Public Health Link

From the Chief Medical Officer for Wales

Distribution:	As Appendix 2
From:	Chief Pharmaceutical Officer, Andrew Evans
Date:	28 November 2019
Reference:	CEM/CPhA/2019/39
Category:	Class 2: Action With 48 Hours
Title:	Class 2 Drug Alert, Action Within 48 Hours, Ceska Republika S.R.O. (An Affiliate Of Bausch And Lomb Uk Limited), Emerade 150 Micrograms Solution For Injection In Pre-Filled Syringe; Emerade 300 Microgram Solution For Injection In Pre-Filled Syringe And Emerade 500 Microgram Solution For Injection In Pre-Filled Syringe
For Action by:	General Practitioners – Action as below. Dispensing General Practitioners – Ensure all working in your dispensary see this alert and a copy is held on your locum file – Action as below. Community Pharmacies – Action as below Hospital pharmacies – Action as below. Chief Pharmacists - Action as below.
For Information:	See Annex 2 – Distribution List
What is this about:	Full details are set out below.
Why has it been sent:	For your information, action and to pass on to colleagues.

Issue:

Pharmaswiss Ceska republika s.r.o. (an affiliate of Bausch & Lomb UK Limited) is recalling all unexpired batches of the above product due to an error in one component of the autoinjector believed to cause some pens to fail to activate and deliver adrenaline. More information is provided in the attached alert.

It is important to note that while Emerade stock held by patients is not being recalled, patients and caregivers in possession of Emerade pens need to be informed of updated safety information about the risk of failure to activate.

Healthcare professionals (GP Practices, Pharmacies) should, where possible, contact patients and carers with Emerade pens, to inform them of the additional advice contained within this alert. Additionally, no further supplies of Emerade will be available on the UK market until the issue has been resolved, therefore patients and carers should be appropriately trained to use other brands.

Full details of the drug alert are included in the attached PDF file. This information is also published on the MHRA website https://www.gov.uk/drug-device-alerts.

Appendix 1

To: Chief Executives of Health Boards and NHS Trusts

Medical Directors of Health Boards

Nurse Directors Health Boards

Directors of Public Health

Hospital Principals and Chief Pharmacists to action as per alert

NHS Direct

To: **NHS Wales Shared Services Partnership to forward to:**

General Practitioners.

Dispensing General Practitioners – Ensure all working in your dispensary see this alert and a copy is held on your locum file.

Community Pharmacies.

Deputising services.

HB Prescribing Advisers.

Independent/Private clinics and Hospitals and Hospices throughout Wales.

MHRA
Regulating Medicines and Medical Devices

Medicines & Healthcare products Regulatory Agency

DRUG ALERT
CLASS 2 MEDICINES RECALL

Action within 48 hours
Pharmacy and Wholesaler Level Recall

Date: 28 November 2019 EL (19)A/39 Our Ref: MDR 57-08/19

Dear Healthcare Professional,

Pharmaswiss Česka republika s.r.o. (an affiliate of Bausch & Lomb UK Limited)

Emerade 150 micrograms solution for injection in pre-filled syringe	**PL 33616/0013**
Emerade 300 micrograms solution for injection in pre-filled syringe	**PL 33616/0014**
Emerade 500 micrograms solution for injection in pre-filled syringe	**PL 33616/0015**

(Adrenaline)

Brief description of the problem
Pharmaswiss Česka republika s.r.o. (an affiliate of Bausch & Lomb UK Limited) is recalling all unexpired batches of the above product due an error in one component of the autoinjector believed to cause some pens to fail to activate and deliver adrenaline. More information is provided.
Emerade stock held by patients is not being recalled, and patients and caregivers in possession of Emerade pens need to be informed of updated safety information about the risk of failure to activate.

Advice for healthcare professionals
Stop supplying the above product immediately. Quarantine all remaining stock and return it to your supplier using your supplier's approved process.

