Department of Health & Social Care

NHS

Supply Disruption Alert

SDA/2019/010 Issued: 29 November 2019 Valid until: 31 January 2020

Emerade® 150 microgram, 300 microgram and 500 microgram adrenaline auto-injector devices

Summary

All Emerade® devices will be unavailable for the foreseeable future. On 28 November, the Medicines and Healthcare products Regulatory Agency (MHRA) issued a Class 2 recall to pharmacy level. No further stocks of Emerade® in all three strengths of 150 microgram, 300 microgram and 500 microgram will be available from this date.

More information is provided in the following link:

https://www.gov.uk/drug-device-alerts/class-2-medicines-recall-emerade-150-300-and-500-microgram-solution-for-injection-in-pre-filled-syringe-mdr-57-08-19?utm_source=01649e53-38ae-49a1-a229-1847087b536b&utm_medium=email&utm_campaign=govuk-notifications&utm_content=immediate

The following management plan has been developed in collaboration with NHS England and NHS Improvement (NHSE&I), the British Society for Allergy & Clinical Immunology (BSACI), the MHRA and National patient groups.

Action

All health care professionals in primary, secondary or specialist healthcare services who prescribe, supply or administer adrenaline auto-injectors (AAIs), or who advise patients and their carers, should ensure that:

1. when patients next request a prescription, they **are reviewed** to ensure their AAI prescription is still appropriate in line with existing guidance (see page 4 for further detail).

2. prescribers issue no more than **two** AAIs per patient (of any brand or strength) unless:
    a. schools require separate AAI(s) to be kept on the school premises (e.g. in a medical room) in which case prescribers may need to consider issuing more than two but no more than four AAIs per child (of any brand or strength). See further information on the use of AAIs in school, page 4;
    b. for the rare scenario where patients might need more than two AAIs prescribed (for example, prior severe reaction resistant to treatment with adrenaline), the prescriber may issue additional AAIs.

3. patients who require replacements for:

    a. expired or used Emerade® **500 microgram** AAIs, prescribers should ensure that:

- the expired or used device is replaced with **one** 300 microgram AAI device of an alternative brand (EpiPen®/Jext®) for each expired Emerade® device;
- on rare occasions at the clinical judgement of the prescribing clinician, consideration is given to prescribing of a vial of adrenaline to be drawn up by the patient for self-administration via the intramuscular route. It should be recognised that although this would allow administration of a dose larger than 300 microgram per injection, use of ampoules will require specific training;

b. expired or used Emerade® **150 microgram** or **300 microgram** AAIs, prescribers should ensure that:

- the expired or used device is replaced with **one** AAI device of an alternative brand (EpiPen®/Jext®) at the same strength for each expired Emerade® AAI;

c. in-date Emerade® AAIs, patients should:

- continue to use the device(s) as instructed until the expiry date at the end of the month listed on the product.

4. adrenaline ampoules, as opposed to AAIs, are stocked when renewing the adrenaline in anaphylaxis kits (ensuring dosing charts, needles and syringes are included).

5. **patients are reminded**:
   - that they should always carry **two** in-date AAIs and are trained in their use (further advice is provided on page 5);
   - not to expose any brand of AAI to temperatures above 25°C. Storage above 25°C may increase the likelihood of a fault occurring with Emerade® AAIs;
   - to ask their healthcare professional to check to see if they currently hold one of the EpiPen®/Jext® batches that can be used beyond the listed expiry (see below*). If one of the listed batches is held, further supplies should be delayed until the extended expiry date;
   - to use their device(s) as instructed until the expiry date/extended expiry date. N.B. a device expiring in 'March 2020' does not expire until 31 March 2020; and
   - of the signs of anaphylaxis and the actions they should immediately take (see Management of Anaphylaxis for further advice).

Please note:

the MHRA has approved the extension of expiry dates for specific batches of EpiPen® 300 micrograms and Jext® 150 micrograms and 300 micrograms by four months beyond the labelled expiry date. Information on the specific batches that can have their original expiry date extended can be found on the company websites:

Mylan UK: http://www.epipen.co.uk/
ALK-Abello Ltd: https://jext.co.uk/

Deadlines for actions

Actions initiated: on receipt of this alert
Actions completed: 31 January 2020

Product details

Emerade® 150 micrograms (adrenaline tartrate) solution for injection in pre-filled pen.
Emerade® 300 micrograms (adrenaline tartrate) solution for injection in pre-filled pen.
Emerade® 500 micrograms (adrenaline tartrate) solution for injection in pre-filled pen.

