

Adrenaline auto- injector prescription for patients at risk of anaphylaxis: BSACI guidance for primary care

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Adrenaline AAI prescription for anaphylaxis guidance for primary care

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Executive Summary

Table 1. Executive summary for adrenaline auto-injectors prescription for primary care

- 1. An allergy focused history supports the risk assessment for anaphylaxis.
- 2. Total and specific IgE blood tests alone are not helpful in predicting future anaphylaxis. If requested this must be done in conjunction with an allergy focused history to enable interpretation of results. Specific IgE testing when the allergen is suspected from the history is of value.
- 3. Prescribe two adrenaline autoinjectors for those at significant risk of anaphylaxis, refer for specialist assessment and train the patient telling them to carry the AAIs at all times. This can be done as part of the referral process prior to being seen at the allergy clinic and ongoing after review if required.
- 4. Training should be specific to the device, ongoing and be incorporated into the prescribing process alongside an individualised action plan.
- 5. Encourage self-management by issuing an allergy action plan supporting the patient to know how and when to use their adrenaline autoinjectors, and avoidance of triggers.
- 6. Optimise asthma control and other comorbidities such as allergic rhinitis.
- 7. Advice on positioning during anaphylaxis. They should sit up if they are having breathing difficulties and lie down if they are feeling faint. Sudden movements to an upright posture should be avoided. Do not stand up.
- 8. Emphasize the early use of an adrenaline autoinjector in anaphylaxis, which is given intramuscularly, administer a second AAI after 5 minutes if no improvement in symptoms. Prompt use of adrenaline can save lives.
- 9. When reviewing patients check their devices are appropriate for weight, that they are carrying their adrenaline autoinjectors, they are in date, they know the process for renewal and have reminders for expiry in place.
- 10. Adolescents and young adults are at risk of fatal anaphylaxis and need an individualised approach. Adolescents and young people may require a specific developmental appropriate approach which may be supported by transition services.
- 11. Refer to patient organisations for resources and peer support.

Introduction

The British Society for Allergy and Clinical Immunology (BSACI) published an expert evidence-based guidance for allergy specialists in 2016 on prescribing adrenaline autoinjectors (AAIs) to improve the management of those at risk of anaphylaxis.¹

This guidance has been written for a primary care healthcare professional managing a patient who has either experienced anaphylaxis or a milder allergic reaction where they may be at risk of anaphylaxis in the future.

It is recognized that primary care physicians and other health care professionals may not feel confident in anaphylaxis recognition and risk assessment as this may not have been covered in their training. This document includes background and context to this area in different sections to support the patient journey, alongside the desktop summary. These include key clinical questions that may arise in the primary care consultation, and an algorithm to guide the prescribing of adrenaline in the community. There is also an ideal service pathway, links to a community referral form template, and information on adrenaline dosages and the different types of AAIs. A 'frequently asked questions' (see appendix 2) for common enquiries and clinical cases to illustrate the guidance (see appendix 3) are also included to reflect real life scenarios. A literature search was performed to support this document (see appendix 6).

Anaphylaxis is 'a severe, life-threatening, generalised or systemic hypersensitivity reaction'.² It is characterised by rapidly developing features involving one or more of the airways (laryngeal oedema and/or bronchospasm) and circulation (hypotension) often with associated skin and mucosal changes (urticaria, angioedema). Many studies show an increase in the incidence of anaphylaxis e.g., 32.19 episodes per 100,000 person-years in 2014, doubled from 2008 (Yang 2017). The incidence of hospital admissions with anaphylaxis has increased seven-fold in the UK over the last ten years.³ NHS digital data shows 28,117 admissions in England due to allergy in 2017/18 – 10% of which were for anaphylaxis (up 52% over 6 years). Despite this, the rate of deaths from anaphylaxis in the UK remains stable at about 20 per year. Fatalities are rare.³ Many more are considered at risk of anaphylaxis and this category accounts for most AAI prescriptions. There are multiple guidelines and guidance on the topic of anaphylaxis and allergy from different organisations and we have tried to distil key points relevant to primary care from them. 4-11

The recent MHRA report has key messages and recommendations for the prescribing of Adrenaline devices. <u>Public Assessment Report: Recommendations to support the effective and safe use of adrenaline auto-injectors - GOV.UK (www.gov.uk)^{12.}</u>

The healthcare professional's task is to ensure the patient (and carer)

- is issued with an AAI prescription.
- always carry their AAI and know how and when to use it.
- receives practical training and regular retraining in the use of their AAI using shared care principles.
- knows how to renew the AAI prescription on expiry and the procedure for this.
- has a treatment plan.
- has the knowledge and ability to avoid triggers.
- is referred to an allergy clinic.
- Is signposted to a patient support organisation

Scope and purpose of the guidance

In preparing this document, the BSACI has worked with the key stakeholders including primary care, pharmacists, patient support groups, ambulance services and allergy specialists.

This guidance has been endorsed by Anaphylaxis UK and Allergy UK.

Other guidelines in this area include:

- NICE Guidelines: food allergy (2011) 4
- NICE Guidelines: anaphylaxis (2012) 2
- NICE Guidelines: drug allergy (2014) 5
- NICE Quality Standards: food allergy (2016) 6
- NICE Quality Standards: anaphylaxis (2016) 7
- European Academy of Allergy and Clinical Immunology (EAACI): food allergy and anaphylaxis guidelines (2014) 8
- BSACI guidelines: adrenaline auto-injectors (2016) ¹
- World Allergy Organisation Anaphylaxis guidance (2020)9
- Resuscitation Council UK Emergency treatment of anaphylactic reactions: Guidelines for healthcare providers (2021) 10
- EAACI guideline: Anaphylaxis (2021 update)¹¹

Stakeholder groups

Stakeholder groups involved in the generation of this guidance were:

- British Society for Allergy and Clinical Immunology (BSACI)
- Allergy UK (Amena Warner, Head of Clinical Services)
- Anaphylaxis UK (Sarah Baker, Head of Heath policy and Developments)
- Asthma UK (Dr Andy Whitamore)
- Pharmacy (Hadar Zaman)
- The BSACI Primary Care Group (Dr Liz Angier and Dr Deepa Choudhury)
- The College of Paramedics (Andy Collen)
- MHRA

The views of all stakeholders have been considered in developing the guidance.