Contact details for further information
For stock enquiries please contact Bausch & Lomb Customer Services, Tel: 0208 781 2991
Email: Pharma_CS@bausch.com

For medical information enquiries please contact the Pharmacovigilance and Medical Information Officer, Tel: 0208 781 5523, Email: Pharmacovigilance.UK@bausch.com

EMERADE PRE-FILLED ADRENALINE AUTOINJECTOR: UPDATE ON FAILURE TO ACTIVATE

Summary

- The MHRA has notified Bausch and Lomb UK Limited of reports that Emerade adrenaline pens (autoinjectors) have failed to activate. A previous drug alert was issued on 03 October 2019.
- The company's investigations have now shown that an error in one component of the autoinjector is believed to cause some pens to fail to activate and deliver adrenaline. There is an increased likelihood of the activation fault occurring when pens are exposed to high temperature. Patients should be advised not to expose pens to temperatures above 25°C as this may increase the likelihood of the fault occurring.
- **On the basis of all the information available, most Emerade pens will activate as normal and patients are advised to continue to follow existing advice to carry two in-date pens with them at all times.**
- Prescribers should prescribe adrenaline pens (autoinjectors) of another brand, until this error has been corrected and ensure that training is provided for the alternative brands.
- In the UK, there are insufficient supplies of alternative brands to replace all the Emerade pens held by patients.
- No further supplies of Emerade will be available until the issue has been fully resolved.
- The advice in the UK therefore is that those patients who have been supplied with Emerade pens should continue to use the pens as instructed. When the Emerade pen has expired, patients should be prescribed a different brand (EpiPen or Jext). Patients and carers will need to be made aware of the difference in administration of the pen they are supplied with, that will require training in use of the new pen. Further information can be found in the Patient Information Leaflets of the different pens.
- The advice to continue using Emerade pens until the expiry date has been considered in order to avoid a serious shortage of adrenaline pens for the wider patient community. The MHRA and Department of Health and Social Care consider that the risk of not having a pen is much higher than having a pen that may not activate.
- Prescribers and patients can be reassured that where a patient has been supplied with Emerade 500 mcg adrenaline pens, EpiPen and Jext in strengths of 300 mcg (0.3 mg) will be appropriate alternatives. The licensed dosing recommendations for each brand of pen are available in the Summary of Product Characteristics (SmPC) and should be followed.
- Patients can be reassured that the majority of Emerade pens will work as intended. However, if the first Emerade pen does not activate, despite use of firm pressure, the patient should immediately use their second pen.
- Patients who have been supplied with Emerade pens should avoid exposing pens to temperatures above 25°C, in line with the recommended storage conditions. If travel to a hot climate is anticipated, the patient is advised to also carry an alternative brand of pen.

Activation issue – further information

- Emerade 150/300/500 micrograms solutions for injection are approved for treating severe acute allergic reactions (anaphylaxis).

- Complaints that Emerade pens (autoinjector) have failed to activate have been received.
- Bausch and Lomb believe a likely contributory cause of the activation failure to be an error in the manufacturing of one of the components of the pen.
- 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, along with the Department of Health and Social Care are working to stabilise the supply of adrenaline pens.

Information for patients:

The MHRA has provided additional information below (see pages 3 and 4) for patients and carers who have Emerade pens. Information is provided on the activation failures and advice on how to handle an emergency event should a pen fail to activate and how to tell whether this has occurred by inspection of the pen. Healthcare professionals are urged to share this information with all patients and carers who have been prescribed an Emerade pen.

It is important to report all suspected adverse reactions or product quality defects via the Yellow Card reporting tool, https://yellowcard.mhra.gov.uk/ - patient should be advised to retain the pen if possible. More information can be found on page 6.

Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Dear Emerade Adrenaline Autoinjector User,

The UK's regulator of medicines (Medicines & Healthcare products Regulatory Agency [MHRA]) has received reports of Emerade pens failing to activate. This means that in some cases, the needle is not released, and the injection of adrenaline is not delivered. This alert is an update to the previous drug alert issued on 03 October 2019. People in the UK who have been supplied with an Emerade are advised of the following:

Don't expose Emerade pens to heat or keep them somewhere hot
The company that makes Emerade (Bausch and Lomb UK Limited) has identified a fault in one part of Emerade autoinjectors that causes some pens not to activate and deliver adrenaline. This fault may be more likely to happen if the pen is exposed to temperatures higher than 25°C. Therefore, make sure you protect it from heat and do not leave your pen in a hot place (for example, in front of a heater, radiator, or fire). This instruction is not new, and you can find out more about how to store your pen safely in the leaflet that comes with it. Contact your doctor if you are planning to travel to somewhere hot since you may need a different pen for this trip.

Most pens will continue to work; carry two pens and use if you need to
In the UK, there are not enough adrenaline pens in alternative brands to replace all the Emerade pens held by patients. Most Emerade pens will continue to work. Therefore, the risk of not having a pen is much higher than the risk of having a pen that may not activate. If you have been given an Emerade pen, continue to use it as instructed (see next page). If your first Emerade pen does not activate despite firm pressure, immediately use your second pen. Always carry two adrenaline pens with you and use them if you need to.

