16/08/2023

Replacement BAXJECT II / BAXJECT II Hi-Flow Reconstitution Devices co-packaged with Recombinate 1000 UI/10 ml polvere e solvente per soluzione iniettabile - 1 flaconcino di polvere + 1 flaconcino di solvente con dispositivo di ricostituzione senza ago

Marketing Authorisation Number(s): n.028687034

Dear Healthcare professional,

Takeda, in agreement with the European Medicines Agency and Italian Medicines Agency, would like to inform you of the following:

Summary

- **Takeda has decided to voluntarily replace BAXJECT II and BAXJECT II Hi-Flow reconstitution devices produced at Takeda's contract device manufacturer between October 2021 and January 2022, co-packaged for use in conjunction with "*Recombinate 1000 UI/10 ml polvere e solvente per soluzione iniettabile - 1 flaconcino di polvere + 1 flaconcino di solvente con dispositivo di ricostituzione senza ago*".**

- **This is a precautionary measure and is due to the potential presence of particulate matter in the luer port of the device. The issue is linked to the device and there is no quality issue with the medicine "*Recombinate 1000 UI/10 ml polvere e solvente per soluzione iniettabile - 1 flaconcino di polvere + 1 flaconcino di solvente con dispositivo di ricostituzione senza ago*" or any other components in the pack.**

- **Takeda will provide replacement BAXJECT II and BAXJECT II Hi-Flow reconstitution devices to those healthcare professionals who have received devices from the impacted batches listed below.**

- **If you require additional devices, please contact the distributor who provides you with "*Recombinate 1000 UI/10 ml polvere e solvente per soluzione iniettabile - 1 flaconcino di polvere + 1 flaconcino di solvente con dispositivo di ricostituzione senza ago*".**

- **BAXJECT II and BAXJECT II Hi-Flow reconstitution devices contained within the below-listed batches should be discarded and the replacement devices should be used for the reconstitution of the "*Recombinate 1000 UI/10 ml polvere e solvente per***

***soluzione iniettabile - 1 flaconcino di polvere + 1 flaconcino di solvente con dispositivo di ricostituzione senza ago*", as instructed in the Product Information.**

- **In case of any delays in receiving replacement devices and if a healthcare professional or patient is in possession of a device from an impacted batch, they should be advised to continue administering the medicinal products using the devices in their possession. Instructions for use should be carefully followed, including inspecting for particulate matter prior to administration. In case of identification of particulate matter, the medicine should not be used.**

- **Healthcare professionals should provide the required number of replacement devices with a copy of *Appendix 1, Instructions for patients who self-administer,* included below, to patients who are self-administering the medicine and are in possession of devices from the impacted batches.**

Nome Prodotto	Dosaggio	Numero di lotto	Data di scadenza
Recombinate	**1000 UI/10ml**	**LE04X808AH**	**31.10.2024**
Recombinate	**1000 UI/10 ml**	**LE04X808AJ**	**31.10.2024**

Background

Recombinate 1000 UI/10 ml is co-packaged with the BAXJECT II / BAXJECT II Hi-Flow device that is used for reconstituting the medicinal product prior to administration.

Takeda has decided to voluntarily replace BAXJECT II and BAXJECT II Hi-Flow reconstitution devices produced at Takeda's contract device manufacturer between October 2021 and January 2022 for use in conjunction with Recombinate 1000 UI/10 ml.

This is a precautionary measure and is due to the potential presence of particulate matter in the luer port of the BAXJECT II / BAXJECT Hi-Flow reconstitution device co-packaged with the medicinal products mentioned

below (See Image in Appendix 1). There has been a small number of complaints **for the BAXJECT II device** that concern the presence of particulate matter before administration.

It is important to note that there is no quality issue with Recombinate 1000 UI/10 ml medicine itself. No particulate matter has been identified in the active product or water for injection (WFI) diluent. The safety profiles of all products remain consistent with the product labels. There have been no adverse events identified that were attributable to the presence of particles in the BAXJECT II / BAXJECT II Hi-Flow devices in our Global Safety databases.

To ensure that patients can continue to receive their needed therapies, **it is important that you carefully read the instructions below and follow them when you are administering these medicinal products.** Additionally, ensure that you communicate these instructions clearly to all patients who self-administer the products or their caregivers, by provision of *Appendix 1: Instructions for patients who self-administer*.

No other products or devices in the Takeda portfolio are impacted by this particle issue in Italy.

Replacement of Impacted Devices
Takeda will provide replacement BAXJECT II / BAXJECT II Hi-Flow reconstitution devices to the Healthcare Professionals who have received impacted batches.

Please carefully follow the below instructions to allow patients to continue their treatment using the replacement devices. If awaiting replacement devices and in possession of devices from an impacted batch, patients should be advised to continue using the devices in their possession. Instructions for use should be carefully followed, including inspecting for particulate matter prior to administration. If you require additional devices, please contact the distributor who provides you with **Recombinate 1000 UI/10 ml.**

For Healthcare Professionals who use devices from the impacted batches on patients:

1. You will receive sufficient quantity of replacement devices to cover the number of units of drug product you have received. Please store the replacement devices alongside the product (in a refrigerator if applicable).
2. Please ensure you carefully follow the instructions for use of the medicine.
3. When prompted in the instructions to open the package of BAXJECT II or BAXJECT II Hi-Flow device, **discard the device co-packed with the**

finished product and substitute it with the replacement device you have received.