Clinical questions

Key clinical questions that might present to primary care are as follows (Box 1):

Box 1. Principal clinical questions

- 1. How are patients at risk of anaphylaxis identified?
- 2. Are tests helpful in primary care and how are they interpreted?
- 3. What can Health Care Professionals (HCP) do to manage patients in the community?
 - What self-management plans should be recommended?
 - What advice can we give about managing an acute reaction including positioning, early use of adrenaline and talking to emergency services?
 - When can children self-administer an adrenaline auto-injector?
 - What device specific training is required, how often do patients require retraining with adrenaline auto-injectors and who could deliver this?
 - How do cofactors affect reactions, and should patients be aware of them?
 - What advice can HCPs give to school, universities, colleges, and employers?
- 4. How many adrenaline auto-injectors should be prescribed?

1. Which patients are at risk of anaphylaxis and require AAIs?

Some patients have an absolute need for prescription of adrenaline auto-injectors (the exception being drug allergy where the drug is mainly easily avoided). In others the assessment of risk of future anaphylaxis is complex as there are limited predictors of future severe reactions that are applicable in all patient's assessment (refer to Figure 1: Algorithm for absolute and relative indications for prescribing).

Where the HCP is uncertain about the risk of anaphylaxis, they can explain that they are prescribing adrenaline as a safety netting procedure pending review in a specialist allergy clinic. The allergist may continue, discontinue, or change the number of Adrenaline Auto-Injectors prescribed. Every patient prescribed AAIs or considered at risk of anaphylaxis must be reviewed by a specialist. Prescription of AAIs is not a substitute for referral.

2. Are tests helpful to decide whether or not to prescribe AAIs in primary care and how are the tests interpreted?

The decision to prescribe AAIs should be based on an allergy focused history and not allergy tests (which by themselves are unhelpful in determining severity).

Validated allergy tests can be helpful in allergy diagnosis, but only in the context of an allergy-focused history. 6,8 Validated tests ordered include serum specific IgE test or a skin prick test, both giving similar results. IgE sensitisation tests need to be interpreted with caution as false positive test results are common. With a positive history of an IgE

mediated allergy (rapid onset of skin, respiratory or gastrointestinal symptoms), a positive specific IgE usually confirms the allergy. A negative test usually excludes allergy (false negatives occur, but infrequently). A baseline serum tryptase measurement is helpful following venom reactions. It may or may not be feasible to request serum tryptase in the primary care setting depending on local laboratory arrangements. Requests for screening serum IgE panels should be avoided due to the frequency of false positive results when allergy does not exist. Total IgE measurement alone is not helpful in primary care. GPs with extended roles (GPWER) can facilitate testing and interpretation of clinical history and results in liaison with allergy networks. Skin prick tests need to be performed by those with the competencies to do the tests and interpret the results with the appropriate equipment and resuscitation facilities available.

3. What can HCPs do to manage patients in the community?

Prescribing adrenaline auto-injectors

There are currently different types of auto-injector devices available in the UK. Training should be specific to the device and practical training with a dummy device should be repeated at every opportunity ideally annually (e.g., each re-prescription). If a prescription of the brand of the AAI devices is changed to another device, then patients will require retraining in the practical use of the new devices as devices require different techniques. Some patients will have had one type for many years with good effect; others may prefer different designs, which they find easier to use. When seeing patients prescribed AAIs remember to always ask to see their devices to check that they are carrying them, and they are in date. It is also helpful to remind them to carry a charged mobile phone in case they need to call for help.

Training and use of self-management plans

AAI training should be incorporated into the process of prescribing and dispensing of the device. AAI - training could be delivered by one of several different health care professionals in the community (e.g., physician associates, practice nurse, pharmacists, paramedics, GPs) provided they have the competencies to do this. It is essential to have training in the administration of AAIs in the settings where patients are seen (Figure 1). Risk factors for fatal anaphylaxis include failure to carry AAIs, lack of knowledge of how to use them, delay in administration of adrenaline, use of out-of-date devices and poorly controlled asthma.¹⁴ Regular retraining, emphasizing the importance of carrying AAIs at all times and going through an updated anaphylaxis plan whilst controlling co-morbidities, such as asthma, is therefore important. Patients should use their AAI if they develop breathing problems or feel they are about to collapse during an allergic reaction. They should sit up if they are having breathing difficulties and lie down if they are feeling faint. Patients should have used their AAI and then called 999 asking for the ambulance service, stating their location, and that they are having an anaphylactic reaction (ANA-FIL-AX-IS phonetically) to ensure the 999 call is appropriately triaged. All these details will be found on the BSACI anaphylaxis management plan (https://www.bsaci.org/about/download-paediatric-allergyaction-plans), which should be provided to the patient. The plans can be tailored according to the presenting patient. The local allergy clinic may provide some more patient specific advice after referral (Figure 2).

Allergy Action Plans - BSACI

In anaphylaxis in children, children at primary school should have the AAI administered by a trained individual; children at secondary school should be trained to carry and administer their AAIs themselves, though this will depend on the individual's maturity and readiness. If necessary, they can have the AAI administered by trained staff as well.

Specialist community dieticians have an important role in advice on food allergen avoidance (e.g., reading labels, food labelling legislation, avoiding cross-contamination, awareness of different ingredient names, avoiding or risk assessing different risk situations such as shared buffets, barbeques, curry houses, restaurants, takeaways, and food stores) as well as ensure that patients continue to have an adequate diet. They can also advise and signpost to awareness of product recalls and signing up to services that that offer text/email alerts.

Replacement of expired auto-injectors and re-training

Patients should be reminded that AAIs expire and to check the date when picking up their prescription. Companies have a reminder system in place for patients using text messaging for which patients can register (http://www.epipen.co.uk/patients/expiry-alert-service/, https://www.emerade-bausch.co.uk & https://adults.jext.co.uk/).

They should be informed about storage of AAIs and the process for renewal. Patients should obtain their own trainer pens (they can get these free from the brand company) and practice with them regularly. Patients should also be retrained with a dummy auto-injector on each re-prescription.

Asthma control

Co-existing asthma, particularly when it is poorly controlled or there is a current exacerbation, can worsen the severity of the allergic reaction. It is important that asthma control should be regularly reviewed and optimised where necessary, which could be done in the annual primary care review.

