

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,