Better Health, Brighter Future

31 August 2023

Direct Healthcare Professional Communication (DHPC)

Replacement BAXJECT II / BAXJECT II Hi-Flow Reconstitution Devices co-packaged with ADVATE or FEIBA

Product Name	Marketing Authorisation Number	Market	Batch Number	Expiry date
ADVATE 250 IU powder and solvent for solution for injection (5ml)	PLGB 06009/0029	Great Britain	BE17C208AA	01/2024
ADVATE 500 IU powder and solvent for solution for injection (5ml)	PLGB 06009/0032	Great Britain	BE01C525AC	03/2024
ADVATE 1000 IU powder and solvent for solution for injection (5ml)	PLGB 06009/0024	Great Britain	BE01C001AD	12/2023
ADVATE 1000 IU powder and solvent for solution for injection (5ml)	PLGB 06009/0024	Great Britain	BE17C205AC	01/2024
ADVATE 1500 IU powder and solvent for solution for injection (5ml)	PLGB 06009/0026	Great Britain	BE01C512AG	01/2024
ADVATE 2000 IU powder and solvent for solution for injection (5ml)	PLGB 06009/0027	Great Britain	BE17C209AC	01/2024
ADVATE 3000 IU powder and solvent for solution for injection (5ml)	PLGB 06009/0030	Great Britain	BE01C533AB	04/2024
ADVATE 1500 IU powder and solvent for solution for injection (5ml)	EU/1/03/271/004	Northern Ireland	BE01C002AM	12/2023
ADVATE 1500 IU powder and solvent for solution for injection (5ml)	EU/1/03/271/004	Northern Ireland	BE01C512AK	01/2024
ADVATE 500 IU powder and solvent for solution for injection (2ml)	EU/1/03/271/008	Northern Ireland	BE01C514AH	01/2024
ADVATE 500 IU powder and solvent for solution for injection (5ml)	EU/1/03/271/002	Northern Ireland	BE01C514AJ	01/2024
ADVATE 250 IU powder and solvent for solution for injection (2ml)	EU/1/03/271/007	Northern Ireland	BE01C502AP	12/2023
ADVATE 250 IU powder and solvent for solution for injection (2ml)	EU/1/03/271/007	Northern Ireland	BE01C518AM	01/2024
ADVATE 250 IU powder and solvent for solution for injection (2ml)	EU/1/03/271/007	Northern Ireland	BE17C208AC	01/2024
ADVATE 250 IU powder and solvent for solution for injection (5ml)	EU/1/03/271/001	Northern Ireland	BE01C518AN	01/2024
ADVATE 250 IU powder and solvent for solution for injection 5ml)	EU/1/03/271/001	Northern Ireland	BE17C208AD	01/2024
FEIBA 50 U/ml powder and solvent for solution for infusion (500 U)	PL 34078/0003	United Kingdom	F2X013AA	03/2024

Takeda UK Limited
Registered office: 1 Kingdom Street, London, W2 6BD, United Kingdom
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www.takeda.com/en-gb
Registered in England & Wales No. 03362860

Dear Healthcare professional,

Takeda UK Limited (acting on behalf of Takeda Manufacturing Austria AG and Baxalta Innovations GmbH), in agreement with the Medicines and Healthcare products Regulatory Agency (MHRA), 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 certain batches of ADVATE and FEIBA.**

- **This is a precautionary measure and is due to the potential presence of particulate matter in the luer port of certain batches of the BAXJECT II / BAXJECT Hi-Flow reconstitution device. The issue is linked to the device and there is no quality issue with the medicine ADVATE or FEIBA or any other components in the pack.**

- **Takeda will provide replacement BAXJECT II and BAXJECT II Hi-Flow reconstitution devices to healthcare professionals who have received devices from the impacted batches (see list provided above).**

- **If you require additional devices, please contact Alloga UK Limited.**

- **BAXJECT II and BAXJECT II Hi-Flow reconstitution devices contained within the above listed batches should be discarded. Please use the replacement devices for the reconstitution of ADVATE or FEIBA, 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 are advised to continue administering the medicinal products using the devices in their possession. Instructions for use should be followed carefully, including inspecting for particulate matter prior to administration. If you identify particulate matter, do not use the medicine.**

- **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.**

Background

ADVATE is co-packaged with the BAXJECT II reconstitution device and FEIBA is co-packaged with the BAXJECT II Hi-Flow reconstitution device, used to reconstitute a medicinal product prior to administration.

Takeda has decided to voluntarily replace certain 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 ADVATE and FEIBA.

This is a precautionary measure and is due to the potential presence of particulate matter in the luer port of certain batches of the BAXJECT II / BAXJECT II Hi-Flow reconstitution device co-

packaged with the medicinal products ADVATE and FEIBA (See Images in Appendix 1). There has been a small number of complaints **regarding 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 either the ADVATE or FEIBA 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 continue to receive their medication, **it is important that you read the instructions below carefully 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 particulate issue in the United Kingdom.