Co-factors

Certain co-factors may worsen the severity of an allergic reaction. Patients need to be aware that these include exercise, lack of sleep, stress, alcohol and NSAIDs. Certain co-factors may worsen the severity of an allergic re-action. These include exercise, lack of sleep, stress, alcohol and NSAIDs, asthma and acute illness. 4,5 Patients should be made aware of these.

Concomitant medications

Beta blockers may impede the response to adrenaline. If a patient has been prescribed these, the indication for the beta blockers should be reviewed to ensure it is still required.⁸

Advice for school, universities, colleges, and employers

It is recommended that patients give a copy of their anaphylaxis management plan to school, universities, colleges, and employers so that staff are aware of their allergies. There is new legislation to allow schools to keep generic adrenaline auto-injectors at school for pupils who already have a prescription of adrenaline (https://www.sparepensinschools.uk).* This does not alter the requirement for the number of auto-injectors to be prescribed. Staff should be aware of how to administer the AAIs.

4. How many AAIs should be prescribed?

The longstanding regulatory advice is that patients should be prescribed two AAIs <u>Public Assessment Report: Recommendations to support the effective and safe use of adrenaline auto-injectors - GOV.UK (www.gov.uk)</u> as the norm, and that the patient should always have immediate access.

This is because of the possibility of a severe reaction that needs more than one dose of adrenaline before the arrival of emergency services, or device failure or misplacement of the first injection.

The BSACI adrenaline guideline for allergy specialists recognised that there is a lack of training and allergy management plans in place and these need to be incorporated into the service delivery.

Parents may request that a total of four AAIs are prescribed, two for school and two for other times. This can be reduced back to two once the child is able to administer and allowed to carry their own AAIs at school. Parents should be reminded that their child should always have access to the AAIs even on the way to school.

Requests for more than two (four, for a child) AAIs should be discouraged. The overriding principle is that the patient should always be carrying the AAIs, rather than having them at multiple locations which might not be accessible at all times.

5. How to recognise at risk groups and at-risk situations and how to manage them?

Adolescents and young adults are at the highest risk of severe/fatal anaphylactic reactions.^{3*} Adolescents and young adults need to know how to tell others about their allergy without being embarrassed within peer groups or other social situations and carry their adrenaline.^{16*} University students may be vulnerable as they are living independently away from home in a new setting. Adolescents and young adults are at risk of fatal anaphylaxis and need an individualised approach. Adolescents and young people may require a specific developmental appropriate approach which may be supported by transition services. Adolescents and young adults are at highest risk of severe or fatal anaphylactic reactions to food, but the elderly have the highest risk of fatal drug anaphylaxis (see online case 5).2,5 Adolescents and young adults need to know how to advocate for their allergy within peer groups or other social situations.

Caution needs to be exercised during parties, roadside vendors, travel in unfamiliar places with different languages, festivals, takeaways, restaurants, and food stores. Curry and oriental restaurants may also have sauces and recipes containing high nut content for nut allergy patients, so an awareness of those dishes, the names of these and their ingredients can be helpful. Patients need to be warned to be particularly vigilant in these circumstances.

https://www.anaphylaxis.org.uk/campaigning/easy-to-ask-campaign/ https://www.allergyuk.org/information-and-advice

Food labels laws can be confusing.¹⁷ Patients should be encouraged to declare their food allergies any time they purchase food even if it does not appear to contain their trigger allergen(s). They should also carry their AAIs at all times.

Travel on airplanes should be covered by carrying the BSACI anaphylaxis action plan to cover carrying AAIs on the plane (see reverse of the BSACI anaphylaxis management plan). The patient support groups give advice on different airlines and travel translator cards. Patients should be advised to contact the airline before travelling to understand the airline policy.

Applicability and utility

The UK has the highest rate of AAI prescriptions, far exceeding other European countries. Studies around the world show both over and under prescribing of adrenaline. 18,19

A UK BSACI nurses audit of children attending allergy clinics showed that within this group many children either did not carry their AAIs with them, the AAIs had expired, or they had not been trained to use it. When primary care had been issued the AAI action plans were often not present²⁰. Appropriate prescribing and focus on training are essential. Further research on prescribing in primary care is required to highlight any gaps in care and actions that can be taken.

Ongoing barriers to care delivery.

UK allergy reports note the barriers to the delivery of effective allergy care. 21,22 These include the lack of both specialist and primary care health care workers with allergy training. fragmented service delivery, long waiting times and inconsistent management advice and referral patterns. Patient support groups are an excellent source of support and guidance.²²

GPs in the UK have no incentive in their current Quality of Frameworks (QOF) payment system for anaphylaxis and food allergy. The quality standards and NICE community guidelines are not mandatory or routinely audited for compliance in the community.⁷

Allergy specialists have reported difficulties with services and triaging patients as the referral letters do not always contain the relevant information.²² There are no agreed national quality standard pathways or templates although recent projects have tried to implement these for some conditions with mixed results.²² Allergy clinic discharge letters should clearly highlight changes to medications, triggers to avoid, required follow up and whether the allergy is considered to be persistent or will be outgrown. Some specialist units request a re-referral in several years' time from discharge or the last appointment, but some children may not have this instigated and therefore be lost to follow up in the system as there are no automatic reminders in the community records to do this. Other patients may be referred from paediatric allergy clinics to adult ones and then do not attend (DNA) and be discharged, but the GP may not be aware of this in their records. These patients may also be lost to follow up on ongoing training and advice. Clearer communication on DNAs of patients between paediatric and adult units and the community teams with the opportunity to follow up and re-access to care and advice would assist in addressing this gap. Patient initiated follow ups may also help to avoid gaps in care.

Many patients prescribed AAIs are not trained on how to use them and studies have shown that health care professionals themselves do not know how to use AAIs.²³ Therefore, ongoing education training of staff to enable them to deliver this care is needed. Studies have shown that some patients are also reluctant to use the AAIs during reactions and may not carry them at all times; concerns and beliefs about treatment should be explored in the consultations with clear explanations.²³ Protective factors for using an AAI include being part of a peer support group, use of a trainer pen, recent training and a severe reaction in the past.21

Some of these barriers of care delivery may be overcome by using imbedded information technology decision support and guidance systems into the GP desktop software.^{24,25} Work with a validated history tool for pollen food syndrome demonstrated that it was as good as a specialist review.²⁶ Other barriers can be overcome with good interdisciplinary care across an integrated health system. A set of competencies for allied health professionals working in allergy has been published by EAACI and a set of competencies for GP with extended roles (GPWER) has been put forward to the RCGP. 13,27 These approaches have the potential to increase the expertise of primary care professions in allergy. The role of pharmacy professionals now working in GP surgeries and across primary care networks (PCN)could be expanded to include re-training patients to use AAIs. The BSACI has developed specialist networks that can support training of allied health and primary care https://www.bsaci.org/professionals/adult-allergy-networks.

