreed to reduce the price protection rebate to five percent.²⁷⁴ Express Scripts was unable to explain to Subcommittee staff why the parties agreed to reduce the price protection rebate to five percent.²⁷⁵

Medicare Part D Rebate Program Agreement. The Medicare Part D Rebate Agreement (“the Medicare Agreement”) between Express Scripts and kaléo to manage prescription benefits for the Medicare Part D program contained similar provisions as the Rebate Savings Agreement. That contract also took effect on October 1, 2014 and included an administrative fee per EVZIO unit of 4.375 percent.²⁷⁶ EVZIO was also listed an unspecified competitive product category with a rebate to Express Scripts of 5 percent and a price protection rebate of 10 percent.²⁷⁷

²⁶⁹ *Id.*

²⁷⁰ *Id.*

²⁷¹ *Id.*; Subcommittee staff briefing with Express Scripts (Sept. 5, 2018).

²⁷² KALEO-PSI-0153760-0153789.

²⁷³ Subcommittee staff briefing with Express Scripts (Sept. 5, 2018).

²⁷⁴ KALEO-PSI-0153790-0153793.

²⁷⁵ Subcommittee staff briefing with Express Scripts (Sept. 5, 2018).

²⁷⁶ KALEO-PSI-0153818-0153846.

²⁷⁷ *Id.*

2. CVS Caremark

Kaléo also signed a “Rebate Agreement” with CVS Caremark (“CVS”) for formulary management of EVZIO.²⁷⁸ CVS covers more than 94 million lives and offers the following services: plan design offerings and administration; formulary management; Medicare Part D services; mail order pharmacy; specialty pharmacy; retail pharmacy network management; prescription management services; clinical services; disease management programs; and medical benefit management.²⁷⁹ CVS reported net revenues of over \$184 billion in 2017.²⁸⁰ In December 2017, CVS announced plans to merge with Aetna Inc. through a transaction valued at almost \$70 billion.²⁸¹ The Department of Justice conditionally approved the merger on October 10, 2018.²⁸²

The Rebate Agreement between CVS and kaléo became effective on October 1, 2014.²⁸³ The contract set administrative fees at four percent.²⁸⁴ In exchange for administrative fees, CVS provided certain services, including, but not limited to:

- “Negotiate and contract with Clients for participation in the Rebates under this Agreement;”
- “Calculate the amount of Rebates applicable to Products for each Plan and invoice Manufacturer for such Rebates;” and
- “Allocate and distribute Rebates to Plans under the terms of its agreements with Clients and provide supporting reports.”²⁸⁵

The Rebate Agreement also specified that the base rate paid to CVS by kaléo for EVZIO was five percent and placed EVZIO in a “1 of 1 Manufacturer Status,” which meant that EVZIO was the only product with preferred formulary position.²⁸⁶ The Rebate Agreement allowed for a drug manufacturer to pay an additional “Incremental Base Rebate for Additional Controls” to exclude other competitive products,²⁸⁷ but at the time no other products were considered a competitor of EVZIO.²⁸⁸

²⁷⁸ KALEO-PSI-0153794-0153817.

²⁷⁹ CVS Health Corporation, Annual Report (Form 10-K), at 3–6 (Feb. 14, 2018).

²⁸⁰ *Id.* at 39.

²⁸¹ CVSHealth.com, *Press Release: CVS Health to Acquire Aetna* (Dec. 3, 2017), <https://cvshealth.com/newsroom/press-releases/cvs-health-acquire-aetna-combination-provide-consumers-better-experience>.

²⁸² Reed Abelson, *CVS Health and Aetna \$69 Billion Merger is Approved with Conditions*, N.Y. TIMES (Oct. 10, 2018), <https://www.nytimes.com/2018/10/10/health/cvs-aetna-merger.html>.

²⁸³ KALEO-PSI-0153794-0153817.

²⁸⁴ *Id.*

²⁸⁵ *Id.*

²⁸⁶ *Id.*

²⁸⁷ *Id.*

²⁸⁸ Subcommittee staff briefing with CVS Caremark (Sept. 13, 2018).

III. KALEO INCREASED THE WHOLESALE ACQUISITION COST OF EVZIO FROM \$575 TO \$3,750 AND CHANGED ITS DISTRIBUTION MODEL

Since setting EVZIO's starting WAC at \$575 in July 2014, kaléo has increased the price of EVZIO three times. Kaléo first increased the price of EVZIO from \$575 to \$750 in November 2015; from \$750 to \$3,750 in February 2016; and once again from \$3,750 to its current WAC of \$4,100 per unit in January 2017 with the launch of EVZIO 2.0 mg.²⁸⁹ This section discusses each EVZIO price increase in chronological order.

A. Kaléo Increased the Price of EVZIO from \$575 to \$750

Kaléo first increased EVZIO's price from \$575 to \$750 in November 2015.²⁹⁰ This represented a 30 percent increase 17 months after the product's launch in July 2014. Mr. Simmons explained that kaléo decided to increase the price from \$575 to \$750 in November 2015 because the company "hadn't taken a price increase."²⁹¹ Mr. Simmons further stated that such post-launch price increases were "standard" in the pharmaceutical industry.²⁹²

An internal document authored by kaléo consultant Todd Smith contained talking points for describing the price increase:

[o]n November 23rd, kaléo increased the EVZIO WAC price to \$750. Through kaléo's managed care contracts with PBMs and MCOs, annual price increases are contemplated in the agreements. kaléo did not take a price increase in 2014 and had not taken a price increase in 2015. This is the first price increase since launch of the product in 2014.²⁹³

Mr. Smith would continue to play a role in how kaléo priced EVZIO.

Kaléo also sought to expand coverage for EVZIO. A PowerPoint presentation designed for the kaléo sales force in 2015 outlined the goal to "improve EVZIO coverage and remove barriers to garner unimpeded access."²⁹⁴ To achieve this goal, kaléo sought to "Increase Evzio payer coverage for [greater than or equal to] 75 % or better access by 12/31/15" through, in part, by "target[ing] accounts: AARP, Humana Commercial/MedD, Aetna Med D, Anthem-Wellpoint,

²⁸⁹ KALEO-PSI-00016478-00016749.

²⁹⁰ Interview of Matthew Simmons, Vice President of Finance and Analytics at kaléo (May 16, 2018).

²⁹¹ *Id.*

²⁹² *Id.*

²⁹³ KALEO-PSI-00083016-00083021.

²⁹⁴ KALEO-PSI-00137826-00137890.

United, Wellcare, Healthspring (Cigna Med D), Silverscript (Caremark MedD), ESI Select Custom Clients.”²⁹⁵

B. Kaléo Hired Consultants Todd Smith and Ben Bove to Change its Distribution Model

In early 2015, kaléo needed advice on how best to capture the naloxone market share for EVZIO. Specifically, kaléo needed help getting EVZIO to patients and commercializing its product. Per Mr. Simmons, the company “had a great product, but no access” to the market.²⁹⁶ Mr. Simmons stated that kaléo believed that the nature of the product itself during an escalating opioid crisis would result in “broad coverage and access,” but that did not occur.²⁹⁷ Mr. Ford explained that the company thought the \$575 WAC would provide for sufficient coverage.²⁹⁸ Instead, kaléo found that “managed care still did not want to cover the drug” at its original WAC of \$575.²⁹⁹

Mr. Ford researched other pharmaceutical companies that had successfully launched their products to determine how kaléo could do the same.³⁰⁰ In 2015, one company that reported success launching a pharmaceutical product was Horizon Pharma, LLC (“Horizon”).³⁰¹ Looking to find a solution to its access and distribution issues, kaléo contacted Valinor Consulting (“Valinor”), a “[s]mall consulting firm based in Chicago, formed by former Horizon Pharma employees, Todd Smith and Ben Bove” for assistance.³⁰² Messrs. Smith and Bove were known to be responsible for the nontraditional approach Horizon took to the pharmaceutical industry.³⁰³

1. The Distribution and Pricing Model used by Horizon

Messrs. Smith and Bove previously worked together at Horizon in Chicago, Illinois. Mr. Smith began at Horizon as a Senior Vice President in 2010 and rose to become Executive Vice President and Chief Commercial Officer (“CCO”) before he

²⁹⁵ *Id.*

²⁹⁶ Interview of Matthew Simmons, Vice President of Finance and Analytics at kaléo (May 16, 2018).

²⁹⁷ *Id.*

²⁹⁸ Interview of Kris Ford, Vice President of Corporate Strategy and Business Development at kaléo (June 28, 2018).

²⁹⁹ *Id.*

³⁰⁰ Interview of Dan Hackman, Vice President of Patient Access at kaléo (July 26, 2018).

³⁰¹ *Id.*

³⁰² Kaleo-PSI-00058576-00058688.

³⁰³ Jared S. Hopkins and Andrew Martin, *These New Pharma Bros Are Wreaking Havoc on Prescription Drug Prices*, BLOOMBERG (Apr. 6, 2018), <https://www.bloomberg.com/news/features/2018-04-06/when-these-new-pharma-bros-show-up-drug-prices-tend-to-go-monumentally-higher>.

left the company.³⁰⁴ Mr. Bove joined Horizon in 2011 and was eventually a Senior Vice President of Marketing and Analytics when he departed in 2014.³⁰⁵

Horizon’s “first product, Duexis, an arthritis treatment that combines ibuprofen and the active ingredient in Pepcid” to decrease the risk of developing stomach ulcers was approved by the FDA in 2011.”³⁰⁶ The company’s initial public (“IPO”) offering in late 2011 did not go as well as planned and the company did not raise as much cash as it anticipated.³⁰⁷ After the IPO, Horizon faced a cash shortfall.³⁰⁸ In response, “Horizon more than doubled the price of a bottle of 90 Duexis pills in March 2013 from \$140 to \$502.”³⁰⁹

While Mr. Smith was CCO, Horizon continued to raise the price of Duexis.³¹⁰ Under Mr. Smith’s direction, Duexis went from \$140 to over \$1,030 per bottle.³¹¹ In 2013, Horizon bought the rights to a competing product, Vimovo, and raised its price as well.³¹² Vimovo is also an arthritis medication that contains naproxen (a nonsteroidal anti-inflammatory drug) and esomeprazole magnesium to reduce the risk of developing stomach ulcers.³¹³ Although Mr. Smith left Horizon in 2014 and Mr. Bove soon followed, a bottle of Duexis now costs over \$2,400 and Vimovo costs nearly \$3,000.³¹⁴ Following these price increases, “Horizon finished 2014 with an estimated \$290 million in revenue, four times its 2013 net sales of \$74 million.”³¹⁵

At Horizon, Mr. Bove “oversaw a program called *Prescriptions Made Easy* (“PME”) that sought to reduce hassles for doctors and costs for patients to mitigate barriers imposed by drug plans. It subsidized copayments and routed prescriptions

³⁰⁴ *Id.*; Horizon Pharma Inc., Soliciting Material Pursuant to 240.14a-12 (Form DEFA14A), at 8 (May 22, 2014).

³⁰⁵ *Id.*

³⁰⁶ Jared S. Hopkins and Andrew Martin, *These New Pharma Bros Are Wreaking Havoc on Prescription Drug Prices*, BLOOMBERG (Apr. 6, 2018), <https://www.bloomberg.com/news/features/2018-04-06/when-these-new-pharma-bros-show-up-drug-prices-tend-to-go-monumentally-higher>.

³⁰⁷ Lynn Cowan, *Horizon Pharma opens flat post-IPO*, MARKETWATCH (July 28, 2011), <https://www.marketwatch.com/story/horizon-pharma-opens-flat-post-ipo-2011-07-28>.

³⁰⁸ Jared S. Hopkins and Andrew Martin, *These New Pharma Bros Are Wreaking Havoc on Prescription Drug Prices*, BLOOMBERG (Apr. 6, 2018).

³⁰⁹ *Id.*

³¹⁰ Jared S. Hopkins and Andrew Martin, *These New Pharma Bros Are Wreaking Havoc on Prescription Drug Prices*, BLOOMBERG (Apr. 6, 2018).

³¹¹ *Id.*

³¹² *Id.*

³¹³ Why VIMOVO?, VIMOVO, https://www.vimovo.com/patient/why_vimovo (last visited Oct. 9, 2018).

³¹⁴ Jared S. Hopkins and Andrew Martin, *These New Pharma Bros Are Wreaking Havoc on Prescription Drug Prices*, BLOOMBERG (Apr. 6, 2018); Matt Egan, *Painkiller that once cost \$138 is now \$2,979*, CNN (Feb. 15, 2018), <https://money.cnn.com/2018/02/15/investing/drug-prices-vimovo-horizon-painkiller/index.html>.

³¹⁵ Mark Guarino, *The pain pill that saved Horizon Pharma*, CRAIN’S CHICAGO BUSINESS (Jan. 8, 2015), <https://www.chicagobusiness.com/article/20150108/ISSUE01/150109926/how-horizon-pharma-developed-breakout-pain-pills-duexis-and-vimovo>.

through a network of specialty pharmacies.”³¹⁶ Mr. Smith explained, however, “[p]hysicians could choose any pharmacy to fill a prescription, and retail pharmacies frequently filled Horizon prescriptions.”³¹⁷

In September 2014, Messrs. Smith and Bove started a specialty pharmacy called Clybourn Park Pharmacy LLC (“CPP”).³¹⁸ Mr. Smith explained the two men “created CPP as a compliant pharmacy.”³¹⁹

2. Messrs. Smith and Bove Established Novum Pharma

Next, Messrs. Smith and Bove established Novum Pharma, LLC (“Novum”) in March 2015.³²⁰ Mr. Smith served as the Chairman and CEO of Novum while Mr. Bove was an officer with the company.³²¹ At Novum, Messrs. Smith and Bove used the same tactics they employed at Horizon. Novum purchased three skin gels in March 2015: (1) Aloquin; (2) Alcortin A; and (3) Novacort.³²² Novum then increased the prices for the three products two months after their acquisition.³²³ Aloquin is an acne cream priced at \$7,968 per tube. Alcortin A, which is used “to treat dermatitis and eczema, went from \$226 to \$7,968.”³²⁴ Novacort treats skin irritation and went from \$4,186 to \$5,952 per tube.³²⁵ While the WAC for these drugs increased, Mr. Smith asserted “the average realized net price for the Novum products was less than \$400, taking into account Novum’s price support.”³²⁶

³¹⁶ Jared S. Hopkins and Andrew Martin, *These New Pharma Bros Are Wreaking Havoc on Prescription Drug Prices*, BLOOMBERG (Apr. 6, 2018). Specialty pharmacies are typically utilized for “complicated and expensive” drugs, but Horizon used them for regular prescriptions. Specialty pharmacies spend more time than regular pharmacies ensuring an insurance company covers a drug. The patient then receives the drug (and any subsequent refills) at their home directly through the mail.

³¹⁷ Letter from David Schumacher, attorney for Todd Smith (Nov. 9, 2018).

³¹⁸ *Id.*; *LLC File Detail Report No. 04929322*, ILL. SEC’Y OF STATE, <https://www.ilsos.gov/corporatellc/CorporateLlcController> (last visited Oct. 9, 2018).

