

## 6.10 ADRENALINE

**300 microgram/0.3 mL injection, 1 x 0.3 mL syringe, EpiPen<sup>®</sup>,  
150 microgram/0.3 mL injection, 1 x 0.3 mL syringe,  
EpiPen Jr<sup>®</sup>,  
Alphapharm Pty Limited**

### 1 Purpose of Application

- 1.1 The minor submission sought to list an auto-injector form of adrenaline (EpiPen<sup>®</sup> and EpiPen<sup>®</sup> Jr) in the Prescriber Bag section of the PBS.

### 2 Background

- 2.1 Adrenaline 1 in 1000 (1 mg/mL) injection, 5 x 1 mL ampoules is currently listed in the Prescriber Bag and the General Schedule of the PBS as an unrestricted benefit.
- 2.2 An application to list EpiPen and EpiPen Jr as Authority Required for emergency treatment for anaphylactic reactions to insect stings, was rejected by the PBAC at the March 1995 meeting. The application was rejected as the Committee could not see that the EpiPen device warranted the vast difference in cost compared to the plain adrenaline injection (the proposed EpiPen price to pharmacist at the time was \$██████, while plain adrenaline injection 1 in 1000 was \$██████ per ampoule).
- 2.3 The PBAC recommended EpiPen and EpiPen Jr for listing in June 2003 on a cost-effectiveness basis compared with no intervention. The PBAC accepted the clinical need for an adrenaline auto-injector, in the context of an ampoule being available on the PBS at a significantly lower price. In its consideration, the PBAC indicated it would support the Pricing Authority recommending a price-volume agreement, due to concerns over potential extensive prescribing of this preparation and the high potential for wastage due to the short effective shelf-life. The auto-injector was recommended for Authority Required listing for:
- initial supply for anticipated emergency treatment of acute allergic reactions with anaphylaxis in a patient who has been assessed to be at significant risk of anaphylaxis by, or in consultation with, a clinical immunologist or allergist; and
  - continuing supply for anticipated emergency treatment of acute allergic reactions with anaphylaxis, where the patient has previously been issued with an authority prescription for this drug.
- A note was included stating that “The auto-injector should be provided in the framework of a comprehensive anaphylaxis prevention program and an emergency action plan including training in recognition of the symptoms of anaphylaxis and the use of the auto-injector device.”
- 2.4 In November 2010, the PBAC deferred a submission for adrenaline auto-injectors requesting a change from an Authority Required to an Authority Required (STREAMLINED) listing to seek comment on the proposed change from Australasian Society of Clinical Immunology and Allergy (ASCIA), before further consideration by the PBAC. The PBAC noted that the shelf-life of the auto-injectors was limited and that a change to a streamlined authority may increase demand by consumers for

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more prescriptions and that this may lead to wastage, as it would be easier for Doctors to write the prescriptions. The PBAC also noted that the two available auto-injectors had different injection mechanisms and if prescribed without receiving the appropriate advice on anaphylaxis management and administration, may lead to quality use of medicines issues.

- 2.5 In March 2011 the PBAC rejected the submission based on advice from ASCIA that a streamlined listing may result in inappropriate prescribing, among other reasons.
- 2.6 The PBAC has not previously considered EpiPen and EpiPen Jr for inclusion in the Prescriber Bag.

*For more details on PBAC's view, see section 7 "PBAC outcome"*

**3 Requested listing**

- 3.1 The submission requested listing on the Prescriber Bag as an alternative to the currently listed ampoule.
- 3.2 The submission did not specify the requested maximum quantity. The pre-PBAC response clarified that a maximum quantity of one was requested.

**Secretariat suggested wording for the restriction:**

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Manufacturer	Name and
ADRENALINE					
300 microgram/0.3 mL injection, 1 x 0.3 mL syringe	1	0	\$ [REDACTED]	EpiPen	Alphapharm Pty Limited
150 microgram/0.3 mL injection, 1 x 0.3 mL syringe	1	0	\$ [REDACTED]	EpiPen Jr	

<b>Category / Program</b>	Emergency Drug Supplies
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Administrative Advice</b>	The auto-injector should be provided in the framework of a comprehensive anaphylaxis prevention program and an emergency action plan including training in recognition of the symptoms of anaphylaxis and the use of the auto-injector device. (For further information see the Australasian Society of Clinical Immunology and Allergy website at <a href="http://www.allergy.org.au">www.allergy.org.au</a> .)

**4 Clinical place for the proposed therapy**

- 4.1 The submission argued that an auto-injector adrenaline is more efficient, easy to administer and eliminates the risk of overdosing than its current counterpart, supported by evidence (ASCIA, A&AA, Kanwar et al) (pg 2 and 3 of submission).

*For more details on PBAC's view, see section 7 "PBAC outcome"*

**5 Comparator**

- 5.1 The minor submission nominated adrenaline ampoule as its comparator.

**6 Consideration of the evidence**

**Sponsor hearing**

- 6.1 There was no hearing for this item as it was a minor submission.

