

United States Senate

WASHINGTON, DC 20510

August 24, 2016

VIA ELECTRONIC TRANSMISSION

Dr. Robert M. Califf
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Commissioner Califf:

We are writing today regarding recent consumer and media reports about the Mylan EpiPen (epinephrine injection) Auto-Injector, which is used in emergency treatment for life-threatening allergic reactions, and concerns with respect to its price and the effect it has on access for patients. Access to epinephrine can mean the difference between life and death, especially for children. That is why the School Access to Emergency Epinephrine Act was signed into law in 2013.¹ The law provides an incentive to states to boost the stockpile of epinephrine at schools. In addition, a number of states have passed laws requiring public schools to have epinephrine.

In 2007, Mylan purchased EpiPen from The Merck Group. The EpiPen has been in use since 1977 and when Mylan bought it in 2007, it cost \$57 each.² Today, the cost of two EpiPens has risen over 400 percent to approximately \$500.³ In France, two EpiPens cost approximately \$85 and in the United Kingdom two cost \$119.⁴ Notably, in Canada, a Mylan brand EpiPen costs \$131.⁵ In addition to the EpiPen, alternatives such as Anapen are available in France, Canada, and the United Kingdom with prices comparable to the EpiPen.⁶ Notably, the United Kingdom offers another competitor, Jext, which is priced at \$32 for one injector.⁷

The cost of the main ingredient in an EpiPen, epinephrine, is extremely inexpensive. According to news reports, it is less than a dollar per milliliter in some parts of the world.⁸ As such, reasonable questions exist with respect to how the product is currently priced. In addition to Mylan's pricing decisions, market competition is an important aspect of medication costs. It would be helpful to understand the Food and Drug Administration's (FDA) role and impact in

¹ <https://www.congress.gov/bill/113th-congress/house-bill/2094/text>

² Aaron E. Carroll, "The EpiPen, a Case Study in Health Care System Dysfunction," *The New York Times* (August 23, 2016). Available at http://www.nytimes.com/2016/08/24/upshot/the-epipen-a-case-study-in-health-care-system-dysfunction.html?smid=tw-upshotnyt&smtyp=cur&_r=0

³ Ben Popken, "EpiPen Price Hike Has Parents of Kids With Allergies Scrambling Ahead of School Year," *NBC News* (August 17, 2016). Available at <http://www.nbcnews.com/business/economy/epipen-price-hike-has-parents-kids-allergies-scrambling-ahead-school-n633071>.

⁴ Cynthia Koons and Robert Langreth, "How Marketing Turned the EpiPen Into a Billion-Dollar Business," *Bloomberg* (September 23, 2015); Lloyds Pharmacy, <https://onlinedoctor.lloydspharmacy.com/uk/allergy/epipen>

⁵ Emma Court, "Mylan's EpiPen price increases are Valeant-like in size, Shkreli-like in approach," *MarketWatch* (August 18, 2016). Available at <http://www.marketwatch.com/story/mylans-epipen-price-increases-are-valeant-like-in-size-shkreli-like-in-approach-2016-07-20>.

⁶ Cost comparison, <http://www.lincolnmedical.co.uk/calculator/Cost-effective%20emergency%20treatment%20of%20anaphylaxis.pdf>

⁷ Pricing information, <http://www.jext.co.uk/healthcare/prescribing-information.aspx>

⁸ Aaron E. Carroll, "The EpiPen, a Case Study in Health Care System Dysfunction," *The New York Times* (August 23, 2016). Available at http://www.nytimes.com/2016/08/24/upshot/the-epipen-a-case-study-in-health-care-system-dysfunction.html?smid=tw-upshotnyt&smtyp=cur&_r=0

this area given the regulatory authority it exerts over the review and approval of the EpiPen and competitor products.

By way of personal example, we've all heard from parents in our respective states who are concerned about the price increase and the financial difficulty it is causing. The high cost has also caused some first responders to consider making their own kits with epinephrine vials and syringes. For example, first responders in Seattle have developed such a kit and have sold them to public health agencies in five other states. Furthermore, there is a demonstration project in New York called "Check and Inject New York" which trains first responders to use syringe epinephrine kits in place of EpiPens to save money.⁹ Although these are examples of ingenuity, an element of patient safety is raised. In the hands of those not trained in medical procedures, this could create a dangerous situation.