³¹⁹ Letter from David Schumacher, attorney for Todd Smith (Nov. 9, 2018).

³²⁰ *LLC File Detail Report No. 04929322*, ILL. SEC’Y OF STATE, <https://www.ilsos.gov/corporatellc/CorporateLlcController> (last visited Oct. 9, 2018).

³²¹ *Id.*; *Todd N. Smith joins BPP Board*, BRIGHT PATH PHARMACEUTICALS (Aug. 28, 2017), <https://brightpathrx.com/todd-n-smith-joins-bpp-board/>.

³²² Ed Silverman, *The curious case of the \$9,500 skin gel*, STAT (Sept. 23, 2016), <https://www.statnews.com/pharmalot/2016/09/23/drug-price-skin-gel/>.

³²³ *Id.*

³²⁴ *Id.*

³²⁵ *Id.*; Letter from David Schumacher, attorney for Todd Smith (Nov. 9, 2018).

³²⁶ *Id.*

C. Kaléo Hired Messrs. Smith and Bove to Change the Way EVZIO Is Distributed

Mr. Ford contacted Mr. Smith on behalf of kaléo in January 2015.³²⁷ Kaléo hoped that the two men could assist with increasing EVZIO sales and the company could see similar successes to what occurred at Horizon.³²⁸

Messrs. Smith and Bove developed a custom distribution plan for EVZIO using an “[e]nhanced consultative selling model coupled with a Specialty Pharmacy” all “designed to reduce the ‘hassle factor’ associated with managed care, copay, and pharmacy issues.”³²⁹ Messrs. Smith and Bove’s plan for kaléo included the following:

- Defined Distribution through CPP
- Modified copay business rules that reduces copays for all commercially approved patients to \$0
- Introduction of an innovative program that allows rejected patients to still have access to EVZIO at \$0
- Unique selling model focused on solution selling to complement product clinical sales
- Applied analytics to determine optimal targets
- Reporting specific to targets and territories.³³⁰

This distribution plan closely mirrored the plan Messrs. Smith and Bove implemented at Horizon.³³¹

1. Kaléo established a pilot program for the new distribution model

Kaléo signed a three-month pilot program consulting agreement with Messrs. Smith and Bove that covered April, May, and June 2015 at a cost of \$50,000 per month.³³² If the pilot was successful and EVZIO sales “increase[d] drastically,” kaléo contemplated increasing the price for EVZIO and paying a royalty fee or bonus to CPP. The agreement also stated CPP would receive a seven percent discount off the WAC for EVZIO as shown below:³³³

³²⁷ Interview of Todd Smith, CEO at Novum Pharma LLC (Aug. 28, 2018).

³²⁸ *Id.*

³²⁹ KALEO-PSI-00058576-00058688.

³³⁰ *Id.*

³³¹ KALEO-PSI-00060770-00060772.

³³² KALEO-PSI-00058576-00058688.

³³³ *Id.* (emphasis added). Mr. Smith stated CCP never bought any product from kaléo. Letter from David Schumacher, attorney for Todd Smith (Nov. 9, 2018).

- Current Pilot Program consulting agreement in place
- 3 months (April – June)
 - \$50K/month
 - Product Purchase Agreement in place with pharmacy (not signed yet)
 - 7% Discount off WAC for Pilot Program
- If Pilot Program is successful and we continue to use program
- 7% Discount off WAC stays in place
 - Dispensing Fee
 - Discuss potential to increase price of drug
 - Discuss some type of small royalty or if volume increases drastically, potential \$50K-\$100k start up fee
 - Cost to buy down Rx's, act as MCO adjudicator
 - Financial Cost Modeling to be done during pilot

A presentation on the pilot program explained that the purpose of the program was “to ensure patients who are prescribed EVZIO are able to receive EVZIO quickly and efficiently.”³³⁴ The “Rx Direct Pilot” program would be run by CPP and focused on three territories: Tampa, Florida; Chicago, Illinois; and Youngstown, Ohio.³³⁵ The pilot program was designed to reduce “the phone calls back to the [health care professional] because [prior authorizations], step edits, etc. are not required to fill EVZIO prescriptions, and the copay will be \$20.”³³⁶ The pilot was scheduled to run from June 1, 2015 to July 31, 2015.³³⁷

The pilot program encouraged the kaléo sales team to use approved talking points. For example, when talking to prescribers, points to emphasize included:

- EVZIO will now be easier to get into your patient[’s] hands.
- This program will allow you to write EVZIO for your commercially insured patients with confidence that those patients will get it filled for no more than a \$20 copay and that no [prior authorizations], step edits or other issues will stop the patient from getting the EVZIO you prescribe.
- Because Rx Direct allows you to prescribe EVZIO without receiving the phone calls back regarding [prior authorizations] and step edits, you can now prescribe EVZIO for all commercial insured patient types you feel are appropriate.
- Multiple units of EVZIO can be prescribed for your commercially insured patients since they will have a maximum of a \$20 copay per prescription. With 2 units your patient can have EVZIO in their home and carry another one with them when they are out.
- Rx Direct ships EVZIO directly to your patient’s home.

³³⁴ KALEO-PSI-00138702-00138726.

³³⁵ *Id.*

³³⁶ *Id.*

³³⁷ *Id.*

- Can I talk to your staff about starting this today?³³⁸

When talking to prescribers' staff, the talking points noted "all the office has to do is e-prescribe EVZIO to Clybourne Park Pharmacy or fax the completed enrollment form to Clybourne Park Pharmacy."³³⁹ The program encouraged "best practices" that included:

- Close for all business. Do not ask for one patient or a "best" patient type; you should have the confidence to now ask for all appropriate Rx based on clinical rationale (cost and complexity have been removed from the equation)
- Ask for two units to be prescribed at the same time (one for home and one for work, car, etc)
 - Note: Only one unit will be shipped if insurance will not adjudicate two
- Call [each] of these offices at least 3 times a week and have a specific objective for each call – high frequency is required!
- Ensure a total office call is made within the practice.³⁴⁰

The Rx Direct Pilot also included weekly reports on: (1) the list of prescribers that CPP has received prescriptions from; (2) the number of prescriptions received into CPP for each prescriber; (3) the number of prescriptions filled by prescriber; and (4) the average number of EVZIO units dispensed by the prescriber.³⁴¹ Reports were also provided to physicians on patients who filled prescriptions.³⁴²

2. Kaléo Cited Barriers to EVZIO in the Traditional Pharmaceutical Market

Mr. Hackman explained that the traditional model for selling a prescription drug did not work for EVZIO.³⁴³ Mr. Hackman believed this was due to a stigma in the market of prescribing a take-home naloxone product.³⁴⁴ He explained that patients thought that their physicians were accusing them of being addicts by prescribing a product to counteract the effect of opioid overdose. At the same time, physicians felt a take-home naloxone product indicated they were overprescribing or mis-prescribing opioids to their patients.³⁴⁵ Mr. Hackman also cited barriers

³³⁸ *Id.*

³³⁹ *Id.*

³⁴⁰ *Id.*

³⁴¹ *Id.*

³⁴² *Id.* Kaléo stated when it learned Messrs. Smith and Bove had an ownership interest in Clybourne Park Pharmacy, kaléo instructed Messrs. Smith and Bove to remove the pharmacy from the network of pharmacies dispensing EVZIO.

³⁴³ Interview of Dan Hackman, Vice President of Patient Access at kaléo (July 26, 2018).

³⁴⁴ *Id.*

³⁴⁵ *Id.*

established by the traditional pharmaceutical reimbursement system, including prior authorizations and requiring patients to try cheaper options first or a “step edit” imposed by PBMs and commercial health plans.³⁴⁶

Mr. Smith asserted pharmacists can mislead patients and give false information about prescribed drugs.³⁴⁷ Mr. Smith noted there are thousands of excuses a pharmacist can give a patient to steer them away from a prescribed drug at the pharmacy.³⁴⁸ As examples, Mr. Smith cited: (1) the product is not available; (2) the product is too expensive; or (3) the product is not on contract. Mr. Smith stated that retail pharmacies have different margins on different products and economic incentives to fill certain products rather than others. Quite often, Mr. Smith believed, patients are unaware of those incentives. He also believed that bonuses are built-in for the store manager for over-the-counter products versus prescription drugs.³⁴⁹

Kaléo was also aware of the impact raising the price of EVZIO would have to its PBM contracts and specifically the price protection rebates.³⁵⁰ Mr. Hackman stated that kaléo knew the company would have to honor those contractual price protection rebates in instances where EVZIO was covered by the agreement.³⁵¹

D. The Kaléo Board of Directors Approved Moving to the New Distribution Model

At kaléo’s June 25, 2015 meeting of the board of directors, the board unanimously resolved to enter into a Commercial Services and Royalty Agreement³⁵² with Messrs. Smith and Bove through Novum. The contract described Novum as:

a pharmaceutical company that has significant expertise in, and proprietary information (including the Novum Commercialization Plan) relating to, the commercialization, marketing and sale of pharmaceutical products, and such expertise and proprietary information (including the Novum Commercialization Plan) is necessary to assist kaleo in the commercialization, marketing and sale of the Product.³⁵³

³⁴⁶ *Id.*

³⁴⁷ Interview of Todd Smith, CEO at Novum Pharma LLC (Aug. 28, 2018).

³⁴⁸ *Id.*

³⁴⁹ *Id.*

³⁵⁰ KALEO-PSI-00047693-00047704.

³⁵¹ Interview of Dan Hackman, Vice President of Patient Access at kaléo, (July 26, 2018).

³⁵² The agreements were combined into one document and signed on December 8, 2015, but were effective retroactively to June 29, 2015. *See* KALEO-PSI-00043111-00043112; KALEO-PSI-00060752-00060768.

³⁵³ KALEO-PSI-0153847.

As such, “[t]he parties desire for Novum to provide significant and substantial proprietary contributions to kaléo’s efforts to commercialize, market, and sell the Product.”³⁵⁴ The agreement created a Joint Operating Committee (“JOC”) that included Messrs. Smith and Bove and two individuals from kaléo, Mr. Williamson and Ned Ruffin.³⁵⁵ The agreement maintained the JOC was to meet soon after signing the agreement and annually in December to work on:

kaleo’s comprehensive annual strategic plan (to include, but is not limited to: pricing, copay, sales force decisions, managed care, trade and any other standard commercial decisions) and budget (collectively, and as may be amended or modified at any subsequent Committee meeting, the “Plan”) relating to the Product shall be discussed with mutually agreed-upon by the Novum Committee Members and the kaléo Committee Members.³⁵⁶

Pursuant to the terms of the contract, Mr. Smith was to join kaléo as its CCO, the same position he held at Horizon.³⁵⁷ Mr. Smith was the “Primary Representative” per the contract, whose responsibilities were to “make and manage all Commercial Operations Decisions, provided that the Primary Representative shall provide periodic updates to kaléo’s Chief Executive Officer.”³⁵⁸ The ultimate decision making responsibilities fell to Mr. Williamson as kaléo’s CEO. Mr. Smith told the Subcommittee he never assumed the official role of CCO at kaléo and was only providing assistance in an acting capacity.³⁵⁹ Mr. Smith assisted kaléo in filling the CCO position with Dan Hackman in September 2015.³⁶⁰

E. The Elements of Kaléo’s New Distribution Model for EVZIO

The distribution model adopted by kaléo was as follows. Kaléo would allow contracts to sell EVZIO through the traditional pharmaceutical market to end, including with PBMs, and would raise EVZIO’s price significantly.³⁶¹ Distribution would then change. A patient would receive an EVZIO unit through the mail direct from a specialty pharmacy if the patient’s insurance plan covered the drug.³⁶² Kaléo would cover any copay so the cost to the patient was \$0,³⁶³ effectively making kaléo a secondary insurer. This meant it would cover the costs not covered by the patient’s primary insurer. If insurance did not cover the prescription, the patient

³⁵⁴ *Id.*

³⁵⁵ Interview of Todd Smith, CEO at Novum Pharma LLC (Aug. 28, 2018).

³⁵⁶ KALEO-PSI-0153847.

³⁵⁷ KALEO-PSI-00060751.

³⁵⁸ KALEO-PSI-0153847.

³⁵⁹ Interview of Todd Smith, CEO at Novum Pharma LLC (Aug. 28, 2018).

³⁶⁰ *Id.*

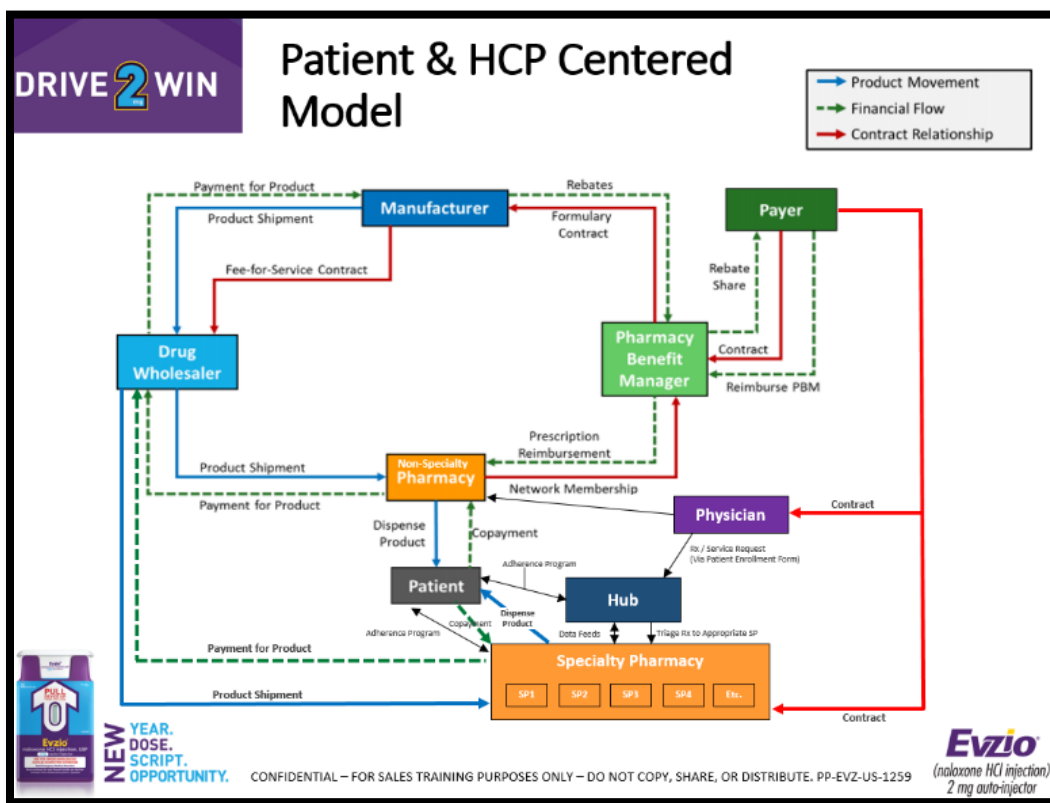
³⁶¹ Subcommittee staff briefing with kaléo (Sept. 7, 2018).

