

**BL 125268 Nplate<sup>®</sup> (romiplostim)**  
**Amgen Inc.**  
One Amgen Center Drive  
Thousand Oaks, CA 91320-1799  
805-447-1000

## **RISK EVALUATION AND MITIGATION STRATEGY (REMS)**

### **I. GOAL**

To inform healthcare providers about the risks of progression of myelodysplastic syndromes (MDS) to acute myelogenous leukemia (AML), thrombotic/thromboembolic complications, bone marrow reticulin formation, bone marrow fibrosis, worsened thrombocytopenia after cessation of Nplate<sup>®</sup>, and Nplate medication errors associated with serious outcomes.

### **II. REMS ELEMENTS**

#### **A. Communication Plan**

Amgen will implement a communication plan to healthcare providers to support implementation of this REMS.

The communication plan will provide for the dissemination of information about the elimination of the elements to assure safe use, inform prescribers and institutions how to obtain Nplate, and remind healthcare providers about the serious risks associated with Nplate and appropriate patient selection in accordance with the approved labeling.

The communication plan consists of:

1. A *Dear Healthcare Provider Letter* will be distributed via direct mail, electronic delivery or via a hand carry program to the following within 15 working days of the most recent REMS approval 12/2011:

- Hematologists
- Oncologists
- Hospitals and Institutions

In addition, Amgen will send the *Dear Healthcare Provider Letter* to MedWatch at the same time it is disseminated to the target audience.

The *Dear Healthcare Provider Letter* is part of the Nplate REMS and is appended.

2. A *Dear Professional Society Letter* will be distributed to the leadership of the following societies via direct mail or electronic delivery within 15 working days of the most recent REMS approval 12/2011:
  - American Society of Clinical Oncology
  - American Society of Hematology

- National Comprehensive Cancer Network
- American Society of Pediatric Hematology/Oncology
- Oncology Nursing Society
- Hematology Oncology Pharmacy Association
- American Society of Health-System Pharmacists

The *Dear Professional Society Letter* is part of the Nplate REMS and is appended.

Both letters will be posted prominently on [www.nplate.com](http://www.nplate.com) and [www.nplatenexus.com](http://www.nplatenexus.com) within 5 working days of the most recent REMS approval 12/2011. This information will remain on [www.nplate.com](http://www.nplate.com) for 6 months and [www.nplatenexus.com](http://www.nplatenexus.com) for 4 weeks.

### **III. TIMETABLE FOR SUBMISSION OF ASSESSMENTS**

Amgen will submit REMS Assessments to the Food and Drug Administration (FDA) on 30 June 2012, 30 June 2015, and 30 June 2019 for the Nplate<sup>®</sup> (romiplostim) 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. Amgen will submit each assessment so that it will be received by FDA on or before the due date.

## IMPORTANT PRESCRIBING INFORMATION

Date: MM/DD/YYYY

- Subject:**
- **Nplate® (romiplostim) REMS Program (Nplate® NEXUS Program): Elimination of Prescriber, Institution, and Patient Enrollment requirements to prescribe and receive Nplate**
  - **Serious risks associated with Nplate**

Dear Healthcare Professional:

As of <insert date of program closure (Day 0)>:

- **Healthcare Professionals/Prescribers** – No longer need to be enrolled to prescribe Nplate® (romiplostim) or complete and submit any Nplate® NEXUS Program Forms
- **Institutions** - No longer need to enroll and verify prescriber and patient enrollment before dispensing Nplate
- **Patients** - No longer need to be enrolled in order to receive Nplate

Any prescriber or hospital will be able to order Nplate without enrolling either themselves or patients.

### **Why are the REMS restricted distribution requirements being eliminated?**

The restrictive elements of the REMS included enrollment of prescribers, patients and institutions to assist in collecting long term safety information. Upon further review, FDA and Amgen have determined that the safety information collected through the REMS, which is based on individual case safety reports, is inherently confounded by underlying medical conditions in the treated patient population and thus cannot be used to determine the precise role of Nplate in the development of the adverse events. Based in part on this determination and the data submitted from clinical trials, FDA and Amgen have concluded that the restricted elements of the REMS can be eliminated. For this reason enrollment of prescribers, patients and institutions and mandatory collection of safety data is no longer required.

### **What has changed?**

#### *Prescribers*

- No longer need to enroll in Nplate® NEXUS Program
- No longer need to enroll patients in Nplate® NEXUS Program
- No longer need to complete and submit the enrollment, baseline, 6-month safety questionnaires, and discontinuation and post-therapy forms

Prescribers should inform their patients currently enrolled in Nplate® NEXUS Program of the elimination of this program.

