RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS

The goals of the NULOJIX REMS are:

1. To inform healthcare providers of the increased risk of post-transplant lymphoproliferative disorder (PTLD), predominantly in the central nervous system (CNS), associated with NULOJIX.

2. To inform healthcare providers of the increased risk of progressive multifocal leukoencephalopathy (PML), a CNS infection, associated with NULOJIX.

3. To inform patients of the serious risks associated with NULOJIX.

II. REMS ELEMENTS

A. Medication Guide

A Medication Guide will be dispensed with each NULOJIX infusion in accordance with 21 CFR 208.24. The Medication Guide is part of the REMS and is appended.

B. Communication Plan

BMS will implement a communication plan to healthcare providers to support implementation of this REMS.
The communication plan will include:

1. A prominent link on the main product webpage that directs healthcare providers to a REMS-specific landing page (www.NULOJIX.com/REMS.aspx). The NULOJIX REMS landing page will include links to the most recently approved full Prescribing Information, Medication Guide, and all approved REMS materials. The link, landing page, and all materials will be available within 2 weeks of approval of the REMS and available for 7 years after approval of the REMS.

   The REMS landing page (www.NULOJIX.com.REMS.aspx) is part of the NULOJIX REMS and is appended.

2. A webinar with voiceover and live support will be available at the time of launch and at least quarterly during the first year after REMS approval via the REMS landing page. In addition, the slides with voiceover will be available on demand for 7 years after approval of the REMS.

   The webinar slides are part of the NULOJIX REMS and are appended.

3. A Dear Healthcare Professional (HCP) Letter along with HCP Fact sheet, full prescribing information, and Medication Guide will be distributed via direct mail and electronic delivery within 2 weeks of approval of the REMS and annually for the three subsequent years. This will be a total of four annual distributions of this material. The target audience will be all potential prescribers of NULOJIX including transplant nephrologists, transplant surgeons, community nephrologists, transplant nurses/coordinators, transplant clinical pharmacists. In addition, this letter will be sent to the leadership of the following professional societies and BMS will request that these societies disseminate this information to their members:

   - American Society of Transplantation (AST)
   - American Society of Transplant Surgeons (ASTS)
   - American Society of Nephrology (ASN)
   - National Association of Transplant Coordinators (NATCO)
   - International Transplant Nurse Society (ITNS, US members only)
   - American College of Clinical Pharmacy (ACCP)
   - American Society of Health-System Pharmacists (ASHP)

   The Dear HCP Letter is part of the NULOJIX REMS and is appended.

   In addition, BMS will send the DHCP Letter to MedWatch at the same time it is disseminated to the target audience.
4. A HCP Fact Sheet will be distributed by BMS field medical liaisons and sales representatives during the first discussion of NULOJIX with a transplant center. The transplant centers that account for 80% of the transplant volume based on 2010 UNOS center level data will be visited within the first 90 days of commercial availability of NULOJIX. The remaining centers will be visited within the first 150 days of commercial availability of NULOJIX.

The HCP Fact Sheet is part of the NULOJIX REMS and is appended.

5. A Dear Infusion Specialist Letter, the Full Prescribing Information, Medication Guide, and Pre-Infusion Checklist will be distributed via direct mail and electronic delivery within 2 weeks of approval of the REMS to infusion nurses, pharmacists, and infusion center directors. In addition, this letter will be sent to the leadership of the following professional societies and BMS will request that these societies disseminate this information to their members:

- Infusion Nurse Society (INS)
- American College of Clinical Pharmacy (ACCP)
- American Society of Health-System Pharmacists (ASHP)

The Dear Infusion Specialist Letter is part of the NULOJIX REMS and is appended.

6. A Pre-Infusion Checklist will be distributed with the Infusion Specialist Letter and separately in tear pads within three weeks of the first order of NULOJIX to a transplant center and to infusion centers that BMS is able to identify for the first seven years after approval of the REMS.

The Pre-Infusion Checklist is part of the NULOJIX REMS and is appended.

7. A Journal Information Piece will be circulated in the following journals

- American Journal of Transplantation
- Journal of the American Society of Nephrology
- Pharmacotherapy
- American Journal of the Society of Health-System Pharmacists

It will appear every 4 months for a total of 3 years.

The Journal Information Piece is part of the NULOJIX REMS and is appended.
III. TIMETABLE FOR SUBMISSION OF ASSESSMENTS

BMS will submit REMS Assessments to FDA annually from the date of the initial approval of the REMS for the first 5 years and again 7 years from the initial date of approval of the NULOJIX 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 of the assessment. BMS will submit each assessment so that it will be received by FDA on or before the due date.