³⁶² *Id.*

³⁶³ *Id.*

received an EVZIO unit through the mail from a consignment pharmacy.³⁶⁴ The patient still paid \$0 and kaléo paid 100 percent.³⁶⁵ A “hub” handled a small percentage of prescriptions,³⁶⁶ which is further explained below.

In short, sales to patients with insurance coverage for EVZIO were intended to cover kaléo’s cost to send the drug to patients whose insurance did not cover kaléo. Thus, the need to raise the price. Mr. Hackman stated kaléo needed to employ this model because the traditional model through PBMs blocked access to EVZIO for patients.³⁶⁷ The new model provided for all patients prescribed an EVZIO to receive one through the mail. This is similar to Horizon’s distribution model that “subsidized copayments and routed prescriptions through a network of specialty pharmacies.”³⁶⁸ The chart below illustrates this new distribution model:³⁶⁹



³⁶⁴ *Id.*

³⁶⁵ *Id.*

³⁶⁶ *Id.*

³⁶⁷ Subcommittee staff briefing with kaléo (Sept. 7, 2018).

³⁶⁸ Jared S. Hopkins and Andrew Martin, *These New Pharma Bros Are Wreaking Havoc on Prescription Drug Prices*, BLOOMBERG (Apr. 6, 2018).

³⁶⁹ KALEO-PSI-00084714.

1. Kaléo Increased the Price of EVZIO to \$3,750

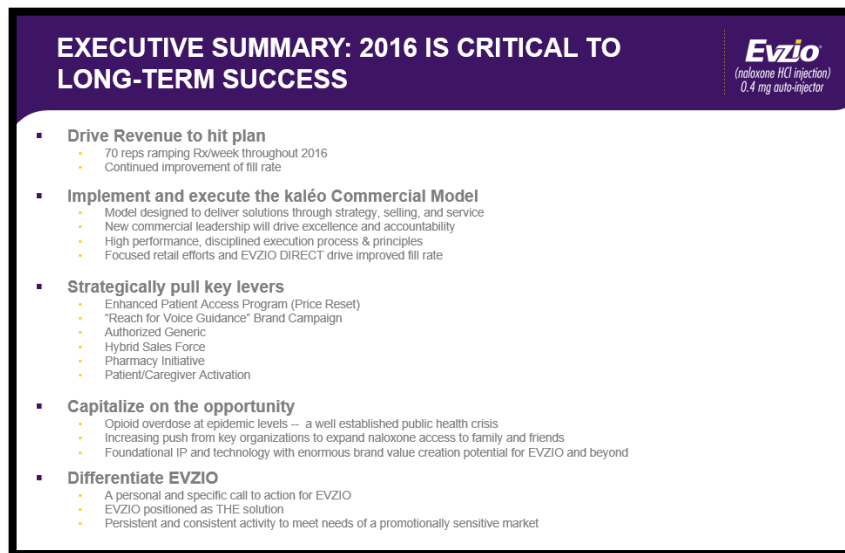
The pricing model required kaléo to increase the price of EVZIO significantly from \$750 to \$3,750 per unit on February 1, 2016.³⁷⁰ Kaléo explained this to providers and other health care professionals as:

[S]etting up a program for commercial patients that ensures that when a physician prescribes EVZIO, the patient will receive the product. Sometimes entities between the physician and the patient intervene to maximize their own profits to the detriment to the patient.³⁷¹

Kaléo asserted the new model “will help commercial covered patients get EVZIO by stepping in as a secondary insurer, when necessary, to assure patients who are prescribed EVZIO by their physician receive EVZIO.”³⁷² Kaléo justified the price increase stating: “The EVZIO WAC price will be higher to support this increased access for patients in need.”³⁷³ According to kaléo, EVZIO’s price increase was necessary to subsidize the cost of the company stepping in to ensure the product got to as many patients as possible once prescribed.³⁷⁴

In conjunction with the price increase, kaléo launched its new business plan. The EVZIO Commercial Update Executive Summary, pictured here, dated April 2016,

noted “2016 is critical to long-term success.”³⁷⁵ With the increased price and new business model, kaléo sought to “[c]apitalize on the opportunity” of “opioid overdose at epidemic levels – a well established public health crisis.”³⁷⁶ The company also



³⁷⁰ KALEO-PSI-00083199-00083207.

³⁷¹ KALEO-PSI-00083016-00083021.

³⁷² *Id.*

³⁷³ *Id.*

³⁷⁴ Interview of Dan Hackman, Vice President of Patient Access at kaléo, (July 26, 2018).

³⁷⁵ KALEO-PSI-00139484-00139543.

³⁷⁶ *Id.*

sought to “differentiate EVZIO” through “persistent and consistent activity to meet [the] needs of a promotionally sensitive market.”³⁷⁷

The 2016 commercial plan acknowledged that a weakness of the new plan was “perceived cost” and “blowback from the price increase.”³⁷⁸ However, kaléo planned to make EVZIO “the brand of choice of Opioid Overdose Emergencies” by highlighting its “cool and innovative technology.”³⁷⁹

The 2016 commercial plan also noted the changing naloxone delivery landscape with the FDA approving Narcan by Adapt Pharma on November 19, 2015.³⁸⁰ One package of Narcan included two 4 mg devices for “intranasal single-use, single spray (one nostril).”³⁸¹ The WAC for Narcan was \$125 with a \$75 bulk pricing for government entities.³⁸²

Kaléo developed scripted responses to media inquiries about its price increase. The company chose not to announce the price increase with a press release due to the increased cost of drugs being “a major topic of discussion among media and this price reset could potentially spur a wave of coverage on the price of EVZIO.”³⁸³ Instead, the “objective [was] to reinforce [kaléo’s] commitment to patient access.”³⁸⁴ As such, one of the core messages to provide to the media was that “kaléo has enhanced our patient access program so we can ensure more patients can obtain this innovative and potentially life-saving prescription product at a low or no [out of pocket] cost.”³⁸⁵

2. Kaléo Increased EVZIO’s Price to \$4,100 When it Launched EVZIO 2.0 mg

Eleven months after its price increase, kaléo launched its new EVZIO 2.0 mg, on January 1, 2017, for an even higher price of \$4,100.³⁸⁶ Kaléo introduced this higher-dosage version of EVZIO to respond to increasingly potent opioids causing overdoses.³⁸⁷ The increase in naloxone qualified EVZIO as a new drug product by the FDA.³⁸⁸ This meant that it was no longer subject to Medicaid rules

³⁷⁷ *Id.*

³⁷⁸ *Id.*

³⁷⁹ *Id.*

³⁸⁰ *Id.*

³⁸¹ *Id.*

³⁸² *Id.*

³⁸³ KALEO-PSI-00083199-00083207.

³⁸⁴ *Id.*

³⁸⁵ *Id.*

³⁸⁶ KALEO-PSI-00016478-00016479. Mr. Smith stated he was not involved in pricing EVZIO 2.0.

³⁸⁷ Interview of Matthew Simmons, Vice President of Finance and Analytics at kaléo, (May 16, 2018).

³⁸⁸ *Id.*

that reduced what the program would pay for a unit of EVZIO to \$0.01 after the initial price increase of the older EVZIO product to \$3,750. With the release of EVZIO 2.0 mg, kaléo increased the amount both Medicare and Medicaid would pay for a unit.³⁸⁹ According to kaléo documents, after the EVZIO 2.0 mg launch, “Medicare is a small [percentage] of unit sales ... but a large [percentage] of net sales.”³⁹⁰ In March 2017, kaléo announced to its Board of Directors that its participation in the Medicaid program would end on March 31, 2017.³⁹¹ The Medicaid program, however, continued to be charged for EVZIO at close to the WAC. The cost to Medicare and Medicaid is explained below.

The kaléo price increase mimicked previous price increases at companies run by Messrs. Smith and Bove. When asked what the difference was between the patient access models of kaléo and Horizon, which also significantly raised the cost of their products, Mr. Hackman stated that kaléo developed its own products and did not purchase an existing drug.³⁹² Mr. Hackman stated that the other company purchased existing drugs that had been in the market a long time and had generic alternatives available at a lower cost. In contrast, kaléo and its founders had taken all of the risk and invested millions of dollars, countless hours, and developed its products itself “by patients for patients.”³⁹³

3. The Distribution Model Sought to Reduce the Prior Authorization Paperwork Burden on Health Care Providers

Kaléo sought to mimic the aspects of Horizon’s distribution model and remove any barriers imposed by the traditional pharmaceutical distribution stream.³⁹⁴ Mr. Hackman stated that kaléo was able to do this by informing doctors that its new access model would get the prescription for EVZIO filled “as written,” regardless of insurance coverage issues.³⁹⁵ Kaléo sought to limit any prior authorization paperwork for the physician to complete or step therapy for the patient to try first.³⁹⁶ If the physician prescribed EVZIO for the patient, kaléo’s new distribution model ensured that the patient received an EVZIO without delay or hassle to the physician.³⁹⁷

Training documents for the launch of EVZIO 2.0 mg detailed how the new model works. The “goal” for the EVZIO sales force was to “drive all new scripts

³⁸⁹ KALEO-PSI-00128146-00128159.

³⁹⁰ *Id.*

³⁹¹ KALEO-PSI-00055051-00055160.

³⁹² Interview of Dan Hackman, Vice President of Patient Access at kaléo, (July 26, 2018).

³⁹³ *Id.*

³⁹⁴ *Id.*

³⁹⁵ *Id.*

³⁹⁶ *Id.*

³⁹⁷ *Id.*

through EvzioDirect.”³⁹⁸ Kaléo’s sales force would identify an “EvzioDirect Champion” in each of their assigned health care provider offices.³⁹⁹ An EvzioDirect Champion handles the paperwork surrounding an EVZIO prescription, but also “educate[s] and train[s] the patient on Evzio.”⁴⁰⁰ Specifically, the presentation suggested the kaléo sales force target the individual in the health care provider’s office responsible for the following tasks:

- Trains patients or provides patient education
- Processes patients through check-in and/or check-out or obtains informed consent forms
- Handles prior authorizations processing and managed care activities
- Helps process prescriptions through the [electronic medical records] system
- Handles forms for specialty pharmacies or hubs.⁴⁰¹

A PowerPoint presentation explained how the EvzioDirect program worked, including the steps the sales force should take to educate each health care provider:

- (1) review the EvzioDirect program with the health care provider;
- (2) determine the best office option for the office to process an Evzio prescription: either eprescription or fax;
- (3) remind the health care provider to provide an EVZIO postcard to the patient about the importance of answering a phone call from EvzioDirect;
- (4) remind the health care provider to remind the patient to answer the phone call from EvzioDirect; and
- (5) remind the health care provider to remind the patient to bring their EVZIO on their follow up appointment.⁴⁰²

The same presentation made clear that education should be “on-going,” including reminding health care providers “and staff they still may receive [prior authorization] forms for commercially insured [patients], but may ignore these.”⁴⁰³ The sales team should also remind health care providers that kaléo is “unable to provide copay support for patients with government insurance.”⁴⁰⁴

The launch presentation also outlined the enrollment process for EvzioDirect. The process begins with an enrollment form or an eprescription signed by the

³⁹⁸ KALEO-PSI-00061403-00061423.

³⁹⁹ *Id.*

⁴⁰⁰ *Id.*

⁴⁰¹ *Id.*

⁴⁰² *Id.*

⁴⁰³ *Id.*

⁴⁰⁴ *Id.*

prescriber.⁴⁰⁵ By signing the “Evzio Direct Patient Enrollment Form” the prescriber allows Asembia, through ASPN Pharmacies, to “act as my prior authorization agent in dealing with prescription and medical insurance companies.”⁴⁰⁶ A call center representative then uses that information to determine the patient’s benefits.⁴⁰⁷ The call center representative then calls the patient within two hours, making four attempts over the course of a week.⁴⁰⁸ If the patient answers, the representative collects any missing information about the patient and validates their shipping address.⁴⁰⁹ The presentation noted that “with the last 4 digits of the patient’s [social security number], Asembia [the service operating the call center is] able to investigate the patient’s drug benefit information 70% of the time.”⁴¹⁰

Next, the call center representative transfers the prescription to the pharmacy “based on region/geographic location, benefit design, and/or patient/prescriber preference.”⁴¹¹ The presentation noted the “pharmacies in the Asembia network are effective at fulfilling the script:

- Established pharmacies with experience, diversified business, high service levels
- Rx will be process[ed] by pharmacy within minutes of transfer
- Rx will be received by patient within 48 hours or less
- Pharmacies are trained on [EVZIO]
- They maintain an inventory [of EVZIO]
- Pharmacies are ready to scale up as Rx volume grows.”⁴¹²

4. Kaléo Used a Hub for a Portion of its Prescriptions through the New Distribution Model

As noted above, a portion of EVZIO prescriptions are routed through Asembia, which is a third-party that either fills the EVZIO prescriptions itself or provides access for the prescriptions to be filled via a network of specialty pharmacies.⁴¹³ Hub service vendors continue to evolve in the pharmaceutical industry and currently offer a wide range of services for their clients, including “benefits investigations and verification, prior authorizations, drug delivery and administration, copay support, financial assistance, and patient education.”⁴¹⁴ The

⁴⁰⁵ *Id.*

⁴⁰⁶ *Id.*

⁴⁰⁷ *Id.*

⁴⁰⁸ *Id.*

⁴⁰⁹ *Id.*

⁴¹⁰ *Id.*

⁴¹¹ *Id.*

⁴¹² *Id.*

⁴¹³ Interview of Dan Hackman, Vice President of Patient Access at kaléo (July 26, 2018).

⁴¹⁴ Jonathan Clark & Atheer Kaddis, *Continuing evolution of hub services*, 23 PHARMACY TODAY 41 (Jan. 2017), [https://www.pharmacytoday.org/article/S1042-0991\(16\)31650-4/pdf](https://www.pharmacytoday.org/article/S1042-0991(16)31650-4/pdf).

hub system evolved to avoid certain barriers that prevent the patient from receiving the prescription as written by their physician, including “copay and coinsurance management, contracted or preferred pharmacy requirements, formulary coverage, step therapy policies, medical necessity requirements, and [prior authorizations].”⁴¹⁵ The goal of hub services is to “address specific issues in the current market to increase patient access.”⁴¹⁶

According to Mr. Hackman, as stated, the traditional pharmacy system through PBMs did not work for kaléo. In fact, Mr. Hackman stated only 19 percent of EVZIO prescriptions were being filled after the company launched.⁴¹⁷ Mr. Hackman stated the low fill rate was due to the barriers kaléo encountered under the traditional pharmacy system, including PBMs and insurers requiring prior authorizations, step therapy edits, or exclusions depending on formulary tier status due to cost.⁴¹⁸

F. The Number of Prescriptions Filled for EVZIO Increased

Mr. Hackman stated that after implementing the new distribution model, EVZIO fill rates increased from around 19 percent to between 60 and 70 percent.⁴¹⁹ He explained that kaléo paid for many of the prescriptions under the new distribution model.⁴²⁰ Mr. Hackman stressed that the company designed the distribution model for patients covered by commercial health plans and did not take into account government payers, like Medicare Part D and Medicaid.⁴²¹

The chart below shows EVZIO’s fill rate starting from September 2015, a few months after implementing its new distribution model, into the first quarter of 2017.⁴²² The EVZIO fill rate improved from 39 percent in September 2015 to a high of 81 percent in March 2016, but then dropped to around 70 percent in January 2017.⁴²³ A percentage of the February and March 2017 fill rates were still in process, but appeared to be in line with fill rates for previous months.⁴²⁴

⁴¹⁵ *Id.*

⁴¹⁶ *Id.*

⁴¹⁷ Interview of Dan Hackman, Vice President of Patient Access at kaléo (July 26, 2018).

