Drug update 🦯

Adrenaline autoinjectors: what you need to know

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Both of the adrenaline autoinjectors available in Australia are now listed on the PBS. The devices have different administration techniques and patients should be trained how to correctly use the device that has been prescribed

for them.

Adrenaline is the first-line treatment for anaphylaxis, and should be administered as soon as possible when a patient is known or suspected to be experiencing anaphylaxis. Delayed administration has been implicated in contributing to fatalities. After administering adrenaline, the patient should be monitored in hospital or another medical facility for at least four hours. What are adrenaline autoinjectors?

Adrenaline autoinjectors are automatic injectors designed for use by nonmedical people. Two brands of adrenaline autoinjectors are available in Australia – the EpiPen and the Anapen. Although they are similar in many ways, they have significantly different administration techniques; these similarities and differences are summarised in Table 1.

Prescribing guidelines for adrenaline autoinjectors

Anapen and EpiPen are Schedule 3 drugs (Pharmacy Only Medicine) and are therefore available without prescription at full price. They are both available through PBS authority prescriptions when risk and clinical need has been assessed by or in consultation with a clinical immunologist, allergist, paediatrician or respiratory physician.¹ General practitioners can contact a specialist if they need to prescribe an initial prescription and should refer the patient to an immunologist, allergist or other appropriate specialist for further assessment. Once a patient has been prescribed an adrenaline autoinjector by

Feature	Anapen	EpiPen
Autoinjector dose	Single premeasured dose Anapen Junior – 0.15 mg Anapen – 0.30 mg	Single premeasured dose EpiPen Jr – 0.15 mg EpiPen – 0.30 mg
Colour of junior device (0.15 mg)	Green	Green
Colour of higher dose device (0.30 mg)	Yellow	Yellow
Availability	S3 (available over the counter at full price) Both devices available on PBS authority prescription	S3 (available over the counter at full price) Both devices available on PBS authority prescription
Trainer devices	Available	Available
Safety	Grey safety cap and black needle shield The needle shield can be replaced over the needle after activation	Grey safety cap Container provided to place device in after activation
Activation of device	Activated by pressing red activation button when device is on outer mid-thigh	Activated by pressing firmly against outer mid-thigh

Table 1. Adrenaline autoinjectors currently available in Australia

Australasian Society of Clinical Immunology and Allergy (ASCIA) Anaphylaxis Working Party; Head of Immunology, Child and Adolescent Health Service, PathWest; and a member of the Western Australia Anaphylaxis Management Implementation Group. Ms Vale is Project Officer for the ASCIA Anaphylaxis Training for Health Professionals Project; WA State Co-ordinator for Anaphylaxis Australia; and a member of the Western Australian Anaphylaxis Management Implementation Group.

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authority prescription, subsequent prescriptions can be provided by general practitioners.

The Australasian Society of Clinical Immunology and Allergy (ASCIA)'s

Table 2. Summary of ASCIA guidelines for prescribing adrenaline autoinjectors^{2*}

Always recommended

History of anaphylaxis

Sometimes recommended

- History of generalised allergic reaction (one or more symptoms or signs of skin, with or without gastrointestinal tract involvement and without respiratory and/or cardiovascular involvement) and one or more of the following risk factors:
 - asthma: current or past history
 - age: children over 5 years, adolescents and young adults
 - specific allergic triggers: nut/peanut allergy or stinging insect allergy in adults (bees, wasps, jumper ants)
 - comorbidity (e.g. ischaemic heart disease)
 - geographical remoteness from emergency medical care

Not normally recommended

- Asthma with no history of anaphylaxis or generalised allergic reactions
- Elevated specific IgE only (positive RAST and/or skin test) without a history of clinical reactions
- Family (rather than personal) history of anaphylaxis or allergy
- Resolved food allergy
- Generalised skin rash (only) to bee stings — in children
- Local reactions to insect stings in adults and children

* Abbreviated from the Australasian Society of Clinical Immunology and Allergy (ASCIA) *Guidelines for Adrenaline Autoinjector Prescribing*. ©ASCIA 2009. ABBREVIATION: RAST = radioallergosorbent test. recommendations for prescribing adrenaline autoinjectors are summarised in Table 2.²

All patients who are prescribed an adrenaline autoinjector should be given an ASCIA Action Plan for Anaphylaxis completed by the medical practitioner. Patients should be educated to always carry their adrenaline autoinjector and ASCIA Action Plan for Anaphylaxis.

ASCIA action plans

ASCIA has four types of action plan for anaphylaxis:

- ASCIA Action Plan for Allergic Reactions (personal) – this action plan is green and is for patients with mild/moderate allergic reactions not thought to be at risk of anaphylaxis and for whom no adrenaline autoinjector has been prescribed.
- ASCIA Action Plan for Anaphylaxis (personal) – this action plan is red and is for patients who are at risk of

Adrenaline autoinjector doses recommended by ASCIA²

- Children weighing under 10 kg (under 1 year of age): adrenaline autoinjectors are not usually recommended; deaths under age 1 year from anaphylaxis are extremely rare
- Children weighing 10 to 20 kg: a junior adrenaline autoinjector (0.15 mg dose) is usually recommended
- Individuals weighing over 20 kg: a higher dose adrenaline autoinjector (0.30 mg dose) is usually prescribed.