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

Please follow the instructions below carefully 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 followed carefully, including inspecting for particulate matter prior to administration.

If you require replacement devices to cover the remaining stock in your possession, please contact Customer Services at Alloga UK Limited to request delivery of replacement devices. Alloga item code APC0890 for a replacement BAXJECT II reconstitution device used with ADVATE, and APC0883 for a replacement BAXJECT II Hi-Flow reconstitution device used with FEIBA, should be quoted on all requests to Alloga UK Limited.

Advice for healthcare professionals who administer the above listed batches to patients:

1. When you order replacement devices, you will receive them within three (3) days as a standard delivery or next day for urgent deliveries to cover the number of units of medicine you have remaining in stock. Please store the replacement devices alongside the product (in a refrigerator if applicable).
2. Please ensure that you follow the instructions for use of the medicine carefully.
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 medicine 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. Follow the

instructions for use carefully, including inspecting for particulate matter prior to administration.

Advice for healthcare professionals who dispense the above listed batches to patients for self-administration:

6. If you are dispensing a unit of one the above listed batches, please ensure that, you inform the patient or caregiver of the situation, and provide them with a replacement BAXJECT II or BAXJECT II Hi-Flow device and a copy of *Appendix 1: Instructions for Patients who self-administer.*
7. Contact patients who have already been dispensed a unit of the above listed batches and 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 Medicines and Healthcare products Regulatory Agency (MHRA) to ensure continuity of supply for patients. We understand and sincerely regret the impact of this issue on patients and healthcare professionals.

Call for reporting
Please report suspected adverse drug reactions (ADRs) or suspected defective medicines to the MHRA through the Yellow Card scheme.

You can report via:

- the Yellow Card website: www.mhra.gov.uk/yellowcard
- the free Yellow Card app available from the Apple App Store or Google Play Store
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals.

Alternatively, you can report a suspected side effect to the Yellow Card scheme by calling 0800 7316789 for free, Monday to Friday between 9am and 5pm.

Healthcare professionals can also report any suspected adverse reactions associated with the use of ADVATE or FEIBA to Takeda UK Ltd via: AE.GBR-IRL@takeda.com

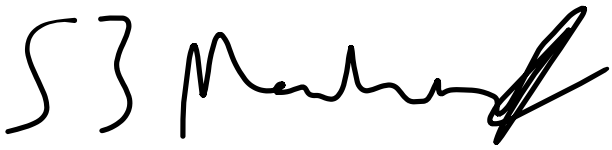
Company Contact Point

Dr Simon Meadowcroft
Medical Director UK & Ireland
Mobile: +44 (0)7766 526 793
1 Kingdom Street
London W2 6BD

Takeda UK Ltd. Medical Information e-mail:
medinfoemea@takeda.com
Med Info. direct line: +44 (0) 3333 000 181
Drug safety e-mail:
AE.GBR-IRL@Takeda.com

Should you have any queries regarding this notification, please contact Takeda using the details provided above.

Yours sincerely,



Dr Simon Meadowcroft
Medical Director UK & Ireland
Takeda UK
BSc MBChB (hons) MRCGP MFPM

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 certain 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 ADVATE or FEIBA.

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.

The issue only affects certain batches of 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 water for injection (WFI) diluent is not affected by any quality issues. No particles have been found in the active drug product or WFI 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 batches of ADVATE or FEIBA medicinal products listed below, 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. Keep these instructions, you may need to read them again.
2. 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 batches listed below. When you are given a product pack from the batches listed below, 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.
3. The replacement devices should be stored with the medicine, in the fridge if required. Please make sure you carefully follow the instructions for use in the package leaflet for the product before you use your medicine.

4. 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.**
5. Follow the remaining instructions for reconstitution and administration of the medicine in the package leaflet.
6. 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. Follow the instructions for use carefully, including inspecting for particulate matter prior to administration. If you identify particulate matter, do not use the medicine.

Impacted batches

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ADVATE 500 IU powder and solvent for solution for injection (2ml)	EU/1/03/271/008	Northern Ireland	BE01C514AH	01/2024
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ADVATE 250 IU powder and solvent for solution for injection (2ml)	EU/1/03/271/007	Northern Ireland	BE17C208AC	01/2024
ADVATE 250 IU powder and solvent for solution for injection (5ml)	EU/1/03/271/001	Northern Ireland	BE01C518AN	01/2024
ADVATE 250 IU powder and solvent for solution for injection 5ml)	EU/1/03/271/001	Northern Ireland	BE17C208AD	01/2024
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Medical Information
You may also contact Takeda medical information department on direct phone line: +44 (0) 3333 000 181 or email medinfoemea@takeda.com if you have any questions about the information contained in this letter or the safe and effective use of ADVATE or FEIBA.