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## United States Senate

October 11, 2016

SUITE SD-255  
DIRKSEN BUILDING  
WASHINGTON, DC 20510-2107  
202-224-2742

975 JFK FEDERAL BUILDING  
15 NEW SUDBURY STREET  
BOSTON, MA 02203  
617-565-8519

222 MILLIKEN BOULEVARD, SUITE 312  
FALL RIVER, MA 02721  
508-677-0523

1550 MAIN STREET, 4TH FLOOR  
SPRINGFIELD, MA 01101  
413-785-4610

The Honorable Andy Slavitt  
Acting Administrator  
Centers for Medicare and Medicaid Services  
200 Independence Avenue, S.W.  
Washington, DC 20201

Dear Acting Administrator Slavitt:

The nation is in the midst of an opioid abuse epidemic that is now claiming approximately 30,000 lives annually.<sup>1</sup> While prescription painkillers like OxyContin and illicit drugs like heroin and illegally manufactured fentanyl have fueled the epidemic, there now appears to be a burgeoning issue with *prescription* fentanyl. I am particularly concerned that Medicare's coverage of prescriptions for the fentanyl drug Subsys — specifically, off-label prescriptions driven by the drug manufacturer's aggressive and illegal marketing activities — may be contributing to the problem.

Fentanyl is a synthetic opioid that is up to 100 times more powerful than morphine.<sup>2</sup> In March 2015, the Drug Enforcement Administration (DEA) issued a nationwide alert on fentanyl as a threat to health and public safety.<sup>3</sup> The consequences of illicit fentanyl use are dire. Across the country, fentanyl-related deaths are continuing to rise at alarming rates. According to the Centers for Disease Control and Prevention, of the almost 30,000 drug overdose deaths nationwide in 2014 that involved some type of opioid,<sup>4</sup> the largest increase in the death rate over the previous year — 80 percent — was due to illicitly-manufactured fentanyl and synthetic opioid pain relievers.<sup>5</sup> In the state of Massachusetts, 66 percent of the more than 400 confirmed opioid deaths in the first half of 2016 involved fentanyl, up from 57 percent in all of 2015.<sup>6</sup>

But illicitly-manufactured fentanyl, which is typically trafficked into the United States from countries like China and Mexico, is not the only problem. Fentanyl prescribed by physicians, and in many instances paid for by Medicare, now appears to be contributing to the epidemic. Specifically, the fentanyl drug Subsys — the subject of a recent article in *STAT*, a

<sup>1</sup> <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm>

<sup>2</sup> <https://www.drugabuse.gov/drugs-abuse/fentanyl>

<sup>3</sup> <http://www.dea.gov/divisions/hq/2015/hq031815.shtml>

<sup>4</sup> <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm>

<sup>5</sup> *Id.*

<sup>6</sup> <https://www.bostonglobe.com/metro/2016/08/03/fentanyl-drives-continuing-rise-opioid-deaths/ymD6jZpMFB4A6z2JA8ImSK/story.html>

health and science publication<sup>7</sup> — has become widely abused, owing to the aggressive and illegal marketing activities of its manufacturer Insys Therapeutics.

In January 2012, the Food and Drug Administration (FDA) approved Subsys “[f]or the management of breakthrough pain in adult cancer patients who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.”<sup>8</sup> The FDA warning accompanying the drug states in part: “SUBSYS is intended to be used only in the care of cancer patients and only by oncologists and pain specialists who are knowledgeable of and skilled in the use of Schedule II opioids to treat cancer pain.”<sup>9</sup> Furthermore, in approving Subsys, the FDA determined that the drug required a risk evaluation and mitigation strategy (REMS) “to ensure the benefits of the drug outweigh the risks of misuse, abuse, addiction, overdose, and serious complications due to medication errors.”<sup>10</sup> In other words, as *STAT* reported: “Subsys is so powerful, and the risk of addiction and overdose so formidable, that the Food and Drug Administration requires doctors to undergo special training before they are allowed to prescribe it. And it has approved Subsys only for cancer patients who suffer intense flares of pain.”<sup>11</sup>

But for the most part, Subsys prescriptions and sales have not come in response to the needs of cancer patients. Rather, by far, Subsys is used “off label” — that is, for a use not specifically approved by the FDA. In fact, as *The New York Times* has reported, “just 1 percent of [Subsys] prescriptions are written by oncologists,” about half are written by pain specialists, and “a wide range of doctors prescribe[] the rest, including general practice physicians, neurologists and even dentists and podiatrists.”<sup>12</sup> As a result, Subsys has proven very profitable for Insys. The year before Subsys — Insys’ only drug — went on the market, the company had no reported revenue; last year it reported revenue of \$330 million and a profit of \$58.5 million.<sup>13</sup>

Insys has aggressively and illegally pushed this off-label prescribing. Its tactics have included Insys’ targeting physicians who do not treat many cancer patients and paying its sales force higher commissions for selling higher doses of the drug.<sup>14</sup> In June 2016, a former district sales manager and a sales representative in New York were arrested in connection with a kickback scheme to increase Subsys prescriptions.<sup>15</sup> In February 2016, a former Insys sales representative in Alabama pled guilty to violating federal kickback laws in connection with a similar scheme.<sup>16</sup> And in September 2016, federal prosecutors in Connecticut charged a former

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<sup>7</sup> <https://www.statnews.com/2016/09/30/fentanyl-opioid-insys-subsys/>

<sup>8</sup> [http://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2012/202788Orig1s000Approv.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/202788Orig1s000Approv.pdf)

<sup>9</sup> [http://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2012/202788Orig1s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/202788Orig1s000lbl.pdf)

