

Request for permission for oral testimony at Idaho  
Medicaid's P&T Committee meeting on 05-22-2014.

Submission # 4

As of 5-7-2015, a portion of this request has been  
approved for oral testimony.



April 30, 2015

Idaho Medicaid P&T Committee

→ Re: May 22<sup>nd</sup> Drug Class review: Analgesics Narcotic Long-Acting

Dear Committee Members,

Pfizer is grateful for the opportunity to comment on the Magellan review of the Long-Acting Analgesics drug class dated February 20th 2015.

The Magellan review does not address the major public health issue concerning abuse of prescription opioid medications and has not included a review of the head to head human abuse potential studies included in the EMBEDA USPI and published in peer review journals.

In 2010-2011, Idaho was one of the top ten states for rates of drug-use in several categories, including: past year non-medical use of pain relievers among persons age 12 or older<sup>1</sup> and we ask the Committee to consider the potential for abuse as a critical consideration in determining opioid product preference, and for the available data for abuse deterrent formulations of opioids to be included in this drug class review.

The FDA has recognized that the development of opioids containing abuse-deterrent properties is an important step towards the goal of creating safer opioid analgesics<sup>2</sup>. FDA deputy director for regulatory programs, Douglas Throckmorton, M.D., stated that the, "development of abuse-deterrent opioid analgesics is a public health priority for the FDA"<sup>3</sup>. Similarly, the White House included expediting the "development of abuse-deterrent formulations (ADFs)" in its action steps for responding to the prescription drug epidemic<sup>4</sup>.

Abuse-deterrent opioids contain the same pain relieving ingredient as opioids currently on the market; however, they also contain technologies designed to deter manipulation of the medication by drug abusers and reduce the "high." Abuse deterrent opioids provide the needed pain relief to patients, but deter those who are crushing and swallowing; snorting; smoking; or injecting from using these important medications inappropriately.

The FDA has released guidance to Industry which provides a roadmap for the development of ADF opioids<sup>6</sup> and it has approved abuse-deterrent labeling for EMBEDA. Based on data from in vitro laboratory studies and clinical studies including abuse potential studies in recreational opioid abusers, the FDA included in the EMBEDA product labeling language describing that these opioid medications are expected to result in a meaningful reduction in abuse.

Reformulated extended release oxycodone was the first abuse deterrent opioid to become available. Abuse of extended release oxycodone decreased by approximately 50% among a group of opioid abusers after its reformulation<sup>5</sup>. Economic modeling suggests that such reductions in abuse on a national level would lead to a decrease in annual healthcare costs by an estimated \$430 million<sup>6</sup>.

Pfizer appreciates the opportunity to comment on the draft drug class review for long-acting opioids and requests, in view of the serious public health concern in Idaho of prescription opioid abuse, that the

Committee consider including drugs that have demonstrated a potential to decrease abuse as preferred agents on the Idaho PDL.

Sincerely,



Roy E. Palmer, PhD  
Field Medical Director  
U.S. Medical Affairs Group  
Pfizer Inc.

<sup>1</sup> US Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Results from the 2013 NSDUH: Detailed Tables. Available at: <http://www.samhsa.gov/data/NSDUH/2013SummNatFindDetTables/DetTabs/NSDUH-DetTabsSect1peTabs1to46-2013.htm#tab1.1a>. Accessed December 12, 2014.

<sup>2</sup> Guidance for Industry Abuse-deterrent Opioids – Evaluation and Labeling. *Draft Guidance January 2013* <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM334743.pdf>. Last accessed Feb 18, 2015

<sup>3</sup> FDA. *FDA approves abuse-deterrent labeling for reformulated OxyContin*. FDA News Press Release. April 16, 2013. Available at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm348252.htm>. Last accessed November 4, 2014.

<sup>4</sup> The White House. *The Administration's Response to the Prescription Drug Epidemic: Action Items*. Available at: [http://www.whitehouse.gov/sites/default/files/ondcp/issues-content/action\\_items\\_response\\_to\\_the\\_prescription\\_drug\\_epidemic.pdf](http://www.whitehouse.gov/sites/default/files/ondcp/issues-content/action_items_response_to_the_prescription_drug_epidemic.pdf). Last accessed November 4, 2014.

<sup>5</sup> Butler SF, Cassidy TA, Chilcoat H, et al. Abuse rates and routes of administration of reformulated extended-release oxycodone: initial findings from a sentinel surveillance sample of individuals assessed for substance abuse treatment. *J Pain*. 2013;14(4):351-358.

