

7.07 ADRENALINE

I.M. injection 150 micrograms in 0.3 mL single dose syringe auto-injector and I.M. injection 300 micrograms in 0.3 mL single dose syringe auto-injector.

AdrenaJect[®], Sun Pharma ANZ Pty Ltd

1 Purpose of Application

- 1.1 The minor resubmission requested the PBAC to reconsider its previous recommendation in July 2016 that AdrenaJect[®] (previously known as Adrenaline Auto Inject Sun-JV) not be considered equivalent for the purposes of brand substitution with the originator brand, EpiPen[®], at the pharmacy level. The sponsor claimed that it is currently not commercially viable to proceed with PBS listing without brand substitution.
- 1.2 The submission also requested to amend the level of authority required for prescribing AdrenaJect[®] from Authority Required to Authority Required (STREAMLINED) listing.
- 1.3 The latter request is similar to the current implementation of a biosimilar uptake driver which applies a lower level of authority to biosimilar brand(s) than exists for the reference brand.
- 1.4 The PBAC noted that biosimilar uptake drivers are designed to supplement existing activities by the Department of Health to improve awareness of, and confidence in, biosimilars for both healthcare professionals and consumers. It is a policy matter as to whether these drivers should be extended to non-biosimilar medicines, in this case, adrenaline. Hence, the latter request is outside the scope of PBAC's consideration.

2 Background

Brand equivalence and substitution at the pharmacist level ('a' flagging)

- 2.1 The Schedule of Pharmaceutical Benefits provide the following definition of brand equivalence:

Extract from the Explanatory Notes

BRAND EQUIVALENCE

'a' located immediately before brand names of a particular strength of an item indicates that the sponsors of these brands have submitted evidence that they have been demonstrated to be bioequivalent or therapeutically equivalent, or that justification for not needing bioequivalence or therapeutic equivalence data has been provided to and accepted by the Therapeutic Goods Administration. It would thus be expected that these brands may be interchanged without differences in clinical effect.

- 2.2 Many medicines are available on the PBS in different brands. The Schedule of Pharmaceutical Benefits indicates where different brands are considered equivalent for the purposes of substitution at the point of dispensing by using 'a' flags.
- 2.3 The ability for prescribers and pharmacists to substitute generic brands for originator brands is an important part of encouraging use of less expensive generics in order to foster market competition which supports the sustainability of the PBS.
- 2.4 For any individual prescription, a prescriber may choose to not permit brand substitution by indicating 'substitution not permitted' on the prescription. Likewise, when substitution is permitted, a patient may nominate which 'a' flagged brand they wish to receive from the pharmacist, except when State or Territory Law prohibits substitution (e.g. for Schedule 8 drugs of dependence). The substitution process allows for patient and prescriber choice and is not automatic.
- 2.5 The *National Health Act 1953* ("The Act") makes it an offence for a pharmacist to supply a pharmaceutical benefit other than the benefit directed to be supplied in a prescription except when, amongst other criteria, the Schedule issued by the Department of Health states that the specified benefit and the substitute benefit are equivalent.
- 2.6 If the PBAC provides advice, the decision to apply brand equivalence ('a' flagging) to listings in the Schedule is made by the Minister for Health (or Delegate).

Previous PBAC considerations for self-administered adrenaline

- 2.7 Adrenaline intra-muscular injection in the form of an auto-injecting pen (EpiPen® and EpiPen Junior®) was first PBS listed on 1 November 2003. Prior to this, adrenaline was available on the PBS in ampoule form only.
- 2.8 In March 2010, a PBAC recommendation was made for Anapen®, a generic brand of adrenaline autoinjector that was delisted on 1 January 2017. The sponsor stated that they had not been able to supply Anapen® since August 2014. This product has since been removed from the Australian Register of Therapeutic Goods (ARTG).
- 2.9 The PBAC considered in March 2010 that specific training for the patient or carer was required for each adrenaline device. This recommendation was also supported by Australasian Society of Clinical Immunology and Allergy (ASCI) at the time of consideration. Online training for the use of Anapen® and anaphylaxis action plans

(Anapen versions) were made available by ASCIA to prevent possible patient confusion.

- 2.10 As part of the consideration for Anapen®, the PBAC recommended the following;
- that a cautionary statement be added to Anapen and EpiPen listings stating ‘EpiPen and Anapen products have different administration techniques and should not be prescribed to the same patient without training in their use’ to aid in alerting prescribers to this issue;
 - the text ‘sole PBS-subsidised supply for anticipated emergency treatment’ be included in the restrictions for Anapen and EpiPen to limit prescribing under the PBS to one brand of adrenaline auto-injector per patient. This will help to prevent patients receiving prescriptions for both Anapen and EpiPen and avoid the associated brand confusion; and
 - requested the National Prescribing Service to educate prescribers on the differences between Anapen and EpiPen.
- 2.11 In July 2016, the PBAC recommended the listing of the adrenaline autoinjector, AdrenaJect®, previously known as Adrenaline Auto Inject Sun-JV, under the same conditions as existing adrenaline autoinjectors (EpiPen®, EpiPen Junior® and Anapen®) on the basis that it is bioequivalent to EpiPen®. Based on previous concerns with adrenaline autoinjectors with differing administration techniques, the PBAC considered that the various brands of adrenaline auto injector should not be considered equivalent for the purposes of substitution (‘a’ flagged) in the Schedule.

For more detail on PBAC’s view, see section 5 PBAC outcome.