#### *Institutions*

- No longer need to complete initial enrollment forms and training
- No longer need to confirm prescriber and patient enrollment in Nplate® NEXUS Program
- No longer need to maintain inventory tracking documentation
- No longer need to undergo periodic audits to ensure Nplate is dispensed in accordance with program requirements

#### *Ordering Nplate*

- There are no restrictions on ordering Nplate
- Ordering Nplate no longer requires an Nplate® NEXUS ID
- Nplate will continue to be available through your normal procurement channels

## What has NOT changed?

### Risks

**Nplate is associated with serious risks, including:**

- **Risk of Progression of Myelodysplastic Syndromes (MDS) to Acute Myelogenous Leukemia (AML):** A randomized, double-blind, placebo-controlled trial enrolling patients with severe thrombocytopenia and International Prognostic Scoring System (IPSS) low or intermediate-1 risk MDS was terminated due to more cases of AML observed in the romiplostim treatment arm.

Nplate is not indicated for the treatment of thrombocytopenia due to MDS or any cause of thrombocytopenia other than chronic ITP.

- **Thrombotic/Thromboembolic Complications** may result from increases in platelet counts with Nplate use. Portal vein thrombosis has been reported in patients with chronic liver disease receiving Nplate. Nplate should be used with caution in patients with ITP and chronic liver disease.
- **Bone Marrow Reticulin Formation and Risk for Bone Marrow Fibrosis:** Nplate administration may increase the risk for development or progression of reticulin fiber formation within the bone marrow. This formation may improve upon discontinuation of Nplate.

If new or worsening morphological abnormalities or cytopenia(s) occur, consider a bone marrow biopsy to include staining for fibrosis.

- **Worsened Thrombocytopenia after Cessation of Nplate:** *Discontinuation of Nplate may result in worsened thrombocytopenia than was present prior to Nplate therapy. Monitor complete blood counts (CBCs), including platelet counts, for at least 2 weeks following Nplate discontinuation.*
- **Medication Error:** Excessive doses of Nplate may increase platelet counts to a level that produces thrombotic/thromboembolic complications.

### Indication

Nplate is indicated for the treatment of thrombocytopenia in patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

- Nplate is not indicated for the treatment of thrombocytopenia due to myelodysplastic syndrome (MDS) or any cause of thrombocytopenia other than chronic ITP.
- Nplate should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increases the risk for bleeding.
- Nplate should not be used in an attempt to normalize platelet counts.

*Please see Prescribing Information for complete description of the safety information.*

### Prescribers

- Discuss the benefits and risks of Nplate with your patients and provide the Medication Guide
- Select the appropriate patients to receive Nplate in accordance with the approved prescribing information
- Monitor your patients as specified in the Prescribing Information
- Report adverse drug reactions to Amgen

### **What about records I collected for the Nplate® NEXUS Program?**

Enrolled prescribers and institutions should maintain patient and Nplate® NEXUS Program records in accordance with state and local records retention requirements.

### **What if I have safety information to submit?**

- Amgen will continue to accept safety information for enrolled patients for an additional 4 weeks faxed to 1-877-NPLATE0 (1-877-675-2830) or via the Nplate® NEXUS Program Patient Management website ([www.nplatenexus.com](http://www.nplatenexus.com)) which will be available until < Day 0 + 4 weeks>
- After <<date>>, report SUSPECTED ADVERSE REACTIONS, to Amgen Inc. at 1-800-77-AMGEN (1-800-772-6436) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

Amgen will not send any additional reminders to prompt safety data collection. This letter serves as the final request for information.

### **What will Amgen do with the patient health information already collected?**

Patient health information and data collected throughout the Nplate® NEXUS Program continues to be protected and will be disclosed only for the purposes described in the patient enrollment form.

### **Further Information**

Should you require additional information about Nplate please refer to the Prescribing Information found at [www.nplate.com](http://www.nplate.com) or contact Amgen Medical Information at 1-800-772-6436.

Sincerely,

Sean E. Harper, MD  
Senior Vice President Global Development and Chief Medical Officer  
Amgen Inc.

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## **What if members of my organization have safety information to submit?**

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**Further Information**

Should your members require additional information about Nplate please refer to the Prescribing Information found at [www.nplate.com](http://www.nplate.com) or contact Amgen Medical Information at 1-800-772-6436.

Sincerely,

Sean E. Harper, MD  
Senior Vice President Global Development and Chief Medical Officer  
Amgen Inc.