When your Emerade pen expires, learn how to use your new type of adrenaline
When your Emerade pen has expired (the end of the month listed on the pen and case), you will be prescribed a different brand of adrenaline (EpiPen or Jext). There are some differences between brands. You and the people around you will need to be aware of these difference in how to use the pen(s) you have been supplied with. The manufacturers of the different devices have training information, including videos of how to use them correctly, on their websites. Trainer pens (mock pens that do not contain adrenaline) are also available to be ordered on the websites.
Further information can be found in the Patient Information Leaflets of the different pens.

- EpiPen - https://www.medicines.org.uk/emc/files/pil.4289.pdf
- Jext - https://www.medicines.org.uk/emc/files/pil.5748.pdf
- Emerade - https://www.medicines.org.uk/emc/files/pil.5278.pdf

What to do if you suspect anaphylaxis
Ensure you **carry two adrenaline pens with you at all times**. If you experience symptoms of anaphylaxis, administer an adrenaline pen without delay, even if you are not sure whether it is anaphylaxis. Early administration is vital. Immediately after administering an adrenaline pen, you or caregiver should dial 999, saying anaphylaxis (pronounced "anna-fill-axis") so that an ambulance is dispatched without delay.

A full investigation is still ongoing. The MHRA and Bausch and Lomb UK Limited will provide updated information to healthcare professionals and affected members of the public as soon as it becomes available.

You can help us by continuing to report any issues directly via the Yellow Card reporting tool, https://www.gov.uk/yellowcard. Always include the brand and batch number included on your pen.

WHAT DOES MY EMERADE PEN LOOK LIKE BEFORE USE? Fig. 1

BEFORE USE

Instructions:

1. An unused Emerade pen, with front cap in place (Fig. 1).

2. For instruction on how to use your Emerade pen please consult the Patient Information Leaflet (PIL).

3. During this period, when activation failure is a possibility, you should press the Emerade pen very firmly against your thigh.

HAS MY EMERADE PEN ACTIVATED? Fig. 2

ACTIVATED
When Emerade Pen has been activated the needle cover will extend and lock.

Instructions:

1. After using an Emerade pen following the instructions found on product labelling, verify that the pen has activated.

2. An Emerade pen that has been activated, will have an extended needle cover (Fig. 2 – circled section of image)

3. Call 999 for an ambulance and state "Anaphylaxis" even if you start to feel better

4. Lie flat with your legs up to keep your blood flowing. However, if you are having difficulty breathing, you may need to sit up to make breathing easier

5. Proceed to administer your second pen if you are not improving after 5 to 15 mins in case you need a second dose of adrenaline

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WHAT DO I DO IF MY EMERADE PEN HAS NOT ACTIVATED? FIG. 3

NOT ACTIVATED
If the needle cover has not extended, the pen has not activated.

Instructions:

1. If the needle cover has not extended, the pen has not activated (Fig. 3 – circled section of image).

2. If the pen has not activated despite firm pressure, use the second pen immediately.

3. Call 999 for an ambulance and state "anaphylaxis" even if you start to feel better.

4. Perform additional attempts to activate, if
- Both pens have failed and no dose has been given;
- One pen has failed, One pen has worked, but a second dose is needed
This should only be attempted once all pens have been tried.

5. Retain any suspected, un-activated pen for reporting to the MHRA via the Yellow Card (further information on page 6) and investigation purposes.

Call for reporting

The reporting of suspected adverse reactions is of great importance. It allows continuous monitoring of the benefit-risk balance of a drug or medical device. Healthcare professionals and patients are encouraged to report any suspected defect or adverse event.

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 Card website - https://yellowcard.mhra.gov.uk/ or via the Yellow Card app available from the Apple App Store or Google Play Store.

Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.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
- by downloading and printing a form from the Yellow Card website (see link above)

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

Contacts for Further Information:

For stock enquiries please contact Bausch & Lomb Customer Services, Tel: 0208 781 2991
Email: Pharma_CS@bausch.com

For medical information enquiries please contact the Pharmacovigilance and Medical Information Officer, Tel: 0208 781 5523, Email: Pharmacovigilance.UK@bausch.com

Further information on Emerade including use of the app can be found at https://www.emerade-bausch.co.uk/

Recipients of this Drug Alert should bring it to the attention of relevant contacts by copy of this letter. NHS Regional Teams are asked to forward this to relevant clinics, general practitioners and community pharmacists for information / action.

Yours faithfully

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