Studies have shown consistent gaps in primary care knowledge and delivery of services in allergy and anaphylaxis management, and we have tried to address most of these.²⁸⁻³⁰ Allergy education could be improved with core competencies such as history taking, diagnosis and management defined.³¹ Further work in this area is recommended.

Summary of the guidance and future recommendations

This guidance highlights how to identify which patients are at risk of anaphylaxis. It describes how to prescribe adrenaline auto-injectors and how to train patients to use them appropriately. The guidance emphasises the need for referral to a specialist allergy clinic and how the specialist and primary care teams should work together to avoid gaps in care. Some allergies are life-long with patients needing regular review and re-training of their AAIs. Although this guidance is primarily aimed at primary care workers, some of the content could be helpful to staff in accident and emergency and secondary care. The recent MHRA report Identifies key areas to improve on with AAI and is a helpful document for primary care. the Fuller stocktake report shows the vision of primary care ahead which will include working across different areas and more integration of services which GPWER can help to implement.

Currently service delivery for patients in the community at risk of anaphylaxis is not ideal. Work is required to strengthen the allergy networks with investment in community services and across primary care networks to widen the access to high quality allergy care. Further qualitative work on communication and patient experience could help inform pathways. Recent international guidance has also been developed for adolescents and young adults as well as transitioning services for asthma and allergy which may help inform service design for this vulnerable group.³²

Work on GP computer systems with system alerts and reminders for AAI prescribing and training could be helpful alongside decision support and template guidance for referrals. Previous studies have shown gaps in knowledge for GP trainees.³³ Some training resources are included in the appendix for interested HCPs such as dieticians and pharmacy and physician associates and nurses. There are good recent examples of successful GPWER allergy clinics emerging with improvements in patient outcomes across the system.³⁴ Integrated Care Systems (ICS) should ensure adequate pathways of care to enhance the patient journey with appropriate advice and guidance where possible. Primary care networks could look at helping their additional roles and staff with training to support this. The framework specifies key competencies and may be of interest to general GPs as well. Integrated care systems should also ensure that there are systems in place for consistent training and retraining of AAIs on an ongoing basis that is accessible to patients and their families alongside safety- netting of pathways to avoid patients being lost to follow up. The recent Fuller report and Hewitt review show potential direction of travel for primary care and working across organisations. A mobile workforce with generalist skills and areas of interest could support the integrated model described looking at adding value to the system and better patient outcomes. They support multi-disciplinary team working and integration of health teams across the system and also encourage patient self-management. Better education and training of health care professionals and improved access to trusted resources for patients could help implement this.35 The GPwER framework will be added to the BSACI website, and the plan is to pilot the accreditation process with a few members this year (2023).

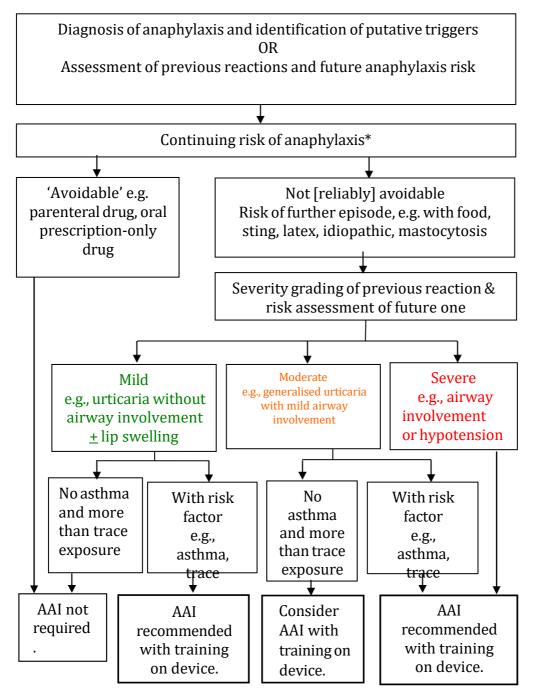
NICE has recently updated their anaphylaxis guidance. Patients with or at risk of anaphylaxis should be issued with two AAIs and be trained on how and when to use them, as well as be advised to carry them.³⁶ This document supports care of patients closer to home and integrated care - these are key components of NHSE policy.³⁷

There is an infographic from MHRA which summarises the key messages. 17002885 The correct use of your Adrenaline Auto-Injector AAI CC V10.pdf (publishing.service.gov.uk)

This guidance is timely as many patients have disclosed possible allergic reactions as part of the history for covid vaccination programme or have possible historic allergies listed or on alerts in their electronic notes without clear clinical detail of anaphylaxis. This guidance aims to give some more clarity on how to approach those situations, to allow a good history

to be taken and to signpost to other services and resources such as the green book for further information.	and to signpost to other services and resources such as the green book for mation.			

Figure 1: Algorithm for support of prescribing AAIs



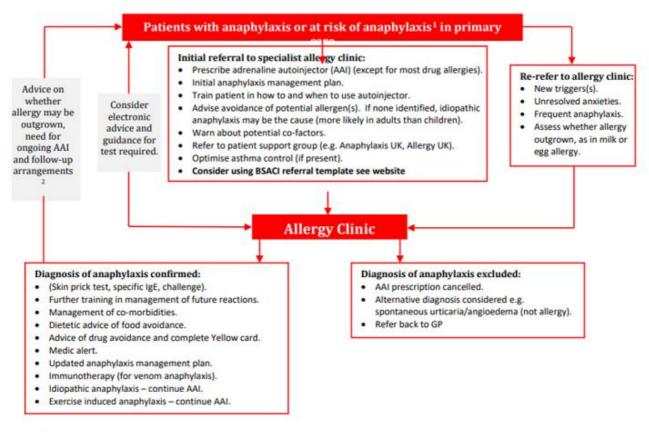
In the absence of additional risk factors, GI symptoms in infants and young children do not usually require adrenaline auto-injectors.

