MPS 3041
MMS 2125

HSC Business Services Organisation

DRUG ALERT

CLASS 1 MEDICINES RECALL

Action Now – including out of hours
Patient/Pharmacy/Wholesaler Level Recall

Dear Healthcare Professional

Pharmaswiss Česka republika s.r.o. and distributor Bausch & Lomb UK Limited

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

SNOMED
Code 23420111000001107

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

SNOMED
Code 23415811000001102

Active Pharmaceutical Ingredients: adrenaline (as tartrate)

Brief description of the problem
Pharmaswiss Česka republika s.r.o. and distributor Bausch & Lomb UK Limited is recalling all unexpired batches of Emerade 500 micrograms and Emerade 300 micrograms adrenaline auto-injectors (also referred to as pens) from patients. This is due to an issue identified during an ISO 11608 Design Assessment study where some auto-injectors failed to deliver the product or activate prematurely.

Specifically, the 1-metre free-fall (vertical orientation) pre-conditioning resulted in damage to internal components of the auto-injector, leading either to failure to deliver the product or premature activation. This damage was not visibly apparent following the pre-conditioning but was evident only on subsequent functional

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testing. It is unclear what impact this has on auto-injectors in clinical use, however as a precautionary measure and owing to the inability to identify this issue before the auto-injectors are used, the auto-injectors are being recalled.

The MHRA, in conjunction with the Department of Health & Social Care (DHSC) has established that there are sufficient supplies of alternative auto-injectors to allow for a recall at patient level. Pharmaswiss Česka republika s.r.o. and distributor Bausch & Lomb UK Limited has confirmed that future production of Emerade 500 micrograms and Emerade 300 micrograms auto-injectors is on hold. Therefore, no further supplies will be available, and patients will need to be switched to an appropriate alternative.

Healthcare professionals should inform patients, or carers of patients, who carry Emerade 300 or 500 microgram auto-injector pens to obtain a prescription for and be supplied with an alternative brand. They should then be informed to return their Emerade 300 or 500 microgram pens to their local pharmacy.

At the point of prescribing and dispensing, it is vital that patients and carers receive training to ensure they are completely familiar with how their new device works. This is because each brand of adrenaline auto-injector works differently. **Patients should continue to carry two devices at all times** in case they need to administer a second dose of adrenaline before the arrival of the emergency services (see links to training material below).

Alternative brands of adrenaline auto-injectors (EpiPen and Jext) are available in a maximum strength of 300 micrograms. There is evidence to suggest that a single EpiPen (300 micrograms) or Jext (300 micrograms) pen will be a suitable replacement for a single Emerade 500 micrograms pen. This is based on recently available results from two studies (including one by the manufacturer of Emerade) which compared blood levels of adrenaline following injection of Emerade 500 micrograms pens with those following EpiPen 300 micrograms or Jext 300 micrograms pens. Patients must continue to always carry two adrenaline pens at all times. Prescribers are to follow dosage guidance in individual Summary of Product Characteristics (SmPC).

Further information is available in the recent Public Assessment Report: Recommendations to support the effective and safe use of adrenaline auto-injectors accessible via the link below. This report provides a combined summary of the conclusions and recommendations of the Commission on Human

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Medicines' Adrenaline Auto-injector Expert Working Group to support the effective and safe use of Adrenaline Auto-injectors.
https://www.gov.uk/government/publications/public-assessment-report-recommendations-to-support-the-effective-and-safe-use-of-adrenaline-auto-injectors

Advice for all healthcare professionals

General Practitioners (GPs) and Pharmacy Teams should send the attached letter "Advice for patients who have been prescribed an Emerade 500 micrograms or Emerade 300 micrograms auto-injectors", to all patients and carers, who have been prescribed an Emerade 500 micrograms or Emerade 300 micrograms auto-injectors.

All healthcare professionals in primary, secondary or specialist healthcare services who prescribe, supply (dispense) or administer adrenaline auto-injectors, or who advise patients and their carers, should note the advice and take appropriate action, as required.

