Adrenaline Auto-Injector Supply Disruption Alert

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.

Actions 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) 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.

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) must only be dispensed in line with the existing established guidance i.e. to children under 30kg. Other children weighing more than 30kg need to be given adult auto-injectors (300mcg) – 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) 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/

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.

Mylan are currently out of stock of the EpiPen Junior 150mcg. Limited supply will be received in October but is not foreseen to be sufficient to fulfil normal demand. Further deliveries are expected in mid-November, therefore there will continue to be intermittent supply constraints. Current prescribing patterns suggest there may be a substantial proportion of children using the Junior EpiPen who under current guidance should already be using 300mcg devices recommended for children over 30kg.

Supplies of EpiPen 300mcg are currently available, but constraints are anticipated to continue for the coming month.

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.

To help manage product availability on an ongoing basis, all suppliers of adrenaline auto-injector devices are working with their wholesaler partners to put processes in place to limit the number of devices that can be supplied per prescription.

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.

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
* 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 30kg can be prescribed 300mcg devices and during current shortages it is particularly important to conform to this existing guidance to preserve the limited supplies of 150mcg devices (junior devices) for smaller children, particularly as there is currently greater availability of the adult devices.

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.