Train in the use of AAIs if prescribed and refer to allergy clinic.

https://www.bsaci.org/wp-content/uploads/2020/01/Ewan_et_al-2016-Clinical_26_Experimental_Allergy.pdf

Figure 2: Service delivery pathway

Algorithm for patient with anaphylaxis or at risk of anaphylaxis* in primary care



Footnotes:

- 1. At risk of anaphylaxis:
 - · Food allergy with unstable or moderate/severe asthma.
 - · Generalised urticaria to bee or wasp sting.
 - · Generalised urticaria to trace amounts of allergen exposure.
 - Mild/moderate allergy reaction with concurrent asthma.
- 2. Retrain on AAI and adjust dose of AAI for age/weight in both primary and secondary care.

Appendix 1: Adrenaline dosages for health care professionals

Adapted from the Resus Council Guideline 2021.

Give intramuscular (IM) adrenaline

Use adrenaline at 1 mg/mL (1:1000) concentration

Adult and child > 12 years: 500 micrograms IM (0.5 mL)

Child 6-12 years: 300 micrograms IM (0.3 mL)

Child 6 months to 6 years: 150 micrograms IM (0.15 mL)

Child <6 months: 100-150 micrograms IM (0.1 -0.15 mL)

The above doses are for IM injection Only

Inject at
anterolateral aspect—
middle third of the thigh





Appendix 2: Frequently Asked Questions (FAQs)

Question: Can an unqualified bystander administer an AAI in the community if needed? **Answer:** Yes, if they are doing this in the best interests of that person in a life-saving situation and they cannot administer it themselves. It is legal to do so and there are no risks associated with the bystander for trying to assist. See FAQs Resus council *

Question: Can pregnant women receive adrenaline via an AAI?

Answer: Pregnant women should be prescribed and have adrenaline administered as normal. Management for anaphylaxis in pregnant women is approached in the same way as for non-pregnant women, alongside modifications to positioning with the mother lying on her left side (left lateral position) to improve venous return to the heart*.

Question: What dose of adrenaline would you give a child under six months?

Answer: Children under 6 months rarely require intramuscular adrenaline, as severe allergy is rare and allergen avoidance is usually easily achieved as the parents control the diet, but it can be prescribed at a dose of 150mcg. The patient should be discussed with the local paediatric allergy clinic.

Question: If you need to give a second dose of adrenaline when can you give it? **Answer:** You should give a second dose of intramuscular adrenaline after 5 minutes, if there is no improvement.

Question: What is biphasic anaphylaxis?

Answer: Biphasic anaphylaxis is the recurrence of anaphylaxis after treatment. This is estimated to occur in up to 20 percent of cases however it is difficult to get accurate numbers as the studies are of poor quality. Most often it occurs within 4-12 hours, but it can occur up to 72 hours afterwards. A delay in giving the initial dose of adrenaline may increase the risk of biphasic reactions.

Question: What is idiopathic anaphylaxis?

Answer: Idiopathic anaphylaxis is thought to occur spontaneously i.e., there is no trigger. It is diagnosed from the history combined with tests to exclude other causes. It can be of slower onset with evolution over an hour or longer, beginning with pruritus then erythema/urticaria often including gastrointestinal features followed by hypotension. There is a higher risk of recurrence.

Question: Which allergies are commonly outgrown?

Answer: Most children outgrow milk allergy. However, when the allergy persists into adulthood, they may have severe reactions. Egg allergy is more common in children than in adults and most children will outgrow this. Peanut allergy tends to persist with only approximately 10 to 20 percent of children outgrowing the allergy.

Question: Why is positioning important during anaphylaxis?

Answer: It is important to maintain blood pressure and circulation if there is hypotension by lying flat, but if breathing difficulty is the main problem (as is usual in food allergy) it is better to support respiration by sitting the patient up. Avoid sudden movements.

For collapse, lie patient flat with legs raised (if breathing is difficult, sit patient up). Do not stand the patient up - this is to avoid empty ventricle syndrome, which can be fatal. Avoid sudden movements in changing in position such as sitting up which can cause hypotension. Patients who are unconscious should be placed in the recovery position*.

Question: What are different causes of anaphylaxis in different age groups?

Answer: The common causes in adults are food, drugs, venom and idiopathic. In children, the main cause is food allergy.

Question: Is the presentation of anaphylaxis different in adults and children? **Answer**: Children mainly present with respiratory difficulty such as breathlessness, stridor or wheeze because the anaphylaxis is usually due to food allergy. In adults, the presentation is often predominantly cardiovascular e.g., in venom or drug allergy.

Question: What are the causes of fatalities?

Answer: Fatal reactions in the United Kingdom are due to drugs (about 50% of those

whose cause was identified), foods (about 25%) and venom (about 25%).

Question: What are the common foods involved in food allergy?

Answer: Cow's milk, eggs, tree nuts, peanuts, shellfish, fish, soy and wheat.

Question: What are the different clinical presentations of anaphylaxis?

Answer: With parental allergens, such as insect or IV drugs, hypotension is the dominant symptom and patients can present with sudden loss of consciousness. This contrasts with foods where airway involvement is dominant (laryngeal oedema and/or asthma)

Question: What is exercise induced anaphylaxis?

Answer: This is a rare condition where anaphylaxis occurs after physical activity. This is more often seen in adults than children.

Question: Are Black and Minority Ethnic (BAME) groups more at risk of anaphylaxis? **Answer:** Limited published data indicate a higher risk of food allergy associated anaphylaxis, ED attendance and shorter specialist follow up. ³⁸

Question: Are there any contraindications to using adrenaline in anaphylaxis?

Answer: There are no absolute contraindications to the use of IM adrenaline in an allergic emergency.

Question: Where can you report adverse events?

Answer: It is important to document these this can be done at

www.mhra.gov.uk/yellowcard

Question: Where is there information about possible reactions to the Covid vaccination? **Answer:** The green book has a chapter on this, available on the BSACI website *

Question: Are there any other conditions that look like anaphylaxis?

Answer: Idiopathic angioedema and urticaria are often confused with anaphylaxis (see clinical cases). Another rare condition is hereditary angioedema, which can cause laryngeal oedema, which is not responsive to adrenaline. These patients need a specialist review and treatment with c1 inhibitor.

Appendix 3: Illustrative cases

Case 1

A 75-year-old woman with no comorbidities comes in for their flu vaccination. They have had a difficult drive in, and they appear to be unsettled. You give the flu vaccination into the left arm. This goes well with no local problems at the site. However, after 5 minutes they start to feel unsteady and unwell and then collapse. What might be the differential diagnosis? What might you look for?