Note that the the approved product informations for the two autoinjectors state that Anapen Junior and EpiPen Jr are intended for children weighing between 15 and 30 kg, and Anapen and EpiPen for children and adults weighing more than 30 kg. anaphylaxis to all allergens expect insect venoms and have been prescribed an adrenaline autoinjector; there are two versions, one for the Anapen and one for the EpiPen (Figure).

- ASCIA Action Plan for Anaphylaxis (insect allergy – personal) – this action plan is yellow and is for patients who are at risk of anaphylaxis to insect venoms and have been prescribed an adrenaline autoinjector; there are two versions, one for the Anapen and the other for the EpiPen.
- ASCIA Action Plan for Anaphylaxis (general) – this action plan is orange and is useful as a poster or for storage with an adrenaline autoinjector in first aid kits; again there is a version for each autoinjector.

The action plans, which are available from the ASCIA website (http://www. allergy.org.au/content/view/10/3), include the signs and symptoms of anaphylaxis and provide instruction on when and how to give the adrenaline autoinjector. A copy of the relevant ASCIA Action Plan for Anaphylaxis (personal) should always be stored with the patient's adrenaline autoinjector. An ASCIA Travel Plan for Anaphylaxis is also available from the ASCIA website for patients carrying adrenaline autoinjectors on aeroplanes.

How are the adrenaline autoinjectors used?

Both types of autoinjector are designed to administer the contained adrenaline into the outer mid-thigh muscle but they differ in their method of administration. The EpiPen is held in the mid-section with the fingers and thumb forming a fist, and is triggered by pressing firmly against the outer mid-thigh until a click is heard. The Anapen is held firmly against the outer mid-thigh and triggered by depressing a red button with the thumb so it clicks. Both injectors should be held in place for 10 seconds after triggering, and may be used through clothing.

ascia www.allergy.org.au	ACTION PLAN FOR Anaphylaxis	ascia www.allergy.org.au	ACTION PLAN FOR Anaphylaxis
Name:	for use with Anapen [®] or Anapen [®] Jr adrenaline autoinjectors	Name:	for use with EpiPen [®] or EpiPen [®] Jr adrenaline autoinjectors
Date of birth:	MILD TO MODERATE ALLERGIC REACTION	Date of birth:	MILD TO MODERATE ALLERGIC REACTION
Photo	 swelling of lips, face, eyes hives or welts tingling mouth, abdominal pain, vomiting 	Photo	 swelling of lips, face, eyes hives or welts tingling mouth, abdominal pain, vomiting
	ACTION		ACTION
Allergens to be avoided:	stay with person and call for help give medications (if prescribed) locate Anapen® or Anapen® Jr contact family/carer	Allergens to be avoided:	stay with person and call for help give medications (if prescribed) locate EpiPen® or EpiPen® Jr contact family/carer
Family/carer name(s):	Watch for any one of the following signs of Anaphylaxis	Family/carer name(s):	Watch for any one of the following signs of Anaphylaxis
	ANAPHYLAXIS (SEVERE ALLERGIC REACTION)	Work Ph:	ANAPHYLAXIS (SEVERE ALLERGIC REACTION)
Work Ph: Home Ph: Mobile Ph: Plan prepared by: Dr Signed	difficult/noisy breathing swelling of tongue swelling/tightness in throat difficulty talking and/or hoarse voice wheeze or persistent cough loss of consciousness and/or collapse pale and floppy (young children)	Home Ph: Mobile Ph: Plan prepared by: Dr Signed	difficult/noisy breathing swelling of tongue swelling/tightness in throat difficulty talking and/or hoarse voice wheeze or persistent cough loss of consciousness and/or collapse pale and floppy (young children)
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<section-header><complex-block><complex-block><complex-block><complex-block><complex-block><complex-block><complex-block><complex-block><complex-block><complex-block><complex-block><complex-block></complex-block></complex-block></complex-block></complex-block></complex-block></complex-block></complex-block></complex-block></complex-block></complex-block></complex-block></complex-block></section-header>	 Give Anapen® or Anapen® Jr Call ambulance*- telephone 000 (Aus) or 111 (NZ) Lay person flat and elevate legs. If breathing is difficult, allow to sit but do not stand Contact family/carer Further adrenaline doses may be given if no response after 5 minutes (if another adrenaline autoinjector is available) If in doubt, give Anapen® or Anapen® Jr Aragent⁴ br is generally rescribed for children aged 15 years. *Media doseration in hospital for at least 4 hours is recommended after anaphylaxis. Additional information 	How to give EpiPen® or EpiPen® Ir Torm figt around EpiPen® and FNUL OF GREY SATET Car Prish Dorbit citic is haved of its and hod TRISH Corrist TRISH Corrist	 Give EpiPen® or EpiPen® Jr Call ambulance*- telephone 000 (Aus) or 111 (NZ) Lay person flat and elevate legs. If breathing is difficult, allow to sit but do not stand Contact family/carer Further adrenaline doses may be given if no response after 5 minutes (if another adrenaline autoinjector is available) If in doubt, give EpiPen® or EpiPen® Jr EpiPen* is pureulty prescued for children aged 1-5 years. *Medical observation in hospital for at least 4 hours is recommended after anaphysics. Additional information

Figure. ASCIA action plans for anaphylaxis (personal) for the Anapen (left) and EpiPen (right). These are downloadable from the ASCIA website (http://www.allergy.org.au/content/view/10/3). (Reproduced with permission of ASCIA.)

