Department of Health & Social Care

Revised Supply Disruption Alert

SDA/2018/001(U) Issued: 15th October 2018 Valid until: 31st December 2018

Update: EpiPen and EpiPen Junior (adrenaline auto-injector devices) – Supply Disruption

Summary

EpiPen and EpiPen Junior will be subject to limited availability for the remainder of 2018. Mylan are now out of stock of EpiPen Junior and interruptions in the supply are anticipated to continue for the coming months.

This alert provides an update to the previous alert from 28 September 2018. Whilst all the information in this alert should be reviewed and actioned as appropriate, the changes from the 28 September alert are highlighted in red text.

For action by

General practices, community pharmacies, acute trusts, community trusts, mental health trusts, ambulance trusts.
Action start date: immediately

Please note that there is an attachment for this revision which is a parent/carer facing letter giving advice about the EpiPen Junior shortage. This alert is requesting GP practices identify registered patients (children) prescribed EpiPen Junior and make contact with their parents in the next five working days to alert on these national contingency arrangements.

Action

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

1) Adult and child auto-injectors are only prescribed and dispensed to those who truly need them, as any additional issuing to patients who are worried about the shortages could exacerbate the overall supply situation.

2) Repeat prescriptions and supply are managed diligently and patients advised of the following:

    a) It is important to note that when validating the expiry date of an adrenaline auto-injector, the product expires on the last day of the month indicated e.g. a device labelled ‘April 2019’ does not expire until the end of April 2019.

b) Certain batches of adult EpiPen can be safely used for four months after the expiry date has passed - please see further information about these batches below. Where possible, prescribers should not prescribe a replacement adult EpiPen whilst the original is within the extended use by date.

c) Patients should be advised not to dispose of their expired devices until they have replaced them. If no new devices can be obtained parents / patients should be advised to use expired devices in an emergency as this is safer than not using them, it will not be dangerous but the potency of the adrenaline may have reduced.

3) Due to ongoing constraints affecting EpiPen 300mcg and Epipen 150mcg devices, some adults and children may need to switch from their usual device to other alternative adrenaline auto-injector devices that may be more readily available. The different brands of adrenaline auto-injectors are not used in exactly the same way and therefore specific training and advice is required for each of the devices- please see information on these alternative devices below.

4) Junior adrenaline auto-injectors (150mcg) in all 3 brands – Epipen, Jext and Emerade - should be reserved for children weighing under 25 kg during this shortage period. Children weighing more than 25 kg should be given adult auto-injectors (300 mcg) – see further guidance below.

5) Prescribers should work in close collaboration with their local pharmacies to understand which devices are available. Prescribers and pharmacists should work together to ensure patients who are switched to an alternative device are trained appropriately and understand how to use the new device.

6) To manage the existing supply of EpiPen Junior® and other replacement products over this short-term period it has been necessary to put in place national contingency arrangements to ensure that those patients with the greatest short-term need have priority access to the 150mcg adrenaline auto-injectors as they become available. We are therefore asking community pharmacies and dispensing practices to validate prescription requests before supply by wholesalers on an individual patient basis in the short term until national supplies can be replenished over the coming months. Specific guidance on this will be issued directly to pharmacies and dispensing practices in the next 24 hours.

7) A patient/parent letter about the EpiPen Junior shortage and relevant advice has been attached below. GPs and Pharmacists should share this with patients/parents affected by this shortage.

20181015 Letter to patients.pdf

8) Prescribers and pharmacies should regularly check the following Specialist Pharmacy Services website for additional updates to supply and clinical guidance.

https://www.sps.nhs.uk/articles/shortage-of-epipen/

Deadlines for actions

Actions initiated:	15/10/2018
Actions completed:	31/12/2018

Product details

Mylan EpiPen and EpiPen Junior (adrenaline auto-injector devices).