<sup>10</sup> [http://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2012/202788Orig1s000Approv.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/202788Orig1s000Approv.pdf)

<sup>11</sup> <https://www.statnews.com/2016/09/30/fentanyl-opioid-insys-subsys/>

<sup>12</sup> <http://www.nytimes.com/2014/05/14/business/doubts-raised-about-off-label-use-of-subsys-a-strong-painkiller.html>

<sup>13</sup> <https://www.statnews.com/2016/09/30/fentanyl-opioid-insys-subsys/>

<sup>14</sup> <http://www.nytimes.com/2014/05/14/business/doubts-raised-about-off-label-use-of-subsys-a-strong-painkiller.html>

<sup>15</sup> <https://www.statnews.com/pharmalot/2016/06/11/fentanyl-opioids-bribes-insys/>

<sup>16</sup> <https://www.statnews.com/pharmalot/2016/02/22/insys-therapeutics-sales-rep-opioid-kickbacks/>



Insys district sales manager with giving kickbacks to doctors and nurses to prescribe Subsys.<sup>17</sup> In August 2015, Insys reached a \$1.1 million settlement with the Oregon attorney general to resolve allegations that Insys improperly marketed Subsys in Oregon for off-label uses such as non-cancer neck and back pain.<sup>18</sup> Other investigations are ongoing. Insys' most recent Form 10-Q filed with the U.S. Securities and Exchange Commission in August 2016 discloses that it has received Civil Investigative Demands or subpoenas from authorities in Massachusetts, Arizona, Illinois, Florida, and New Hampshire for documents relating to the company's Subsys sales and marketing practices.<sup>19</sup> Insys has also disclosed that it has received a subpoena from the Office of the Inspector General of the U.S. Department of Health and Human Services (HHS) in connection with potential violation of HHS programs.<sup>20</sup>

Insys' improprieties involving the marketing and sales of Subsys have proven costly to the federal government. *STAT* recounted how, for one patient's Subsys prescription from January 2015 to March 2016 — just 15 months — Medicare paid \$250,544.<sup>21</sup> That patient, 32-year-old Sarah Fuller, who died with a lethal dose of fentanyl in her blood, had not been suffering pain from cancer, but rather neck and back pain from an automobile accident.<sup>22</sup> In connection with the arrest of the Subsys sales personnel in New York, authorities alleged that Medicare reimbursed approximately \$1.2 million in prescription costs.<sup>23</sup> And in the recent prosecution of the former Insys sales manager in Connecticut, the U.S. Attorney alleged that Medicare lost an estimated \$1.3 million.<sup>24</sup>

These Medicare Part D reimbursements for off-label use of Subsys add up and have resulted in the federal government's payment of tens of millions of dollars for questionable Subsys prescriptions that may have also led to the overdose deaths of people who should never have received the drug in the first place. In 2013, Medicare paid \$30 million for Subsys prescriptions.<sup>25</sup> Only one year later, in 2014, it paid more than three times that — \$97 million.<sup>26</sup>

CMS must not become complicit in the growing prescription fentanyl problem this country is combating. By reimbursing prescriptions for improper off-label use of Subsys, CMS appears to be contributing to the opioid abuse epidemic, rewarding Insys for its wrongdoing, and costing taxpayers millions of dollars. Accordingly, by November 1, 2016, I would appreciate answers to the following questions:

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<sup>17</sup> <https://www.statnews.com/pharmalot/2016/09/29/insys-manager-arrested-kickback/>

<sup>18</sup> <http://www.doj.state.or.us/releases/Pages/2015/re1080515.aspx>

<sup>19</sup> <http://secfilings.nasdaq.com/filingFrameset.asp?FilingID=11527974&RcvdDate=8/5/2016&CoName=INSYS%20THERAPEUTICS%2C%20INC.&FormType=10-Q&View=html>

<sup>20</sup> *Id.*

<sup>21</sup> <https://www.statnews.com/2016/09/30/fentanyl-opioid-insys-subsys/>

<sup>22</sup> *Id.*

<sup>23</sup> <http://freepdfhosting.com/e2d586b32f.pdf>

<sup>24</sup> <http://freepdfhosting.com/43f2d02f77.pdf>

<sup>25</sup> <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Medicare-Provider-Charge-Data/PartD2013.html>

<sup>26</sup> <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Medicare-Provider-Charge-Data/PartD2014.html>

1. For CMS data available since Subsys went on the market in 2012, how many Subsys prescriptions for cancer patients did Medicare Part D reimburse annually, and how many were off-label?
2. Medicare Part D reimburses off-label prescriptions when there is a “medically accepted indication” for a drug.<sup>27</sup> Please explain how CMS has determined that there is a medically accepted indication for Subsys in patients who are not suffering from cancer.
3. Is CMS taking any steps to ensure that Medicare Part D is not reimbursing for improper off-label Subsys prescriptions that resulted from Insys’ illegal marketing tactics? If so, what steps is CMS taking? If not, why not?
4. In light of Insys’ pattern of aggressive and illegal off-label marketing of Subsys, is CMS engaging in extra scrutiny of off-label prescriptions for Subsys presented to CMS for reimbursement? If so, what additional scrutiny is CMS applying to those requests for reimbursement? If not, why not?
5. Is CMS taking any steps to recoup from Insys Medicare Part D reimbursements for off-label Subsys prescriptions that resulted from Insys’ illegal marketing tactics? If so, what steps is CMS taking? If not, why not?

Thank you in advance for your assistance and your cooperation in responding to these requests. Should you have any questions, please contact Andrew Cohen of my staff at 202-224-2742.

Sincerely,

  
Edward J. Markey  
United States Senator

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<sup>27</sup> 42 C.F.R. § 423.100.