

Request for permission for pharmaceutical industry oral testimony at Idaho Medicaid's P&T Committee meeting on 5-20-2016.

Submission # 1

As of May 2, 2016, this submission has not been accepted for oral presentation at the meeting.

Gennrich, Jane - Medicaid

From: Eide, Tamara J. - Medicaid
Sent: Monday, April 25, 2016 8:51 AM
To: Gennrich, Jane - Medicaid
Subject: FW: Pfizer Medical Information: Response to your request for information (US16-024065)
Attachments: MedInfo Letter No 3395452.PDF; Idaho medicaid testimony letter _final 4.22.16.pdf

Tami Eide, Pharm.D., BCPS

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From: Pfizer USMedInfo [<mailto:RSCGRO-USMIADMIN@pfizer.com>]
Sent: Friday, April 22, 2016 5:56 PM
To: Eide, Tamara J. - Medicaid
Subject: Pfizer Medical Information: Response to your request for information (US16-024065)

Dear Dr Eide,

We would like to request that our Field Medical Director, testify on Embeda at the Idaho Medicaid P&T Committee meeting on May 20th 2019. Please communicate directly with our local Medical Outcomes Specialist, Dr. Lori Blackner at Lori.Blackner-Brown@pfizer.com or by phone at (801) 390-8976 regarding this request.

The enclosed document contains relevant clinical and economic data for your review. Please keep in mind that this information was prepared with the understanding that it should not be disclosed to anyone other than those who in the course of their job responsibilities require access to this document.

Thank you for your inquiry to Pfizer Medical Information. We are pleased to provide you with the attached information in response to your specific request. To view our response to your inquiry, double-click on the attached PDF icon. By opening the attached PDF icon, you are acknowledging that you specifically requested the information attached to this email. PLEASE NOTE: This e-mail is intended only for the specific person who has requested information about a specific Pfizer Inc product.

Please contact Pfizer Medical Information at (800) 438-1985, or Hospira, a Pfizer Company, at (800) 615-0187:

- If you did NOT request this information
- If you have any other questions regarding Pfizer products

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MEDICAL INFORMATION

April 22, 2016

Dear Dr Eide,

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I hope the information enclosed proves to be of help and interest. Please do not hesitate to contact us at 1-800-438-1985, or via www.pfizermedinfo.com, should you require anything further.

Sincerely,

A handwritten signature in cursive script that reads "Ellen Shulman".

Ellen Shulman, PharmD.
Pfizer Medical Information

US16-024065



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SR - the Brief Product Summary

EMBEDA® CII (morphine sulfate/naltrexone hydrochloride) Extended Release (ER) capsules
Idaho Medicaid written testimony

The purpose of this document is to provide the clinical and/or pharmacoeconomic information regarding EMBEDA that was requested on the Idaho Medicaid website; it is not intended to be used for any other purpose. This document contains relevant information for EMBEDA, which may or may not be included in the U.S. Prescribing Information (USPI). Pfizer does not suggest or recommend the use of EMBEDA in any manner other than as described in the USPI.

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>. In the event these links should not work, please access the product's approved Prescribing Information at www.pfizer.com. Please refer to the full Prescribing Information for complete BOXED WARNING: ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; and INTERACTION WITH ALCOHOL.

SUMMARY

The points below include brief summaries of recent clinical and epidemiologic evidence published concerning opioid misuse, abuse epidemic as well as economic data on Embeda that were not part of the last (2015) submission.

Opioid medication abuse and Societal and Economic Costs of Opioid Medication Abuse, Dependence

The Centers for Disease Control and Prevention (CDC) recently reported that drug overdose deaths in the US significantly increased from 2013 to 2014 mainly due to an increase in opioid overdose deaths. In 2014 opioids were involved in 28,647 deaths, more than in any previous year on record.⁶ In 2014, almost 2 million Americans abused or were dependent on prescription opioids.⁹

Product manipulation is more common with extended-release opioids than with immediate-release opioids due to a higher drug content.¹⁰ While overconsumption of prescription opioid medications is a common method of abuse, findings from the National Health and Wellness Survey (NHWS) showed that approximately half of surveyed participants reporting the use of opioid medications to get high had tampered with the medication by swallowing it with alcohol, chewing it, or crushing it to enable abuse by other routes (eg, IV injection, snorting).⁷ Additionally, based on analysis of RADARS Poison Center data (2006-2014), intentional abuse exposures involving prescription opioid medication tampering associated with injection or inhalation were more likely associated with death or major medical outcome than exposures from oral ingestion (87% and 76% greater risk, respectively). Prescription opioid medication tampering associated with injection or inhalation vs oral ingestion accounts for a disproportionate share of serious health consequences including death (% of cases leading to death or a major medical outcome: 13.4% vs 12.5% vs 7.2%, respectively).⁸

