

May 5, 2015

Hon. Elijah Cummings  
Ranking Member  
Committee on Oversight and Government Reform  
United States House of Representatives  
2157 Rayburn Office Building  
Washington, DC 20510

Hon. Bernard Sanders  
Ranking Member  
Subcommittee on Primary Health and Retirement Security  
Committee on Health, Education, Labor and Pensions  
United States Senate  
SD-428 Dirksen Senate Office Building  
Washington, DC 20510

Re: Naloxone

Dear Ranking Member Cummings and Sanders:

On behalf of my client, Amphastar Pharmaceuticals, Inc. (“Amphastar”), I am responding to your March 2, 2015 correspondence inquiring about the drug product, naloxone, and its intranasal use as “...an antidote [used] to treat the life-threatening effects of opiate overdoses.” Naloxone is manufactured by Amphastar’s subsidiary, International Medication Systems, Ltd. (“IMS”), and is an FDA approved *injectable* product for use by medical personnel in a hospital/clinical setting for the treatment of “...complete or partial reverse of opioid overdose, postoperative opioid depression and septic shock.” **Exhibit #1**. Please note that IMS’s naloxone product is *not* FDA approved as an intranasal product, and as such, any use to fight opiate overdoses by intranasal delivery is an off label use, which Amphastar and IMS are strictly prohibited from promoting (and that Amphastar and IMS do not, in fact, promote).

By way of background, the majority (if not all) of Amphastar’s naloxone sales are to wholesalers and the Veterans’ Administration. Our product is manufactured and designed to be used in a hospital/medical clinic setting. We manufacture two styles of naloxone syringes for injectable use. One style has a needle at the end of the syringe for injection. The other style is a syringe having a Luer Lock threaded tip for screwing into an IV medicine port. It is this threaded syringe with its universal Luer Lock tip that allows third parties that are beyond Amphastar’s control to independently package Amphastar’s naloxone syringe with a separate plastic intranasal adapter made by a third party, which readily connects to the Luer Lock threaded tip syringe for the intranasal dispensing of naloxone. Again, sales of such third party packaged intranasal products are *not* made by Amphastar or IMS (nor can they be), given the prohibition against promoting off label use.

Indeed, as your correspondence acknowledges, police departments, law enforcement agencies, and public health officials across the country purchase “kits” containing naloxone. Hence, neither Amphastar nor IMS manufacture these “kits,” and we do not directly supply any known manufacturer of these “kits” with naloxone. It is our understanding that police departments, law enforcement agencies and public health officials prefer to administer naloxone via intranasal delivery because they believe it is a more convenient way to deliver this life saving drug to an unconscious person in what could likely be a tense or otherwise difficult situation. Again, however, the intranasal use by first responders in an overdose situation is considered an “off-label” use that Amphastar and IMS cannot (and does not) promote or market.

Because we share your public health concerns, Amphastar has submitted a pre-IND (investigative new drug) to the FDA for intranasal delivery of naloxone. We are actively working with the FDA to determine whether it is feasible to develop and obtain FDA approval of an “intranasal” delivery of naloxone. You must recognize, however, that the challenges the developer of any new drug application (NDA) faces include potentially years of development and the expenditure of million(s) of dollars. The application fee alone on an NDA with clinical trials is over *two million dollars!* **Exhibit #2.** Not only are there challenges in terms of cost, but there are certain unique challenges to the design of clinical trial(s) supporting approval of an intranasal naloxone product. Notwithstanding these costs and challenges, Amphastar is committed to developing an FDA approved intranasal naloxone product because it believes such a product will greatly benefit patients.

Thus, there can be no question that Amphastar and IMS are committed to working to provide safe and effective pharmaceutical products to better the overall public health in this country, and it was for this very reason that they *did* respond when the New York Attorney General (and other states) questioned the increased cost of the “kits.” Amphastar and IMS believe that transparency on the cost issue demonstrates that their recent price increase was *not* to “take advantage” of increased demand for naloxone from police departments and other first responders using naloxone to treat heroin over-dosages. Instead, there were several unrelated, legitimate business factors that led to their pricing increase.

First, Amphastar and its subsidiaries manufacture all of their drug products in the United States. As you may be aware, like other companies in the industry, manufacturing costs for our entire portfolio of products, including naloxone, have been steadily increasing due to the continued rise in costs for raw materials, energy, and labor over the recent several years. In fact, Amphastar currently operates at a loss as a direct result of such rising costs, which dictated the need for Amphastar to raise the price of the majority of its products. **Exhibit #3.**

Second, when considering any price increase, Amphastar strives to meet the goal of providing safe and effective drug products at an affordable price. It should be noted that our recent price increase brings the price of our naloxone product closer to (but still well below) the current market price. Indeed, our price for naloxone after the increase is still the lowest among similar products in the United States when considering the price per milligram of naloxone. As summarized in the table below, which compare the prices of naloxone products on the U.S. market, our price is not only the lowest among our competitors, *but it is significantly lower than the market price set by our peer group, and*

*the increase hardly even matches the market price* (Please note that the comparison in the table below is made by using the published wholesaler acquisition cost, or WAC price (i.e., a list price before discounts and rebates).)