Background

There has been an ongoing supply issue affecting EpiPen, supplied by Mylan for several months. The issue is due to manufacturing delays from Mylan's contract manufacturer, Meridian Medical Technologies, a Pfizer company in the US. Stabilising supply is taking longer than anticipated and is affecting countries globally. Initially the delays affected the 300mcg preparation of EpiPen, however these have recently been extended to the EpiPen Junior 150mcg device.

In the UK there are two alternative adrenaline auto-injector devices available, Emerade, supplied by Bausch and Lomb and Jext, supplied by ALK. Both companies manufacture adult and paediatric presentations of adrenaline auto-injectors. Both companies are aware of the supply disruptions affecting EpiPen and EpiPen Junior and have been working with their supply chains to increase supplies to the UK for the remainder of this year.
Supplies of EpiPen 300mcg are currently available, but constraints are anticipated to continue for the coming month. Supplies of Jext 300mcg, Emerade 300mcg and 500mcg are currently available.

Mylan are currently out of stock of the EpiPen Junior 150mcg and further supplies are not expected until the end of October. Further supplies of Jext 150mcg and Emerade 150mcg are expected to be made available at UK wholesalers during the w/c 15th October, but it is not foreseen to be sufficient to fulfil normal demand and there will be a backlog of patients with already expired devices who will receive priority. Further deliveries all of three auto-injectors are expected during November, but there may be ongoing constraints until the end of this year.

To help manage product availability on an ongoing basis, all suppliers of adrenaline auto-injector devices are working with their wholesaler partners. Processes are being put in place by wholesalers to help support ensuring that devices get to those with the greatest need.

Current prescribing patterns suggest there may be a substantial proportion of children using the Junior EpiPen brand who under current guidance should already be using the Epipen 300mcg devices recommended for children over 25kg. The guidance on weight varies by device between 25-30kg for use of adult pens but for the period of this reduced supply expert clinical guidance is to use 25kg as the cut off for switching from 150mcg to 300mcg dosage for all devices. For two of the devices this will be an off-label change.

Extended use beyond labelled expiry date

Mylan UK have obtained acceptance from the MHRA to extend the use of specific batch numbers of EpiPen 300mcg auto-injectors, beyond the labelled expiry date by four months. The affected lot numbers, which have labelled expiry dates between July 2018 and November 2018, are listed in the table below. EpiPen 300mcg auto-injectors within these batches will have likely already been dispensed by pharmacies and will therefore be in patients' possession. To the extent possible, clinicians should defer prescribing a replacement adult EpiPen for a pen in one of the lots in the table which is within the extended use by date.

LOT	Labelled Expiry Date (end of the month)	Extended Use by Date (end of the month)
6FA794J	07.2018	11.2018
6FA795Y	07.2018	11.2018
7FA112F	09.2018	01.2019
7FA106B	09.2018	01.2019
7FA283B	10.2018	02.2019
7FA251D	10.2018	02.2019
7FA250B	10.2018	02.2019
7FA265C	11.2018	03.2019
7FA265B	11.2018	03.2019

The extended use only applies to the lots of Epipen 300mcg auto-injectors listed above. Patients can continue to use the Epipen 300mcg auto-injectors of these specified lots safely until the extended use by date in the table above.

Important: This extended use does not apply to EpiPen 150mcg auto-injectors or any lot number of Epipen 300mcg auto-injectors not specified. Patients must continue to adhere to the labelled expiry date on any EpiPen not covered by the lot numbers above.

However please note if no new devices can be obtained parents / patients should be advised to use expired devices in an emergency as this is safer than not using them, it will not be dangerous but the potency of the adrenaline may have reduced.

During clinical conversations with patients please stress that using an in-date device (if one can be supplied), even if not of the usual brand, is preferable to using an expired device.