<sup>6</sup> Rossiter LF, Kirson NY, Shei A, et al. Medical cost savings associated with an extended-release opioid with abuse-deterrent technology in the US. *J Med Econ*. 2014;17(4):279-287



## COMMENTS ON THE MAGELLAN REVIEW OF NARCOTIC ANALGESICS, LONG ACTING

### General comments:

The EMBEDA label was significantly revised in October 2014. The review appears to have been written based upon the old label and several sections should be updated. Approved Prescribing Information on Embeda and the Medication Guide, can be accessed via the following links, respectively:

<http://labeling.pfizer.com/ShowLabeling.aspx?id=694> and

<http://labeling.pfizer.com/ShowLabeling.aspx?id=875>, or via [www.pfizer.com](http://www.pfizer.com)

The review does not discuss the results of human abuse potential studies which are described in detail in the new EMBEDA label<sup>1</sup>. Four head to head human abuse potential studies<sup>2,3,4,5</sup> have been conducted and published for EMBEDA and the results of these studies should be included in the class review as they provide important information on the expected likelihood of a product being abused as outlined in the FDA Guidance to Industry<sup>6</sup>.

### Specific comments on Magellan Review:

Page 2: Indication for EMBEDA is incorrect. Correct indication should read *“EMBEDA is a combination opioid agonist/opioid antagonist product indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.”*

Page 6, line 29: The boxed warning for alcohol interaction is missing: *“Instruct patients not to consume alcohol or any products containing alcohol while taking EMBEDA because co-ingestion can result in fatal plasma morphine levels.”*

Page 16, lines 34-41: This paragraph was based upon language in the old label and does not reflect the new language the FDA has granted EMBEDA which includes the results of human abuse potential studies. In section 9.2 of the EMBEDA USPI it is stated that *“The in vitro and pharmacokinetic data demonstrate that crushing EMBEDA pellets results in the simultaneous release and rapid absorption of morphine sulfate and naltrexone hydrochloride. These data along with results from the oral and intranasal human abuse potential studies indicate that EMBEDA has properties that are expected to reduce abuse via the oral and intranasal route. However, abuse of EMBEDA by these routes is still possible.”*

Page 19, lines 10-17: This section should be updated to include the results of the human abuse potential studies described in Section 9.2 of the EMBEDA USPI<sup>1</sup> and published in peer reviewed journals<sup>2,3,4,5</sup>.

Page 22, lines 8-11: This statement *“... but considering the lack of evidence to suggest that the abuse-limiting mechanism is effective”* is not consistent with the FDA labeling language in section 9.2 of the new EMBEDA label which states *“These data along with results from the oral and intranasal human abuse potential studies indicate that EMBEDA has properties that are expected to reduce abuse via the oral and intranasal route. However, abuse of EMBEDA by these routes is still possible.”*

References:

1. EMBEDA<sup>®</sup> CII (morphine sulfate and naltrexone hydrochloride) Package Insert, Oct 2014. Pfizer Inc.
2. Stauffer J, Setnik B, Sokolowska M, Romach M, Johnson F, Sellers S, Subjective Effects and Safety of Whole and Tampered ALO-01 (Morphine Sulfate and Naltrexone Hydrochloride) Extended Release Capsules Versus Morphine Sulfate Solution and Placebo. *Clin Drug Investig.* 2009; 29(12): 777-790.
3. Setnik B, Sommerville K, Goli V, Han L, Webster L. Assessment of pharmacodynamic effects following oral administration of crushed morphine sulfate and naltrexone hydrochloride extended-release capsules compared with crushed morphine sulfate controlled-release tablets and placebo in nondependent recreational opioid users. *Pain Med.* 2013 Aug;14(8)
4. Setnik B, Goli V, Levy-Cooperman N, Mills C, Shram M, Smith I., Assessing the subjective and physiological effects of intranasally administered crushed extended-release morphine formulations with and without a sequestered naltrexone core in recreational opioid users. *Pain Res Manag.* 2013 Jul-Aug;18(4)
5. Webster LR, Johnson FK, Stauffer J, Setnik B, Ciric S: Impact of intravenous naltrexone on intravenous morphine-induced high, drug liking, and euphoric effects in experienced, nondependent male opioid users. *Drugs R D* 2011, 11:259–275.
6. FDA. *Guidance for Industry: Abuse-deterrent Opioids—Evaluation and Labeling* . Rockville, MD: FDA; 2015; <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>