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Naloxone Switch NDA Submitted As US FDA Signals Nonprescription Access Looks Safe, Effective

by Malcolm Spicer

Harm Reduction Therapeutics submits NDA for OTC approval of a 3-mg naloxone nasal spray branded RiVive. CEO Michael Hufford says the NDA touches all the bases FDA detailed in notice it published on what's needed in naloxone OTC switch proposals.

Some questions the US Food and Drug Administration announced on 15 November about safe and effective use of naloxone as a nonprescription product could be answered in a new drug application submitted three weeks earlier.

Harm Reduction Therapeutics Inc. on 28 October submitted to the FDA its NDA for OTC approval of a 3-mg intranasal naloxone product branded RiVive. The Pittsburgh nonprofit intends to provide naloxone available OTC at little or no cost to consumers.

Despite the agency providing a model Drug Facts label as encouragement for a naloxone switch NDA and even as the number of US opioid overdose deaths continues to climb, the antagonist that reverses the effects of respiratory depression and sedation by displacing opioids from the mu-opioid receptor in the central nervous systems remains available only by prescription.

The FDA is ready to change that, it indicates in a notice released a day ahead of its publication in the Federal Register.

The agency's Center for Drug Research and Evaluation states in the notice that naloxone nasal spray up to 4 mg and intramuscular- or subcutaneous-delivery autoinjectors up to 2 mg "have the

US FDA Serves Notice: Approval Of OTC

potential to be safe and effective for use as directed in nonprescription drug labeling without the supervision of a healthcare practitioner" *(see related story)*.

HRT cofounder and CEO Michael Hufford considers the CDER notice as tracking with the information the firm provided in its NDA for RiVive, which delivers an atomized form of 0.1-mL naloxone, and as a sign that the FDA has moved to becoming assured that OTC access to some naloxone products is merited.

"What I saw was one incredibly compelling and well-articulated public health rationale for the need for OTC naloxone. In fact, much of this really mirrors the NDA that we just submitted, a lot of the same rationale was in place," Hufford told HBW Insight.

Naloxone Could Close Prescription Sales

By Malcolm Spicer

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Agency signals assurance about making naloxone available OTC, so much so that firms with approved NDAs for Rx products should prepare for an all-nonprescription market. After offering model DFl to spur OTC switch NDAs, FDA notice about OTC assessment is second unprecedented step on its naloxone journey since opioid crisis declared a public health emergency in 2017.

Read the full article here

He said information the notice identified as needed at the agency is part of HRT's NDA, data from a human factors study.

"Our work I think shows very clearly and compellingly that based on the Drug Facts label that the FDA created, we found in our own human factors study that, in fact, lay people were able to both understand the instructions and appropriately use and administer the product in a simulated overdose setting," Hufford said.

He said HRT's proposal also answers the FDA's questions about relative bioavailability of naloxone though a nasal spray. In March, it announced Phase 1 bioavailability study results comparable to Rx intramuscular naloxone available in the US. (Also see "*HRT Reports 'Remarkable Achievement' In OTC Naloxone Phase 1 Clinical Trial Results*" - HBW Insight, 1 Mar, 2022.)

"We had to check all the boxes of relative bioavailability as well as the human factors work, and we did that," Hufford said.

He expects to learn around the end of 2022 whether the FDA has accepted the NDA for filing, which would mark the start of its review with an eight-month deadline for a decision. HRT also has asked the agency for priority review, which would trim the FDA's review deadline to six

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months after filing the NDA.

“Right now, that’s when we expect to hear about that,” Hufford said.

HRT, which launched in 2017 after the FDA published the model DFl firms could use in preparing NDAs for a naloxone OTC switch, also is interested in comments submitted in response to the notice, due by mid-January, and whether the FDA will schedule an advisory committee meeting to discuss the NDA.

The firm, which relies entirely on grants and donations to operate and would make RiVive available for free or as low-priced as possible, has a contract with a contract manufacturer to begin making RiVive pending FDA approval. It’s also talking with other manufacturers about licensing the product and expanding the number which would be available.

MICHAEL HUFFORD: "WE HAD TO CHECK ALL THE BOXES OF RELATIVE BIOAVAILABILITY AS WELL AS THE HUMAN FACTORS WORK, AND WE DID THAT.” *Source: Source: Harm Reduction Therapeutics*

“Once we're fully up and running, our current target is manufacturing about 2 million devices a year. We would love to increase that and give away more of it for free. But that just all comes down to funding,” Hufford.

HRT estimates that following FDA’s review and potential approval and after its supply and production operations are ready, its most likely commercial launch date would be in early 2024.

Hufford in March acknowledged frustration with the FDA officials’ response to HRT’s outreach on submitting a naloxone OTC switch proposal. (Also see "*Drivers For Allowing OTC Naloxone In US Include Social Justice As Well As Public Health Need*" - HBW Insight, 31 Mar, 2022.)

However, since then the firm’s NDA received fast track designation from the FDA. The designation helps NDA sponsors primarily by allowing more meetings with FDA officials during development of their proposals and by allowing for rolling reviews – submitting parts of an NDA before completing an application, which helps the FDA manage time for evaluations. (Also see "*OTC Naloxone NDA In US Gets Fast Track Status*" - HBW Insight, 10 Aug, 2022.)

“Since the submission of the NDA, we've been thrilled that the FDA has clearly really dug in, they've been asking some great clarifying questions. Every indication is, since the submission of the full NDA, that it certainly appears to us the FDA is fully engaged in the preliminary review of the NDA,” Hufford said.