PUBLIC SUMMARY DOCUMENT

Product: Anecortave Acetate, depot suspension, 15 mg in 0.5 ml, Retaane®

Sponsor: Alcon Laboratories (Australia) Pty Ltd

Date of PBAC Consideration: November 2006

1. Purpose of Application

The re-submission requested a Section 100 (Direct Supply Program) listing for treatment of subfoveal choroidal neovascularisation (CNV) due to exudative age related macular degeneration (AMD) where the CNV is composed predominantly (≥50%) of classic lesions.

2. Background

At the March 2006 meeting, the PBAC rejected a submission for a restricted benefit listing because of inadequate evidence to support the claim that anecortave acetate is no worse than photodynamic therapy (PDT) with verteporfin, in terms of effectiveness and safety.

3. Registration Status

Anecortave acetate was registered on 16 December 2005 for the treatment of subfoveal choroidal neovascularisation (CNV) due to exudative age-related macular degeneration (AMD) where there is a classic component.

4. Listing Requested and PBAC's View

Option 1

Section 100

For the treatment of subfoveal choroidal neovascularisation (CNV) due to exudative age related macular degeneration (AMD) where the CNV is composed predominantly (≥50%) of classic lesions.

Treatment can only be undertaken by designated trained specialist ophthalmologists.

Option 2

Section 100

For the treatment of subfoveal choroidal neovascularisation (CNV) due to exudative age related macular degeneration (AMD) where the CNV is composed predominantly (≥50%) of classic lesions.

Treatment can only be undertaken by designated trained specialist ophthalmologists.

Anecortave acetate and photodynamic therapy (PDT) with verteporfin are not subsidised for adjunctive use.

See Recommendation and Reasons for the PBAC's view.

5. Clinical Place for the Proposed Therapy

Age-related macular degeneration (AMD) is a leading cause of new blindness in the elderly patient. There are two forms of AMD- atrophic, or dry macular degeneration and exudative or wet, macular degeneration. Dry AMD occurs in 85-90% of patients with macular degeneration. Exudative age-related macular degeneration (AMD) occurs only in 10-15% of patients with AMD. It is usually more severe and causes more vision loss.

Exudative macular degeneration is characterised by choroidal neovascularisation (CNV), or abnormal growth of blood vessels in the choroid membrane beneath the retina near the macula. Vision loss in the disease is as a direct result of leakage and haemorrhage into the sub retinal space near the macular.

Treatment of exudative AMD include laser photocoagulation, photodynamic therapy, macular translocation, submacular surgery, vitamin supplements, transpupillary thermotherapy, and a variety of drug therapies including anecortave acetate.

6. Comparator

The submission nominated PDT with verteporfin. This was as previously agreed by the PBAC. *See Recommendations and Reasons.*

7. Clinical Trials

No changes had been made to the trial data presented in the previous submission.

The trials that had been published at the time of submission are as follows:

Key trial

Trial/First author	Publication title	Publication citation
C-01-99		
Slakter JS et al (2006)	Anecortave acetate (15 milligrams) versus photodynamic therapy for treatment of subfoveal neovascularization in age-related macular degeneration.	Ophthalmology, 113(1): 3-13

Supportive trials

Trial/First author	Publication title	Publication citation
C-98-03		
Augustin AJ et al (2005)	Safety of posterior juxta-scleral depot administration of the angiostatic cortisene anecortave acetate for treatment of subfoveal choroidal neovascularization in patients with age-related macular degeneration.	Graefe's archive for clinical and experimental ophthalmology 2005; 243:9-12.
D'Amico DJ et al (2003)	Anecortave acetate as monotherapy for treatment of subfoveal neovascularization in age-related macular degeneration: twelve month clinical outcomes.	Ophthalmology 2003; 110:2372-83; discussion 2384-5.
D'Amico DJ et al (2003)	Anecortave acetate as monotherapy for the treatment of subfoveal lesions in patients with exudative age-related macular degeneration (AMD): Interim (month 6) analysis of clinical safety and efficacy.	Retina 2003; 23:14-23.
Schmidt-Erfurth U et al (2005)	Anecortave acetate for the treatment of subfoveal choroidal neovascularization secondary to age-related macular degeneration.	European Journal of Ophthalmology 2005; 15:482-5.
Regillo CD et al (2002)	Safety of anecortave acetate administered as posterior juxtascleral injection in patients with subfoveal	American Academy of Ophthalmology 2002; 282pp.

Trial/First author	Publication title	Publication citation
	choroidal neovascularization.	
C-00-07		
Regillo CD et al (2002)	Safety of anecortave acetate administered as posterior juxtascleral injection in patients with subfoveal choroidal neovascularization.	American Academy of Ophthalmology 2002; 282pp.

8. Results of Trials

There were no changes to the key results presented in the previous submission. The results of the trials had previously been described in the March 2006 Public Summary Document (PSD).

9. Clinical Claim

The submission described anecortave acetate as safe, well tolerated and as effective as PDT with verteporfin for the treatment of age-related macular degeneration in patients with classic lesions.