⁴¹⁸ *Id.*

⁴¹⁹ *Id.*

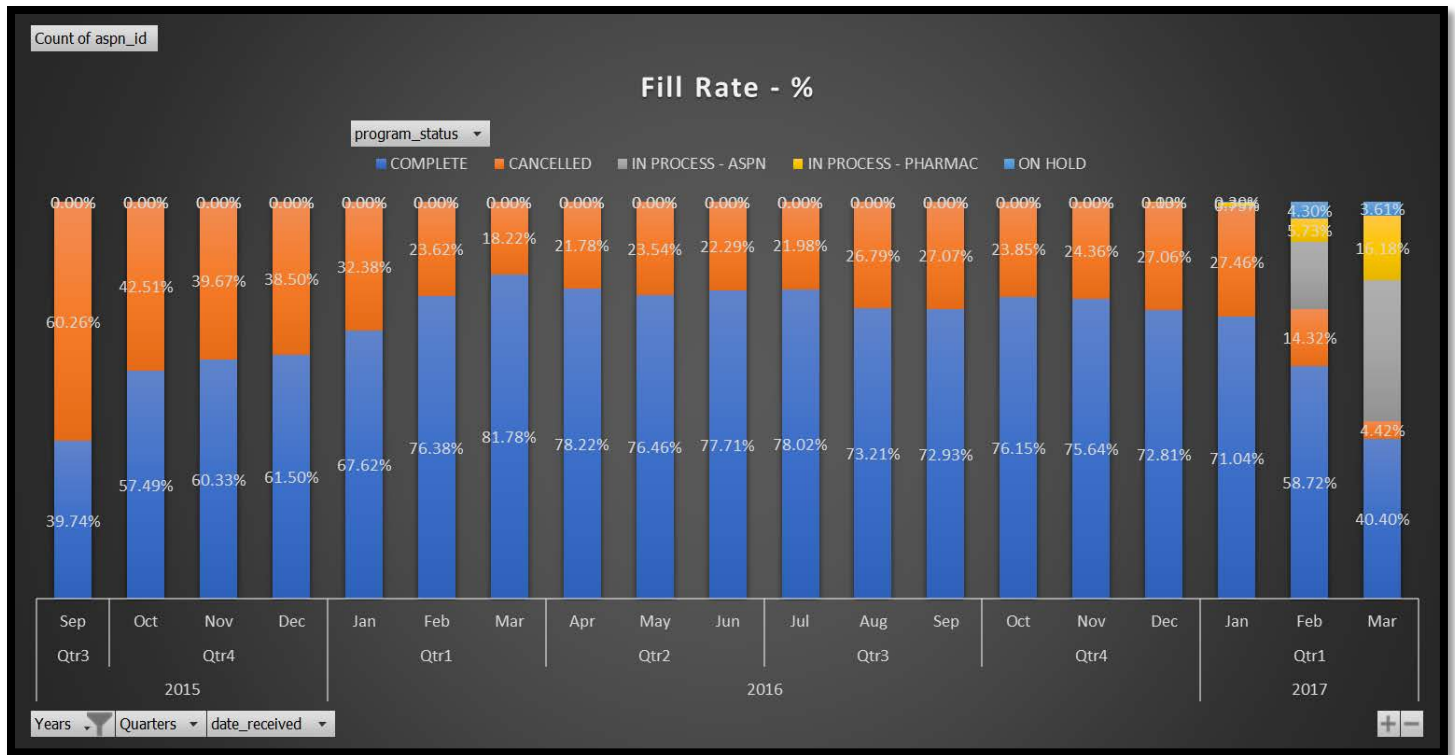
⁴²⁰ *Id.*

⁴²¹ *Id.*

⁴²² KALEO-PSI-00019015-00019018.

⁴²³ *Id.*

⁴²⁴ *Id.*



I. Messrs. Smith and Bove were Compensated Based on the Success of the Distribution Model they Helped Install

The compensation package for Messrs. Smith and Bove’s services through Novum included a royalty calculation that was based on the Adjusted Net Revenue (“ANR”) for kaléo’s product.⁴²⁵ The following excerpt shows how much Novum stood to gain if kaléo was able to increase its ANR due to the success of the “Novum Commercialization Plan” and its use of the “Novum Know-How.”⁴²⁶

⁴²⁵ KALEO-PSI-0153847-0153862.

⁴²⁶ *Id.*

4. **CONSIDERATION FOR THE NOVUM KNOW-HOW**

4.1 **Royalty.** In exchange for Novum's provision and disclosure of the Novum Commercialization Plan and provision of the Services (subject to Section 6.4), kaleo shall pay to Novum (payable quarterly in accordance with Section 4.2 below) an aggregate annual royalty (the "Novum Royalty") determined as follows:

(a) if kaleo's Adjusted Net Revenue for the applicable calendar year is less than \$25,000,000, the Novum Royalty shall be zero;

(b) if kaleo's Adjusted Net Revenue for the applicable calendar year is between \$25,000,000 and \$49,999,999.99, the Novum Royalty shall be an amount equal to five percent (5%) of such cumulative Adjusted Net Revenue;

(c) if kaleo's Adjusted Net Revenue for the applicable calendar year is between \$50,000,000 and \$249,999,999.99, the Novum Royalty shall be an amount equal to ten percent (10%) of such cumulative Adjusted Net Revenue; and

(d) If kaleo's Adjusted Net Revenue for the applicable year is \$250,000,000 or more, the Novum Royalty shall be an amount equal to fifteen (15%) of such cumulative Adjusted Net Revenue.

(e) For calendar year 2015 only, with respect to the calculation of the Novum Royalty due to Novum for any Adjusted Net Revenue received between October 1, 2015 and December 31, 2015, the thresholds listed in paragraphs (a) through (d) above shall be prorated by multiplying each threshold by 0.25.

For the avoidance of doubt, the applicable percentages set forth above with respect to the calculation of the Novum Royalty shall be based on aggregate Adjusted Net Revenue during each calendar year and the applicable percentage shall apply to all Adjusted Net Revenue during such calendar year (and not only to the incremental portion of Adjusted Net Revenue that exceeds the relevant Adjusted Net Revenue threshold corresponding to such percentage). By way of example, if aggregate Adjusted Net Revenue during a calendar year were \$255,000,000, the aggregate Novum Royalty would be equal to fifteen percent (15.0%) of \$255,000,000 (i.e. \$38,250,000).

Nine months after signing the original contract between kaléo and Novum, Messrs. Smith and Bove indicated to kaléo the need to create a new corporate entity for EVZIO-related work.⁴²⁷ Therefore, kaléo contracted with Messrs. Smith and Bove as Underhill Pharma, LLC ("Underhill") on September 23, 2016, with a retroactive effective date of July 1, 2016.⁴²⁸ The contract with Underhill spells out the duties and responsibilities among the parties to include:⁴²⁹

(b) Todd Smith will attend in person certain kaleo meetings, including Commercial Alignment, EVZIO Execution, Auvi-Q Execution and sales leadership meetings. In addition, Todd Smith and Ben Bove will be available and attend various telephonic and/or video conference meetings that are scheduled at mutually convenient times.

⁴²⁷ Interview of Todd Smith, CEO at Novum Pharma LLC (Aug. 28, 2018).

⁴²⁸ Underhill was incorporated on September 15, 2015, and lists Todd Smith and Ben Bove as two of its managers along with three other individuals. *LLC File Detail Report No. 05094917*, DEL. DEP'T. OF ST.: DIV. CORPS., <https://icis.corp.delaware.gov/ecorp/entitysearch/NameSearch.aspx>.

⁴²⁹ KALEO-PSI-00060752-00060768.

The contract identified Mr. Smith as having the responsibility for “managing, coordinating and performing the Services on behalf of Underhill.”⁴³⁰ The contract also included a clause that prevented Underhill from substituting another person for Mr. Smith without kaléo’s permission.⁴³¹ Mr. Smith stated he and Mr. Bove created Underhill because they realized they were consulting out of Novum, which had its own pharmaceutical products.⁴³² The two men believed they needed to establish a second entity to handle the consulting business, which was Underhill.⁴³³

Messrs. Smith and Bove were compensated through the Underhill contract. The compensation for the “Underhill Know-How” was also based on the adjusted net revenue kaléo earned from its EVZIO product in the following way:⁴³⁴

(a) if kaleo’s Adjusted Net Revenue for EVZIO for the applicable calendar year is between \$0 and \$50 Million, the Underhill Royalty shall be an amount equal to five percent (5%) of such cumulative Adjusted Net Revenue for EVZIO;

(b) if kaleo’s Adjusted Net Revenue for EVZIO for the applicable calendar year is greater than \$50 Million, the Underhill Royalty shall be an amount equal to ten percent (10%) of such cumulative Adjusted Net Revenue; and

(c) If kaleo’s Adjusted Net Revenue for Auvi-Q for the applicable year is greater than \$0, the Underhill Royalty shall be an amount equal to two and half percent (2.5%) of such cumulative Adjusted Net Revenue for Auvi-Q.

Underhill’s royalty package incentivized the success of kaléo’s EVZIO by providing as compensation a percentage of kaléo’s adjusted net revenue, which is net sales minus the cost of goods sold.⁴³⁵ The royalty was paid quarterly with estimates every three months and a year-end calculation.⁴³⁶

Overall, kaléo paid Underhill \$10,247,559 for the work performed by Messrs. Smith and Bove.⁴³⁷ The majority of that amount, \$9,421,203 or 92 percent, was paid for work during 2016 and 2017, including \$5.6 million as a contract termination fee.⁴³⁸ Kaléo had to pay this fee because it terminated its contract with Messrs. Smith and Bove before the contract had expired. Mr. Smith stated his work at kaléo covered more than just pricing EVZIO, and included improving kaléo’s

⁴³⁰ *Id.*

⁴³¹ *Id.*

⁴³² Interview of Todd Smith, CEO at Novum Pharma LLC (Aug. 28, 2018).

⁴³³ *Id.*

⁴³⁴ KALEO-PSI-00060752-00060768 (emphasis added).

⁴³⁵ *Id.*

⁴³⁶ *Id.*

⁴³⁷ KALEO-PSI-00153951.

⁴³⁸ *Id.*

commercial strategy and execution, operations, sales analytics, forecasting, and marketing.

G. Kaléo Ended its Relationship with Messrs. Smith and Bove

According to Mr. Hackman, kaléo parted ways with Messrs. Smith and Bove in summer 2017 because the company felt that it no longer needed their services.⁴³⁹

⁴³⁹ Interview of Dan Hackman, Vice President of Patient Access at kaléo (July 26, 2018).

IV. PHARMACY BENEFIT MANAGERS RESPONDED TO KALEO'S PRICE INCREASE BY EXCLUDING EVZIO FROM FORMULARIES

Following EVZIO's price increase, PBMs took steps to exclude EVZIO from their formularies. Also, around the same time kaléo increased the price of EVZIO, the FDA approved Adapt's Narcan, which was a cheaper take-home naloxone nasal spray for \$125 per unit. Both Express Scripts and CVS included Narcan on their formularies in place of EVZIO, which kaléo expected following such a dramatic price increase. This further limited kaléo's access to the traditional pharmaceutical market, increasing the need for the success of the new distribution model. This section details the traditional pharmaceutical market's reaction to kaléo's price increase and distribution model.

A. CVS Added Narcan to its Formulary and Ended Coverage of EVZIO

Following the FDA approval of Narcan in November 2015, CVS added Narcan to its formulary in the same tier as EVZIO, effective July 1, 2016. Mr. Hackman wrote to CVS to explain that, because of Narcan's tier placement, kaléo believed it owed no rebates under its contract:

Caremark placed Narcan on tier 2 preferred status, which is the same category and status as EVZIO. As both EVZIO and Narcan have been approved by the FDA as take home naloxone/opioid antagonists, EVZIO and Narcan are clearly competitive products that have been actively competing in the market since Narcan's approval in November 2015. As a result of Caremark's placement of Narcan on the same category and status as EVZIO, effective July 1, 2016, EVZIO is no longer in the 1 of 1 Manufacturer Status category, but rather is in the 1 of 2 Manufacturer Status category. Under our agreement, kaléo does not owe Caremark administrative fees, base rebates, or price protection rebates in this category.⁴⁴⁰

Mr. Hackman explained to the Subcommittee that kaléo believed it was ridiculous for CVS to assert kaléo owed it rebates because Narcan was not a competing product with EVZIO, since both products were designed to be take-home naloxone devices.⁴⁴¹ CVS responded on September 30, 2016:

Narcan Nasal Spray is not a Competitive Product of EVZIO and is not part of the Competitive Category as defined in the agreement. Therefore Narcan would not be considered as a competing product of EVZIO and would have no impact on the Rebate eligibility.⁴⁴²

⁴⁴⁰ KALEO-PSI-00012945.

⁴⁴¹ Interview of Dan Hackman, Vice President of Patient Access at kaléo (July 26, 2018).

⁴⁴² KALEO-PSI-00132390.

CVS explained to the Subcommittee that among the reasons it placed Narcan on its formulary with EVZIO, following Narcan’s approval by the FDA and review by the PBM’s independent pharmacy and therapeutics committee, were: (1) kaléo’s price increase was unacceptable, especially during a public health crisis and (2) Narcan was \$125 versus EVZIO’s price of \$3,750.⁴⁴³ Given these factors, CVS felt it was appropriate to add Narcan to the formulary.⁴⁴⁴ Kaléo believed that, according to its rebate agreement with CVS, it only owed rebates if CVS placed EVZIO on a formulary with no other competitive products. It believed Narcan qualified as a competing product. As a result, once CVS placed Narcan on its formulary, kaléo withheld paying any fees and rebates to CVS under the agreement.

The dispute between the two parties centered on \$19,967,492 in fees that kaléo refused to pay.⁴⁴⁵ CVS and kaléo ultimately settled the dispute.⁴⁴⁶ However, kaléo notified CVS that it would not be renewing its Rebate Agreement with the PBM, which meant the contract terminated on June 30, 2017.⁴⁴⁷ CVS excluded EVZIO from its formulary in 2017 and listed Narcan as the preferred drug option on its formulary in place of EVZIO.⁴⁴⁸

From 2015 to present, CVS processed claims for 9,241 EVZIO units.⁴⁴⁹ The Rebate Agreement between kaléo and CVS provided for administrative fees, base rebates, and price protections. The chart below represents the amounts kaléo paid CVS.