Further information about this can be found here: http://www.epipen.co.uk/

Clinical advice to consider for patients who require adrenaline auto-injector devices:
NOTE: the main body of the Alert outlines the actions that are required. This section summarises the existing guidance that those actions are based on. It is intended as an easy reference summary of the existing guidance, especially as it applies to children. All prescribers should review the current guidance for the prescription of an adrenaline auto-injector 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) as the definitive version, and also refer to the guidance in BNF and provided by manufacturers as appropriate.

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

All patients should be reminded that in the onset of symptoms of anaphylaxis, they should:

- **Immediately use an adrenaline auto-injector device.**
- Immediately call an ambulance or send someone to do this. Say this is an emergency case of anaphylaxis*

**Please note- ambulances carry adrenaline 1mg/1ml (1 in 1,000) ampoules, which are not affected by the shortage*
In view of the current shortage of adrenaline auto-injectors (AAIs), notably the junior versions, the following is considered necessary and appropriate advice to manage the supply disruption with least risk to patients and is to be applied across England. This advice may need to be reviewed as the supply situation changes over time.

Consider if the initial prescription of AAIs is appropriate

Patients at risk of anaphylaxis that should be considered for long-term provision of an adrenaline auto-injector include those:

- who have suffered a severe systemic reaction where the allergen cannot be easily avoided
- 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.

Adrenaline auto-injectors should be discontinued if the original prescription was inappropriate or the child has outgrown the allergy.

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.

If it has been recommended that 2 AAI devices are to be available both at school and outside school but if inadequate AAIs are available, consideration should be given to leaving only one device on school premises, relying then on the backup (non-personal) device(s) available at the school, if the school has availed itself of this opportunity under the change in legislation as laid out in the current Department of Health and Social Care guidance.

Which AAI devices can be used?

The most commonly used devices in the UK are branded Epipen®. Alternative devices also exist e.g. Jext®, Emerade® and can be prescribed. 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
- EpiPen Training video: https://www.medicines.org.uk/emc/product/4289/rmms
- EpiPen Junior Training Video: https://www.medicines.org.uk/emc/product/4290/rmms
- 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 Training Video: 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

Guidance on paediatric dosing:

Children weighing above 25kg can, during this shortage, period be prescribed 300mcg devices in all brands to preserve the limited supplies of 150mcg devices (junior devices) for smaller children, particularly as there is currently greater availability of the adult devices. This advice is off-label for Jext and Emerade devices but is recommended by clinical allergy specialists during this shortage period.

Whilst at present it is believed careful management of existing supply will avoid the need to use expired devices other than for batch numbers where it is known to be safe to do so, patients should be advised not to dispose of their expired devices until they have replaced them. This is because AAIs will not actively cause harm if used after expiry but they may be less effective at treating the anaphylactic episode as the potency of the adrenaline gradually reduces (and is also dependent on the conditions they were stored in). It is still preferable to use a device even if it has expired, rather than no device at all, if an in-date device is not available.

Adrenaline for anaphylaxis kits

Some healthcare professionals may be holding EpiPens, or other 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 adrenaline from ampoules with a normal syringe and needle.

Due to the shortage, we ask that when you renew the adrenaline in your anaphylaxis kits, you alert all your staff 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. Pharmacists providing vaccination services may also wish to refer to PSNC FAQs. Supplies of adrenaline ampoules are currently available and there is an expectation that healthcare professionals should use these in preference to the EpiPen or similar devices.

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
- Scholl nursing/medical services
- Emergency Preparedness and Response officer
- Medical directors
- Pharmacists
- Paediatricians
- Paediatrics departments

Please note: CQC and OFSTED do not distribute these alerts. Independent healthcare providers and social care providers can sign up to receive Supply Disruption Alerts directly from the Medicines and Healthcare products Regulatory Agency's Central Alerting System (CAS) by sending an email to: safetyalerts@mhra.gov.uk and requesting this facility.

Enquiries

Please send enquiries about this notice to the DH Supply Resilience Team, quoting reference number SDA/2018/001.

Email: supplyresiliencemd@dh.gsi.gov.uk

Addressees may take copies for distribution within their own organisations