In fact, the WAC price (in dollars per milligram) of other naloxone products (in vials) are as follows:

- the price from Firm-X1 is 240% of that of our naloxone prefilled syringe;
- the price from Firm-X2 is 288% of that of our naloxone prefilled syringe; and
- the price from Firm-X3 is 150% of that of our naloxone prefilled syringe.

#	Manufacturers	Product Description				Price and Evaluation		
		Product Style	Strength/ Size	Units per Box	mg/Unit	Price (WAC) \$ per Box	Price (WAC) per milligram of Naloxone	Percentage of Amphastar's Price, %
1	Amphastar	Pre-filled Syringe	2mg/2mL	10	2	330.00	<b>16.50</b>	-
2	Firm-X1	Vial	0.4 mg/mL	10	0.4	158.3	<b>39.58</b>	<b>240%</b>
3	Firm-X2	Vial	0.4 mg/mL	10	0.4	189.78	<b>47.45</b>	<b>288%</b>
4	Firm-X3	Vial	4mg/10mL	25	4	2,467.50	<b>24.68</b>	<b>150%</b>
5	Firm-X4	Auto injector	0.4mg/0.4mL	2	0.4	575.0	<b>718.75</b>	<b>4356%</b>
<b>Average Price of Naloxone in Vials (Items 2 to 4)</b>							<b>37.23</b>	<b>226%</b>

The fact that we have the lowest naloxone price on the market is all the more remarkable because it is manufactured in a pre-filled syringe associated with a higher manufacturing cost. Our naloxone pre-filled syringe has a higher cost to manufacture than that of naloxone vial products due to our more sophisticated manufacturing process and strict quality control and assurance, which includes the use of more materials and the exertion of more manpower. Further, our naloxone in a pre-filled syringe provides the added benefits of a more convenient delivery method and value for users. Despite these factors, our prefilled syringe naloxone product remains at the lowest (WAC) per milligram than any other naloxone product on the market today. On average, the price of naloxone in the U.S. market (in vial form) is \$37.23 per milligram, or 226% of the price of Amphastar’s naloxone (in a prefilled syringe), when compared as WAC price per milligram of naloxone. *Even more astounding is the fact that the price for an auto-injector naloxone product (Firm-X4 above) is more than 43 times of the price of Amphastar’s naloxone product, as shown in the table above.*

Third, it should be noted that a certain purported \$34.50 price for Amphastar’s naloxone product has been cited by others (for example, by the New York Attorney General) as being higher than our WAC for naloxone (\$33.00). We believe that the higher \$34.50 price likely is a price that was charged by a distributor, *not* by Amphastar. And, in fact, our actual direct contract price is always lower still than our WAC price. We mention these facts because,

notwithstanding Amphastar's already reasonably and relatively low price for naloxone, Amphastar always welcomes the opportunity to help the government wherever it can, just as it did with the state of New York and other states.

Indeed, for the states of New York and Ohio, Amphastar has entered into agreements effectively granting a rebate of \$6.00 for each naloxone syringe. Further, it is in process of working on similar agreements with several other states, including Massachusetts, New Jersey, and Vermont. It should be noted that because our proposed intranasal naloxone product will be considered a new drug, it will include clinical trial data as required by FDA. In that regard, we are working with several states, including New York, Ohio, New Jersey, Massachusetts, and Vermont, to request their assistance in providing certain naloxone usage data that they have, in order to further our efforts to obtain FDA approval of an intranasal naloxone product, which we believe is so critically needed for the epidemic facing our country. We would very much appreciate the support of you and your Committee(s) on this project for our proposed intranasal naloxone product.

Also note further evidence of Amphastar's commitment to providing safe and effective pharmaceutical products to better the overall public health in this country is its contract with the Veterans' Administration. Amphastar currently provides naloxone at a price of \$13.87 per syringe to the Veterans' Administration, greatly below the WAC, and a price that Amphastar has not raised in any significant way for many years. **Exhibit #4.**

Finally, you should understand that it is difficult (if not impossible) to determine yearly naloxone sales in light of its intranasal off label use by third parties. Nevertheless, in reviewing the IMS Health Report for the past two years, it is fair to say that while Amphastar has the lowest price for naloxone, it is by no means the largest manufacturer of naloxone. **Exhibit #5.**

On behalf of my clients Amphastar and IMS, I look forward to developing a positive relationship with the Committee(s) in furtherance of the public health and safety of the American people. Please do not hesitate to contact me anytime with any comments or questions.

Sincerely,

Hon. Bart Stupak  
Counsel to Amphastar/IMS

Enclosures: Exhibits #1-#5

Cc: Hon. Jason Chaffetz  
Hon. Lamar Alexander  
Hon. Patty Murray  
Hon. Michael Enzi