Schools are also feeling the budgetary effects of needing EpiPens on hand in order to be prepared for emergency situations. The cost of an EpiPen prescription has implications for the federal taxpayers as well. Over 40% of children are insured through Medicaid or the Children's Health Insurance Program (CHIP). It follows that many of the children who are prescribed EpiPens are covered by Medicaid and therefore the taxpayers are picking up the tab for this medication.

We are concerned that Mylan has not faced much competition for its product. One of its competitors, Auvi-Q, was recalled in October 2015 giving Mylan a near monopoly with its product. News reports indicate that generic versions of the EpiPen have been subject to additional questioning by the FDA and have yet to be approved.¹⁰ We have always championed access to safe, efficacious, and affordable medications. It would be helpful if the FDA could clarify whether any barriers exist to the approval of safe alternative products to the EpiPen.

We are also concerned that the substantial price increase from Mylan could limit access to a much-needed medication. Given the importance of this topic, it is imperative to understand the FDA's role with respect to EpiPens and its approval of generic equivalents that could help to increase competition and lower prices if introduced.

Please answer the following:

1. Self-injectable epinephrine has been on the FDA's drug shortage list since 2012. With the tripling of the number of people diagnosed with peanut allergies in the past 20 years, what steps has FDA taken to ensure that there is an adequate supply of self-injectable epinephrine? Should this product be considered in shortage? Please explain.
2. What steps, if any, has the FDA taken to ensure an efficient and safe approval process for competitive alternatives to the EpiPen is not hampered by backlogs? Please explain. In addition, please describe situations that warrant changes to the typical

⁹ Ike Swetlitz, "America has a dangerous EpiPen crisis," The Week (July 28, 2016). Available at <http://theweek.com/articles/634878/america-dangerous-epipen-crisis>.

¹⁰ Lydia Ramsey, "Why the price of prescription drugs in the US is out of control," Business Insider (August 23, 2016). Available at <http://www.businessinsider.com/why-the-us-pays-more-for-prescription-drugs-2016-8>

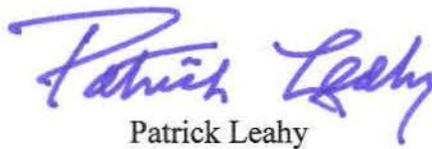
FDA approval timeline, such as drug shortages, and the nature of any resource constraints you face in ensuring timely approvals.

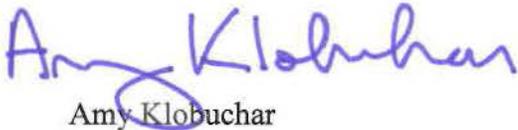
3. Has the FDA looked into whether the EpiPen can become an over-the-counter medication rather than requiring a prescription? If not, why not? If so, what has the FDA concluded? Please explain.
4. Please describe the standard and process by which a product can become an over-the-counter medication.
5. How many alternatives to Mylan's EpiPen are currently being reviewed by the FDA? Please detail where each alternative is in the review process.

Thank you in advance for your cooperation with this request. Please number your responses according to their corresponding questions and respond no later than September 8, 2016. In addition to the questions, we request that you meet with our staff to discuss your answers. If you have questions, please contact Karen Summar in Senator Grassley's office at [REDACTED] or (202) 224-5225, Sean Riley in Senator Johnson's office at [REDACTED] or (202) 224-5323, [REDACTED] in Senator Leahy's office at [REDACTED] [REDACTED] Michael Kades in Senator Klobuchar's office at [REDACTED] or (202) 224-8998, and Khaliyl Lane in Senator Blumenthal's office at [REDACTED] or (202) 224-2823.

Sincerely,


Charles E. Grassley


Patrick Leahy


Amy Klobuchar


Richard Blumenthal


Ron Johnson

Ron Johnson