

## **Report to the Legislature by the Governor’s Criminal Justice and Substance Abuse Cabinet and the Attorney General Regarding Naloxone**

The Governor’s Criminal Justice and Substance Abuse Cabinet (“Substance Abuse Cabinet”) and the Attorney General (AGO) submit this report in response to the Legislature’s request for an investigation into the cause for the “recent excessive price increase” of Naloxone and to “explore the legislative, regulatory, policy, and legal options to ensure that Naloxone is available to Vermonters at reasonable prices.” The findings and recommendations requested by the Legislature are set forth below.

### **Current Availability of Naloxone Products**

Naloxone is an opioid antagonist. With proper, timely administration, it negates or neutralizes the effects of an overdose of heroin or another opioid. It is used in Vermont to reduce the rates of death due to overdoses.

Naloxone hydrochloride (“naloxone”) is the active ingredient in brand name drug Narcan® and its generic forms. Naloxone, the generic drug manufactured by Amphastar Pharmaceuticals, Inc., is approved by the FDA for use by injection, but can also administered “off-label” as a nasal spray.<sup>1</sup> Until November 2015, all FDA-approved formulations of naloxone were injectables.

Injectable naloxone is sold in numerous forms, including a multi-dose vial and a pre-filled syringe with and without a needle. Nasal administration of Naloxone using the pre-filled syringe (without needle) is a widely accepted medical practice, with low risk and complication rates for both the patient and rescuers (such as friends, family members, medical and non-medical professionals). While it is more expensive to use Naloxone as a spray than by injection,<sup>2</sup> it addresses the view of first responders and primary caregivers that a spray eliminates the risk of injury from a contaminated needle and is easier to deliver.

The Vermont Department of Health (VDH) believes that use of the spray is the appropriate public health strategy because it mitigates rescuers’ risk of exposure to HIV and/or Hepatitis B or C. By avoiding use of needles, which are considered potentially contaminated/hazardous after use for injection, the safety of the non-healthcare “citizen rescuers” is greatly enhanced. To use Naloxone as a nasal spray, the rescuer puts a syringe of Naloxone into an atomizer and sprays it into the nasal passage of the overdose victim. Training can be completed in under a half hour.<sup>3</sup> “Rescue kits,” such as those provided by VDH, include both a syringe and an atomizer.

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<sup>1</sup> When a drug is used in a way that is different from the use described in the FDA-approved label, it is referred to as “off-label”. <http://www.fda.gov/forpatients/other/offlabel/default.htm>

<sup>2</sup> The spray version requires a higher concentration of naloxone because it is not put directly into the bloodstream.

<sup>3</sup> Vermont Department of Health, “Overdose Rescue Kit: How to give nasal naloxone for suspected opioid overdose,” Feb. 2014, available at

In recognition of the number of drug overdose deaths and to address the widespread off-label use of injectable naloxone as a nasal spray, in July 2015, the FDA granted Fast Track designation to Adapta Pharma for its Narcan® Nasal Spray. The FDA moved quickly and approved the product in November 2015. It delivers a dose of naloxone in a nasal spray. According to Adapta's press release, group purchasers such as law enforcement, first responders, and health departments that order directly from Adapta may be eligible for a "discounted Public Interest Prices" of \$37.50 per device.<sup>4</sup> Adapta expects its Nasal Spray to be available for purchase in early 2016.<sup>5</sup> In October 2015, the FDA also granted Fast Track designation to Insys Therapeutics, Inc. for its naloxone sublingual spray. Insys has not announced what its product will cost.

Naloxone is also currently available via EVZIO, an automatic injector made by kaléo. The auto-injector functions like an Epi-pen and has a retractable needle.<sup>6</sup> It has been on the market since 2014, but, the electronic device (with visual and voice instructions) is far more expensive than an intranasal kit, at about \$350 per injector.<sup>7</sup>

### **The Cost of Naloxone in Vermont**

The State of Vermont, together with other states across the country, purchases naloxone (and other drugs) at the price negotiated by the Minnesota Multistate Contracting Alliance for Pharmacy (MMCAP), a consortium of 46 states and two cities that have joined together in a cooperative purchasing agreement. Vermont government entities that provide human services and law enforcement receive the benefit of the MMCAP naloxone purchase price. Currently, the Vermont Department of Health (VDH) purchases the naloxone and distributes it to those entities under the Pilot Program authorized by the Legislature in 2015. The Vermont State Police (VSP) have acquired naloxone through VDH at the request of the VSP Commissioner. Currently, VDH and the Department of Corrections (DOC) are working toward a solution that will allow DOC to place orders of naloxone directly from Cardinal Health, the State's pharmaceutical distributor. VDH will also cooperate with other State entities to make purchases under the contract, but does not have plans to open up such purchases to Emergency Medical Services, the majority of which are not municipal entities, in the near term.

