05 Sept 2023

Direct Healthcare Professional Communication (DHPC)

Subject: ADVATE 500 IU, MID, BAXJECT II - Replacement BAXJECT II Reconstitution Devices co-packaged with AfDVATE 500 IU, MID, BAXJECT II

ADVATE 500 IU, MID, BAXJECT II batch number: BE01C525AN & BE01C515AG

Dear Healthcare Professional,

Takeda, in agreement with the Saudi Food and Drug Authority, would like to inform you of the following:

Summary

- **Takeda has decided to voluntarily replace BAXJECT II reconstitution devices produced at Takeda's contract device manufacturer between October 2021 and January 2022, co-packaged for use in conjunction with ADVATE 500 IU, MID, BAXJECT II - batch number: BE01C525AN & BE01C515AG.**
- **Takeda will provide replacement BAXJECT II reconstitution devices to those Healthcare Professionals who have received the impacted batches listed above.**
- **If you require additional devices, please contact the distributor who provides you with ADVATE 500 IU, MID, BAXJECT II**
- **BAXJECT II reconstitution devices contained within the above-listed batches should be discarded and the replacement devices should be used for the reconstitution of the powder with the provided solvent, as instructed in the Product Information**
- **In case of any delays in receiving replacement devices and if a patient is in possession of an impacted lot, the patient should be advised that they should continue to administer 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.**
- **There is no quality issue with the ADVATE 500 IU drug products or any other components in the pack**
- **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 medicinal product and are in possession of the impacted lots**

Background

ADVATE 500 IU may be co-packaged with the BAXJECT II device that is used for reconstituting the medicinal product prior to administration.

Takeda has decided to voluntarily replace BAXJECT II reconstitution devices produced at Takeda's contract device manufacturer between October 2021 and January 2022, for use in conjunction with ADVATE 500 IU in KSA -- batch number: BE01C525AN & BE01C515AG.
This is a precautionary measure and is due to a potential issue, related to particulate matter that originates in the luer port of the BAXJECT II reconstitution device co-packaged with the medicinal products mentioned above (See Image in Appendix 1). There has been a small number of complaints **for the BAXJECT II device** that have reported the presence of the particulate matter before administration.

It is important to note that there is no quality issue with the ADVATE 500 IU drug product itself. No particulate matter has been identified in the active product or 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 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 ADVATE 500 IU in KSA.

Replacement of Impacted Devices
Takeda will provide replacement BAXJECT II reconstitution devices to the Healthcare Professionals who have received impacted lots.

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 an impacted lot, patients should be advised that they should continue to administer the medicinal products using the devices in their possession. If you require additional devices, please contact the distributor who provides you with ADVATE 500 IU.

For Healthcare Professionals who administer the impacted batches to patients:

1. You will receive a 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 drug product.

3. When prompted in the instructions to open the package of BAXJECT II 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 drug product
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:

6. 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 and provide them with a copy of *Appendix 1: Instructions for Patients who Self-administer*

7. For patients who have already been dispensed the above-listed lots, contact those patients to establish if they have any unused units 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 Saudi Food and Drug Authority 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 reconstitution device, used in combination with ADVATE 500 IU to **Takeda LOC at:**

E-mail: AE.SaudiArabia@takeda.comand PQC@takeda.com
Mobile: +966549993493
Website: https://www.takeda.com/worldwide/saudi-arabia/

SFDA National Pharmacovigilance and Drug Safety Center (NPC):
SFDA National Pharmacovigilance Center (NPC):
SFDA call center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa

Company Contact Point

You may also contact our medical information department at Amer Alsiddik Amer.ALSIDDIK@takeda.com if you have any questions about the information contained in this letter or the safe and effective use of ADVATE 500 IU.

Sincerely,

Rasha Elbohi

Quality Lead – Middle East Cluster

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

As a precautionary measure after receiving a small number of complaints, Takeda has decided to voluntarily replace BAXJECT II reconstitution devices at Takeda's contract device manufacturer between October 2021 and January 2022, for use with **ADVATE 500 IU - batch number: BE01C525AN & BE01C515AG.**

The issue only affects the BAXJECT II reconstitution devices (see images below). These devices are included inside the medicinal product pack of the above products. All complaints received have reported the presence of the particles before administration.

BAXJECT II 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 needed therapies, you will be provided with replacement reconstitution devices by your doctor or pharmacist.

If you were given one of the batches of ADVATE 500 IU - batch number: BE01C525AN & BE01C515AG medicinal products, read all the information carefully before you use this medicine because it contains important information for you.

Instructions on how to use the Replacement Baxject II Reconstitution Device

1. Your doctor or pharmacist will contact you if you have received a product pack containing a BAXJECT II device from the above listed batches.
2. If you still have any unused devices with you, your doctor or pharmacist will give you the required number of replacement BAXJECT II devices
3. If you will receive a product pack from the above-listed batches, your doctor or pharmacist will provide the required number of replacement devices with the drug product
4. The replacement devices should be stored with the drug product, 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.
5. When you reach the step in the instructions that asks you to open the package of Baxject II device, **discard the device in the pack and replace it with the new device given to you by your doctor or pharmacist**
6. Follow the remaining instructions for reconstitution and administration of the drug product in the package leaflet

Please contact KSA Medical Affairs at Takeda Amer.ALSIDDIK@takeda.com 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 reconstitution device, used in combination with ADVATE 500 IU - batch number: BE01C525AN & BE01C515AG to

Takeda KSA LOC at:
Email: AE.SaudiArabia@takeda.com
Mobile: +966549993493
Website**:** https://www.takeda.com/worldwide/saudi-arabia/

SFDA National Pharmacovigilance and Drug Safety Center (NPC):
SFDA call center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa

Medical Information
You may also contact our medical information department at Amer Alsiddik Amer.ALSIDDIK@takeda.com if you have any questions about the information contained in this letter or the safe and effective use of ADVATE 500 IU.