Problem / background

Further to Caution in Use Drug Alerts issued on 11 July and 2 October 2019 by the MHRA, the current issue affecting all strengths of Emerade® AAIs globally is caused by an error in one component of the AAI which can cause some devices to fail to activate as intended. This error may under some circumstances, such as exposure to high temperature, cause misalignment of two components, and could potentially lead to failure to activate, even if higher activation force is used. The MHRA has therefore taken the decision to issue a Class

2 recall to pharmacy level so that no further potentially defective Emerade® AAIs are supplied to patients. More information is provided in the following link:

https://www.gov.uk/drug-device-alerts/class-2-medicines-recall-emerade-150-300-and-500-microgram-solution-for-injection-in-pre-filled-syringe-mdr-57-08-19?utm_source=01649e53-38ae-49a1-a229-1847087b536b&utm_medium=email&utm_campaign=govuk-notifications&utm_content=immediate

Patients who require a replacement for an Emerade® AAI that has expired or been used will therefore need to be prescribed an AAI of an alternative brand (Epipen®/Jext®). Many patients are supplied with AAIs from the same batch that have concurrent shelf-lives that will expire at the same time. These patients will therefore be switched completely to a new brand.

For those patients who require a single expired AAI to be replaced, owing to the supply situation it is not possible to replace this with two AAIs of a different brand. Therefore, these patients will, for a period of time, be carrying two AAIs of different types. It is important that they and their caregiver are confident in the way each AAI is used and they should decide in advance which type of AAI they feel most confident to administer as the first AAI to be used in an anaphylactic emergency.

The advice to continue using Emerade® AAIs until the expiry date has been given in order to avoid a serious shortage of AAIs for the wider patient community. The MHRA and Department of Health and Social Care (DHSC) consider that the risk of not having an AAI is much higher than having an AAI that may not activate.

In the UK there are two alternative AAI devices available, EpiPen®, supplied by Mylan and Jext®, supplied by ALK-Abello. Neither of these companies supply a 500 microgram strength AAI. Both companies manufacture 150 microgram and 300 microgram AAI devices are aware of the supply disruptions affecting Emerade®. Jext® and EpiPen® AAIs are currently available in quantities sufficient to support the Emerade® shortage going forward, however, there are insufficient supplies to replace all Emerade® AAIs already held by patients.

The advice from national experts is that, in the absence of an Emerade® 500 microgram, affected patients should be prescribed a 300 microgram AAI and, as per existing guidance, advised to keep **two** AAIs with them at all times. Patients and prescribers can be confident in the safety and effectiveness of Epipen® and Jext® 300 microgram as alternatives to Emerade® 500 microgram. Prescribers can find more information in the Summary of Product Characteristics for the Epipen® and Jext® devices.

To ensure equitable distribution, suppliers have put management processes in place to control stock. The EpiPen® range remains on a prescription validation protocol. As per the EpiPen® website, pharmacies presented with a prescription for EpiPen® or EpiPen® Junior can place an order for up to a maximum of two AAIs per prescription. Anonymised prescriptions should be sent to Alliance Healthcare's prescription validation service, either by fax (0330 332 8126) or email (scriptvalidation@alliance-healthcare.co.uk) and should include the pharmacies Alliance Healthcare account number.

The supplier of Jext® has also placed quotas on the number of devices that can be obtained by each community pharmacy per day or per month. If the pharmacy exceeds this limit and is presented with a prescription for an AAI, they are able to contact the company directly, who may approve further supplies.

Management of anaphylaxis

All patients should be made aware of the signs of anaphylaxis and reminded that at the onset of symptoms of anaphylaxis, they should:

- use an AAI device immediately;
- call an ambulance (**999**) immediately or send someone to do this. Say this is an emergency case of anaphylaxis*;

- await the response to the first AAI, before administering a second AAI 5 minutes after the initial dose, if no improvement is seen;
- use a second AAI immediately if an Emerade® AAI fails to activate despite pressing firmly against the thigh (see page 5 of Class 2 Medicines Recall Emerade for further info); and
- make further attempts to activate a failed AAI while waiting for the ambulance if the patient is not improving, suggesting a need for a second dose.

*Please note - ambulances carry adrenaline 1mg/1ml (1 in 1,000) ampoules, which are not affected by the shortage.

Existing Guidance

This section summarises the existing guidance that the actions are based on. It is intended as an easy reference summary of the existing guidance. All prescribers should review current guidance for when to prescribe AAIs for adults and children that has been developed by the Standards of Care Committee (SOCC) of the British Society for Allergy and Clinical Immunology (BSACI) and the MHRA, and also refer to the guidance in BNF and training material provided by manufacturers as appropriate.

https://www.bsaci.org/Guidelines/adrenaline-auto-injector

Regulatory advice for two AAIs as the norm for most patients, once a need for an AAI prescription has been confirmed, should continue to be adhered to:

https://www.gov.uk/drug-safety-update/adrenaline-auto-injectors-updated-advice-after-european-review

https://assets.publishing.service.gov.uk/media/5b644e25ed915d377695c83d/AAI-PDF-v4.pdf

Guidance on the use of AAIs in schools
For more information on the use of AAIs in schools, see the link below:

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/645476/Adrenaline_auto_injectors_in_schools.pdf

Children at risk of anaphylaxis should have their prescribed AAI(s) at school for use in an emergency. The MHRA recommends that those prescribed AAIs should carry **two** devices at all times.

