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April 27, 2016

Senate Special Committee on Aging
Attention: Phylcia Woods, Minority Staff

Re: Massive Recent Price Increase in CaEDTA, a Drug Used to Treat Life-Threatening Lead Poisoning, after Its Acquisition by Valeant Pharmaceuticals

Dear Ms. Woods:

In view of the Senate Special Committee on Aging hearing this afternoon on Valeant Pharmaceuticals drug pricing practices, I want to draw to the attention of the Senators, and submit for the public record, a copy of the attached letter. A colleague and I prepared this letter on this topic for the House of Representatives in January. The letter remains current and relevant to the Senate hearing.

Sincerely,

A handwritten signature in black ink that reads "Michael J. Kosnett". The signature is written in a cursive style with a long horizontal line extending to the right from the end of the name.

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January 28, 2016

The Honorable Elijah E. Cummings
United States House of Representatives
Ranking Member, House Committee on Oversight and Government Reform
Washington, DC

Re: Massive Recent Price Increase in CaEDTA, a Drug Used to Treat Life-Threatening Lead Poisoning, after Its Acquisition by Valeant Pharmaceuticals

Specific Request: Prompt action that will either result in a marked lowering of the cost of Valeant brand Calcium Disodium Edetate (also known as CaEDTA or Calcium EDTA), or that will enable United States hospitals to acquire CaEDTA from other international manufacturers who make their drug available at a far lower price.

Dear Representative Cummings:

We are writing to communicate our public health concern regarding the recent massive increase in the price of a generic drug, CaEDTA, that is used for the emergency treatment of severe and life-threatening lead poisoning in children and adults. The sole source for CaEDTA in the United States is a generic brand manufactured by Valeant Pharmaceuticals.

CaEDTA entered the US pharmacopoeia in the 1950s as a chelating agent that accelerates the removal of lead from the body. When prescribed by medical toxicologists, it is administered by parenteral (i.e. intravenous or intramuscular) injection in a hospital setting to patients with extremely high blood lead concentrations, usually in excess of 100 µg/dl, who are suffering from severe or life-threatening complications of lead intoxication, such as encephalopathy or colic. Because the incidence of severe lead poisoning in the United States is currently limited (around one hundred identified cases per year) and because CaEDTA has few other indications, use of the drug by any one hospital is limited. Nevertheless, because severe lead poisoning such as lead encephalopathy requires prompt emergency treatment with CaEDTA, the California Poison Control System recommends that hospitals that treat medical emergencies maintain a minimum stock of CaEDTA ampules for injection on hand.

Until the past few years, it had been common for many major emergency hospitals in the United States to stock CaEDTA in their pharmacies. In the mid 2000s through 2011, the drug was manufactured by Graceway Pharmaceuticals. After Graceway was purchased by Medicis Pharmaceutical in late 2011, production temporarily stopped. In 2012, Valeant Pharmaceuticals acquired Medicis. By 2013 or 2014, Valeant had resumed the manufacture and sale of CaEDTA. However, as shown in the table below, the price of CaEDTA produced by Valeant increased progressively by an enormous amount – 7150 % from the Graceway product wholesale price in 2008 to the Valeant product wholesale price at the end of 2014. This huge price increase resulted in the inability of some hospitals to stock the drug in their emergency department pharmacy. Indeed, we became aware of this problem when Children’s Hospital in Oakland, CA informed the California Poison Control System that it could not afford the wholesale price of approximately \$25,000 it was quoted in 2015 by a distributor, AmerisourceBergen, to purchase one box of 5 ampules of CaEDTA. One box of 5 ampules would typically be the amount needed to treat one young child with lead encephalopathy with a 5 day course of chelation (1 ampule per day).

Table: Wholesale Prices for Calcium Disodium Edetate (Calcium EDTA) – 5 ml ampules (200mg/ml) [Source: Red Book Online Database – Micromedex Solutions® accessed 1/23/2016]

Manufacturer	Package Size (# of ampules)	Effective Date	Wholesale Acquisition Cost - Package	Average Wholesale Price - Package	Average Wholesale Price per ml	Percent Increase per ml
Graceway Pharmaceuticals	6	10/02/2008	\$464.24	\$557.09	\$18.57	
Valeant Pharmaceuticals North America	5	12/22/2014	\$26,927.33	\$33,659.16	\$1346.37	7,150 %

Additional Red Book data accessed on 1/23/2016 indicates that in 2014 alone, the unit wholesale price of the Valeant brand of CaEDTA increased by 278 percent, from \$355.81 per ml on 01/06/2014 to \$1346.37 on 12/22/2014. The massive nature of this ongoing increase in the Valeant drug was qualitatively confirmed by information we received from several hospital pharmacies. UCSF pharmacy paid a wholesale price of \$179.36 for two 2.5 ml ampules (5 ml) in 2012. However, in February 2015 they paid \$3,044.78 for a 5 ml ampule of the Valeant brand drug, and in December 2015 they paid \$4995.02 for a 5 ml ampule of the Valeant brand drug, the latter representing a unit price increase of 2685% since 2012. San Francisco General Hospital paid \$2904.81 for five 5 ml ampules in 2013. They are currently quoted a wholesale price of \$26,927.33, an 822% increase in two years.

Valeant Pharmaceuticals is the only source of CaEDTA ampules available to hospitals in the United States. This week we conducted an investigation to determine whether the drug was for sale to hospitals in Canada by another drug manufacturer(s) at lower wholesale cost. Canadian colleagues at the IWK Regional Poison Centre in Halifax, Nova Scotia informed us that they obtain CaEDTA through Canada’s Special Access Program from SERB Laboratories, France. In the recent past they purchased a box of

ten 10 ml ampules (50 mg CaEDTA/ml) for \$45 CND, or approximately \$36 USD (at 2015 currency rates). This equates to a price of \$7.20 per one gram dose of CaEDTA, (an amount typically needed to treat a severely lead poisoned child for 1 day). Last week we contacted Laboratoire SERB in Paris directly to learn the current price. The current price of a box of ten 10 ml ampules (50 mg CaEDTA/ml) is 69.00 Euro (\$75.17), equivalent to \$15.03 per gram. If the price of the French drug is compared to the price of the Valeant drug purchased by UCSF last month, it can be seen that Valeant brand CaEDTA costs 332 times as much as SERB Laboratories brand CaEDTA.

It should be noted that CaEDTA is an off-patent generic drug that was developed in the 1950s and initially introduced by other pharmaceutical companies. Research and development costs for the drug were expended long before the drug was produced by Valeant. The cost of producing or purchasing CaEDTA as a commodity chemical is low. One kilogram (1000 grams) of sodium calcium edetate is currently advertised for sale in the Sigma Aldrich chemical company internet catalog for \$333.00, or the equivalent of \$0.33 per gram.

We consider the extremely high price of pharmaceutical CaEDTA ampules sold exclusively in the United States as a product manufactured by Valeant Pharmaceuticals to be an obstacle to the availability of a potentially life-saving medicine to patients who may require it for severe lead poisoning. Prior to Valeant's recent acquisition and manufacture of the drug, CaEDTA was available in the United States for decades from a succession of other pharmaceutical companies at far lower cost. Hospitals in Canada and Europe continue to be able to acquire CaEDTA ampules for treatment of their severely lead-poisoned patients at a small fraction of the cost of the Valeant brand drug sold in the United States.

In the interest of public health, we encourage prompt action that will either result in a marked lowering of the cost of Valeant brand CaEDTA, or that will enable United States hospitals to acquire CaEDTA from other international manufacturers who make their drug available at a far lower price.

Sincerely,



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