Total US societal and economic costs due to prescription opioid medication abuse, dependence, or misuse are substantial and are estimated to be > \$50 billion annually.¹² Several analyses have been conducted of Medicaid populations and have found that prescription opioid medication abusers, compared to non-abusers, have substantially greater annual health care costs, resource utilization, and prevalence of comorbidities.² Recent data show that excess annual medical cost in Medicaid patients with diagnosed opioid abuse and dependence is ~\$15,000/patient.³

Economic Model

Economic models demonstrate that the larger costs associated with opioid abuse and dependence are driven by direct medical costs of abuse (eg, hepatitis, HIV, trauma) and related medical events such as emergency department (ED) visits, hospitalizations and substance abuse treatment. A model was developed to assess the quantitative relationship between positive subjective measures (PSM) i.e., drug liking and high from human abuse liability studies and real-world non-medical use (NMU); a PSM-NMU model. The PSM-NMU model demonstrated a significant relation between reductions in the PSM of overall drug liking and real-world NMU rates. Using this PSM-NMU model for an ER morphine ADO (i.e., EMBEDA) with a previous budget-impact model allowed an estimation of medical events avoided and cost savings based on the overall US population covered by a single payer. This analysis estimated annual reductions in NMU rates in the range of 45.1% to 98.8% and estimated health care savings in the range of \$147.7 million to \$323.6 million annually in the US for EMBEDA, assuming it replaced the branded non-abuse-deterrent formulation ER morphine products currently available.⁵

Clinical safety/Indication/ Dosage and administration

EMBEDA is contraindicated in patients with significant respiratory depression, acute or severe bronchial asthma, known or suspected paralytic ileus, or hypersensitivity to morphine or naltrexone. The most common adverse reactions (> 10%) are constipation, nausea, and somnolence. In a long-term, open-label 12-month safety study, the distribution of adverse reactions was similar to that seen in the controlled studies and was consistent with the most common opioid-related adverse reactions. Please refer to the full Prescribing Information for complete information on warnings, precautions and adverse events.⁴

EMBEDA (morphine sulfate and naltrexone hydrochloride extended release capsules) 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.⁴

EMBEDA is available in six dosage strengths: 20 mg/0.8 mg, 30 mg/1.2 mg, 50 mg/2 mg, 60 mg/2.4 mg, 80 mg/3.2 mg and 100 mg/4 mg. Embeda 100/4 mg capsules are only for patients in whom tolerance to an opioid of comparable potency is established. Patients considered opioid-tolerant are those taking, for 1 week or longer, at least 60 mg of morphine daily, at least 30 mg of oral oxycodone daily, at least 8 mg of oral hydromorphone daily, or an equianalgesic dose of another opioid. EMBEDA is administered at a frequency of either once daily (every 24 hours) or twice daily (every 12 hours). Because steady-state plasma concentrations are approximated within 24 to 36 hours, EMBEDA dose may be adjusted every 1 to 2 days. Do not abruptly discontinue EMBEDA in a physically-dependent patient. Instruct patients to swallow EMBEDA capsules intact, or to sprinkle the capsule contents on applesauce and immediately swallow without chewing. The pellets in the capsule are not to be crushed, dissolved, or chewed. If the pellets in EMBEDA capsules are crushed, dissolved or chewed it will result in uncontrolled delivery of morphine and can lead to overdose or death. They can release sufficient naltrexone to precipitate withdrawal in opioid-dependent individuals.⁴

Additional details regarding the economic model are provided below:

Quantitative Link Between Human Abuse Liability Studies and Real-World Nonmedical Use

Overview

Human abuse liability studies, also known as clinical abuse potential studies, are important for assessing the abuse potential of new drug formulations. Study participants typically have a history of recreational drug use, are not dependent on opioids, and are administered specific doses of study drug, active comparator, and placebo. The participants are asked to rate their experience with each product on a range of positive subjective measures (PSMs). PSMs of "overall drug liking," "drug liking," and "high" are evaluated using a 100-point VAS, in which larger values represent a greater degree of drug liking or high. In human abuse liability studies of abuse-deterrent formulations (ADFs), the ADFs have been shown to exhibit lower PSM scores than non-ADF controls. However, the extent to which these reductions in PSM scores translate to reductions in real-world abuse rates is unknown.⁵

Economic models, such as the budget impact model described above, demonstrate that the larger costs associated with opioid abuse and dependence are driven by direct medical costs of abuse (eg, hepatitis, HIV, trauma) and related medical events such as ED visits and stays in substance abuse treatment centers.⁵ Whereas ADFs have been shown to decrease PSM scores compared to non-ADF, the extent by which these reductions in PSMs are associated with reductions in real-world abuse rates and associated costs has not been established.