الملحق 1: تعليمات المريض / مقدم الرعاية حول استخدام أجهزة إعادة التكوين BAXJECT II البديلة

كإجراء وقائي بعد تلقي عدد صغير من الشكاوى ، قررت تاكيدا استبدال أجهزة إعادة تكوين BAXJECT II طواعية لدى الشركة المصنعة لجهاز تاكيدا المتعاقد عيه في الفترة ما بين أكتوبر 2021 ويناير 2022, لاستخدامها مع:
- ADVATE 500 IUرقم الدفعة BE01C525AN :وBE01C515AG

تؤثر المشكلة فقط على أجهزة إعادة التكوين BAXJECT II (انظر الصور أدناه). يتم تضمين هذه الأجهزة داخل باقة المنتجات الطبية للمنتجات المذكورة أعلاه. أبلغت جميع الشكاوى الواردة عن وجود الجسيمات قبل الإعطاء

جهاز BAXJECT II

لا يتأثر المنتج الطبي نفسه والمخفف بأي مشاكل تتعلق بالجودة. لم يتم العثور على جزيئات في المنتج النشط أو المادة المخففة. تظل ملفات تعريف السلامة لجميع المنتجات متسقة مع ملصقات المنتج.

للتأكد من أنه يمكنك الاستمرار في استخدام العلاجات التي تحتاجها ، سيتم تزويدك بأجهزة إعادة التكوين البديلة من قبل طبيبك أو الصيدلي.

إذا تم إعطاؤك إحدى دفعات ADVATE 500 IU - رقم الدفعة: BE01C525ANوBE01C515AG المنتجات الطبية, اقرأ جميع المعلومات بعناية قبل استخدام هذا الدواء لأنه يحتوي على معلومات مهمة لك.

تعليمات حول كيفية استخدام جهاز إعادة التكوين BAXJECT II البديل:

1. سيتواصل معك طبيبك أو الصيدلي إذا تلقيت باقة منتج تحتوي على جهاز BAXJECT II من الدفعات المذكورة أعلاه.
2. إذا كان لا يزال لديك أي أجهزة غير مستخدمة معك ، فسوف يمنحك طبيبك أو الصيدلي العدد المطلوب من أجهزة BAXJECT II البديلة
3. إذا كنت ستتلقى باقة منتج من الدفعات المذكورة أعلاه ، فسيوفر طبيبك أو الصيدلي العدد المطلوب من الأجهزة البديلة مع منتج الدواء
4. يجب تخزين الأجهزة البديلة مع منتج الدواء ، في الثلاجة إذا لزم الأمر. احتفظ بهذه التعليمات ، قد تحتاج إلى قراءتها مرة أخرى. يرجى التأكد من اتباع تعليمات الاستخدام الموجودة في نشرة العبوة للمنتج بعناية قبل استخدام هذا الدواء.
5. عندما تصل إلى الخطوة في التعليمات التي تطلب منك فتح باقة جهاز Baxject II, تخلص من الجهاز الموجود في العبوة واستبدله بالجهاز الجديد الذي أعطاه لك الطبيب أو الصيدلي
6. اتبع التعليمات المتبقية لإعادة تكوين وإعطاء المنتج الدوائي في نشرة العبوة

يرجى الاتصال بالشؤون الطبية بتاكيدا على Amer.ALSIDDIK@takeda.com إذا كان لديك أي أسئلة.

تلتزم تاكيدا بالإمداد بنزاهة ونحن نعمل على ضمان استمرارية الإمداد للمرضى. نحن نفهم ونأسف بصدق لتأثير هذه المشكلة على المرضى.

الإبلاغ عن الآثار الجانبية
يتم تشجيع مقدمي الرعاية الصحية والمرضى على الإبلاغ عن الآثار الجانبية و / أو مشاكل الجودة المتعلقة بجهاز إعادة التكوين BAXJECT II ، المستخدم مع ADVATE 500 IU - رقم الدفعة: BE01C525AN & BE01C515AG
إلى تاكيدا السعودية عن طريق
الايميل: AE.SaudiArabia@takeda.com
رقم الهاتف: +966549993493
الموقع الإلكتروني: **https://www.takeda.com/worldwide/saudi-arabia/**

المركز الوطني للتيقظ والسلامة الدوائية
مركز الاتصال الموحد: 19999
الإيميل: npc.drug@sfda.gov.sa
الموقع الإلكتروني: https://ade.sfda.gov.sa

معلومات طبية
يمكنك أيضًا الاتصال بقسم المعلومات الطبية لدينا على Amer.ALSIDDIK@takeda.com إذا كان لديك أي أسئلة حول المعلومات الواردة في هذه الرسالة أو الاستخدام الآمن والفعال لـ ADVATE 500 IU.