Initial REMS approval 03/2012

NDA 202799

OMONTYS® (peginesatide) Injection
An erythropoiesis-stimulating agent (ESA)

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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS

- To inform healthcare professionals that OMONTYS Injection is indicated only for use in the treatment of patients with anemia due to chronic kidney disease on dialysis.

- To inform healthcare professionals of the serious risks associated with the use of OMONTYS Injection including potentially fatal cardiovascular and/or thromboembolic adverse events, and the increased risk of these events in non-dialysis patients.

II. REMS ELEMENTS

A. Communication Plan

Affymax, Inc. will implement the following elements of a communication plan:

1. A Dear Healthcare Professional (DHCP) letter will be sent within 60 days of product approval or at the time of product launch, whichever is sooner, and again after 12 months. The letter will be available via a REMS-specific link from the OMONTYS website and through Affymax's medical information department for 2 years following approval of the REMS. The intended audience for this letter is the nephrology community of Healthcare Professionals (HCPs) who are likely to prescribe OMONTYS.

The letter will be sent to all nephrologists, to related professional societies, and to dialysis facilities. Dialysis facilities and professional societies receiving the DHCP letter will be requested to distribute the DHCP letter to their staff, including other HCPs, or membership.

In addition, for 18 months following approval of the REMS, new nephrologists and new dialysis facilities ordering OMONTYS will receive the letter if they have not previously received it. The list of HCPs to receive the letter will be derived from a comprehensive commercially available database.

Within 60 days of product approval or at the time of product launch, whichever is sooner, and again after 12 months, Affymax, Inc. will send the DHCP letter to the following professional organizations, and will request that the letter be provided to the members of the professional organizations:

National Renal Administrators Association (NRAA)
American Society of Nephrology (ASN)
Renal Physicians Association (RPA)
American Nephrology Nurses Association (ANNA)
National Kidney Foundation (NKF)

The letter will be available at the OMONTYS booth at the following scientific meetings for the two years following approval of OMONTYS:

American Nephrology Nurses Association (ANNA)
National Kidney Foundation (NKF)
National Renal Administrators Association (NRAA)
American Society of Nephrology (ASN)
Renal Physicians Association (RPA)

The letter will be provided to MedWatch at the same time it is provided to the professional organizations.

The Dear Healthcare Professional letter is part of the REMS and is appended.

The communication plan will be updated to reflect any changes in labeling for the risks outlined above.

Affymax, Inc. will make the REMS, the DHCP letter, and professional labeling available via a REMS-specific link from the OMONTYS website as well as through the medical information department for 2 years after the initial date of approval.

The OMONTYS REMS web page is part of the REMS; the landing page screen shot is appended.

B. Timetable for Submission of Assessments

Affymax, Inc. will submit REMS Assessments to FDA at 12 months, 24 months, 36 months and 7 years from the date of initial approval of the REMS. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by

each assessment should conclude no earlier than 60 days before the submission date for that assessment. Affymax, Inc. will submit each assessment so that it will be received by the FDA on or before the due date.

Appendix 1: Dear Healthcare Professional Letter

IMPORTANT DRUG WARNING

Subject: **Increased risk of cardiovascular events in patients with Chronic Kidney Disease (CKD) not on dialysis**

Dear Healthcare Professional:

Affymax, Inc. and Takeda Pharmaceuticals America, Inc. would like to inform you that OMONTYS® (peginesatide) Injection, an erythropoiesis-stimulating agent (ESA) for once monthly administration, has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of anemia associated with chronic kidney disease (CKD) in adult patients on dialysis only.

In collaboration with the FDA, a Risk Evaluation and Mitigation Strategy (REMS) has been developed to ensure the benefits of Omontys outweigh the risks.

Omontys is not indicated in patients with CKD not on dialysis

- In two trials of Omontys, patients with CKD not on dialysis experienced increased specific cardiovascular events.

We remind you that all ESAs, including Omontys have a **boxed warning** containing the following:

ESAs increase the risk of death, myocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access and tumor progression or recurrence

- In controlled clinical trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered ESAs to target a hemoglobin level of greater than 11 g/dL
- No trial has identified a hemoglobin target level, ESA dose, or dosing strategy that does not increase these risks
- Use the lowest Omontys dose sufficient to reduce the need for red blood cell transfusions

Medication Guide
A Medication Guide is provided to medical personnel and nephrology societies to facilitate the education of dialysis patients on the risks of Omontys.

[Guidance for Medical Personnel- include in Dear HCP letter]:

- At the start of Omontys therapy, when needed to reinforce patient knowledge, and when new information is included in the Medication Guide, provide and review the current Medication Guide with each patient and/or patient caregiver

IMPORTANT DRUG WARNING

[Guidance for Nephrology societies – include in professional society letter]

- Raise awareness among the membership for the need of the medical personnel to provide a Medication Guide as outlined above

Copies of the Omontys Medication Guide, may be obtained from the website www.omontys.com or by calling Affymax at 1-855-466-6689.

Reporting Adverse Events
To report all adverse events suspected with the use of Omontys contact:

- Affymax at 1-855-466-6689.
- FDA's MedWatch reporting system by phone (1-800-FDA-1088), or online (www.accessdata.fda.gov/scripts/medwatch)

This letter is not a comprehensive description of the risks associated with the use of Omontys. Please read the accompanying Full Prescribing Information and Medication Guide for a complete description of these risks.

Affymax and Takeda are committed to working in partnership with you to support medical personnel and patient education regarding the safe use of Omontys in patients with anemia of CKD on dialysis.

Sincerely,

Appendix 2: REMS-specific Link on OMONTYS Website – Landing Screen Shot

Important Safety Information | Prescribing Information | Medication Guide

OMONTYS® (peginesatide) Injection

Risk Evaluation and Mitigation Strategy (REMS)

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks.

OMONTYS is an erythropoiesis-stimulating agent (ESA) indicated for the treatment of anemia due to chronic kidney disease (CKD) in adult patients on dialysis only.

OMONTYS is not indicated in patients with CKD not on dialysis.

- **In two trials of OMONTYS, patients with CKD not on dialysis experienced increased specific cardiovascular events**

OMONTYS has a **boxed warning** containing the following language:

ESAs increase the risk of death, myocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access and tumor progression or recurrence.

Use the links below to access important REMS documents:

- Dear Healthcare Professional Letter
- Prescribing Information
- Medication Guide

Limitations of Use

OMONTYS is not indicated and is not recommended for use in patients with CKD not on dialysis, in patients receiving treatment for cancer and whose anemia is not due to CKD, or as a substitute for RBC transfusions in patients who require immediate correction of anemia. OMONTYS has not been shown to improve symptoms, physical functioning, or health-related quality of life.

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/s/

RICHARD PAZDUR
03/27/2012