Kaléo’s Payments to CVS under the Rebate Agreement⁴⁵⁰

	2015	2016	2017	Total
Administrative Fees	\$40,838.84	\$1,016,440.81	(\$2,233.06)	\$1,055,046.59
Formulary Rebates	\$51,048.22	\$1,282,268.32	(\$2,791.32)	\$1,330,525.22
Price Protection	\$111,706.25	\$20,245,346.39	(\$51,540.26)	\$20,305,512.38
Total Amount	\$203,593.31	\$22,544,055.52	(\$56,564.64)	\$22,691,084.19

⁴⁴³ Subcommittee staff briefing with CVS (Sept. 13, 2018).

⁴⁴⁴ *Id.*

⁴⁴⁵ KALEO-PSI-00136229.

⁴⁴⁶ Subcommittee staff briefing with CVS (Sept. 13, 2018).

⁴⁴⁷ KALEO-PSI-00012935-00012938.

⁴⁴⁸ *Formulary Drug Removals*, CVS CAREMARK (Oct. 2017), https://2wt0853vtha23hf7qg2rwk3g-wpengine.netdna-ssl.com/wp-content/uploads/2017/12/Caremark_Tasigna_Formulary_Exclusion_Drug_List.pdf.

⁴⁴⁹ Subcommittee staff briefing with CVS Caremark (Sept. 13, 2018).

⁴⁵⁰ CVS Health Response to Further Questions Regarding EVZIO Submitted to the Homeland Security and Government Affairs Permanent Subcommittee on Investigations (October 2, 2018).

Of the \$22,691,084.19 collected from kaléo in administrative fees, rebates and price protections for EVZIO, CVS returned \$20,305,541.00 to its clients, or about 90 percent of the amounts collected.⁴⁵¹ The amount returned included \$19,650,547.00 in formulary rebates and price protections and \$654,994.00 in administrative fees.⁴⁵²

B. Express Scripts Allowed Plans to Impose a Cheaper Alternative to EVZIO and Then Replaced it with Narcan

Kaléo's contract with Express Scripts did not forbid Express Scripts from allowing a client insurance plan to require a cheaper option (commonly called a "step edit") before a patient received an EVZIO. However, kaléo and Express Scripts disagreed about whether the contract required kaléo to pay rebates when a step edit was imposed on EVZIO. While step edits were employed in only 110 cases, ultimately the price increase was too much for Express Scripts and the PBM excluded EVZIO from its PBM's formulary replacing it with Narcan.

1. Express Scripts Allowed its Member Plans to Impose Step Edits before a Patient Received an EVZIO

The Rebate Savings Agreement between kaléo and Express Scripts did not prohibit an Express Scripts client from requiring that a patient take certain actions before receiving an EVZIO. These included a "preferred specialty management" and "preferred step therapy." Under the terms for the contract, the "Preferred Specialty Management" is defined as:

[A] utilization management tool offered by [Express Scripts] to Plans that requires a Participant to satisfy prior authorization criteria prior to gaining access to a therapeutic category and, once prior authorization criteria are satisfied, is required to try a Preferred specialty product prior to a non-Preferred specialty product or pay 100% of the cost of their non-Preferred branded product. In limited circumstances, the Participant may try the non-Preferred specialty product when the Preferred specialty product is not clinically appropriate but only after prior authorization criteria are satisfied.⁴⁵³

In practice, this meant a prescribing physician would need to fill out additional paperwork before the patient could receive an EVZIO.⁴⁵⁴ Despite the terms of the

⁴⁵¹ Email from CVS to Subcommittee staff (Oct. 31, 2018).

⁴⁵² *Id.*

⁴⁵³ KALEO-PSI-0153760-0153789.

⁴⁵⁴ Interview of Dan Hackman, Vice President of Patient Access at kaléo, (July 27, 2018).

contract, Express Scripts stated it did “not employ a prior authorization program for EVZIO.”⁴⁵⁵

The Rebate Savings Agreement also did not prohibit Express Scripts member plans from imposing a “Preferred Step Therapy” before a patient could receive an EVZIO. A Preferred Step Therapy is defined in the contract as

A program, developed and administered by Express Scripts or a Plan, in which one or more products (each “Step Agent”) must first be tried by the Participant or, as a consequence of not trying the Step Agent: (i) the Participant is required to pay 100% of the cost of the non-Step-Agent branded product regardless of whether the applicable deductible has been satisfied, or (ii) the Plan imposes [a national drug code] block against coverage benefits for the non-Step Agent, or (iii) the Participant must obtain the non-Step Agent branded product upon appeal. Provided, however, in each case Participant may obtain the non-Preferred or non-covered product when medically necessary. For the purpose of this definition, Step Agents may include branded and/or generic pharmaceutical products. Existing users of a non-Step Agent branded products will not be grandfathered beyond statutory requirements, unless mutually agreed otherwise.⁴⁵⁶

Express Scripts began to offer the preferred step therapy on EVZIO on July 1, 2016, to its commercial clients; it was not an option for Medicare clients.⁴⁵⁷ At that time, the step therapy a member health plan could impose required that “injectable generic naloxone must be tried before using EVZIO.”⁴⁵⁸ If a person failed at using the injectable generic naloxone, they were eligible for an EVZIO. Express Scripts explained to Subcommittee staff that it was impossible to imagine a scenario where someone actively overdosing would go to a pharmacy and stand in line for a naloxone prescription.⁴⁵⁹ The PBM’s representative asserted that the generic version was for someone to have on hand as a pre-emptive option.⁴⁶⁰ However, “an exception may be granted if the physician can confirm that a patient is blind or significantly visually impaired.”⁴⁶¹

Since July 1, 2016, Express Scripts commercial client plans initiated 110 step therapies reviews for EVZIO prescriptions and of those, 58 (or 53 percent) were

⁴⁵⁵ Email from Express Scripts to Subcommittee staff (Oct. 1, 2018).

⁴⁵⁶ KALEO-PSI-0153760-0153789.

⁴⁵⁷ Letter from Express Scripts to Subcommittee staff (Sept. 17, 2018).

⁴⁵⁸ *Id.*

⁴⁵⁹ Subcommittee staff briefing with Express Scripts (Sept. 5, 2018).

⁴⁶⁰ *Id.*

⁴⁶¹ *Id.*

ultimately approved. The remaining 52 prescriptions were denied.⁴⁶² Step therapies were not an option to Express Scripts' Medicare line of business.⁴⁶³

2. Express Scripts Excluded EVZIO from its Formulary

In March 2016, Express Scripts decided to exclude EVZIO from its formulary based on the increase in the price to \$3,750.⁴⁶⁴ After exclusion, Express Scripts no longer covered EVZIO, unless the patient's physician applied for a medical exception.⁴⁶⁵ Applying for a medical exception requires additional paperwork and waiting for a determination. Express Scripts explained to Subcommittee staff that at the same time it excluded EVZIO, it added Narcan to its formulary, which the FDA approved on December 28, 2015 at a WAC of \$125.⁴⁶⁶

Following the exclusion by Express Scripts, Mr. Hackman emailed kaléo employees to explain that this action was "as expected."⁴⁶⁷ Mr. Hackman wrote that "the potential for this action was very much a part of our analysis and calculation as we designed the strategy and offering of our unrivaled patient access program."⁴⁶⁸ Express Scripts also excluded EVZIO 2.0 mg when kaléo introduced it in January 2017.⁴⁶⁹

Following the exclusion, in May 2016, kaléo refused to pay Express Scripts rebates.⁴⁷⁰ Kaléo asserted the contract only required it to pay rebates if Express Scripts offered EVZIO "at the lowest branded copay tier in the applicable CPC." Kaléo believed Express Scripts was not offering EVZIO on that tier. In contrast, Express Scripts asserted kaléo owed a total of \$12,104,827 under the Rebate Savings Agreement and \$1,224,909 under the Medicare Part D Rebate Program Agreement.⁴⁷¹

3. Express Scripts Sued Kaléo

The parties failed to reach agreement on the amount owed and Express Scripts filed a breach of contract lawsuit against kaléo demanding \$14.5 million.⁴⁷² In the complaint, Express Scripts alleged "the lawsuit [was] necessary to prevent kaléo from profiteering at the expense of Express Scripts, its client health plans,

⁴⁶² Email from Express Scripts to Subcommittee staff (Oct. 1, 2018).

⁴⁶³ Letter from Express Scripts to Subcommittee staff (Nov. 9, 2018).

⁴⁶⁴ Subcommittee staff briefing with Express Scripts (Sept. 5, 2018).

⁴⁶⁵ *Id.*

⁴⁶⁶ *Id.*

⁴⁶⁷ KALEO-PSI-00081594-00081595.

⁴⁶⁸ *Id.*

⁴⁶⁹ Subcommittee staff briefing with Express Scripts (Sept. 5, 2018).

⁴⁷⁰ *Id.*

⁴⁷¹ KALEO-PSI-00132391-0013292.

⁴⁷² Complaint at 20, *Express Scripts, Inc. v. kaleo Inc.*, No. 4:17-cv-01520-RLW (E.D. Mo. May 16, 2017).

and the members of those plans to whom EVZIO is administered or dispensed.”⁴⁷³ Kaléo counterclaimed alleging breach of contract by Express Script and resulting damages of \$5.3 million.⁴⁷⁴ Kaléo denied that “it unreasonably raised the prices of its drugs” and asserted Express Scripts “extracts excessive fees and ‘rebates’ from pharmaceutical manufacturers like kaléo to drive up its own profits while providing little, if anything, of value to the pharmaceutical supply chain.”⁴⁷⁵ The two parties settled the lawsuit out of court for an undisclosed amount.

4. Kaléo’s Payments to Express Scripts

Over the course of the relationship, kaléo paid Express Scripts in administrative fees, formulary rebates, and price protections. The chart below shows those payments under both contracts Express Scripts had with kaléo.

Kaléo’s Payments to Express Scripts under the Preferred Savings Grid Rebate Program Agreement⁴⁷⁶

	2014	2015	2016	Totals
Administrative Fees	\$5,413.26	\$52,673.87	\$321,166.17	\$379,253.30
Formulary Rebates	\$215.63	\$3,777.22	\$40,762.50	\$44,755.35
Price Protection	\$0	\$35,121.02	\$4,901,228.47	\$4,936,349.49
Total Amount	\$5,628.89	\$91,572.11	\$5,263,157.14	\$5,360,358.14
Total Shared with Clients	\$3,915.22	\$73,381.29	\$805,175.36	\$882,471.87
Percent Shared with Clients	70%	80%	15%	16%

Express Scripts told the Subcommittee that starting in 2016 it “launched the Inflation Protection Program to protect [Express Scripts] clients from rising brand inflation.”⁴⁷⁷ Express Scripts explained that “at that time, [the PBM] classified information protection amounts independently from rebates, offering clients specific guarantees.”⁴⁷⁸ Express Scripts noted “[t]he underlying economics for

⁴⁷³ Complaint at 3, *Express Scripts, Inc. v. kaleo Inc.*, No. 4:17-cv-01520-RLW (E.D. Mo. May 16, 2017).

⁴⁷⁴ Defendant kaleo, Inc.’s Answer to Plaintiffs’ Complaint and Counterclaims at 36, *Express Scripts, Inc. v. kaleo Inc.*, No. 4:17-cv-01520-RLW (E.D. Mo. June 22, 2017).

⁴⁷⁵ Defendant kaleo, Inc.’s Answer to Plaintiffs’ Complaint and Counterclaims at 5, 16, *Express Scripts, Inc. v. kaleo Inc.*, 17-cv-01520-RLW (E.D. Mo. June 22, 2017).

⁴⁷⁶ Email from Express Scripts to Subcommittee staff (Sept. 27, 2018).

⁴⁷⁷ Letter from Express Scripts to Subcommittee staff (Sept. 17, 2018)

⁴⁷⁸ *Id.*

inflation payments are separate and apart from plan’s rebates. Any inflation payments paid are in addition to rebates under” its agreements.⁴⁷⁹ Express Scripts stated the program is designed to shift the risk to the PBM. Express Scripts extended the program to Medicare clients in 2017.⁴⁸⁰ With the advent of this program, specific to EVZIO, Express Scripts clients only received 15 percent of the fees and rebates paid by kaléo to Express Scripts, given the higher WAC of \$3,750 in 2016.

Kaleo’s Payments to Express Scripts under the Medicare Part D Agreement⁴⁸¹

	2014	2015	2016	Totals
Administrative Fees	\$1,113.32	\$12,779.29	\$31,483.80	\$45,376.41
Formulary Rebates	\$215.65	\$1,413.14	\$10,537.50	\$12,166.29
Price Protection	\$0	\$9,142.97	\$603,480.24	\$612,623.21
Total Amount	\$1,328.97	\$23,335.40	\$645,501.54	\$670,165.91
Total Shared with Clients	\$1,175.24	\$16,394.41	\$445,658.30	\$463,227.95
Percent Shared with Clients	88%	70%	69%	69%

Overall, Express Scripts adjudicated claims for approximately 17,379 EVZIO units from 2014 through the end of 2017 and charged clients \$60,368,846 for those claims.⁴⁸²

Average Cost of EVZIO by Year for Express Scripts Clients⁴⁸³

Year	No. of EVZIO Claims	Amount Billed to Clients	Average cost per EVZIO
2014	304	\$152,452.90	\$501.49
2015	2,662	\$1,573,622.68	\$591.14
2016	8,842	\$34,317,118.67	\$3,881.15
2017	5,571	\$24,325,651.86	\$4,366.48

Express Scripts continues to cover EVZIO to patients under its Medicare Part D contract with kaléo. That contract terminates on December 31, 2018 and

⁴⁷⁹ *Id.*

⁴⁸⁰ *Id.*

⁴⁸¹ *Id.*

⁴⁸² *Id.*

⁴⁸³ Email from Express Scripts to Subcommittee staff (September 28, 2018).

according to Express Scripts, there is no plan to renew the Medicare Part D contract.⁴⁸⁴

⁴⁸⁴ Subcommittee staff briefing with Express Scripts (Sept. 5, 2018).

V. THE COST OF KALÉO'S PRICE INCREASE ON GOVERNMENT FUNDED PRESCRIPTION DRUG PROGRAMS

EVZIO's price increases over the past several years considerably affected several state and federal government health care programs. Specifically, due to their size and purchasing power, Medicare Part D and Medicaid experienced the most significant impact. Kaléo's own internal documents show that actual net sales of EVZIO by Medicare and Medicaid were dramatically higher than the company originally planned. Additionally, the price increases also squeezed the ability of the Department of Defense to purchase EVZIO.

Despite charging these programs over \$140 million, kaléo has not turned a profit on EVZIO for the four years the product has been on the market. This section of the report details how the price increase affected the cost of EVZIO to government prescription drug programs.

