

<http://www.latimes.com/business/la-fi-naloxone-sales-20160707-snap-story.html>

As need grows for painkiller overdose treatment, companies raise prices.

By **Melody Petersen**. Los Angeles Times. July 17, 2016.



Aimee Dunkle of Rancho Santa Margarita holds a portrait of her son Ben, who died from a drug overdose four years ago. Dunkle has distributed hundreds of doses of naloxone, a drug that she believes would have saved her son. (Los Angeles Times)

Aimee Dunkle began helping to distribute the drug naloxone -- the life-saving antidote to prescription painkiller overdoses -- after her son died.

Ben Dunkle, 20, was with three people when he overdosed in 2012, she said. She believes he would be alive today if they had naloxone.

“They panicked,” Dunkle said, “and dumped him in a parking lot.”

Naloxone works by blocking the effect that painkillers and heroin have in the brain and reversing the slowed breathing and unconsciousness that come with an overdose.

The Solace Foundation in Orange County, the group that Dunkle co-founded, says the drug has been used since February to reverse 128 overdoses that otherwise probably would have been fatal.

But as the demand for naloxone has risen -- overdose deaths now total 130 every day, or roughly the capacity of a Boeing 737 -- the drug's price has soared.

Not long ago, a dose of the decades-old generic drug cost little more than a dollar. Now the lowest available price is nearly 20 times that.

One manufacturer, Kaleo of Richmond, Va., increased the wholesale price of its auto-injector to \$4,500 this year for a package of two from \$690 in 2014.

Increased access to naloxone is among the measures included in federal legislation that Congress passed last week in response to the painkiller deaths. The White House has said that President Obama plans to sign the bill.

Last month, U.S. Sens. Susan Collins (R-Maine.) and Claire McCaskill (D-Mo.) wrote to Kaleo, Rancho Cucamonga's Amphastar Pharmaceuticals and three other drug makers, asking why they had hiked prices for naloxone during a public health crisis.

"At the same time this epidemic is killing tens of thousands of Americans a year," said McCaskill, "we're seeing the price of naloxone go up by 1,000% or more."

The companies separately defended their prices. One said it was spending millions to innovate and make naloxone easier to administer. Another said investments were needed to maintain the drug's high quality.

Kaleo said it increased the list price of its drug Evzio after deciding to cover patients' insurance co-pays to ease access to it.

Lora Grassilli, a spokeswoman for Kaleo, noted that the company had donated 150,000 of the auto-injectors to more than 250 groups.

Kaleo and other manufacturers also said they had given most customers discounts and rebates. “The list price is not a true net price to anyone,” Grassilli said.

In 2014, more than 47,000 Americans died from drug overdoses -- nearly 60% of them from drugs called opioids, which include prescription painkillers such as OxyContin and fentanyl as well as the illegal drug heroin.

That was 50% more deaths than from highway accidents, according to the [Centers for Disease Control and Prevention](#), and more overdose deaths than any year on record.

The overdose crisis has its roots in the 1990s, when doctors began prescribing more and higher doses of painkillers. The physicians were responding to campaigns, often funded behind the scenes by drug makers, that urged doctors to prescribe the strongest painkillers not just to cancer patients and others in severe pain, but also to those with milder pain, including backaches, migraines and sports injuries.

The narcotic manufacturers’ funding of those campaigns -- and the groups that promoted them, including the now-defunct American Pain Foundation -- came to light through evidence unearthed in lawsuits and investigative journalism reports.

Since 1999, the amount of prescription opioids such as oxycodone, morphine and hydrocodone sold in the U.S. nearly quadrupled, even though there has been no overall change in the amount of pain reported by Americans, according to the CDC.

During that same time, deaths from those drugs quadrupled.

The lethal side effects of that booming prescription painkiller market has now sparked a moneymaking opportunity with naloxone.

For years, Hospira in Lake Forest, Ill., dominated the naloxone market. In July 2005 its average wholesale price for a vial of the injectible drug was \$1.10, according to Truven Health Analytics.

By 2014, the price was almost \$19 a vial.

In July 2014, privately-held Kaleo added competition to the market by introducing its auto-injector Evzio. It was the first naloxone product approved for use by people without medical training.

Kaleo designed the auto-injector so that people taking painkillers, and those concerned about them, could carry naloxone in their purse or pocket. About the width and height of a credit card, the device has a robotic voice that tells how to administer the drug.