3 Requested listing

- 3.1 The resubmission requested the PBAC to reconsider its previous recommendation on brand equivalence (‘a’ flagging) between AdrenaJect® and EpiPen® from the July 2016 PBAC meeting.
- 3.2 No change to the wording of the existing listing was proposed.

For more detail on PBAC’s view, see section 5 PBAC outcome.

4 Consideration of the evidence

- 4.1 The PBAC noted that the submission provided data from a study conducted in the USA which aimed to demonstrate the effectiveness, readability and usability of the instruction of AdrenaJect® for the intended user populations (i.e. juveniles and adults currently prescribed an adrenaline auto injector). The resubmission noted PBAC’s previous concern regarding the different administration techniques between the two adrenaline auto injector brands.

- 4.2 In summary, the study was conducted with a total of 90 participants. Participants consisted of 30 adult patients, 30 juvenile patients and 30 caregivers that have or might have administered a rescue injection of adrenaline. There were two subgroups in the study, one group was trained in a representative manner and the other was given time to self-familiarise for a length of time. Participants were then asked to return approximately one week later for the second session to perform an unaided rescue attempt followed by an open-ended feedback on the preparation and injection process.
- 4.3 Across all participants in the study, 87 out of 90 (97%) successfully injected a full dose of adrenaline from AdrenaJect®. The Sponsor also claimed that the failures appeared more attributed to a lack of attention (or interest) by the user than the design flaws of the device or labelling based on the participants' feedback.
- 4.4 The Sponsor concluded that no patterns of preventable failures between the two subgroups of participants, and that AdrenaJect® could correctly, safely, and effectively be used in the intended user populations.
- 4.5 The PBAC noted that all failures occurred in the group that did not receive training, especially within the juvenile users. The PBAC also questioned the applicability of the study as it was not based in Australia. The Sponsor stated that training for a new adrenaline device may not always occur (page 13 of the validation report), however the Sponsor expects that the intended user populations will receive ongoing and frequent training through schools, childcare centres or via ASCIA.

Sponsor hearing

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

Consumer comments

- 4.7 The PBAC noted the advice received from six organisations, Asthma Australia, ASCIA, Allergy & Anaphylaxis Australia, Pharmacy Guild of Australia, Australian Pharmaceutical Industries (API) and Mylan Australia clarifying the likely use of adrenaline in clinical practice. The PBAC noted the concerns around potential for confusion due to the different administration devices. There was a strong emphasis on the importance of training and education for the new device if the PBAC was to recommend AdrenaJect® for brand substitution at the pharmacy level.
- 4.8 On the other hand, most of the organisations and individuals also acknowledged the current shortage of EpiPen®. The PBAC specifically noted anecdotal reports that some patients were relying on expired products due to the shortages.

For more detail on PBAC's view, see section 5 PBAC outcome.

5 PBAC Outcome

- 5.1 The PBAC deferred making a recommendation on the brand equivalence of

AdrenaJect® with the originator brand, EpiPen®, for the purposes of brand substitution at the pharmacy level. The PBAC requested further information from the Sponsor regarding their education plan to support the PBS listing of AdrenaJect®. The PBAC also requested further information from the Department regarding possible alternative measures to support safe uptake.

- 5.2 The PBAC recalled that at the time of recommending the listing of AdrenaJect®, in July 2016, the Committee considered these auto-injectors to have significantly different administration techniques and advised that the various brands of adrenaline auto injector should not be considered equivalent for the purposes of substitution (i.e. 'a' flagged in the Schedule).
- 5.3 The PBAC acknowledged the current shortage of EpiPen® and noted that the TGA has been proactively seeking alternative supply to address the current shortage. The PBAC considered an alternative brand of adrenaline autoinjector on the PBS would be appropriate to ensure patient access. The TGA have recently granted a Section 19A approval to Link, to import and supply an alternative UK based product which also has a different device to EpiPen.
- 5.4 The PBAC noted the supporting study and educational materials provided by the sponsor in addressing previous concerns raised by the committee. However, the PBAC questioned the applicability of the supporting study as it was not based in an Australian population. The PBAC also considered the clarity and quality of the educational materials and the samples of autoinjector provided, did not sufficiently minimise the risk for a possible medication misadventure due to the different administration techniques.
- 5.5 The PBAC specifically noted advice from the ASCIA, that if AdrenaJect® is available with brand equivalence ('a' flagged) on the PBS, there should be widespread, quality education and training for all health professionals, school teachers, early childhood education/care staff, first aid officers, patients and their families/carers to avoid misadventure such as fatal anaphylaxis due to incorrect device use.
- 5.6 The PBAC noted that options were discussed at the meeting to address the issues of consumer confusion, including the suggestion of having a non-brand-specific action plan available from ASCIA and improved clarification on the labelling and packaging of AdrenaJect®. The PBAC suggested that the Sponsor liaise with relevant organisations (i.e. ASCIA) to obtain advice and assistance to address the concerns raised.
- 5.7 The PBAC acknowledged the sponsor's concern around commercial viability and considered that brand equivalence ('a' flagging) is one mechanism which may assist uptake. The PBAC sought policy advice from the Department to support safe uptake of this alternative brand given the current supply issues with the originator brand.
- 5.8 The PBAC noted that this submission is not eligible for an Independent Review as it was deferred.

Outcome:

Deferred

6 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.

7 Sponsor's Comment

Sun Pharma will continue to work with the PBAC and relevant Stakeholders to list AdrenaJect on the PBS as an equivalent brand for EpiPen.