The below actions should be initiated by General Practitioners (GPs) and Pharmacy Teams immediately:

- stop supplying the impacted products immediately. Quarantine all remaining stock and return it to your supplier/MAH using your supplier's approved process

- identify patients who have been supplied with Emerade 500 micrograms and Emerade 300 micrograms auto-injectors and ensure that they are reviewed by their prescriber to determine whether their adrenaline auto-injector prescription is still appropriate and in line with existing guidance

- immediately inform patients and carers to request a new prescription to replace each Emerade 500 micrograms and Emerade 300 micrograms auto-injector with an equivalent strength adrenaline pen in an alternative brand. Healthcare professionals should be aware that the licensed dosing recommendations for each brand of pen are not identical. Dosing recommendations are available in the Summary of

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Product Characteristics (SmPC) and should be followed (see links below)

- inform patients to return Emerade 500 micrograms and Emerade 300 micrograms auto-injectors to any pharmacy after they have obtained a total of two equivalent strength adrenaline auto-injectors in an alternative brand;
    - Pharmacies that receive Emerade 500 micrograms and Emerade 300 micrograms auto-injectors from patients should quarantine the pens and return them to the supplier using the supplier's approved process

- Inform patients:
    - that they should carry two in-date adrenaline auto-injectors with them at all times in case they need to administer a second dose of adrenaline before the arrival of the emergency services
    - that they need to receive training, so they are confident in being able to use any new devices (see further information in the attached document)
    - of the signs of anaphylaxis and the actions they should take immediately (see Management of Anaphylaxis in the alert for further advice)

- be aware that this recall also applies to Emerade 500 micrograms and Emerade 300 micrograms auto-injectors that are in emergency anaphylaxis kits held by healthcare professionals, such as dental surgery kits etc.

- stock adrenaline ampoules, as opposed to auto-injectors, when renewing the adrenaline in anaphylaxis kits (ensuring dosing charts, needles and syringes are included). See further information below

- be aware that this recall also applies to Emerade 500 micrograms and Emerade 300 micrograms auto-injectors that are currently held by schools. See further information below

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Prescribers should issue no more than two adrenaline auto-injectors per patient (of any brand or strength) unless:

- schools require separate pens 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 pens per child (of any brand or strength). See further information on the use of pens in schools below
- patients rarely need more than two adrenaline pens prescribed (for example, a prior severe reaction resistant to treatment with adrenaline), where the prescriber may issue additional pens

Different brands of adrenaline pens work differently. Patients and carers should be told of these important differences.

- Healthcare professionals – doctors, nurses and pharmacists – should, where possible, ensure that they provide training to patients and carers in the correct use of the new pen. Instructions for use can be found in the SmPC (prescriber's information) and in the Patient Information Leaflets (PILs) that are supplied with the different pens and on the respective manufacturers' websites where training videos are available. Training pens that do not contain adrenaline can also be obtained free of charge from the manufacturers. Healthcare professionals and patients are strongly recommended to obtain these to assist with training. The trainer pens can be used repeatedly, allowing patients to practice regularly with them so they are prepared for use in an emergency.

- The following links provide training materials for the different devices:

  EpiPen
  - EpiPen® devices: http://www.EpiPen.co.uk/patients/EpiPenr-user-guide
  - EpiPen® 0.15mg: https://www.medicines.org.uk/emc/product/4290/rmms
  - EpiPen® 0.3mg: https://www.medicines.org.uk/emc/product/4289/rmms

  Jext
  - Jext® devices: https://jext.co.uk/
  - Jext® 150 Training Video: https://www.medicines.org.uk/emc/product/5747/rmms
  - Jext® 300 Training Video:

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https://www.medicines.org.uk/emc/product/5748/rmms

Emergency Use Adrenaline Auto-injectors in the Healthcare setting: Adrenaline pens that are currently held by healthcare professionals, i.e., in emergency anaphylaxis kits, dental kits etc. are subject to the recall.

- Healthcare professionals providing services where anaphylaxis treatment may be required should be competent to administer intramuscular adrenaline from ampoules with a syringe and needle. These services should use adrenaline from ampoules in preference to adrenaline auto-injectors. This is to preserve supplies of adrenaline pens for patients to self-administer, during the ongoing global fragile supply situation for all adrenaline auto-injectors.