MMCAP purchases Naloxone at a wholesale price, and VDH receives a "cost of goods" discount from that price. The current MMCAP price per dose is \$30.45 and the current non-MMCAP price is \$39.60 per dose. Under its current contract (which runs from July 1, 2015 to

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[http://www.healthvermont.gov/adap/treatment/naloxone/documents/naloxone\\_od\\_rescue\\_howto\\_brochure.pdf](http://www.healthvermont.gov/adap/treatment/naloxone/documents/naloxone_od_rescue_howto_brochure.pdf)

<sup>4</sup> <http://www.adaptpharma.com/press-releases/>. Adapta also said it expects its product to have "broad coverage with affordable co-pays" for people with health insurance coverage.

<sup>5</sup> <http://www.ashp.org/menu/News/PharmacyNews/NewsArticle.aspx?id=4287>

<sup>6</sup> <http://www.evzio.com/patient/>

<sup>7</sup> <http://www.goodrx.com/evzio>

June 30, 2016), VDH pays \$29.21 per dose, up from the \$13.74 per dose it paid under its July 1, 2013 to June 30, 2014 contract. Naloxone is produced for use by injection so when it is administered as a nasal spray, as is the case in Vermont, an atomizer is also required, at a cost of \$3.86 per atomizer.

Amphastar denied accusations of price gouging when it increased the price of Naloxone by nearly double in October 2014,<sup>8</sup> and attributed the price hike to the increased price of energy, labor and raw materials. Amphastar said that its price was the lowest among similar products in the U.S. Nonetheless, a number of government officials, including Governor Shumlin, and U.S. Senator Sanders, demanded that Amphastar provide relief from the price increases.

### **AGO Settlement with Amphastar**

A Vermont agreement for a reduction in the price of Naloxone followed agreements negotiated in New York, New Jersey, Massachusetts, Ohio, Delaware, and Rhode Island. In December 2015, the Vermont Attorney General entered into an agreement (“Agreement”) with Amphastar pursuant to which the State will receive a \$6.00 per syringe rebate on each syringe purchased by a Vermont government entity until December 16, 2016. The rebate will automatically increase, dollar-for-dollar, if Amphastar raises its WAC price during that time. The Vermont Agency of Administration (“AOA”) will submit the State’s combined Naloxone purchase data to Amphastar on a quarterly basis and Amphastar will remit the total rebate payment to AOA which will, in turn, send the appropriate rebate amounts to the government entities that made the Naloxone purchases. The Agreement is attached to this Report.

### **Recommendations**

Given that VDH has recommended the continuation of the State’s Opioid Antagonist Pilot Program,<sup>9</sup> the State should explore additional options for reducing its Naloxone cost.

The entry into the market of competitive new naloxone products may result in lower naloxone prices. Assuming that the Adapta and Amphastar nasal sprays are comparable, we recommend that the State ask MMCAP to engage in discussions with Adapta for a group purchase price, and/or that the State explore such discussions on its own.

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<sup>8</sup> <http://blogs.wsj.com/pharmalot/2015/03/03/lawmakers-pressure-amphastar-over-price-hikes-for-its-heroin-antidote/>. Amphastar’s President attributed the price hike to overall rising costs.

<sup>9</sup> VDH recommended continuation of the Pilot Program in its January 6, 2016 “Report Evaluating the Statewide Opioid Antagonist Pilot Program (From Inception to November 2015).”

VT SUPERIOR COURT  
WASHINGTON UNIT  
CIVIL DIVISION

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**STATE OF VERMONT  
SUPERIOR COURT  
WASHINGTON UNIT**

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IN RE )  
AMPHASTAR PHARMACEUTICALS, INC. )

CIVIL DIVISION  
Docket No. 800-12-15 Wncw

**ASSURANCE OF DISCONTINUANCE**

Vermont Attorney General William H. Sorrell (“the Attorney General”) and Amphastar Pharmaceuticals, Inc. (“Amphastar”) hereby agree to this Assurance of Discontinuance (“AOD”) pursuant to 9 V.S.A. § 2459.