A. Medicare Part D

Kaléo's price increase significantly impacted EVZIO's cost to the Medicare Part D program. From January to August 2018, Medicare paid approximately \$45.8 million (including rebates) for EVZIO.⁴⁸⁵ Last year, the Medicare Part D program paid over \$60 million (including rebates).⁴⁸⁶ The chart below shows the increased impact to Medicare Part D as kaléo continued to increase the price of EVZIO from 2014 to 2018.⁴⁸⁷

*Estimated Amounts Charged to Medicare for EVZIO*⁴⁸⁸

Year	Units Sold	Total Paid	Rebates	Total Cost to Part D	Average Cost per Unit
2014*	266	\$149,931	\$1,329	\$148,602	\$558
2015	3,162	\$2,012,388	\$84,611	\$1,927,777	\$609
2016	11,360	\$40,709,738	\$3,097,845	\$37,611,893	\$3,310
2017	14,861	\$60,615,963	\$3,369,131	\$57,246,832	\$3,852
2018**	13,509	\$45,846,395	\$522,496	\$45,323,899	\$3,355

*July 2014 to December 2014

**January to August 2018

Federal law prohibits Medicare from negotiating directly with pharmaceutical drug companies such as kaléo over drug prices.⁴⁸⁹ Instead, the government relies on private plans and competition to drive down Medicare Part D

⁴⁸⁵ KALEO-PSI-0153899.

⁴⁸⁶ *Id.*

⁴⁸⁷ *Id.*

⁴⁸⁸ *Id.*; KALEO-PSI-00153949.

⁴⁸⁹ 42 U.S.C. §1395w-111 (2018).

drug prices.⁴⁹⁰ As kaléo raised the price of EVZIO, Medicare Part D’s average price for EVZIO also increased.⁴⁹¹ Medicare beneficiaries would have to pay more out of their own pockets in the form of a copay or would not be able to fill the prescription for EVZIO due to their inability to pay the higher price at the pharmacy.⁴⁹²

The focus of the kaléo sales force on individuals in physicians’ offices that completed prior authorization forms had an impact on Medicare Part D. As stated, a plan is required to give a prior authorization request for coverage of a non-formulary drug for medical necessity “great weight.”⁴⁹³ This standard increases the likelihood a plan would approve the request for a formulary exception for medical necessity and Medicare would cover the drug, less any patient copay. Examples of requests for formulary exceptions for medical necessity are annexed to this report.⁴⁹⁴

Further, a training presentation for the launch of EVZIO 2.0 mg dated January 25, 2017 highlighted “Government [Prior Authorization] Enhancements” that appear intended to increase the likelihood that physicians would complete any prior authorizations for EVZIO.⁴⁹⁵ These included: (1) some government claims have a low out of pocket or simple [prior authorization] process; (2) Asembia provides [prior authorization] forms and digital signature on the [health care provider] portal to make this easier; and (3) Asembia will not call the [health care provider] more than twice to minimize hassle.⁴⁹⁶

DRIVE 2 WIN

6. Government PA Process Enhancements

- Some government claims have low out of pocket or simple PA process
- Asembia provides PA forms and digital signature on the HCP portal to make this process easier
- Asembia will not call the HCP more than twice to minimize hassle

NEW YEAR. NEW RECIPE. OPPORTUNITY.

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Evzio
(naloxone HCl) injection
2 mg subcutaneous

⁴⁹⁰ CTRS. FOR MEDICARE AND MEDICAID SERVS., MEDICARE PART D PREMIUMS CONTINUE TO DECLINE IN 2019 (July 31, 2018), <https://www.cms.gov/newsroom/press-releases/medicare-part-d-premiums-continue-decline-2019>.

⁴⁹¹ CMS Data – Medicare Part D Naloxone Drug Utilization and Cost Summary for 2011-2017; KALEO-PSI-0153899.

⁴⁹² KALEO-PSI-00047693-00047704.

⁴⁹³ Medicare Part D Prescription Drug Benefit Manual, Ch. 18, *Part D Enrollee Grievances, Coverage Determinations, and Appeals*, pgs. 39-40 (May 12, 2014).

⁴⁹⁴ The names of the patients, prescribers, and plans are redacted.

⁴⁹⁵ KALEO-PSI-00018384-00018420.

⁴⁹⁶ *Id.*

Medicare and Medicaid net sales resulted in a disproportionate amount of revenue compared to kaléo’s commercial net sales. For example, in the first quarter of 2017, Medicare and Medicaid combined accounted for 24 percent of units sold, but accounted for 75 percent of net sales totaling \$7,947,980.⁴⁹⁷ Kaléo forecasted that commercial sales would be 84 percent of unit sold (9,792 units) with net sales of \$7.66 million.⁴⁹⁸ Medicare and Medicaid were only forecasted to be 10 percent of units sold (1,121 units) representing 29 percent of forecasted sales (\$3.02 million) as seen below.⁴⁹⁹

COMPARED TO PLAN - YTD

Overall Medicare is a small % of unit sales (16%) but a large % of net sales \$ (56%).

Customer Mix--Units

	Actual		Plan		Difference	
	Units	%	Units	%	Units	%
Commercial	7,127	66%	9,792	84%	(2,665)	-18%
Medicare	1,680	16%	796	7%	885	9%
Cash	1,140	11%	714	6%	425	4%
Medicaid	842	8%	325	3%	517	5%
Total	10,789	100%	11,627	100%	(838)	

Customer Mix--Net Sales

	Actual		Plan		Difference	
	Net Sales	%	Net Sales	%	Net Sales	%
Commercial	\$ 2,616,555	25%	\$ 7,656,359	75%	(5,039,804)	-50%
Medicare	\$ 5,916,662	56%	\$ 2,388,880	23%	3,527,782	33%
Cash	\$ (85,790)	-1%	\$ (421,662)	-4%	335,872	3%
Medicaid	\$ 2,031,318	19%	\$ 633,285	6%	1,398,032	13%
Total	\$ 10,478,745	100%	\$ 10,256,862	100%	221,883	

An internal accounting chart for kaléo on Average Net Realized Price (“ANRP”), or “Pocket Price” shows that Medicare had the highest ANRP for the EVZIO product when compared to commercial, cash, and Medicaid.⁵⁰⁰ ANRP represents the list price minus any discounts or rebates. The chart below shows Medicare’s ANRP averages at \$3,517 per sale with Medicaid second highest at \$2,708 in March 2017.⁵⁰¹

⁴⁹⁷ KALEO-PSI-00128146-00128159.

⁴⁹⁸ *Id.*

⁴⁹⁹ *Id.*

⁵⁰⁰ *Id.*

⁵⁰¹ *Id.*

Commercial ANRP is currently in line with COGS & Salesforce costs of ~\$300, Medicare has the highest ANRP.

Latest Finance GTN estimate by Channel (current month)

	Commercial	Cash	Medicaid	Medicare
<i>Prompt Pay Discounts</i>	2.0%	2.0%	2.0%	2.0%
<i>Product Returns</i>	2.3%	2.3%	2.3%	2.3%
<i>Fee For Service (FFS)</i>	6.4%	6.4%	6.4%	6.4%
<i>Chargebacks</i>			0.2%	
<i>Industrial Funding Fee</i>	0.0%			
<i>Commercial Rebates</i>	7.2%			
<i>Medicaid Rebates</i>			23.1%	
<i>Tricare Rebates</i>	1.2%			
<i>Part D-Rebates</i>				1.0%
<i>Part D-Coverage Gap ("Donut Hole")</i>				2.5%
<i>Co-Pay Programs</i>	64.6%	91.2%		
<i>Consigned Goods</i>	9.2%			
Total Channel GtN %	7.1%	-1.9%	66.0%	85.8%
Total Channel ANRP	\$ 290	\$ (79)	\$ 2,708	\$ 3,517

When asked how his distribution model affected the price paid by Medicare, Mr. Smith stated that by law there was nothing kaléo could do to help Medicare beneficiaries or other government programs with the price of EVZIO.⁵⁰² Mr. Smith explained the federal anti-kickback law prohibited kaléo from providing copayment support to patients with federal insurance. While kaléo advocated for generic naloxone or Narcan for government-covered patients, kaléo's distribution model for EVZIO had turned its focus to commercial insurance coverage.⁵⁰³

Medicare Part D benefits managed by PBMs also reflected an increased average cost of EVZIO. The charts below reflect those price increases.

⁵⁰² Interview of Todd Smith, CEO at Novum Pharma LLC (August 28, 2018).

⁵⁰³ *Id.*

Average Cost of EVZIO for Express Scripts Medicare Part D Clients⁵⁰⁴

Year	Units	Amount Paid by Medicare Clients	Average Cost per Unit
2014	42	\$23,235.88	\$553.24
2015	446	\$253,912.05	\$569.31
2016	1,197	\$4,208,917.85	\$3,516.22
2017	1,259	\$5,010,909.98	\$3,980.07

Average Cost of EVZIO for CVS Medicare Part D Clients⁵⁰⁵

Year	Units	Medicare Charges	Average Cost per Unit
2014	49.25	\$28,318.75	\$575
2015	871.75	\$532,581.25	\$610.93
2016	4,486.25	\$16,323,937.50	\$3,638.66
2017	5,419	\$22,137,575.00	\$4,085.18
2018	5,961.5	\$24,437,950.00	\$4,099.30

B. Medicaid

Kaléo's price increases also impacted the cost of EVZIO to the Medicaid program.⁵⁰⁶ From July 2014 through March 2017, nearly 7,500 units of EVZIO were provided to Medicaid recipients.⁵⁰⁷ However, kaléo likely lost money on EVZIO through the program in 2016 due to Medicaid rules that reduced what the program would pay for EVZIO to \$0.01 due to kaléo raising the price of the drug faster than the inflation rate.⁵⁰⁸ The chart below uses data provided by CMS and kaléo to show an estimated breakdown of EVZIO units covered through the Medicaid program from July 2014 through 2017.⁵⁰⁹

⁵⁰⁴ Email from Express Scripts to Subcommittee staff (Oct. 26, 2018); email from Express Scripts to Subcommittee staff (Nov. 5, 2018).

⁵⁰⁵ Email from CVS to Subcommittee staff (Oct. 31, 2018).

⁵⁰⁶ CMS Data – Medicare Part D Naloxone Drug Utilization and Cost Summary for 2011-2017; KALEO-PSI-0153899; KALEO-PSI-0154931.

⁵⁰⁷ *Id.*

⁵⁰⁸ *Id.*

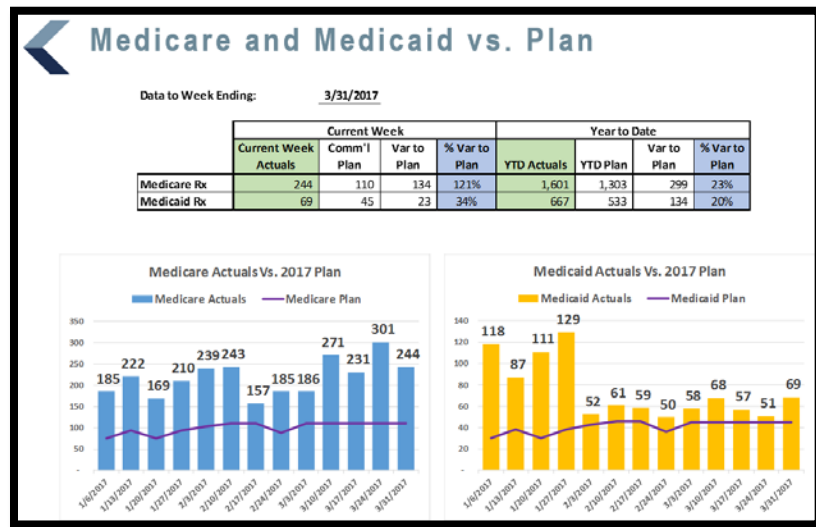
⁵⁰⁹ *Id.*

Estimated Amounts Charged to Medicaid for EVZIO⁵¹⁰

Year	Units Sold	Total Paid	Rebates	Total Cost	Average Cost per Unit
2014*	73	\$31,624	\$6,814	\$24,810	\$339.86
2015	2,301	\$1,440,921	\$406,312	\$1,034,609	\$449.63
2016	4,085	\$17,919,661	\$18,630,936	(\$711,275)	(\$174.12)
2017	1,634	\$3,980,939	\$1,700,980	\$2,279,959	\$1,395.32

*July 2014 to December 2014

Kaléo tracked the EVZIO units sold to the Medicare and Medicaid programs and compiled the information in weekly charts.⁵¹¹ As an example, the chart to the right shows that once EVZIO 2.0 mg launched on January 1, 2017, kaléo included Medicare and Medicaid unit sales as part of its plan.⁵¹² As the chart shows, the actual weekly sales for



Medicare for the last week in March 2017 were 121 percent higher than planned, while the year-to-date sales were 23 percent higher.⁵¹³ During the same week, Medicaid sales were 34 percent higher than planned, while year-to-date sales were 20 percent higher than planned.⁵¹⁴

In March 2017, kaléo announced to its Board of Directors that its participation in the Medicaid program would end on March 31, 2017.⁵¹⁵ Kaléo's

⁵¹⁰ This chart reflects totals paid produced by CMS and unit sales and rebates paid produced by kaléo. CMS Data – Medicare Part D Naloxone Drug Utilization and Cost Summary for 2011-2017; KALEO-PSI-0153899; KALEO-PSI-0154931.

⁵¹¹ KALEO-PSI-00061708-00061728.

⁵¹² *Id.*

⁵¹³ *Id.*

⁵¹⁴ *Id.*

⁵¹⁵ KALEO-PSI-00055051-00055160.

explanation was that, “many state Medicaid plans restrict patients to only one preferred product on their formularies. To help meet the needs of the community and ensure patients at risk for an opioid emergency have access to EVZIO, we are no longer participating in Medicaid.”⁵¹⁶ Despite ending its contract, the Medicaid program continued to pay for EVZIOs.⁵¹⁷ As such, PBMs continued to process Medicaid claims for EVZIO. For example, the chart below shows claims for EVZIO processed by CVS, including an increase in the average cost per EVZIO to the program.

Average Cost to Medicaid for EVZIO Units Processed by CVS⁵¹⁸

Year	Units	Amount Charged to Medicaid	Claims requiring Prior Authorization	Average Cost per Unit
2014	8	\$4,114	6	\$514.25
2015	479	\$291,719	242	\$609.02
2016	586	\$1,903,941	204	\$3,249.05
2017	400	\$1,564,143	85	\$3,910.36
2018*	152.5	\$666,149	87	\$4,368.19

*January through August 2018

Kaléo reported that 1,238 units were sold through the Medicaid program from January to August 2018.⁵¹⁹ EVZIO claims processed through CVS in 2018 averaged \$4,368.19 per claim.⁵²⁰ If the Medicaid program processed all claims at that rate (for 1,238 EVZIO units through August 2018 as reported by kaléo), the cost would be \$5,407,819.22 in 2018 for EVZIOs.

Express Scripts also continued to process EVZIO claims through the Medicaid program. The chart below shows the units, amount charged, and average cost per EVZIO for those claims.

