Public Summary Document

Product:	Moxonidine, tablets, 200 microgram and 400 microgram, Physiotens®
Sponsor:	Solvay Pharmaceuticals Pty Ltd
Date of PBAC Consideration:	March 2006

1. Purpose of Application

This re-submission sought listing on the Pharmaceutical Benefits Scheme (PBS) as a restricted benefit for the treatment of hypertension.

2. Background

At its March 2005 meeting, the Pharmaceutical Benefits Advisory Committee (PBAC) rejected a cost-minimisation submission from the sponsor requesting a Restricted benefit listing of moxonidine on the PBS for hypertension based on a comparison with angiotensin converting enzyme inhibitor (ACEIs).

The PBAC rejected the submission because of doubts overall that moxonidine is no worse than the ACEIs in terms of effectiveness and safety and thus uncertain but unacceptable cost-effectiveness.

3. Registration Status

Moxonidine was approved by the TGA on 28 October 2004 for the 'treatment of hypertension'.

4. Listing Requested and PBAC's View

Restricted Benefit

Treatment of hypertension.

The PBAC considered it appropriate to initially list moxonidine as a restricted benefit, in order to highlight its clinical place as add-on therapy in the treatment of hypertension, where a centrally acting agent is required, and as an alternative to clonidine.

5. Clinical Place for the Proposed Therapy

Moxonidine is a centrally acting antihypertensive agent structurally related to clonidine that provides an alternative treatment for hypertension.

6. Comparator

The March 2005 submission used ACEIs as the comparators whereas clonidine was nominated as the comparator in the submission to the March 2006 meeting. Although the PBAC had previously accepted ACEIs were the appropriate comparator, the PBAC agreed that clonidine was an acceptable comparator to use.

7. Clinical Trials

The submission presented two double-blind, randomised, comparative trials using moxonidine and clonidine hydrochloride (individually titrated daily doses) in the treatment of hypertension as the key evidence: Plänitz (1987) and study K.220.5908.

The published trial included in the submission is below:

Trial/first author	Protocol/Publication title	Publication citation
Plänitz V	Comparison of moxonidine and clonidine HCL in treating in treating patients with hypertension.	J. Clin. Pharmacol. 1987; 24:46-51.

In support of the two pivotal studies, the submission presented two double-blind, randomised, cross-over studies of moxonidine and clonidine hydrochloride similarly focussed on the treatment of hypertension: Plänitz (1984) and Plänitz (1985).

8. Results of Trials

The results of the key trials showed that for both treatments, systolic and diastolic treatment pressures fell significantly ($p<0.001$) but there were no statistically significant differences between moxonidine and clonidine treatment.

The key results are summarised in the table below:

Mean reductions in blood pressure for Planitz 1987

Key trial	Moxonidine † (N=115)	Clonidine † (N=27)
Supine diastolic blood pressure (mmHg)		
Before treatment	100	99
After titration	88	89
After treatment	87	87
Difference in sDBP *	-13.5	-11.8
3-day withdrawal period	98	98
Supine systolic blood pressure (mmHg)		
Before treatment	177	176
After titration	151	151
After treatment	151	147
Difference in sSBP *	-26.0	-29.4
3-day withdrawal period	171	169

† Difference between groups was not statistically significant ($p>0.05$)
* Statistically significant ($p<0.001$) reduction

Similar results were observed in study K220.5908.

In the Planitz (1987) trial, the total incidence of adverse reactions was statistically significantly greater ($p=0.031$) in patients receiving clonidine (53%) as compared with moxonidine (30%). Dryness of mouth occurred more frequently with clonidine (47%) than with moxonidine (20%) ($p=0.005$). Oedema was observed in 17% of the patients during clonidine therapy but only in 1% of moxonidine-treated patients ($p=0.001$). Weight gain was not observed in either treatment group. In trial K.220.5908, there were no statistically significant differences in the rates of adverse events between moxonidine and clonidine.

9. Clinical Claim

The submission claimed moxonidine is no worse than clonidine in terms of effectiveness and toxicity. This was considered by the PBAC to be a reasonable description for moxonidine as an add-on therapy for hypertension.

10. Economic Analysis

An updated preliminary economic evaluation was presented. The PBAC considered the choice of a cost-minimisation approach valid.

11. Estimated PBS Usage and Financial Implications

The submission claimed that the listing of moxonidine would provide a net cost saving to the PBS of <$10 million.

The trial evidence did not support the extent of the claim of financial savings. A number of factors were taken into account by the PBAC when the estimate was recalculated and the sponsor agreed with a new smaller estimate.

12. Recommendation and Reasons

The PBAC recommended listing on a cost-minimisation basis, concluding that moxonidine is no worse than clonidine as add-on therapy for the treatment of hypertension, and overall, appears to be less toxic. The equi-effective doses are moxonidine 380 micrograms per day and clonidine 357 micrograms per day, based on the average dose at steady state across the two key trials included in the submission. The final PBS price of moxonidine should take into account available tablet strengths and pack sizes.

The PBAC considered it appropriate to initially list moxonidine as a restricted benefit, in order to highlight its clinical place in the treatment of hypertension, that is, as add-on therapy, where a centrally acting agent is required, and as an alternative to clonidine. The Committee requested that the National Prescribing Service consider publishing a RADAR article on moxonidine to coincide with the PBS listing

Recommendation

Moxonidine, tablets, 200 microgram and 400 microgram

Restriction:	Restricted Benefit Hypertension in patients receiving concurrent antihypertensive therapy.
Maximum Quantity:	30 (Both strengths)
Repeats:	5 (Both strengths)

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

Moxonidine was first registered in Germany in 1991 and is now available in over 50 countries around the world as a treatment for hypertension, either as monotherapy or in combination with other antihypertensive agents.