Soon after Kaleo introduced Evzio at an average wholesale price of \$690 for a package of two auto-injectors, Amphastar doubled the price of its syringes that are pre-filled with naloxone. In Oct. 2014, the company's average wholesale price for a pre-filled syringe jumped to \$39.60 from \$20.30, according to Truven.

Kaleo then continued to increase the price of Evzio. On Feb. 1, the drug's price rose to \$4,500 from \$900 for an Evzio package -- a 400% jump.

The price increases on top of rising demand have caused overall sales of naloxone to nearly quadruple in the last four years, according to prescription-tracking company IMS Health, increasing to \$81.9 million last year from \$21.3 million in 2011.

Eliza Wheeler at the Harm Reduction Coalition in San Francisco, which works to reduce overdoses, said the price increases are causing more nonprofit groups distributing naloxone to limit their operations.

“To reduce mortality you need to flood the community of drug users with naloxone,” she said. “That model is only effective if we have a low-cost product.”

Kaleo had donated 800 Evzio packages to Dunkle’s Orange County group. Now with that supply nearly gone, it has declined to provide more, she said.

“If we don’t have naloxone,” Dunkle said, “we’ll start losing people.”

Kaleo said that “due to overwhelming demand” the company had “exhausted our charitable donation supply for the balance of this year, and are not likely to be able to review applications for free product again until January.”

Company officials say there are valid reasons for the price increases.

Bill Peters, Amphastar’s chief financial officer, said the company raised its price in October 2014 because manufacturing costs were rising.

The company had also invested millions of dollars, he said, into the development of a new naloxone product that avoids injections by allowing for intranasal delivery.

Hospira was purchased by pharmaceutical giant Pfizer in Sept. 2015. Rachel Hooper, a Pfizer spokeswoman, said Hospira’s prices “take into account the investments necessary to produce high-quality generic drugs as well as ensure appropriate distribution.”

“As other manufacturers have exited the naloxone market over the years,” she said, “Hospira worked hard for more than three decades to maintain the availability of this important, medically necessary product.”

The other two naloxone manufacturers that received the senators' letters were Mylan, which sells a vial for an average wholesale price of \$23.70, according to Truven and Adapt Pharma of Dublin, Ireland.

Late last year, Adapt introduced a naloxone nasal spray named Narcan for a average wholesale price of \$150 for two units, according to Truven.

Adapt said in an email that it had not raised that price and is offering the package to law enforcement agencies and community groups for \$75 -- half the listed price. The company is also offering the drug for free to some groups, including school nurses. Last week, Adapt sent 200 packages to Dunkle's Solace Foundation.

Mylan, which moved its headquarters from Pennsylvania to the Netherlands in 2014 to lower its tax rate, declined to comment.

First approved in 1971, naloxone has been shown in studies to reduce deaths.

Overdose deaths plummeted after San Francisco's public health department began distributing naloxone to heroin users in 2003, said Phillip Coffin, the city's director of substance use research. In a new study, San Francisco found that by co-prescribing naloxone with painkillers, emergency room visits declined 47% over the next six months compared with pain patients who didn't receive naloxone.

The drug comes with risks, including rare cases of heart attacks, seizures and death after the abrupt reversal of an overdose. And an ambulance must be called even if the victim wakes up, since naloxone does not work as long as most painkillers.

As the overdose toll keeps rising, states have passed laws making it easier to get naloxone. Most states now allow good Samaritans to administer the drug in emergencies. In January, new California regulations allowed pharmacists to begin furnishing naloxone without a prescription.

Paramedics have long stocked naloxone, but more cities are now requiring police to carry it.

Jim Davis, assistant fire chief in Columbus, Ohio, said the city's firefighters last year used 2,250 naloxone doses, or about 6 doses a day -- at a cost of \$147,000. Recently, Columbus also stocked the drug in 115 police cruisers, he said.

In Huntington, W. Va., where the overdose rate is among the nation's highest, the city began distributing Evzio to members of the public in February after receiving 2,200 free packages from Kaleo. The city's firefighters have also begun carrying the drug.

"I'm sure we have had dozens of overdose reversals," said Michael Kilkenny, the physician director of the Cabell-Huntington Health Department.

But the city couldn't afford the drug's price without the company's donation, he said. "We would not be able to purchase it."