Average Cost to Medicaid for EVZIO Units Processed by Express Scripts⁵²¹

Year	Units	Amount Charged to Medicaid Less Rebates	Average Cost per Unit
2014	10	\$5,376.67	\$537.67
2015	135	\$79,042.42	\$585.50
2016	726	\$2,333,864.70	\$3,214.69
2017	325	\$1,322,492.47	\$4,069.21

⁵¹⁶ KALEO -PSI-00017714-00017716.

⁵¹⁷ 42 U.S.C. 1396r-8 (2018).

⁵¹⁸ Email from CVS to Subcommittee staff (Oct. 31, 2018).

⁵¹⁹ KALEO-PSI-00153949.

⁵²⁰ Email from CVS to Subcommittee staff (Oct. 31, 2018).

⁵²¹ Email from Express Scripts to Subcommittee staff (Oct. 26, 2018); email from Express Scripts to Subcommittee staff (Nov. 5, 2018).

Kaléo representatives stated they were surprised the Medicaid program would continue to pay for EVZIO after kaléo ended its participation.⁵²² Since the company ended its participation, it has not received a request for rebates from the program.⁵²³ Kaléo reported they provide EVZIO to the wholesaler and any payment from Medicaid for EVZIO would be based on agreements between Medicaid and pharmacies or PBMs (or both) that kaléo is neither privy to nor has control over.⁵²⁴ The company designed its patient assistance program to provide EVZIO to patients covered by Medicaid with free product without requiring reimbursement from Medicaid.⁵²⁵

In place of participating in the Medicaid program, kaléo encouraged patients to use its KALÉO CARES Patient Assistance Program (“PAP”) by filling out a two-page form on kaléo’s EVZIO website.⁵²⁶ To receive an EVZIO at \$0 cost, kaléo’s PAP requires that a patient must: (1) be a legal U.S. resident; (2) not have any government or commercial drug coverage; (3) not have commercial insurance or be eligible for state or federal government insurance such as Medicare and Tricare; and (4) have an annual household income of less than \$100,000.⁵²⁷ Patients who are eligible for Medicaid coverage may be eligible for assistance to receive EVZIO at no cost.⁵²⁸ The prescriber signs a statement “certify[ing] that this EVZIO prescription fits the indication and is medically appropriate for this patient.”⁵²⁹ The form also includes special instructions for prescribers in New York and Tennessee.⁵³⁰ Representatives from kaléo stated they did not submit these forms to Medicaid for reimbursement.⁵³¹

Kaléo’s PAP provided a total of 2,624 units of EVZIO since it began in 2014.⁵³² Of those, kaléo distributed 2,114 units of EVZIO (more than 80 percent) under the PAP after it ended its Medicaid participation.⁵³³

In addition to its PAP, kaléo reported to the Subcommittee that it maintains a donation program to state and local entities. Since October 2014, kaléo has

⁵²² Conference call with kaléo employees and Subcommittee staff (Nov. 2, 2018).

⁵²³ *Id.*

⁵²⁴ *Id.*

⁵²⁵ Email from Michael Bopp, attorney for kaléo to Subcommittee staff (Nov. 3, 2018).

⁵²⁶ *EVZIO KALÉO CARES Patient Assistant Program Enrollment Form*, EVZIO, <https://evzio.com/patient/pdfs/Evzio-Enrollment-Form.pdf> (Aug. 2017).

⁵²⁷ *Id.*

⁵²⁸ *Id.*

⁵²⁹ *Id.*

⁵³⁰ *Id.*

⁵³¹ Conference call with kaléo employees and Subcommittee staff (Nov. 2, 2018).

⁵³² KALEO-PSI-0154931.

⁵³³ *Id.*

donated 177,784 cartons of EVZIO to state and local entities, including first responders.⁵³⁴

C. Department of Veterans Affairs

Kaléo reached out to the VA to initiate the VA Federal Supply Schedule (“FSS”) contracting process in 2014.⁵³⁵ The VA FSS is used for health care acquisitions by the Department for commercial products and services. Kaléo and the VA reached an interim agreement later that year – referred to as a “letter contract” – that was in effect until 2016, when a full five-year contract running through September 14, 2021 was executed.⁵³⁶

The WAC at the start of the kaléo contract with the VA was \$3,750.⁵³⁷ The VA price for EVZIO 0.4 mg under the 2014 letter of contract was \$428.26. When the five-year FSS contract went into effect in 2016, the contract price was \$428.61.⁵³⁸ According to Mr. Simmons, the company negotiated the VA contract with a discount of 88 percent off the WAC, which kaléo believed was standard for the FSS.⁵³⁹ In 2017, when kaléo launched EVZIO 2.0 mg, it continued to offer the VA a discount, charging the agency \$426.47.⁵⁴⁰

Later in 2017, kaléo implemented a lower price of \$360 for the VA and as of August 2018, that remained the price the VA pays for EVZIO.⁵⁴¹ The VA has spent a total of \$13,220,694.71 for 73,518 units of EVZIO.⁵⁴²

Kaléo also worked out an additional arrangement with the VA. When kaléo was transitioning to its new version of EVZIO, which contained a 2.0 mg dosage, the company reached out to the VA to negotiate a bulk sale of 5,000 0.4 mg dosage units for \$750,000.⁵⁴³ These units had a twenty-month shelf life.

⁵³⁴ KALEO-PSI-00153948.

⁵³⁵ Subcommittee staff briefing with U.S. Dep’t of Veterans Affairs (July 26, 2018).

⁵³⁶ *Id.*

⁵³⁷ *Id.*

⁵³⁸ *Id.*

⁵³⁹ Interview of Matthew Simmons, Vice President of Finance and Analytics, kaléo (May 16, 2018).

⁵⁴⁰ Subcommittee staff briefing with U.S. Dep’t of Veterans Affairs (July 26, 2018).

⁵⁴¹ *Id.* The \$360 price has also been extended to all federal agencies. Subcommittee briefing with U.S. Dep’t of Veterans Affairs (June 7, 2018); Interview with Matthew Simmons, Vice President of Finance and Analytics, kaléo (May 16, 2018).

⁵⁴² Information provided by U.S. Dep’t of Veterans Affairs.

⁵⁴³ Subcommittee staff briefing with U.S. Dep’t of Veterans Affairs (July 26, 2018).

D. Department of Defense TRICARE Health Care Program

Through the TRICARE program, the Department of Defense (“DOD”) has purchased an increasing number of both EVZIO and Narcan, as depicted in the chart below.⁵⁴⁴

Total Units of Naloxone Take-Home Products Dispensed

Drug	2014	2015	2016	2017
EVZIO 2.0 mg				784
EVZIO 0.4 mg	252	750	2,520	188
Narcan 4 mg			933	7,161
Total	252	750	3,452	8,133

In 2014, the net cost of EVZIO prescriptions under the TRICARE program to DOD was \$46,869 (an average of \$315 per unit).⁵⁴⁵ In 2015, that amount went up to \$296,907 (an average of \$442 per unit) as the price of EVZIO increased to \$750 towards the end of the year.⁵⁴⁶ Kaléo’s EVZIO price increase in early 2016 to \$3,750 increased the DOD’s net payments for the drug to \$5,780,610 (an average of \$3,008 per unit).⁵⁴⁷ In contrast, the average cost of Narcan to TRICARE was \$70 per unit.⁵⁴⁸

In August of 2016, during the DOD’s drug bid review period, the Pharmacy and Therapeutics Committee recommended placing EVZIO as non-formulary with a Tier-3 copay. A medical necessity form signed by the prescribing physician allows for lowering to the Tier-2 copay.⁵⁴⁹ As an incentive to encourage use of Narcan over EVZIO, the Committee recommended Narcan have a reduced Tier 1 copay and designated Narcan as a Basic Core Formulary drug.⁵⁵⁰ That recommendation was implemented on January 11, 2017, shortly after kaléo launched its EVZIO 2.0 mg product and increased the price to \$4,100 on January 1, 2017.⁵⁵¹ The DOD’s net cost for EVZIO in 2017 was \$2,409,057 (an average of \$2,633 per unit).⁵⁵²

⁵⁴⁴ U.S. Dept. of Defense Naloxone Report provided to the Subcommittee (Aug. 10, 2018).

⁵⁴⁵ U.S. Dept. of Defense Naloxone Report provided to the Subcommittee (Aug. 10, 2018).

⁵⁴⁶ *Id.*

⁵⁴⁷ *Id.*

⁵⁴⁸ Email from Department of Defense to Subcommittee staff (Nov. 16, 2018).

⁵⁴⁹ Subcommittee staff briefing with Department of Defense (Oct. 4, 2018).

⁵⁵⁰ Email from Department of Defense to Subcommittee staff (Nov. 16, 2018).

⁵⁵¹ *Id.*

⁵⁵² U.S. Dept. of Defense Naloxone Report provided to the Subcommittee (Aug. 10, 2018).

Total Cost of Naloxone Take-Home Products

Drug	2014	2015	2016	2017
EVZIO 2.0 mg				\$2,334,126
EVZIO 0.4 mg	\$46,869	\$296,907	\$5,780,610	\$74,931
Narcan 4 mg			\$71,693	\$531,650
Total	\$46,869	\$296,907	\$5,852,303	\$2,940,707

The DOD told the Subcommittee that in 2018, although it purchased nine times more Narcan, the EVZIO prescriptions still cost more overall.⁵⁵³ The average net cost per prescription filled for EVZIO and Narcan in 2016 were \$2,866.80 and \$38.45, respectively.⁵⁵⁴ In 2017, the average net cost per prescription filled for EVZIO and Narcan were \$3,720.32 for EVZIO 2.0 mg, \$498.88 for EVZIO 0.4 mg, and \$37.12 for Narcan, as shown in the chart below.⁵⁵⁵ DOD explained that EVZIO cannot be substituted with Narcan at the point of dispensing since it is not an AB rated generic. This designation allows for interchange between drugs at the point of dispensing. The FDA is the sole entity that can designate a drug with AB rating and subsequent interchangeability.⁵⁵⁶

Average Cost per Unit of Naloxone Take-Home Products

Drug	2014	2015	2016	2017
EVZIO 2.0 mg				\$3,720.32
EVZIO 0.4mg	\$232.72	\$495.17	\$2,866.80	\$498.88
Narcan 4mg			\$38.45	\$37.12

⁵⁵³ Subcommittee staff briefing with U.S. Dep't of Defense (Oct. 4, 2018).

⁵⁵⁴ U.S. Dept. of Defense Naloxone Report provided to the Subcommittee (Aug. 10, 2018).

⁵⁵⁵ *Id.*

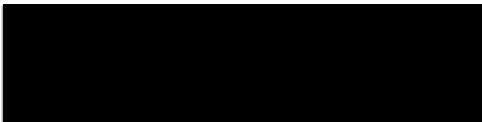
⁵⁵⁶ Email from Department of Defense to Subcommittee staff (Nov. 16, 2018).

VI. CONCLUSION

As explained above, in the midst of a national crisis, kaléo increased the price of its naloxone drug EVZIO by more than 600 percent, resulting in charging taxpayers, to date, more than \$142 million in just the last four years.

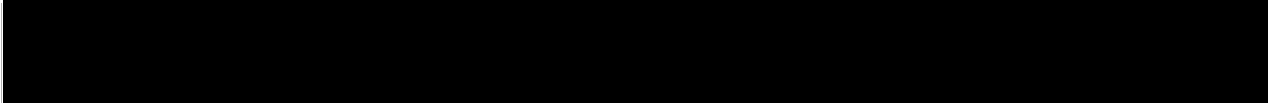
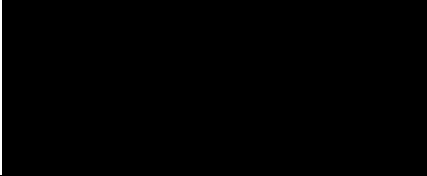
Kaléo raised the price in February 2016 from \$575 to \$3,750 and launched its new distribution model planning to “[c]apitalize on the opportunity” of “opioid overdose at epidemic levels” and a “well established public health crisis.” Eleven months later, kaléo raised the price to \$4,100. As part of its new distribution model, the company’s sales force focused on ensuring doctor offices signed any necessary paperwork (called prior authorizations) for the EVZIO prescription to be covered, including that EVZIO was medically necessary, which ensured it would be covered by government programs like Medicare and Medicaid for the Wholesale Acquisition Cost, less any patient copays.

ANNEX



**REQUEST FOR
MEDICARE PRESCRIPTION DRUG COVERAGE DETERMINATION**

This form may be sent to us by mail or fax:



Who May Make a Request: Your prescriber may ask us for a coverage determination on your behalf. If you want another individual (such as a family member or friend) to make a request for you, that individual must be your representative. Contact us to learn how to name a representative.

Enrollee's Information

Enrollee's Name _____ Date of Birth _____

Enrollee's Address _____

City _____ State _____ Zip Code _____

Phone _____ Enrollee's Member ID # _____

Complete the following section ONLY if the person making this request is not the enrollee or prescriber:

Requestor's Name _____

Requestor's Relationship to Enrollee _____

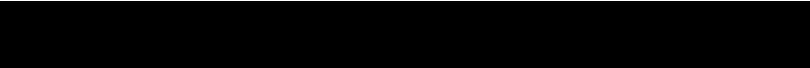
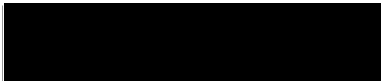
Address _____

City _____ State _____ Zip Code _____

Phone _____

Representation documentation for requests made by someone other than enrollee or the enrollee's prescriber:

Attach documentation showing the authority to represent the enrollee (a completed Authorization of Representation Form CMS-1696 or a written equivalent). For more information on appointing a representative, contact your plan or 1-800-Medicare (1-800-633-4227), TTY: 1-877-486-2048, 24 hours per day, 7 days a week.



Name of prescription drug you are requesting (if known, include strength and quantity requested per month):

EVZIO 2MG/0.4ML, 0 8ML/30days

Type of Coverage Determination Request

- I need a drug that is not on the plan's list of covered drugs (formulary exception).*
- I have been using a drug that was previously included on the plan's list of covered drugs, but is being removed or was removed from this list during the plan year (formulary exception).*
- I request prior authorization for the drug my prescriber has prescribed.*
- I request an exception to the requirement that I try another drug before I get the drug my prescriber prescribed (formulary exception).*
- I request an exception to the plan's limit on the number of pills (quantity limit) I can receive so that I can get the number of pills my prescriber prescribed (formulary exception).*
- My drug plan charges a higher copayment for the drug my prescriber prescribed than it charges for another drug that treats my condition, and I want to pay the lower copayment (tiering exception).*
- I have been using a drug that was previously included on a lower copayment tier, but is being moved to or was moved to a higher copayment tier (tiering exception).*
- My drug plan charged me a higher copayment for a drug than it should have.
- I want to be reimbursed for a covered prescription drug that I paid for out of pocket.

***NOTE: If you are asking for a formulary or tiering exception, your prescriber MUST provide a statement supporting your request. Requests that are subject to prior authorization (or any other utilization management requirement), may require supporting information. Your prescriber may use the attached "Supporting Information for an Exception Request or Prior Authorization" to support your request.**

Additional information we should consider (*attach any supporting documents*):
 EVZIO IS THE ONLY FDA APPROVED AUTO-INJECTOR TO BE USED BY THE PATIENT OR OTHER NON-MEDICAL PERSONNEL IN THE EVENT OF AN OPIOID OVERDOSE.