**Consumer comments**

- 6.2 The PBAC noted that while no consumer comments were received for this item, the submission included correspondence from Allergy & Anaphylaxis Australia and the Australasian Society of Clinical Immunology and Allergy. The correspondents

outlined that the adrenaline auto-injectors are quickly administered as they come in pre-measured doses. The correspondents also outlined that delay in, or lack of, administration of adrenaline was a factor contributing to mortality in anaphylaxis cases, and was due to a range of factors, including not recognising anaphylaxis, difficulty in measuring the correct dose, lacking clarity around the method of administration and not using the right equipment. The correspondents considered that the auto-injector form of adrenaline would both reduce the delay in treatment and increase the use of adrenaline in anaphylaxis cases through quicker and easier administration in the context of a single pre-measured dose.

***Clinical trials***

- 6.3 As a minor submission, no clinical trials were presented in the submission. The basis of the submission's request was:
- ease and timeliness of administration compared with the ampoule;
  - clinical support for use of the auto-injector over the ampoule, with supportive correspondence provided by Allergy & Anaphylaxis Australia, Australasian Society of Clinical Immunology and Allergy; and
  - an anecdote on the use of auto-injectors in emergency medical kits on domestic flights.

***Clinical claim***

- 6.4 The submission claimed superior ease and timeliness of administration and decreased risk of overdosing to adrenaline ampoule. The PBAC considered this claim to be difficult to assess due to inadequate evidence.

***Economic analysis***

- 6.5 The minor submission did not present an economic comparison or state on what basis it was seeking listing for EpiPen and EpiPen Jr on the Prescriber Bag.
- 6.6 The current Approved Ex-Manufacturer Price (AEMP) for EpiPen and EpiPen Jr is \$██████ per injection. The submission requests the same AEMP for the Prescriber Bag listing. The AEMP of the form of adrenaline currently listed on the Prescribers Bag is \$██████ for five ampoules.

***Estimated PBS usage & financial implications***

- 6.7 The minor submission did not provide financial estimates.
- 6.8 Listing EpiPen and EpiPen Jr on the Prescriber Bag would result in a cost to the PBS. The extent of that cost would depend on the extent of substitution for the ampoule adrenaline (assuming both would be available as an either/or option).

*For more details on PBAC's view, see section 7 "PBAC outcome"*

## **7 PBAC Outcome**

- 7.1 The PBAC decided not to recommend the listing of auto-injector adrenaline on the Prescriber Bag section of the PBS. This was on the basis of an unacceptably high cost compared with the comparator, adrenaline ampoule, and a lack of evidence to support the clinical claim of superior ease and timeliness of administration and decreased risk of overdosing.
- 7.2 The PBAC accepted that adrenaline ampoule was the appropriate comparator.
- 7.3 The PBAC noted that no clinical trials were presented in the submission, which relied upon supportive correspondence provided by Allergy & Anaphylaxis Australia and the Australasian Society of Clinical Immunology and Allergy and an anecdote on the use of auto-injectors in emergency medical kits on domestic flights.
- 7.4 The PBAC considered that the claim of superior ease and timeliness of administration and decreased risk of overdosing compared with adrenaline ampoule was not supported due to inadequate evidence.
- 7.5 The PBAC noted the correspondence from Allergy & Anaphylaxis Australia and the Australian Society of Clinical Immunology and Allergy which argued that the adrenaline auto-injector was easier and quicker to administer, presented less dosing issues as the dose was pre-measured, and would increase the use of adrenaline. The PBAC considered that the auto-injector may be quicker to administer, however considered this would only occur if the practitioner had experience with the product. The PBAC also considered that dosing issues were generally related to ascertaining the correct dose based on patient's weight, rather than the actual administration. The PBAC further considered that the auto-injector form was unlikely to increase the use of adrenaline as there was no evidence it would improve the recognition of anaphylaxis, which the PBAC considered was one of the factors contributing to under-administration of adrenaline.
- 7.6 The PBAC also noted that the submission did not present an economic comparison or state on what basis it was seeking listing. The PBAC noted that the current AEMP for auto-injector adrenaline is approximately forty times greater than the currently listed adrenaline ampoule, and considered that the listing of the auto-injector form would result in a significant cost to the PBS for no or minor additional health benefits.
- 7.7 The PBAC further noted that Prescriber Bag items are provided without charge to prescribers on a monthly basis, where they can receive the maximum quantity of each item listed on the Prescriber Bag provided they do not have the maximum quantity on hand. The PBAC considered it was highly unlikely that prescribers would administer the maximum quantity of adrenaline each month, and so considered that significant wastage would occur due to the short shelf life of adrenaline. In the context of the high cost of the drug, the PBAC was particularly concerned about the cost implications wastage of the product would present for the PBS.

**Outcome:**  
Rejected

**8 Context for Decision**

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

**9 Sponsor's Comment**

The sponsor had no comment.