Bristol-Myers Squibb Pharmaceuticals Limited

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13th March 2017

Direct Healthcare Professional Communication
Manufacturing related supply constraints for Nulojix®
(belatacept) 250mg powder for concentrate for solution for infusion

Dear Healthcare Professional,
Bristol Myers Squibb (BMS) in agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA) would like to inform you of the following:

Summary

- **As of March 15, 2017, distribution of Nulojix (belatacept) will be restricted to existing patients worldwide for the remainder of 2017.**
- **New patients should not start treatment with Nulojix (belatacept).**
- **The supply shortage is related to a temporary production capacity issue. It is not related to a quality defect of the product or a safety issue.**

Background on the supply shortage

Effective March 15, 2017, BMS aims to restrict distribution of Nulojix (belatacept) to existing patients worldwide for the remainder of 2017, as a necessary measure to ensure adequate supplies for patients under belatacept therapy while the company completes its transition to a new manufacturing process. Under this condition, BMS does not anticipate any disruption of supply to existing patients.

BMS anticipates that, subject to regulatory approval, the transition to the new manufacturing process will be completed at the end of 2017, which will enable supply to new patients again starting in 2018.

In October 2016, BMS initiated communications with the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), and local health authorities in applicable European and South American countries to notify them that a delay in transition to a new manufacturing process, which is needed to meet growing demand for belatacept, will create a potential supply constraint in 2017. Steps have been taken to mitigate the potential supply constraint. Based on worldwide growth in new prescriptions, BMS projects that the supply of belatacept in 2017 will not be sufficient to enable **new** patients to start treatment with Nulojix.
Nulojix (belatacept), in combination with corticosteroids and a mycophenolic acid, is indicated for the prophylaxis of graft rejection in adults receiving renal transplant [1]. Belatacept is not recommended as an option for use within the NHS as stated by NICE, SMC and AWMSG [2,3,4].

[1] Nulojix (belatacept) Summary of Product Characteristics. Available at www.medicines.org.uk/emc.
[2] https://www.nice.org.uk/guidance/GID-TAG348/documents/final-appraisal-determination-document (accessed 15/02/2017)
[3] https://www.scottishmedicines.org.uk/SMC_Advice/Advice/786_12_belatacept_Nulojix (accessed 15/02/2017)
[4] www.awmsg.org/awmsgonline/app/appraisalinfo/430 (accessed 15/02/2017)

BMS is committed to maintaining supply for existing patients being treated with belatacept.
This includes patients who are on a post study drug supply programme and patients on commercial supply. In order to manage demand, BMS will not be able to supply the product for any new patients being prescribed belatacept. This measure is in place to preserve the available stock for existing patients to receive belatacept.
Effective immediately, BMS will be introducing a formal monthly quota for hospitals in the NHS and private providers to ensure continuity of supply to existing patients. These quotas will be determined by the average historical demand required in 2016.
If a quota applies to a hospital, BMS will be in contact with the trust/private provider in the coming days to share the quota volumes allocated, and the interim ordering process for obtaining stocks moving forward.
BMS anticipates that the transition to the new manufacturing process will be completed at the end of 2017, which will enable supply to new patients again starting in 2018. BMS will update both the MHRA and healthcare professionals when supply constraints are resolved.

Bristol-Myers Squibb contact information and enquiries
If you have further questions or require additional information, please contact the BMS Medical Information department (Telephone: 0800 731 1736; Email: medical.information@bms.com).

Reporting adverse events
Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme. Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.

- all suspected ADRs associated with new drugs and vaccines identified by the black triangle▼

It is easiest and quickest to report ADRs online via the Yellow Cards website - https://yellowcard.mhra.gov.uk/ .

Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gsi.gov.uk
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- or by downloading and printing a form

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.'

Adverse events should also be reported to Bristol-Myers Squibb Medical Information on 0800 731 1736 or medical.information@bms.com.

Kind regards,

Dr. Faisal Mehmud BSc, MBBChir, MRCP, MFPM
Executive Medical Director, UK & Ireland
Bristol-Myers Squibb Pharmaceuticals Ltd