4. Follow the remaining instructions for reconstitution and administration of the medicine.
5. In case of any delays in receiving replacement devices, you should continue administering the medicinal products using the devices in your possession. Instructions for use should be carefully followed, including inspecting for particulate matter prior to administration.

For Healthcare Professionals who dispense the above-listed batches to patients for self-administration:

5. In case you are dispensing a unit of one the above-listed batches, ensure that, upon dispensing to the patient or caregiver, they are made aware of the situation, provided with a replacement BAXJECT II or BAXJECT II Hi-Flow device and provided with a copy of *Appendix 1: Instructions for Patients who self-administer.*

6. For patients who have already been dispensed a unit of the above-listed batches, contact those patients to establish if they have any unused devices remaining. If they do, please arrange provision of the required number of replacement devices, plus a copy of *Appendix 1: Instructions for Patients who Self-administer.*

Takeda is committed to supply with integrity, and we are working closely with the AIFA to ensure continuity of supply for patients. We understand and sincerely regret the impact this issue has on patients and healthcare professionals.

Call for Reporting

Healthcare professionals and patients are encouraged to report adverse reactions and/or quality problems related to the BAXJECT II / BAXJECT II Hi-flow reconstitution device, used in combination with **Recombinate 1000 UI/10 ml** to Takeda (AE.ITA@takeda.com) and/or AIFA(https://www.aifa.gov.it/content/segnalazioni-reazioni-avverse)

Appendix 1: Patient/Caregiver Instructions on use of the replacement BAXJECT II and BAXJECT II Hi-Flow reconstitution devices

As a precautionary measure after receiving a small number of complaints, Takeda has decided to voluntarily replace BAXJECT II and BAXJECT II Hi-Flow reconstitution devices produced at Takeda's contract device manufacturer between October 2021 and January 2022, for use with <insert product names per market> .

The issue only affects the BAXJECT II / BAXJECT II Hi-Flow reconstitution devices (see images below) and not the medicine that is co-packed with it. All complaints received concern the presence of the particles in the luer port of the device before administration.

BAXJECT II Device

BAXJECT II Hi-flow Device

The medicinal product itself and diluent is not affected by any quality issues. No particles have been found in the active product or diluent. The safety profiles of all products remain consistent with the product labels.

To ensure that you can continue to use your medicine, you will be provided with replacement reconstitution devices by your doctor or pharmacist.

If you were given one of the below-listed batches of <insert product names per market> medicinal products, read this section carefully before you use this medicine, because it contains important information for you.

Instructions on how to use the Replacement BAXJECT II or BAXJECT II Hi-Flow Reconstitution Device

1. Your doctor or pharmacist will contact you if you have received a product pack containing a BAXJECT II or BAXJECT II Hi-flow device from the below-listed batches.

   When you are given a product pack from the below-listed batches or if you already have them in your possession, your doctor or pharmacist will give

you the required number of replacement BAXJECT II or BAXJECT II Hi-flow devices.

2. The replacement devices should be stored with the medicine, in the fridge if required. Keep these instructions, you may need to read them again. Please make sure you carefully follow the instructions for use in the package leaflet for the product before you use this medicine.
3. When you reach the step in the instructions that asks you to open the package of BAXJECT II or BAXJECT II Hi-Flow device, **discard the device in the pack and replace it with the new device given to you by your doctor or pharmacist.**
4. Follow the remaining instructions for reconstitution and administration of the medicine in the package leaflet.
5. If you are awaiting replacement devices and in possession of devices from an impacted batch, you should continue to use the devices in your possession. Instructions for use should be carefully followed, including inspecting for particulate matter prior to administration. In case of identification of particulate matter, the medicine should not be used.

<LOC to tabulate Product Batches impacted in their country>

Please contact <insert Country> Medical Affairs at Takeda at <Insert relevant number> if you have any questions.

Takeda is committed to supply with integrity and we are working to ensure continuity of supply for patients. We understand and sincerely regret the impact this issue has on patients.

Reporting Side Effects
Healthcare providers and patients are encouraged to report side effects and/or quality problems related to the BAXJECT II / BAXJECT II Hi-flow reconstitution device, used in combination with <insert product names> to Takeda <adapt according to country> and/or the <national competent authority>.

Medical Information
You may also contact our medical information department at <adapt according to country> if you have any questions about the information contained in this letter or the safe and effective use of <insert product names>.

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substances	ADVATE (octocog alfa), FEIBA (Factor VIII Inhibitor Bypassing Activity), RECOMBINATE (octocog alfa) and RIXUBIS (nonacog gamma)
Marketing authorisation holder(s)	ADVATE: Takeda Manufacturing Austria AG, Industriestrasse 67, A-1221 Vienna, Austria RIXUBIS: Baxalta Innovations GmbH Industriestrasse 67, A-1221 Vienna, Austria
Safety concern and purpose of the communication	Replacement of the BAXJECT II and BAXJECT II Hi-flow reconstitution particles due to potential presence of particles
DHPC recipients	Hospital and community pharmacists, hospital and other healthcare professionals dispensing or administering the involved products. Appendix 1, for patients who self-administer
Member States where DHPC will be distributed	In all EEA member states where ADVATE, FEIBA, RECOMBINATE or RIXUBIS are distributed, whether commercially or via clinical trials or named patient programs

Timetable	**Date**
DHPC and communication plan (in English) agreed by CHMP	1st August, 2023
Submission of translated DHPCs to national competent authorities for review	4th August, 2023
Agreement of translations by national competent authorities	10th August, 2023
Dissemination of DHPC	14th August, 2023