Nulojix (belatacept): Risk of medication errors due to change in maintenance dose from 5 mg/kg to 6 mg/kg

Dear Healthcare professional,

Bristol Myers Squibb in agreement with the European Medicines Agency and the <National Competent Authority> would like to inform you of the following:

Summary

- With the implementation of a new manufacturing process, **the maintenance dose for Nulojix (belatacept) will be changed to 6 mg/kg every 4 weeks.**
- For approximately one to two months starting <month/year>, Nulojix from both the previous and the new manufacturing processes will coexist on the market.
- Healthcare professionals must carefully check the dose for the specific product to be administered, to make appropriate adjustments for weight-based dosing calculations.
- The dosage during the induction phase (i.e. the first four months post-transplant) is unchanged (10 mg/kg).

Changes to the NULOJIX outer packaging, vial label, and product information have been made to aid in identifying the new supply and are described in detail below.

Background on the safety concern

Nulojix, in combination with corticosteroids and a mycophenolic acid (MPA), is indicated for prophylaxis of graft rejection in adult recipients of a renal transplant.

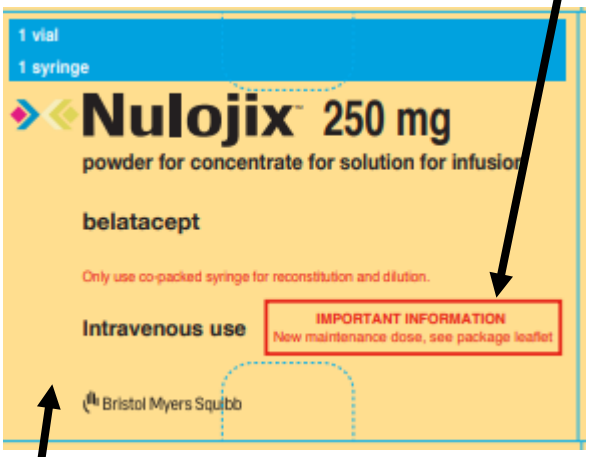
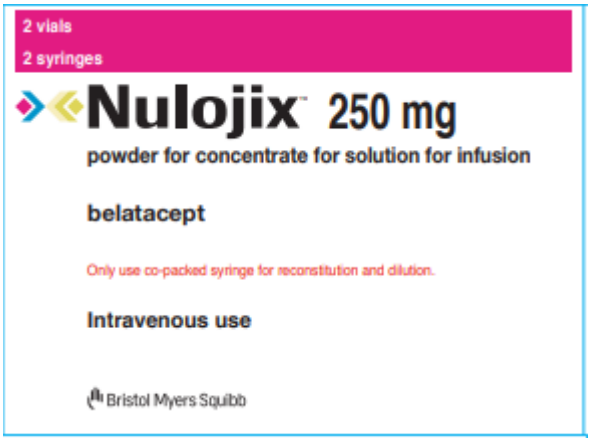
The manufacturing process of Nulojix drug substance (belatacept) has been changed. This is referred to as a change from Process C (current process) to Process E (new process).

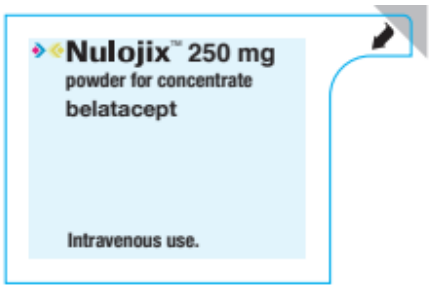
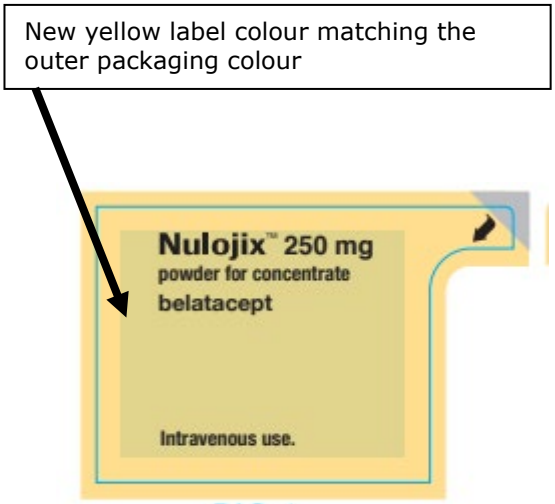
Elimination of belatacept manufactured by Process E is faster than for Process C. Faster elimination is expected to result in a lower minimum concentration (C_{min}) of belatacept during the maintenance phase when a patient is given belatacept from Process E compared to Process C at the same dose level.

To account for the faster elimination of belatacept with Process E, the maintenance dose has been increased to 6 mg/kg. The Process E maintenance dose of 6 mg/kg is to be administered by intravenous infusion every 4 weeks (± 3 days), starting at the end of week 16 after transplantation.

For approximately one to two months, Nulojix from Process C and Process E will coexist on the market. A mix-up between the products may lead to medication errors resulting in over- or underdosing of belatacept. It is therefore important that the healthcare professional checks the dosing for the specific product to be administered, to make the appropriate dosing adjustments for weight-based dosing calculations.

In order to alert healthcare professionals to the posology change and mitigate the risk of dosing errors during the transition phase, the following changes are made to the packaging for Nulojix Process E finished product:

	Current Packaging 5mg/kg maintenance dose (Process C)	**New Packaging** **6mg/kg maintenance dose (Process E)**
1 vial 1 syringe outer packaging		Warning alerting HCPs to the new maintenance dose and instructing them to refer to the package leaflet  New yellow outer packaging colour
2 vials 2 syringes outer packaging		Warning alerting HCPs to the new maintenance dose and instructing them to refer to the package leaflet  New yellow outer packaging colour

	Current Packaging 5mg/kg maintenance dose (Process C)	**New Packaging** **6mg/kg maintenance dose (Process E)**
Vial Label	 PAG. 1	 PAG. 1

The product information, including outer packaging and vial label, are being updated to reflect this dosing change.

Call for reporting

<A reminder of the need and how to report adverse reactions and batch details in accordance with the national spontaneous reporting system, including the details (e.g. name, postal address, fax number, websiteaddress) on how to access the national spontaneous reporting system will be included.>

Company contact point

<Contact point details for access to further information, including relevant website address(es),telephone numbers and a postal address>

DHPC COMMUNICATION PLAN	
Medicinal product(s)/ active substance(s)	NULOJIX 250 mg powder for concentrate forsolution for infusion
Marketing authorisation holder(s)	Bristol Myers Squibb EEIG
Safety concern and purpose of the communication	The proposed change in the maintenance dose with Process E drug product introduces a potential risk of medication errors
DHPC recipients	Healthcare Professionals involved in the prescribing and/or preparation of NULOJIX for administration: • Transplant Centers • Transplant Surgeons and Nephrologists • Transplant Coordinators • Transplant Nurses • Professional Transplant Societies • Pharmacists/Pharmacies • General Nephrologists • Nurses for Home Infusion (France-specific) The target group should be further defined at national level, in agreement with the respective national competent authority.
Member States where the DHPC will be distributed	All EU/EEA Member States where Nulojix is marketed.

Timetable	Date
DHPC and communication plan (in English)agreed by PRAC	05 April 2022
DHPC and communication plan (in English)agreed by CHMP	07 April 2022
Submission of translated DHPCs to the nationalcompetent authorities for review	14 April 2022
Agreement of translations by national competentauthorities	25 April 2022
Dissemination of DHPC	Shortly ahead of the launch of Process E finished product (with the new packaging) in the respective MS