**REGULATORY FRAMEWORK**

1. Vermont’s Consumer Protection Act prohibits “[u]nfair methods of competition in commerce, and unfair or deceptive acts or practices in commerce.” 9 V.S.A. § 2453

**BACKGROUND**

2. Amphastar is a Delaware corporation with its principal offices and place of business located at 11570 6<sup>th</sup> Street, Rancho Cucamonga, California 91730. It is a specialty pharmaceuticals company that is engaged in the development, manufacture and marketing of proprietary and generic injectable and inhalation products, including the generic drug Naloxone.

3. Naloxone is an opioid antagonist. With proper, timely administration, it negates or neutralizes the effects of an overdose of heroin or another opioid. Naloxone is used in Vermont to reduce the rates of death due to overdose.

4. Vermont and other states are confronting a profound public health challenge, as the number of heroin and opioid-related deaths continues to increase.

5. The State of Vermont, local governments in Vermont, and associated public entities, including but not limited to the Vermont Department of Health and the governments of individual Vermont municipalities, counties and communities, likewise established programs to respond to the heroin and opioid epidemic by distributing, purchasing, or funding the purchase of Naloxone.

6. Amphastar raised prices for its current Naloxone products in or about the fall of 2014.

7. The Governor of Vermont transmitted a letter to Amphastar dated April 8, 2015 in which he expressed concern that the increase in the price of Naloxone could adversely affect access to the drug in Vermont.

8. While the Attorney General alleges that the increase in Naloxone prices constitutes an unfair and deceptive act and practice under 9 V.S.A. § 2453, Amphastar maintains that its pricing of Naloxone is based upon legitimate and lawful business factors.

9. In a mutual good faith effort to amicably resolve VTAG's stated pricing concerns, the parties have engaged in discussions regarding Amphastar's Naloxone pricing. Amphastar and VTAG each believe that the obligations imposed by this agreement are beneficial to the public and will improve access to Naloxone, and will potentially save lives.

#### **TERMS OF AGREEMENT**

10. Payment Amount

- a. Amphastar shall make a payment ("Payment") in the amount of \$6.00 (the "Payment Amount") for each Amphastar Naloxone Syringe (a "Syringe") purchased by a Public Entity in Vermont, or where the purchase price is

reimbursed by a Public Entity in Vermont. For purposes of this Agreement, a "Public Entity" is any non-federal governmental entity located in Vermont, including but not limited to state agencies, county or other local governments and their agencies, or law enforcement agencies. In the event that a Public Entity distributes or resells Syringes to other Public Entities, the Vermont Agency of Administration ("AOA"), on behalf of the State of Vermont, will only permit the last purchaser to receive reimbursement for a Syringe.

- b. Amphastar shall pay the Payment Amount associated with a given Syringe regardless of whether the Syringe was purchased directly from Amphastar or from a third party (including wholesale distributors). In no event shall the Payment Amount be reduced.

11. Payment Increase. Notwithstanding paragraph 10, in the event Amphastar increases its wholesale acquisition cost ("WAC") of a Naloxone Syringe ("WAC Increase"), Amphastar shall increase the Payment Amount by the actual dollar amount of the WAC Increase to offset any increase in the Syringe price. However, in no event shall the Payment Amount be reduced. During the Term (as defined in paragraph 15 below), Amphastar shall notify AOA within 30 days following any wholesale price increase of Naloxone to Public Entity Purchasers.

12. Payment Procedures. When seeking Payments under this Agreement, AOA shall request from the Minnesota Multistate Contracting Alliance for Pharmacy ("MMCAP") (the group purchasing organization for state governments which negotiates the purchase price paid to Amphastar for Naloxone by state governments, including Vermont) and submit to Amphastar, the Vermont Naloxone Detailed Report of the number of Naloxone Syringes

purchased or reimbursed by a Public Entity during a given quarter, i.e., a three (3) month time period, within sixty (60) days of the conclusion of the quarter. Within sixty (60) business days of receipt of the Vermont Naloxone Detailed Report, Amphastar shall pay the total accrued Payment Amounts reflected in the Consolidated Request to AOA. AOA shall thereafter disburse the Payments to the Vermont Agencies as required, in a timely manner.