- Therefore, when re-stocking adrenaline in anaphylaxis kits, all staff are alerted to stock these with ampoules (together with dosing charts for use of intramuscular adrenaline to treat anaphylaxis, needles and syringes) and not adrenaline pens (of any brand).

- The Green Book and Resuscitation Council guidance provides additional advice to healthcare professionals on the use of adrenaline in response to anaphylaxis.

Guidance on the use of adrenaline auto-injectors in schools:

For more information on the use of adrenaline auto-injectors 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 adrenaline auto-injectors at school for use in an emergency.
- Depending on their level of understanding and competence, children and particularly teenagers should carry their adrenaline pens with them at all times or the pens should be quickly and easily accessible at all times. If the adrenaline auto-injectors 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.

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Advice for patients

The MHRA is aware of a safety issue, potentially impacting all Emerade 500 micrograms and Emerade 300 micrograms auto-injectors (also referred to as pens). The issue may mean that pens fail to activate and deliver adrenaline if they have been dropped. Premature activation was also detected in one Emerade pen after it had been dropped, meaning that the adrenaline solution may be released prior to administration. As a precautionary measure and due to the inability to identify this error before the auto-injector is used, the autoinjectors are being recalled.

If you have been given an Emerade pen, continue to use it as instructed. 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.

Your GP/doctor, pharmacist, or other healthcare professional will contact you to make sure you get a new prescription for an alternative product. Once you have a replacement, you should return your Emerade auto-injectors to any pharmacy. You can contact your healthcare professional directly if you are worried.

What to do if you suspect anaphylaxis

All patients should be made aware of the signs and symptoms of anaphylaxis and that at the first onset of any signs or symptoms of anaphylaxis, they or a carer/bystander should:

- administer an adrenaline auto-injector device without delay, even if there is doubt whether it is anaphylaxis
- call an ambulance (999) immediately after giving the injection and say this is an emergency case of anaphylaxis
- administer a second auto-injector 5 to 15 minutes after the initial dose, if no improvement is seen or if the patient deteriorates after an initial improvement
- patients should be advised to use a second adrenaline auto-injector immediately if the first adrenaline autoinjector pen fails to activate despite pressing firmly against the thigh (pictorial guidance on whether an Emerade pen has activated or not is given below)
- make further attempts to activate a failed adrenaline autoinjector pen while waiting for the ambulance if the patient is not improving, even if one pen has worked, as this may suggest a need for a second or more doses. The purpose of

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adrenaline pens is to start treatment for anaphylaxis that is continued by the emergency services.

We encourage patients and carers to read this fact sheet with advice on the use of adrenaline auto-injectors. The risk of device mishandling or device failure exists with all adrenaline auto-injectors and is something that patients and carers should be aware of.

The chance of a successful outcome is increased if adrenaline is administered promptly at the first signs of anaphylaxis. Even with an apparently successful response to adrenaline auto-injector administration, patients may relapse some hours later, which underlines the importance of the emergency services always being called.

Call for reporting

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 ▼

You can report via:

- the Yellow Card website
- 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 731 6789 for free, Monday to Friday between 9am and 5pm.
When reporting please provide as much information as possible, including information about medical history, any concomitant medication, timing onset, treatment dates, and product brand name.

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Further Information

For stock enquiries, please contact Bausch & Lomb Customer Services, Tel: 020 8781 2991
Email: Pharma_CS@bausch.com

For medical information enquiries please contact the Medical Information Team, Email: medinfo.europe@bauschhealth.com

Recipients of this Medicines Notification should bring it to the attention of relevant contacts by copy of this notice. RQIA should bring this information to the attention of private hospitals/clinics registered with them and any other relevant care facilities.

The Business Services Organisation is asked to bring this information to the attention of Community Pharmacists and General Medical Practitioners directly.

Recipients of this Drug Alert should bring it to the attention of relevant contacts by copy of this letter.

TO ALL CHEMISTS, DOCTORS ON THE LISTS

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Pharmaceutical website: http://www.hscbusiness.hscni.net