The PBAC considered that, on the basis of the evidence provided in the submission, it could not rule out the possibility that anecortave is less effective than verteporfin with PDT (verteporfin) in terms of the proportion of patients experiencing a less than 3 point loss in visual acuity after 12 months. *See Recommendations and Reasons.*

10. Economic Analysis

An updated preliminary economic evaluation was presented. The resources included in the evaluation were drug costs, cost of drug administration, cost of assessing patient outcomes and specialist consultations.

A modelled economic evaluation was presented.

The incremental cost per additional QALY gained from treatment with PDT with verteporfin versus anecortave acetate was estimated to be in the range $105,000 – $200,000.

11. Estimated PBS Usage and Financial Implications

The likely number of patients/year was estimated to be < 10,000 in Year 3. The PBAC considered this might be an underestimate.

The financial savings/year to the PBS (excluding co-payments) minus any savings in use of other drugs was estimated to be < $10 million in Year 3. The PBAC considered this might be an overestimate in the re-submission.

12. Recommendation and Reasons

The PBAC recommended listing for the treatment of subfoveal choroidal neovascularisation (CNV) due to exudative age related macular degeneration (AMD) where the CNV is composed predominantly (≥50%) of classic lesions in a patient with a baseline visual acuity equal to or better than 6/60 (20/200), on the basis of acceptable cost-effectiveness compared with verteporfin (ie anecortave is less effective and less costly).

The PBAC considered that, on the basis of the evidence provided in the submission, it could not rule out the possibility that anecortave is less effective than verteporfin with PDT

(verteporfin) in terms of the proportion of patients experiencing a less than 3 point loss in visual acuity after 12 months. The Committee considered that anecortave would most likely be used in patients in whom verteporfin cannot be used and, to a lesser extent, as a replacement for verteporfin in patients that live in areas where access to a laser machine is difficult. Placebo is therefore an appropriate comparator to the extent that anecortave is used in patients in whom verteporfin cannot be used, while verteporfin is an appropriate comparator in the remaining group of patients. On the basis of these considerations the PBAC recommended listing at the price proposed in the submission.

The PBAC recommended that anecortave be used as monotherapy and requested that the Secretariat advice the MSAC Secretariat of this recommendation with a view to similarly limiting verteporfin to use as monotherapy. The PBAC noted that there were a number of other unresolved issues with the listing wording, including whether or not a Section 100 listing was the most appropriate listing to ensure patient access and whether to apply an upper limit to the number of PBS-subsided treatments per eye. The PBAC requested that these issues be resolved by the RWG in consultation with the sponsor and other relevant stakeholders.

[Following the meeting, the post-PBAC RWG recommended that a Section 85 authority listing be used for anecortave, as (a) anecortave will principally be used by ophthalmologists in private rooms in the community setting thus making a Section 85 listing appropriate and (b) a Section 85 listing does not create any obvious obstacle to patient access].

Recommendation

ANECORTAVE ACETATE, depot suspension, 15 mg in 0.5 ml

Restriction: **To be finalised**

Authority Required

Initial treatment by an ophthalmologist, as the sole subsidised therapy, of predominantly (≥50%) classic, subfoveal choroidal neovascularisation (CNV) due to age related macular degeneration (AMD), as diagnosed by fluorescein angiography, in a patient with a baseline visual acuity equal to or better than 6/60 (20/200).

No more than 10 treatments per eye will be authorised.

Authority approvals will be administered by the PBS and Specialised Drugs Branch of Medicare Australia.

The first authority application for each eye must be made in writing, and must include:

(a) a completed authority prescription form;
(b) a completed Subfoveal Choroidal Neovascularisation (CNV) – PBS Supporting Information Form [www.medicare.gov.au]; and
(c) a copy of the fluorescein angiogram demonstrating that the CNV is predominantly classic (≥50%).

Written applications for authority to prescribe anecortave should be forwarded to:

Medicare Australia
Prior Written Approval of Specialised Drugs
Reply Paid 9826
GPO Box 9826
HOBART TAS 7001

Alternatively, the first authority application may be faxed to Medicare Australia on (03) 6215 5474 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Medicare Australia will then contact the prescriber by telephone. The original documentation must be posted to the above address after approval has been gained.

Authority Required
Continuing treatment by an ophthalmologist, as the sole subsidised therapy, of predominantly (≥50%) classic, subfoveal choroidal neovascularisation (CNV) due to age related macular degeneration (AMD) where the patient has previously been granted an authority prescription for the same eye.

No more than 10 treatments per eye will be authorised.

Authority approvals will be administered by the PBS and Specialised Drugs Branch of Medicare Australia. Authority applications for continuing treatment in the same eye may be made by telephone on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

Max Quantity: 1
Number of Repeats: 0

Pack: 1

13. 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.

14. Sponsor's Comment

The sponsor welcomes the PBAC recommendation and would be willing to participate in further discussion regarding access mechanisms that would allow direct supply via ophthalmologists' rooms. A direct supply mechanism would significantly improve the convenience and timely treatment in this patient group that is frequently hampered by mobility and transport issues.

The sponsor would also like to stress that the efficacy estimates used in the cost effectiveness submission included the 50% of patients in whom leakage (reflux) of medication occurred due to incorrect injection technique. There is considerable evidence that avoidance of leakage

will result in improved efficacy. To this end, Alcon encourages all prospective users to be trained on the correct injection technique.