13. Term and Termination. This Agreement shall apply to Syringes purchased within one (1) year following the Effective Date of this Agreement (the "Term"). Following the payment of all Payment Amounts accrued during the Term and submitted for reimbursement pursuant to paragraph 3, this Agreement shall terminate ("Termination"), except for paragraphs 15 through 21, which shall survive Termination.

14. Liability Exclusion. Except as otherwise may be stated herein, Amphastar's liability under this Agreement is limited to payment of the Payment Amount for Syringes purchased during the Term, and Amphastar otherwise shall assume no further liability pursuant to this Agreement, including liability for damages of any type (including direct, indirect, and consequential damages). Except as provided in paragraph 16 below, however, nothing in this Agreement shall be construed to alter or limit Amphastar's existing legal obligations or liabilities, including but not limited to those arising from the manufacture or marketing of Naloxone.

#### **OTHER TERMS**

15. The Attorney General finds the financial relief and other obligations set forth in this agreement to be in the public interest, accepts the terms of this Agreement, pursuant to 9 V.S.A. § 2459, in lieu of the commencement of any legal proceeding, and agrees not to take legal action against Amphastar or any of its Affiliates, predecessors, successors, parents,

subsidiaries, assigns, agents, administrators, attorneys, directors, shareholders, officers, employees, or representatives in connection with its 2014 pricing of Naloxone.

16. Nothing in this Agreement shall be construed as an admission or concession by Amphastar of any liability in connection with Naloxone, including with respect to Amphastar's pricing, sales, manufacture, and marketing thereof.

17. Amphastar expressly disclaims any endorsement or promotion of off-label use by VTAG and/or any Vermont Agency of any of Amphastar's products, including Amphastar's Naloxone.

18. Unless otherwise provided herein, this Agreement may not be changed, waived, discharged, or terminated orally, but instead only by a written document that is signed by the duly authorized officers of both Parties.

19. Whenever possible, each provision of the Agreement shall be interpreted in such manner as to be effective and valid under applicable law, but if any term or provision of this Agreement is held to be prohibited by or invalid under applicable law, such provision shall be ineffective only to the extent of such prohibition or invalidity, without invalidating the remainder of the Agreement and this Agreement shall be interpreted and construed as if such provision had never been contained herein.

20. This Agreement shall be governed by and interpreted under the laws the State of Vermont without regard to its conflict or choice of law provisions. Amphastar agrees not to raise or interpose in any way their state of incorporation as a defense on grounds of personal jurisdiction as to any cause of action, claim, or argument arising from the enforcement of this Agreement by the Attorney General or any Vermont Agency.

21. The Parties agree that any Vermont Agency purchasing Naloxone during the Term constitutes an intended third-party beneficiary of this Agreement.

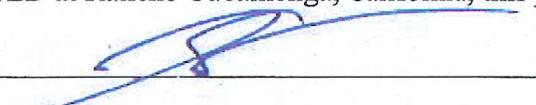
22. This Agreement constitutes the entire agreement by and between the Parties as to the subject matter hereof.

23. This Agreement may be executed in any number of counterparts, each of which shall be an original, but all of which together shall constitute one instrument. This Agreement may be executed and delivered electronically or by facsimile and upon such delivery such electronic or facsimile signature will be deemed to have the same effect as if the original signature had been delivered to the other Party.

24. The Superior Court of the State of Vermont, Washington Unit, shall retain jurisdiction over this AOD and the parties for the purpose of enabling the Attorney General to apply to this Court at any time for orders and directions as may be necessary or appropriate to enforce compliance with or punish violations of this AOD.

25. By signing below, Amphastar voluntarily agrees with, and submits to, the terms of this AOD.

DATED at Rancho Cucamonga, California, this 14<sup>th</sup> day of December, 2015.

By: 

Jason Shandell

Title: President

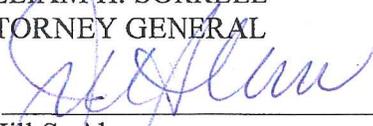
Amphastar Pharmaceuticals, Inc.

ACCEPTED on behalf of the Attorney General

DATED at Montpelier, Vermont this 16<sup>th</sup> day of December, 2015.

STATE OF VERMONT

WILLIAM H. SORRELL  
ATTORNEY GENERAL

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