Important Note: Expedited Decisions

If you or your prescriber believe that waiting 72 hours for a standard decision could seriously harm your life, health, or ability to regain maximum function, you can ask for an expedited (fast) decision. If your prescriber indicates that waiting 72 hours could seriously harm your health, we will automatically give you a decision within 24 hours. If you do not obtain your prescriber's support for an expedited request, we will decide if your case requires a fast decision. You cannot request an expedited coverage determination if you are asking us to pay you back for a drug you already received.

- CHECK THIS BOX IF YOU BELIEVE YOU NEED A DECISION WITHIN 24 HOURS**
 (If you have a supporting statement from your prescriber, attach it to this request).

I attest that the medication requested is medically necessary for this patient. I further attest that the information provided is accurate and true, and that documentation supporting this information is available for review if requested by the health plan sponsor, or, if applicable, a state or federal regulatory agency. I understand that any person who knowingly makes or causes to be made a false record or statement that is material to a claim ultimately paid by the United States government or any state government may be subject to civil penalties and treble damages under both the federal and state False Claims Acts. See, e.g., 31 U.S.C. §§ 3729-3733.

Signature of person requesting the coverage determination (the enrollee, or the enrollee's prescriber or representative): _____

Date: _____

Type of Coverage Determination Request

FORMULARY and TIERING EXCEPTION requests cannot be processed without a prescriber's supporting statement. PRIOR AUTHORIZATION requests may require supporting information.

REQUEST FOR EXPEDITED REVIEW: By checking this box and signing below, I certify that applying the 72 hour standard review timeframe may seriously jeopardize the life or health of the enrollee or the enrollee's ability to regain maximum function.

Prescriber's Information

Name: [REDACTED]

Address: [REDACTED]

City: [REDACTED] State: [REDACTED] Zip Code: [REDACTED]

Office Phone: 253944128 [REDACTED] Fax: [REDACTED]

Prescriber's Signature: [REDACTED] Date: [REDACTED] 18

Diagnosis and Medical Information

Medication: EVZIO AUTO-INJECTOR	Strength and Route of Administration: 2MG/0.4ML	Frequency: PRN FOR OPIOID EMERGENCY
New Prescription OR Date Therapy Initiated: NEW RX	Expected Length of Therapy: INDEFINITE	Quantity: 1 CARTON
Height/Weight:	Drug Allergies:	Diagnosis: [REDACTED]

Rationale for Request

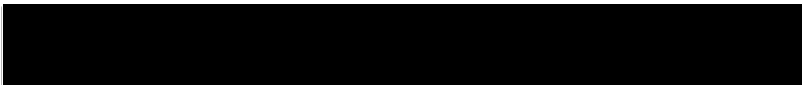
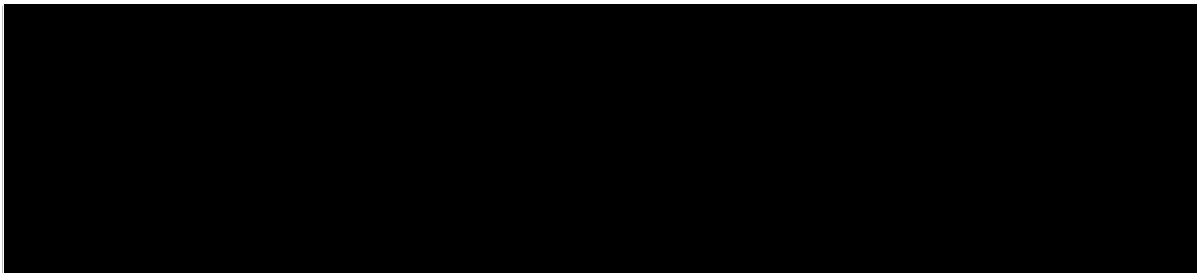
Alternate drug(s) contraindicated or previously tried, but with adverse outcome, e.g., toxicity, allergy, or therapeutic failure Specify below: (1) Drug(s) contraindicated or tried; (2)



adverse outcome for each; (3) if therapeutic failure, length of therapy on each drug(s)

- Patient is stable on current drug(s); high risk of significant adverse clinical outcome with medication change** Specify below: Anticipated significant adverse clinical outcome
- Medical need for different dosage form and/or higher dosage** Specify below: (1) Dosage form(s) and/or dosage(s) tried; (2) explain medical reason
- Request for formulary tier exception** Specify below: (1) Formulary or preferred drugs contraindicated or tried and failed, or tried and not as effective as requested drug; (2) if therapeutic failure, length of therapy on each drug and adverse outcome; (3) if not as effective, length of therapy on each drug and outcome
- Other** (explain below)

Required Explanation: WAC 246-840-4980



Evzio, a take-home naloxone auto-injector, is appropriate and medically necessary because the patient is at increased risk of opioid overdose due to opioid analgesics taken outside of a medically supervised setting.

Opioid overdose, as manifested by opioid-induced respiratory depression, is a well-documented, serious side effect that can occur in the presence of certain risk factors. Recent government publications have endorsed co-prescribing of the opioid antagonist naloxone for those at increased risk for life-threatening opioid-induced respiratory depression. Without immediate intervention, opioid overdose may result in severe clinical consequences, such as brain injury or death within minutes. Most opioid overdose occurs in the home and is witnessed by friends or family who may be in the best position to intervene quickly.

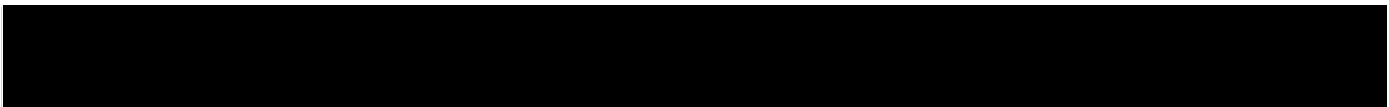
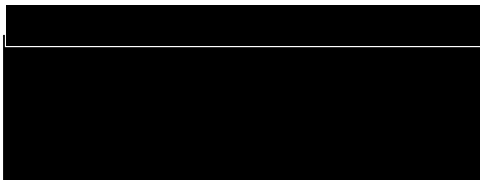
Evzio is the only FDA approved product indicated for the emergency treatment of opioid overdose and intended for immediate administration by friends or family members outside of medically supervised settings such as the home. Evzio is the only opioid overdose treatment that automatically delivers a predetermined dose of naloxone to rapidly reverse opioid overdose and contains visual and voice instructions to make it easy to use correctly by family members and other caregivers in an emergency situation. Evzio verbally instructs the caregiver and patient to immediately seek emergency medical attention once the injection is complete.

Therefore, prescribing Evzio for this patient is appropriate and medically necessary. There is no generic equivalent to Evzio.



**REQUEST FOR
MEDICARE PRESCRIPTION DRUG COVERAGE DETERMINATION**

This form may be sent to us by mail or fax:



Who May Make a Request: Your prescriber may ask us for a coverage determination on your behalf. If you want another individual (such as a family member or friend) to make a request for you, that individual must be your representative. Contact us to learn how to name a representative.

Enrollee's Information

Enrollee's Name  Date of Birth 

Enrollee's Address 

City  State  Zip Code 

Phone  Enrollee's Member ID # 

Complete the following section ONLY if the person making this request is not the enrollee or prescriber:

Requestor's Name _____

Requestor's Relationship to Enrollee _____

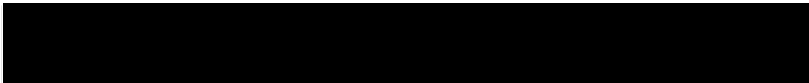
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City _____ State _____ Zip Code _____

Phone _____

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Attach documentation showing the authority to represent the enrollee (a completed Authorization of Representation Form CMS-1696 or a written equivalent). For more information on appointing a representative, contact your plan or 1-800-Medicare (1-800-633-4227), TTY: 1-877-486-2048, 24 hours per day, 7 days a week.



Name of prescription drug you are requesting (if known, include strength and quantity requested per month):

EVZIO, 2MG/0.4ML, 0.8ML/30 days

Type of Coverage Determination Request

- I need a drug that is not on the plan's list of covered drugs (formulary exception).*
- I have been using a drug that was previously included on the plan's list of covered drugs, but is being removed or was removed from this list during the plan year (formulary exception).*
- I request prior authorization for the drug my prescriber has prescribed.*
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- I have been using a drug that was previously included on a lower copayment tier, but is being moved to or was moved to a higher copayment tier (tiering exception).*
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Additional information we should consider (*attach any supporting documents*):

EVZIO IS THE ONLY FDA APPROVED AUTO-INJECTOR TO BE USED BY THE PATIENT OR OTHER NON-MEDICAL PERSONNEL IN THE EVENT OF AN OPIOID OVERDOSE.

Important Note: Expedited Decisions

If you or your prescriber believe that waiting 72 hours for a standard decision could seriously harm your life, health, or ability to regain maximum function, you can ask for an expedited (fast) decision. If your prescriber indicates that waiting 72 hours could seriously harm your health, we will automatically give you a decision within 24 hours. If you do not obtain your prescriber's support for an expedited request, we will decide if your case requires a fast decision. You cannot request an expedited coverage determination if you are asking us to pay you back for a drug you already received.

- CHECK THIS BOX IF YOU BELIEVE YOU NEED A DECISION WITHIN 24 HOURS**
(If you have a supporting statement from your prescriber, attach it to this request).

I attest that the medication requested is medically necessary for this patient. I further attest that the information provided is accurate and true, and that documentation supporting this information is available for review if requested by the health plan sponsor, or, if applicable, a state or federal regulatory agency. I understand that any person who knowingly makes or causes to be made a false record or statement that is material to a claim ultimately paid by the United States government or any state government may be subject to civil penalties and treble damages under both the federal and state False Claims Acts. See, e.g., 31 U.S.C. §§ 3729-3733.

Signature of person requesting the coverage determination (the enrollee, or the enrollee's prescriber or representative):

Date: _____

Type of Coverage Determination Request

FORMULARY and TIERING EXCEPTION requests cannot be processed without a prescriber's supporting statement. PRIOR AUTHORIZATION requests may require supporting information.

REQUEST FOR EXPEDITED REVIEW: By checking this box and signing below, I certify that applying the 72 hour standard review timeframe may seriously jeopardize the life or health of the enrollee or the enrollee's ability to regain maximum function.

Prescriber's Information

Name: _____

Address: _____

City: _____ State: _____ Zip Code: _____

Office Phone: _____ Fax: _____

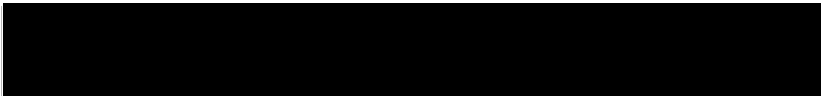
Prescriber's Signature: _____ Date: _____/_____/_____

Diagnosis and Medical Information

Medication: EVZIO	Strength and Route of Administration: 2MG/0.4ML	Frequency: PRN FOR OPIOID EMERGENCY
New Prescription OR Date Therapy Initiated:	Expected Length of Therapy: INDEFINITE	Quantity: 1
Height/Weight:	Drug Allergies:	Diagnosis: _____

Rationale for Request

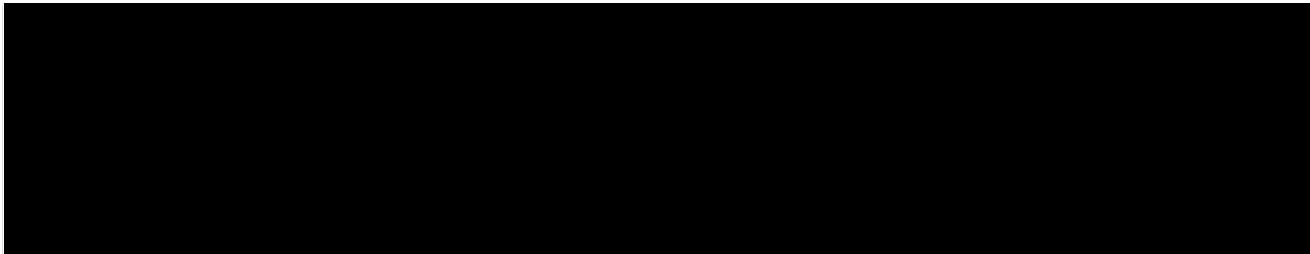
Alternate drug(s) contraindicated or previously tried, but with adverse outcome, e.g., toxicity, allergy, or therapeutic failure Specify below: (1) Drug(s) contraindicated or tried; (2)



adverse outcome for each; (3) if therapeutic failure, length of therapy on each drug(s)

- Patient is stable on current drug(s); high risk of significant adverse clinical outcome with medication change** Specify below: Anticipated significant adverse clinical outcome
- Medical need for different dosage form and/or higher dosage** Specify below: (1) Dosage form(s) and/or dosage(s) tried; (2) explain medical reason
- Request for formulary tier exception** Specify below: (1) Formulary or preferred drugs contraindicated or tried and failed, or tried and not as effective as requested drug; (2) if therapeutic failure, length of therapy on each drug and adverse outcome; (3) if not as effective, length of therapy on each drug and outcome
- Other** (explain below)

Required Explanation: ***SEE BELOW



*** GENERIC NALOXONE HCL FOR INJECTION (VIAL OR SYRINGE) IS INAPPROPRIATE FOR THIS PATIENT BECAUSE IT IS NOT INTENDED FOR IMMEDIATE ADMINISTRATION BY A FAMILY MEMBER OR OTHER NON-HEALTHCARE PROFESSIONAL AS EMERGENCY THERAPY IN SETTINGS WHERE OPIOIDS MAY BE PRESENT, SUCH AS THE HOME. GENERIC NALOXONE PRODUCTS ARE INTENDED FOR ADMINISTRATION IN MEDICALLY SUPERVISED SETTING. EVZIO IS THE ONLY PDA APPROVED PRODUCT INDICATED FOR THE EMERGENCY TREATMENT OF OPIOID OVERDOSE AND INTENDED FOR IMMEDIATE ADMINISTRATION BY FRIENDS OR FAMILY MEMBERS OUTSIDE OF MEDICALLY SUPERVISED SETTINGS SUCH AS THE HOME.

EVZIO IS THE ONLY OPIOID OVERDOSE TREATMENT THAT AUTOMATICALLY DELIVERS A PREDETERMINED DOSE OF NALOXONE TO RAPIDLY REVERSE OPIOID OVERDOSE AND CONTAINS VISUAL AND VOICE INSTRUCTIONS TO MAKE IT EASY TO USE CORRECTLY BY FAMILY MEMBERS AND OTHER CAREGIVERS IN AN EMERGENCY SITUATION. EVZIO VERBALLY INSTRUCTS THE CAREGIVER AND PATIENT TO IMMEDIATELY SEEK EMERGENCY MEDICAL ATTENTION ONCE THE INJECTION IS COMPLETE.