The aim of this study⁵ was to:

- Assess the relationship between PSMs from human abuse liability studies and real-world non-medical use
- Evaluate the healthcare resource utilization and cost impacts of these relationships

Methods

The study involved two components:

- 1) **Multivariate Econometric Model** – A quantitative evaluation of the association between PSMs and real-world nonmedical use rates was calculated using an ordinary least-squares regression. The dependent variable was nonmedical use, and the independent variable was each PSM. The model controlled for prescription volume and indicators for opioids and controlled substance schedule.
- 2) **Budget Impact Model** – The budget impact model translated the estimated relation to an implied measure of health care utilization and cost savings. Using a budget impact model developed by White et al, 2009¹¹, the health care events avoided and cost savings associated with a reduction in PSM score due to the introduction of an abuse-deterrent opioid were calculated.

Data Sources: Several data sources were used to obtain the following information:

- Nonmedical use: 2010 NSDUH and 2010 DAWN
- PSMs: Post hoc analysis of human abuse liability studies. These studies provided the average peak effects (E_{-ax}) for "overall drug liking," "drug liking," and "high."
- Prescription drug volume: IMS Health

Model Assumptions: Model assumptions included:

- The ADF effectiveness was varied over a range of 20 to 80 percent to determine the average number of healthcare events avoided and cost savings
- The ADF was priced at par with the branded opioid.
- The ADF replaced the branded opioid of the same molecule 100%
- Prescription volume remained stable.
- Generics were assumed to still be available at the same prescription volume.

Results

Based on human abuse liability studies of (ER morphine abuse deterrent formulation (Embeda), the reductions observed in the overall drug liking E_{-ax} are associated with private payer cost reductions using this model in the range of \$147.97–\$323.6 million (Table 1).⁵

Table 1. Impact of Reduced Overall Drug Liking E_{-ax} Observed in Human Abuse Liability Studies for ER morphine Abuse-Deterrent Formulation (Embeda) Relative to Comparator Non-Abuse-Deterrent Formulation⁵

	Drug Introduced ER Morphine Abuse-Deterrent Formulation
Predicted percent decrease in nonmedical use rate	45.1%–98.8%
Estimated number of Emergency department visits avoided	
Per 1% decrease in nonmedical use rate	249.8
Total predicted for percent decrease	11,262–24,673
Estimated number of Hospitalizations avoided	
Per 1% decrease in nonmedical use rate	165.4
Total predicted for percent decrease	7,457–16,337
Estimated Health care cost savings	
Per 1% decrease in nonmedical use rate	\$3.28 million
Total predicted for percent decrease	\$147.7 million–\$323.6 million

ER = extended release

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1) Birnbaum HG et al. Pain Med. 2011;12(4):657-667; 2) Hansen RN et al. Clin J Pain. 2011;27(3):194-202; 3) Oderda GM et al. Journal of Pain & Palliative Care Pharmacotherapy 2015;29(4):388-400; 4) EMBEDA (morphine sulfate and naltrexone hydrochloride) extended-release capsules, CII Package Insert; 5) White AG et al. J Opioid Manag. May-Jun 2015;11(3):199-210; 6) Rudd RA et al. MMWR Morb Mortal Wkly Rep 2015;64:1378-1382; 7) Vietri J, Joshi AV, Barsdorf AI, et al. Prescription opioid abuse and tampering in the United States: results of a self-report survey. Pain Med. 2014;15(12):2064-74; 8) Bucher-Bartelsson B, Claire Le Lait M, Dart R, et al. Medical outcome associated with unintended

Embeda- April 2016

routes of prescription opioid abuse. *Postgrad Med.* 2015;127(Sup1):S54-55; 9) Substance Abuse and Mental Health Services Administration, National Survey on Drug Use and Health, 2014; 10) Katz N et al. Tampering with prescription opioids: nature and extent of the problem, health consequences, and solutions. *Am J Drug Alcohol Abuse.* 2011;37(4):205-217. 11) White AG, Birnbaum HG, Rothman DB, et al. Development of a budget-impact model to quantify potential cost savings from prescription opioids designed to deter abuse or ease of extraction. *Appl Health Econ Health Policy.* 2009;7(1):61-70.