It is important to educate patients on how to the use the particular device that has been prescribed for them. Trainer devices are available from pharmacies, Anaphylaxis Australia and the distributors of the pens.

Adrenaline autoinjector dose guidelines

The recommended doses for Anapen and EpiPen are given in the box on page 82.²

What needs monitoring? The device

The expiry date on an adrenaline autoinjector needs to be checked regularly, as with adrenaline ampoules. The EpiPen injector has a viewing window enabling the checking of the adrenaline to see if it is discoloured or contains a precipitate, which may reduce its effectiveness. Adrenaline is heat sensitive and ideally should be stored at room temperature. Adrenaline autoinjectors should not be refrigerated as this can affect the autoinjector mechanism.

Side effects

Transient and minor side effects occur in most patients and include anxiety, fear, restlessness, headache, dizziness, palpitations, tremor and pallor. Serious side effects are rare.

Studies have shown minimal cardio - vascular effects in children.³ Intramuscular adrenaline (1:1000) in doses of 0.01 to

0.4 mg/kg is not associated with clinically significant cardiotoxicity, even if given inadvertently in the absence of acute anaphylaxis.⁴

Important precautions and interactions

Precautions are relative as adrenaline autoinjectors are intended for use in lifethreatening anaphylaxis. There are no absolute contraindications to the administration of adrenaline for anaphylaxis.⁵ The reluctance to administer adrenaline because of fear of adverse cardiac effects should be countered by the awareness that coronary artery spasm, myocardial ischaemia and infarction and dysrhythmias can occur in patients with untreated anaphylaxis.⁶⁷

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The effects of adrenaline may be potentiated by monoamine oxidase inhibitors, tricyclic antidepressants, thyroid hormones and certain antihistamines such as diphenhydramine. Patients receiving stimulant medications such as amphetamines or methylphenidate (used in the treatment of attention deficit hyperactivity disorder) or abusing cocaine may be at higher risk for adverse effects from adrenaline. Patients taking nonselective β -blockers may experience severe hypertension and bradycardia if they are administered adrenaline.

Some caution may be required for patients with certain preexisting conditions, such as recent intracranial surgery, aortic aneurysm, uncontrolled hyperthyroidism or hypertension, or other conditions that might place them at higher risk for adverse effects related to adrenaline.

Summary

Adrenaline is the first-line treatment for anaphylaxis and adrenaline autoinjectors are designed for use by the general population. There are no absolute contraindications to the administration of adrenaline in the treatment of anaphylaxis. The EpiPen and the Anapen devices enable patients at risk of anaphylaxis to carry and administer the life-saving medication if they have an anaphylactic reaction. An ASCIA Action Plan for Anaphylaxis, completed by a medical practitioner, should always be carried with an adrenaline autoinjector as it provides instruction on when and how to use the injector.

References

1. PBS for health professionals. Canberra: Australian Government Department of Health and Ageing. Available online at: http://www.pbs.gov.au/html/healthpro/home (accessed August 2010).

2. Australasian Society of Clinical Immunology and Allergy (ASCIA). Guidelines for adrenaline autoinjector prescribing. Sydney: ASCIA; 2009. Available online at: http://www.allergy.org.au/content/view/11/319 (accessed August 2010).

3. Simons FE, Roberts JR, Gu X, Simons KJ. Epinephrine absorption in children with a history of anaphylaxis. J Allergy Clin Immunol 1998; 101(1 Pt 1): 33-37.

 Bentley A, Luyt D. Adrenaline use in anaphylaxis: friend or foe? Medicine On-line. First published 2006. http://priory.com/med/adrenaline.htm (accessed August 2010).

5 Simons FE. Epinephrine (adrenaline) in the first-aid, out-of-hospital treatment of anaphylaxis. Novartis Found Symp 2004; 257: 228-243; discussion 243-247, 276-285.

6. Triggiani M, Patella V, Staiano RI, Granata F, Marone G. Allergy and the cardiovascular system. Clin Exp Immunol 2008; 153 Suppl 1: 7-11.

7. Biteker M, Duran NE, Biteker FS, et al. Allergic myocardial infarction in childhood: Kounis syndrome. Eur J Pediatr 2010; 169: 27-29.

This article is intended for general information purposes only, and the full product information should be consulted before prescribing any of the mentioned medications.

COMPETING INTERESTS: None.

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