Department of Health

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Ms Hassell
HM Senior Coroner, Inner North London
St Pancras Coroners Court
Camley Street
London
N1C 4PP

Friday 7th July 2017

Dear Ms Hassell

Thank you for your letter of 12 May 2017 following the conclusion of the Inquest into the death of Nasar Ahmed.

I was very saddened to read of the circumstances surrounding Nasar's death. Please pass my condolences to his family and loved ones.

Your Report asked if consideration could be given to making generic adrenaline auto-injectors available in public spaces, in a similar way to that for defibrillators. This followed evidence heard at Inquest that the lifesaving potential of their use could outweigh the risks of harm in similar situations.

In giving this consideration, I have taken advice from the Medicine and Healthcare Products Regulatory Agency (MHRA). The MHRA, having deliberated on this, considers such an action could pose substantial risks that outweigh potential for benefit and would need careful evaluation. The MHRA has both clinical and technical concerns.

Clinical concerns

Adrenaline auto-injectors are indicated solely for the emergency treatment of anaphylaxis and are intended for self-administration by the patient, their carer or another suitably trained person. Patients known to be at risk of anaphylaxis are strongly recommended to carry their prescribed adrenaline auto-injectors with them at all times https://www.gov.uk/drug-safety-update/adrenaline-auto-injector-advice-for-patients . This recommendation was endorsed by the European Medicines Agency in 2015 following an Article 31 safety referral:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Adrenaline_auto_injectors/human_referral_000367.jsp&mid=WC0b01ac05805c516f

The provision of communal adrenaline auto-injectors alongside defibrillators in public places would require a member of the public to make a distinction between collapse due to anaphylaxis and collapse for other reasons, including a primary cardiac event such as a myocardial infarction or an arrhythmia. The importance of this distinction is that inappropriate administration of an adrenaline auto-injector to someone suffering from collapse for a primary cardiac reason could increase the likelihood of precipitating a fatal cardiac rhythm disturbance.

Automated defibrillators (particularly newer generation defibrillators) have the diagnostic capability to detect the presence and type of heart rhythm abnormality and whether a shock should be delivered. Modern defibrillators are equipped to deliver shock at the appropriate point in the cardiac cycle. Adrenaline auto-injectors have no ability to detect the cause of the collapse (anaphylaxis or other) and therefore, the decision to administer adrenaline will be dependent on the awareness of the public, an uncertain scenario.

The prescriber's information for Epipen, and the Company's website, carry the following caveat; "*Use with extreme caution in patients with heart disease…. Cardiac arrhythmias may follow administration of adrenaline.*" An incorrect choice to use an adrenaline auto-injector in someone suffering from collapse due to a heart attack or other cardiac disturbance could lead to fatal consequences.

While it is recognised that during resuscitation for cardiac arrest, particularly for patients in asystole, bolus doses of adrenaline are used, for tachy-arrhythmic events such as ventricular tachycardia, defibrillation is the first choice treatment. Any unintended, inappropriate administration of adrenaline could precipitate a fatal arrhythmia and will therefore require reliance on a considered judgement. Provision of adrenaline alongside defibrillators may introduce an additional decision step about which treatment to administer. Furthermore, administration of adrenaline in cardiac arrest is currently under review, due to uncertainty over benefit-risk.

Automated defibrillators have the important safeguard that they only deliver a shock if this is required. The UK resuscitation council guideline on automated defibrillators states: "*They are safe and will not allow a shock to be given unless the heart's rhythm requires it.*"

In summary, the MHRA consider that the benefit-risk of defibrillators in public places is clearly favourable (in that the benefits outweigh the risks). Conversely, the benefit-risk of adrenaline auto-injectors in public places is considered to be unfavourable. If adrenaline auto-injectors are made available alongside defibrillators in public places, this risks

conflation of their use for "collapse" with potentially fatal consequences. An additional decision step may also deter or delay the appropriate use of a defibrillator.

Technical and practical concerns

I am advised that there are additional significant technical and practical challenges with the provision of adrenaline auto injectors in public places as outlined below.

I. The adrenaline auto-injector devices marketed in the UK each have different instructions for use and are intended to be used by patients or other suitably trained persons to enable correct deployment of the drug. Their use is not intuitive and for an untrained individual seeking to provide emergency assistance, there is a risk that they may either inadvertently self-inject the drug or administer it incorrectly.

II. The adrenaline active substance is relatively unstable in solution and particularly sensitive to high temperatures. All the adrenaline auto-injector devices have a short time to expiry of 18 – 20 months from the date of manufacture and need to be protected from extremes of temperature. Above 25°c, the adrenaline auto-injector may well have reduced potency due to increased degradation of drug. In freezing temperatures there is a risk of the drug solidifying making it unable to be delivered. Low temperatures might also cause the device to malfunction (the devices should not be refrigerated). These failures might not be evident to the user.

III. It would be highly impractical to provide temperature-controlled storage units for adrenaline auto-injector devices held in public places. Even if correctly stored, the device would have to be replaced on its expiry date which would require a responsible person to monitor this. Two or more devices would have to be made available in case needed, introducing further complexity in storing them.

IV. The adrenaline auto-injector devices are marketed in three strengths (150, 300 and 500 micrograms) and with differing needle lengths. The prescribing physician will have determined the type of adrenaline auto-injector and strength as appropriate for an individual. In public places, there is a risk of using an inappropriate device potentially delivering an ineffective dose or an excessive dose depending on the circumstances.

Permitting adrenaline auto-injectors to be made available in public places would also require a change in the law and therefore a formal review and public consultation process.

Based on the complexities involved in the appropriate use of adrenaline auto-injectors, in the clinical situations described above and taking into account the technical and practical

issues outlined, the MHRA does not recommended that adrenaline auto-injectors are stored in public places in the same way as defibrillators. On the basis of this advice, I am not currently intending to pursue further the making of generic adrenaline auto-injectors available in public places.

However, I am hopeful that work underway to change the law to allow schools to hold spare auto-injectors without a named individual prescription, for use as emergency back-up to treat anaphylaxis in children registered by the school as being in receipt of a medical prescription for an auto-injector, will tackle some of the challenges which staff faced in this sad case, and which were set out in your determination.

Our amendments to the Human Medicines Regulations 2012, Parliament permitting, will come into effect on 1 October 2017. Officials are currently working on guidance for school staff in how to obtain and use these auto-injectors appropriately, and the guidance will also provide advice on use of adrenaline more generally. Clinicians from the Anaphylaxis Campaign, as well as lay people, are advising on the content of this guidance, and we are hoping to also bring together training videos on different auto-injectors in a single website.

I hope that this guidance, which we will bring to the attention of schools, will greatly reduce the likelihood of a repetition of the tragic events which led to the death of Nasar Ahmed, and so save other lives.

Thank you for bringing the circumstances of Nasar Ahmed's death to our attention.

Yours ever

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CHIEF MEDICAL OFFICER