Anaphylaxis is rare after vaccination with an approximate rate of 1 per million. Other differentials more commonly seen could include faint/syncope or panic attack and these should be considered and assessed. If there is uncertainty as to the diagnosis between fainting and anaphylaxis and no initial improvement, anaphylaxis can be presumed, and the appropriate management started.

In a syncope or faint some features could include bradycardia but with a strong central pulse, transient hypotension improved by a supine position, pallor and transient loss of consciousness improved by supine position. Respiration should be normal but may be shallower. There should be recovery with positioning and symptoms should be transient. Timing can be before, during or within minutes of the injection.

In a panic attack there might be hyperventilation and paraesthesia and pins and needles of the arms and legs and hands. There may be an erythematous rash associated with anxiety. There might be anxiety about the vaccination or needle phobia or something else that has occurred on that day or an anxiety disorder. There should be no hypotension. Response to reassurance and control of breathing should help alleviate symptoms. Timing can be before, during, or within minutes of the injection.

In anaphylaxis there could be acute onset with initial tachycardia and weak central pulse. There might be itch, coughing wheeze, stridor and cyanosis and tachypnoea, rapid onset and sustained hypotension, urticaria and they might feel a sense of impending doom. Skin changes could also include angioedema, pallor and flushing. In cases of anaphylaxis, 20 percent do not have urticaria and urticaria alone is not anaphylaxis. There may be gastrointestinal symptoms such as vomiting and abdominal pain. There may be anxiety and distress and loss of consciousness. Timing of reaction can be within minutes after the injection or up to two hours.

The criteria for anaphylaxis are, anaphylaxis is 'a severe, life-threatening, generalised or systemic hypersensitivity reaction'. It is characterised by rapidly developing features involving one or more of the airways (laryngeal oedema and/or bronchospasm) and circulation (hypotension), often with associated skin and mucosal changes (urticaria, angioedema).

Check for ABCDE as per the algorithm from Resus Council (Appendix 7). Lie the patient down and elevate the legs; if respiratory symptoms predominate, adjust posture to one of comfort avoiding sudden movements (see positioning FAQS). Call for help, state location and administer adrenaline IM in the doses recommended into the mid part of the anterolateral aspect of the thigh. Record the time of administration of adrenaline. If no response, repeat after 5 minutes. If there is oxygen at the surgery and it is indicated can give high flow at 6-8 l/min. Crystalloid Fluids can be given. If deterioration and if indicated, perform CPR (see algorithm)

Do not try to move or sit the patient up suddenly as this may cause severe hypotension and deterioration. Do not walk to the ambulance. Wait for ambulance crew who can transfer them by stretcher.

See table below taken from green book chapter 8 v4 and resources green book and algorithm attached in appendix 7.

Clinical Features of Fainting and Anaphylaxis

Clinical Features of Fainting and Anaphylaxis				
ONSET	FAINTING	ANAPHYLAXIS		
	Before, during or within 5 minutes of vaccine administration	Usually within minutes of vaccine administration but can be up to two hours.		
Symptoms/signs	3			
Skin	Generalised pallor, cold clammy skin	Skin itchiness, pallor or flushing of skin, red or pale urticaria (wheals) or angioedema		
Respiratory	Normal respiration – may be shallow, but not laboured	Cough, wheeze, stridor, or signs of respiratory distress (tachypnoea, cyanosis, rib recession)		
Cardiovascular	Bradycardia, but with strong central pulse; hypotension – usually transient and corrects in supine position	Tachycardia, with weak/absent central pulse; hypotension - sustained		
Neurological	Sense of light- headedness; loss of consciousness – improves once supine or head down position; transient jerking of the limbs and eye-rolling which may be confused with seizure; incontinence	Sense of severe anxiety and distress; loss of consciousness – no improvement once supine or head down position		

Case 2

A 3-year-old boy is brought in by his mother. She tells you that he has had a reaction to a small amount of peanut butter on toast at home. He immediately became wheezy and had an altered hoarse voice with angioedema of his lips with vomiting and generalised urticaria. He had severe eczema as a baby and now has rhinitis and asthma. Does this boy need to be prescribed AAIs?

Answer: Yes, he needs to be prescribed AAIs. The timing of the reaction and symptoms suggest an IgE-mediated allergy with systemic features. Children often present with respiratory symptoms with food allergy. The altered voice suggests laryngeal oedema. The child should be referred to the allergy clinic, prescribed AAIs and his parents/carers should be trained in when and how to use them. An initial anaphylaxis plan can be given with advice to avoid peanuts and tree nuts until assessed. Patients can be directed to Allergy UK or Anaphylaxis!! who can provide advice such as how to inform schools. Allergy tests can be done at the allergy unit when he is reviewed. His rhinitis and asthma should be treated to ensure that they are optimally controlled.

Case 3

A 12-year-old girl has noticed itching in her mouth for ten minutes after eating raw apples. She can eat apple pie and apple sauces without problems. She also has mild tingling of her lips after eating cherries and plums. She has springtime hay fever but no asthma. How would you manage her?

Answer: She does not need an AAI. This is pollen food syndrome which causes symptoms with raw fruits but not cooked as the allergenic protein is denatured by heating. This is usually a mild condition and should be treated by washing out the mouth with water, followed only if needed, by an antihistamine. She has no concerning symptoms, and they resolve quickly. She could avoid the raw fruits or peel them or eat the heated form. This is a common allergy. She can be managed in primary care if only a few fruits are involved and mild symptoms. Any symptoms with nuts should prompt a referral to the local allergy clinic as it is difficult to distinguish this from true nut allergy. Referral to a patient support website may be helpful.

Case 4

A 65-year-old man taking beta-blockers for anxiety collapses after being stung by a bee whilst tending his roses. He was treated in the local emergency department and was advised to attend his GP a few days later for review. What would your management be?

Answer: In venom allergy patients with anaphylaxis can present with hypotension alone. Ask about other features such as urticaria, angioedema or wheeze. Management includes issuing AAIs and training in when and how to use the AAIs. His beta-blocker prescription should be reviewed, and alternative options discussed as this may interfere with the action of adrenaline if it is required. An initial anaphylaxis plan could be issued with information on support groups. He should be referred to the local allergy clinical for confirmation of allergy and consideration of venom immunotherapy.