Depending on their level of understanding and competence, children and particularly teenagers should carry their AAI(s) on their person at all times or they should be quickly and easily accessible at all times. If the AAI(s) are not carried by the pupil, then they should be kept in a central place in a box marked clearly with the pupil's name but NOT locked in a cupboard or an office where access is restricted.

It is not uncommon for schools (often primary schools) to request a pupil's AAI(s) are left in school to avoid the situation where a pupil or their family forgets to bring the AAI(s) to school each day. Where this occurs, the pupil must still have access to an AAI when travelling to and from school.

Consider if the initial prescription of AAIs is appropriate
Patients at risk of anaphylaxis that should be considered for long-term provision of an AAI include those:

- who are allergic to high-risk allergens, for example nuts with other risk factors (such as asthma), even if the reaction was relatively mild
- who had a reaction in response to trace amounts of allergen/trigger
- who cannot easily avoid the allergen
- with continuing risk of anaphylaxis (e.g. food dependent, exercise-induced)
- with idiopathic anaphylaxis

- with significant co-factors (e.g. raised baseline serum tryptase)

The decision to prescribe requires a tailored, individual decision as part of a package of measures and is not a substitute for a referral to an allergy specialist. The decision to prescribe should be made by a clinician experienced in risk assessment in this context.

AAIs should be discontinued if the original prescription was inappropriate.

How many AAIs are required?
The majority of patients should have two AAI devices available at all times but there is existing flexibility within the prescriber information for the clinician, in exceptional cases, to prescribe one AAI, based on careful assessment of individual risk factors. Prescribers should issue no more than two AAIs per patient (of any brand or strength) – see page 1 for exceptions.

Training needs for different brands of AAIs
There are three AAI devices available in the UK; EpiPen®, Jext® and Emerade®. The devices differ slightly in the administration technique and specific training is required for each device. The devices are not interchangeable without specific training on the device being issued to the patient. This is the responsibility of the prescriber and training may be accessed via pharmacists, practice nurses or allergy services.

The following links provide training materials for the different devices:

- EpiPen® devices: http://www.epipen.co.uk/patients/epipenr-user-guide
- Jext® devices: https://jext.co.uk/
- Jext® 150 Training Video: https://www.medicines.org.uk/emc/product/5747/rmms
- Jext® 300 Training Video: https://www.medicines.org.uk/emc/product/5748/rmms
- Emerade® devices: https://www.emerade-bausch.co.uk/patient/how-to-use-emerade
- Emerade® 150: https://www.medicines.org.uk/emc/product/5278/rmms
- Emerade® 300: https://www.medicines.org.uk/emc/product/5280/rmms
- Emerade® 500: https://www.medicines.org.uk/emc/product/5279/rmms

Adrenaline for anaphylaxis kits

Some healthcare professionals may be holding AAIs in preference to adrenaline ampoules, to treat anaphylactic reactions; this should not be necessary.

All healthcare professionals providing services where anaphylaxis treatment may be required, including but not exclusive to flu vaccination services, should have the competency to draw up and administer intramuscular adrenaline from ampoules with a normal syringe and needle.

Due to the shortage, we ask that, when renewing the adrenaline in your anaphylaxis kits, all staff are alerted to please stock ampoules (ensuring you also include dosing charts, needles and syringes) and not AAIs.

The Green Book and Resuscitation Council guidance provides additional advice to healthcare professionals on the use of adrenaline in response to anaphylaxis. Supplies of adrenaline ampoules are currently available and there is an expectation that healthcare professionals should use these in preference to AAIs.

Distribution

If you are responsible for cascading these alerts in your organisation, these are our suggested distribution lists; however, each organisation needs to ensure a senior clinician takes responsibility for coordinating all actions that need to be taken.

- General Practitioners
- Practice Nurses
- Chief Pharmacist
- Allergy specialists/allergy teams
- School Nursing/Medical Services
- Emergency Preparedness and Response Officer
- Medical Directors
- Pharmacists
- Paediatricians
- Paediatrics departments

Enquiries

England
Send enquiries about this notice to the DHSC Supply Resilience Team, quoting reference number SDA/2019/010

Email: supplyresiliencemd@dhsc.gov.uk

Addressees may take copies for distribution within their own organisations