

## Important Information About



### **Increased Risk of Post-Transplant Lymphoproliferative Disorder (PTLD), predominantly involving the Central Nervous System (CNS), and Progressive Multifocal Leukoencephalopathy (PML) with NULOJIX**

NULOJIX® is a selective T-cell costimulation blocker indicated for the prophylaxis of organ rejection in adult patients receiving a kidney transplant. NULOJIX is to be used in combination with basiliximab induction, mycophenolate mofetil (MMF), and corticosteroids. NULOJIX is indicated for use only in patients who are Epstein-Barr virus (EBV) seropositive. Use of NULOJIX for the prophylaxis of organ rejection in other transplanted organs has not been established.

#### **Increased Risk of Post-Transplant Lymphoproliferative Disorder (PTLD)**

NULOJIX treated patients have an increased risk for PTLD, predominantly in the CNS

- ◆ The highest risk of PTLD is in EBV seronegative patients; therefore, NULOJIX is contraindicated in transplant recipients who are EBV seronegative or with unknown serostatus
- ◆ In clinical trials of kidney transplant recipients, PTLD was seen in 13 out of 949 NULOJIX-treated patients, including patients receiving the recommended dosage regimen and a dosage higher than the recommended regimen
  - 8 of 13 cases of PTLD in NULOJIX-treated patients presented in the CNS
  - 5 of those 8 CNS cases were fatal
- ◆ At the recommended clinical dose in the EBV seropositive population, 3 cases of PTLD were reported
  - 1 of those 3 cases presented in the CNS and that case was fatal
- ◆ Other known risk factors for PTLD include T-cell depleting therapy and cytomegalovirus (CMV) infection
  - T-cell depleting therapy for the treatment of acute rejection should be used with caution in patients who are on NULOJIX
  - CMV prophylaxis is recommended for at least 3 months after transplantation

#### **Increased Risk of Progressive Multifocal Leukoencephalopathy (PML)**

Patients in clinical trials exposed to NULOJIX at higher or more frequent dosing than the recommended regimen have developed PML

- ◆ 2 cases of PML were reported: 1 case occurred in a renal transplant recipient and 1 case occurred in a liver transplant recipient
- ◆ Do not exceed the recommended doses of NULOJIX and concomitant immunosuppressants

#### **Patient Monitoring and Counseling**

Monitor patients for new or worsening neurologic, cognitive, or behavioral signs or symptoms. If detected, consideration should be given to:

- ◆ Appropriate neurologic work-up including consideration for consultation with a specialist (e.g., neurologist and/or infectious disease)
- ◆ Dose reduction or discontinuation of immunosuppressive therapy taking into account the risk to the graft

Prescribers should counsel patients to:

- ◆ Immediately report changes in thinking, memory, speech, mood or behavior, confusion, weakness, change in vision, episodes of fever, night sweats, prolonged tiredness, weight loss, and swollen glands
- ◆ Adhere to all prescribed medications including those for prophylaxis

#### **ENLIST Registry – Evaluating NULOJIX Long-Term Safety in Transplant**

- ◆ BMS established the ENLIST Registry to further evaluate the safety profile of NULOJIX
- ◆ ENLIST is intended to enroll all adult kidney transplant patients who are treated with NULOJIX
- ◆ The primary objective of ENLIST is to determine the incidence of PTLD, CNS PTLD, and PML in US adult EBV seropositive kidney transplant recipients treated with NULOJIX
- ◆ Data collection will include the patients' EBV and CMV serostatus as well as when NULOJIX was initiated relative to time of transplant
- ◆ BMS encourages your center to participate in the ENLIST Registry. For more information on how to enroll in ENLIST and answers to other questions regarding the registry, please call 1-800-321-1335. Find out more about the protocol at [www.clinicaltrials.gov](http://www.clinicaltrials.gov)

**Adverse events** with the use of NULOJIX should be reported to:

- ◆ Bristol-Myers Squibb at 1-800-721-5072 and/or
- ◆ FDA MedWatch program by phone at 1-800-FDA-1088 or online at [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)

All REMS materials, including a NULOJIX REMS webinar, are accessible at [www.NULOJIX.com/REMS.aspx](http://www.NULOJIX.com/REMS.aspx).

**Please refer to the complete Prescribing Information for further information which is available at [www.NULOJIX.com](http://www.NULOJIX.com).**