Case 5

A teenager comes in for an asthma review. He has allergic rhinitis, asthma and sesame allergy. He has previously had anaphylaxis to eating sesame. You notice that he has not had a recent prescription for AAIs. On further enquiry he tells you he has been busy going out to parties, he likes the gym, festivals, late nights out, and has takeaways often. What would you do?

Answer: He is in an at-risk group for anaphylaxis. He needs to have up to date AAIs, these should be checked if he has them with him, if not you should re-prescribe them and advise to carry them at all times. He should be warned about at-risk situations and cofactors to reactions such as exercise and alcohol. You should check if he has a written emergency treatment plan and optimise his asthma management. Advise on patient support groups. Warn him about confusing labelling laws and that foods prepared on the premises currently don't have mandated labelling meaning he always needs to ask about ingredients with any transaction with foods.

Case 6

A 35-year-old woman presents with a five-week history of intermittent urticarial rashes with no temporal relationship to foods. The rashes last for a few days and there is no bruising with them. How would you manage her?

Answer: She does not require an AAI. This presentation is characteristic of chronic spontaneous urticaria. Try regular non-sedating long-acting antihistamines. Refer to local allergy clinic and guidance if not settling on increased doses of antihistamines.

Case 7

A 45-year-old man with diabetes and recurrent infections presents with a possible penicillin allergy. He collapsed and had a severe breathing problem after the second dose of amoxicillin for a chest infection. He has had penicillin before with no problems. How would you manage him?

Answer: He does not require AAIs as the medication penicillin can be easily avoided. He needs a referral to an allergy unit as he will have an ongoing requirement for antibiotics. The features in history are of a systemic anaphylactic reaction. He could be given advice on medic alerts and a warning about penicillin allergy placed on the GP records until the clinic review him. The allergy unit may do the following investigations: skin prick tests, intradermal tests to penicillin's and blood tests. A drug challenge may be performed in the specialist unit. The allergy unit, after confirming an allergy, will write with advice on which alternative drugs can be used and those which must be avoided.

Case 8

A 68-year-old man comes to see you. He has been waking up with tongue swelling at 5am for three months. He has been on the antihypertensive treatment ramipril for 5 years for hypertension. How would you manage him?

Answer: Stop the ramipril as ACE inhibitors can cause angioedema after any period of time and can cause fatal airway obstruction. There is no temporal relationship to foods in the history. Cessation of the drug usually improves symptoms, but there is often a lag of a few months. If symptoms are ongoing, other causes of angioedema should be considered and advice sought from the allergy unit with a referral instigated.

Case 9

A 10-year-old boy with asthma is brought to your surgery by his parents after having a reaction with swelling of his lips and wheeze after eating peanuts. How would you manage him?

Answer: The wheeze suggests that it is a severe reaction. Asthma is a potential cofactor; subsequent reactions may be worse if the asthma is uncontrolled or another cofactor such as exercise is present. This patient should be referred to an allergy clinic for management. In the meantime, it would be reasonable to prescribe AAIs and train both the child and parents how and when to use. Advice should be given on support groups, an anaphylaxis plan provided, advice on avoidance given and asthma control optimised.

Appendix 4: Summary

Identify

Consider prescribing AAIs if:

- •Anaphylaxis: if history of acute attack of one or more of wheeze, breathlessness, stridor, collapse, hypotension (+/- angioedema (swelling)/urticaria).
- •With no previous anaphylaxis, but at-risk: -Food allergy with co-existing unstable or moderate to severe asthma*
- -Generalised urticaria to bee or wasp stings.
- -Generalised urticaria to trace amounts of allergen exposure.

Patients with allergies have differing levels of risk for anaphylaxis. The level of risk should therefore be considered when deciding a patient's need to carry AAIs.

Think about increased risk with these red flags:

- •asthma (unstable or severe)
- •cardiovascular disease
- beta-blockers
- •allergy to peanuts, tree nuts, shellfish
- severe milk allergy
- •systemic mastocytosis*

Cases not requiring AAIs include:

- •mild food allergy without asthma
- drug allergy if easily avoided
- •angioedema/urticaria alone (unless angioedema involves the airway includingtongue swelling)
- •if on an ACE inhibitor and have developed isolated facial/tongue/laryngeal oedema,consider stopping the ACE inhibitor medication and review as this may be the cause.

Prescribe

Prescribe initial AAIs, pending specialist appointment. The MHRA recommends patients should always have two in-date AAIs available:

<u>Public Assessment Report: Recommendations to support the effective and safe use of adrenaline auto-injectors - GOV.UK (www.gov.uk)</u>

Inform patient/carer about AAI expiry reminder services:

https://www.bsaci.org/wp-content/uploads/2023/05/AAI-Frequently-Asked-Questions.pdf

Inform about any AAI alerts, extended expiry dates or supply issues. For correct dosage, see Appendix 1. Children should be weighed to check they have the right dose of AAI.

Train

- •Educate patient/carer on how to use the AAIs (using trainer devices).
- •Recognition and prompt treatment of allergic reactions.
- •Annual re-training in AAIs technique on when and how to use.
- •AAI should be by given by the intramuscular route in the mid outer thigh -anterolateral aspect of middle third of thigh.
- •Training should be device specific. If a patient is switched to an alternative brand of AAIs, advice on how to use them should always be provided.
- □Educate patients about carrying their AAIs at all times and appropriate allergen avoidance measures. https://www.bsaci.org/about/download-paediatric-allergy-action-plans
- •Give information about avoiding trigger(s)https://www.allergyuk.org, https://www.anaphylaxis.org.uk/

Practical AAI training is essential and could be provided by a competent health care professionals (e.g., trained practice nurses, pharmacist etc.) https://www.bsaci.org/wp-content/uploads/2023/05/AAI-Frequently-Asked-Questions.pdf

It is vital that health professionals also keep up to date with devices and meet relevant competency requirements.

https://www.bsaci.org/wp-content/uploads/2019/12/AllergyNurseCompetences_Edition1_Nov2014.pdf

Refer

Refer to Allergy specialist http://www.bsaci.org/find-a-clinic/index.htm) with symptoms and suspected trigger(s) with temporal relationship, GP referral form.

Support

- •Anaphylaxis treatment plans are available (https://www.bsaci.org/about/download- paediatric-allergy-action-plans)
- •Optimise asthma management.
- •Inform patient/carer about support organisations.

https://www.allergyuk.orghttps://www.anaphylaxis.org.uk/

Home - AllergyWise - Online training for Healthcare Professionals and Patients / Carershttps://www.asthma.uk

- •To support education about trigger avoidance, asthma, and anaphylaxis.
- •Follow up to ensure AAI renewals/re-training and identify if new allergies (can be done with asthma review).

Appendix 5 – Definitions and resources

BSACI website https://www.bsaci.org

MHRA: Public Assessment Report: Recommendations to support the effective and safe use of adrenaline auto-injectors - GOV.UK (www.gov.uk)

17002885 The correct use of your Adrenaline Auto-Injector AAI CC V10.pdf (publishing.service.gov.uk)

Food allergy definition NICE guideline and Quality Standards

https://www.nice.org.uk/guidance/cg116

Food allergy has been defined as 'an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food'. It can be classified into IgE-mediated and non-IgE-mediated reactions (although some responses can involve both types). IgE-mediated reactions (difficulty swallowing or feeling sick or vomiting) are often immediate and have a rapid onset whereas non IgE-mediated reactions (redness and itchiness of the skin or heartburn) are generally characterised by delayed reactions.

BSACI Allergy Action Plans:

https://www.bsaci.org/professional-resources/allergy-action-plans

Definition mastocytosis NHS website

https://www.nhs.uk/conditions/mastocytosis/

Mastocytosis is a rare condition caused by an excess number of mast cells gathering in the body's tissues.

There are 2 main types of mastocytosis:

- Cutaneous mastocytosis, which mainly affects children where mast cells gather in the skin, but are not found in large numbers elsewhere in the body
- Systemic mastocytosis, which mainly affects adults where mast cells gather in body tissues, such as the skin, internal organs and bones

There are also several subtypes of systemic mastocytosis, depending on the symptoms. Patients with mastocystosis have an increased risk of anaphylaxis.

Guideline on asthma BTS 2019-BTS

https://www.brit-thoracic.org.uk/about-us/pressmedia/2019/btssign-british-guideline-on-the-management-of-asthma-2019/

Asthma UK videos

https://www.asthma.org.uk/advice/manage-your-asthma/

Easy to ask campaign

https://www.anaphylaxis.org.uk/campaigning/easy-to-ask-campaign/

Expiry alert services

http://www.epipen.co.uk/patients/expiry-alert-service/

https://adults.jext.co.uk

https://www.emerade-bausch.co.uk/patient

Product recall services FSA /AA

https://www.food.gov.uk/news-alerts

Definition mastocytosis NHS website

https://www.nhs.uk/conditions/mastocytosis/

Patient organisation helpline numbers

https://www.allergyuk.org/get-help

https://www.anaphylaxis.org.uk/contact-us/helpline/

Translation cards Allergy UK

https://www.allergyuk.org/get-help/translation-cards, https://www.anaphylaxis.org.uk/living-with-anaphylaxis/travelling/translation-cards/

Adolescent Guidelines EAACI with advice on transition services

https://onlinelibrary.wiley.com/doi/full/10.1111/all.14459

Resuscitation Council FAQ

https://www.resus.org.uk/home/fags/fags-anaphylaxis

Resuscitation Council guidelines

https://www.resus.org.uk/library/additional-guidance/guidance-anaphylaxis

AAI information sites

http://www.epipen.co.uk/demonstrationvideo/https://adults.iext.co.uk

http://www.emerade-bausch.co.uk

Spare Pens in school resources for HCPs and public

https://www.sparepensinschools.uk, https://www.rpharms.com/resources/quick-reference-guides/supply-of-spare-adrenaline-auto-injectors-aais

Positioning in anaphylaxis

https://www.nhs.uk/conditions/anaphylaxis/treatment/

Adverse events and Green Book

Reporting of Adverse Events www.mhra.gov.uk/yellowcard

https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book (Vaccine Safety and adverse events Chapter 8v4)

Training resources HCP

https://www.bsaci.org/education-and-events/primary-care-education/

Allergy wise training

https://www.anaphylaxis.org.uk/information-training/allergywise-training/

https://www.imperial.ac.uk/continuing-professional-development/short-courses/medicine/allergy/

https://www.southampton.ac.uk/medicine/postgraduate/taught_courses/msc_allergy.page

Appendix 6: Literature search strategy

Data base:

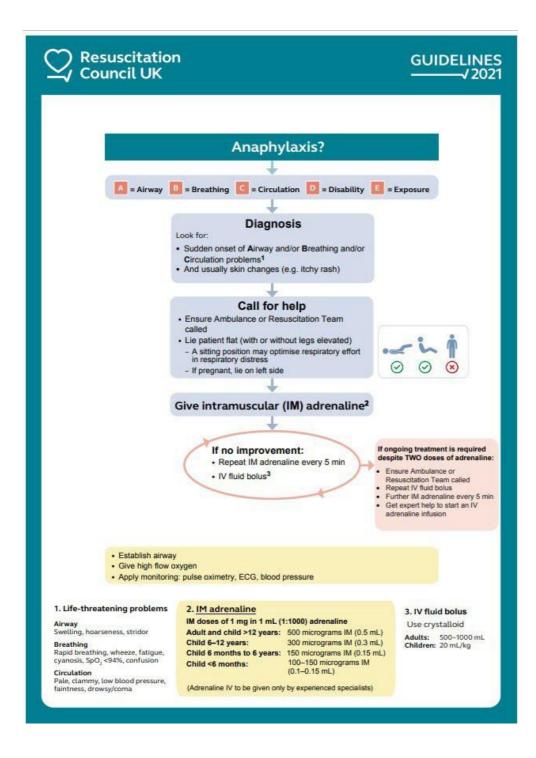
- Embase <1980 to 2019 Week 47>
- Ovid MEDLINE(R) without Revisions <1996 to November Week 4 2019>

Search Strategy:

- 1 adrenaline.mp. (22748)
- primary care.mp. (221786)anaphylaxis.mp. (56140)
- 4 epinephrine.mp. (60413)
- 5 1 or 4 (77855)
- 6 2 and 3 and 5 (111)

Known papers to the authors have also been referenced.

Appendix 7 – Management of Anaphylaxis



Appendix 8: The correct use of your Adrenaline Auto- injector (AAI)

17002885 The correct use of your Adrenaline Auto-Injector AAI CC V10.pdf (publishing.service.gov.uk)



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