PUBLIC SUMMARY DOCUMENT

Product: Varenicline tartrate, tablets, 0.5 mg, 11 and 1 mg, 14 and 1 mg, 28 and tablets 1 mg, 56, Champix®

Sponsor: Pfizer Australia Pty Ltd

Date of PBAC Consideration: July 2007

1. Purpose of Application

The submission sought authority required listings on the Pharmaceutical Benefits Scheme for short-term treatment to aid the goal of achieving abstinence in those patients aged 18 years and over who have indicated they are ready to cease smoking and meet specified criteria.

2. Background

This drug had not previously been considered by the PBAC.

3. Registration Status

Varenicline tartrate was registered by the TGA on 15 February 2007 as an aid for smoking cessation in adults over the age of 18 years.

4. Listing Requested and PBAC's View

NOTE:
Only one treatment course of varenicline per 12 months with no increased maximum quantities or repeats will be authorised.

Authority required
Commencement of short-term treatment to aid the goal of achieving abstinence for adults aged 18 years or over who have indicated that they are ready to cease smoking and:
(a) who have entered a comprehensive support and counselling program; or
(b) who are entering a comprehensive support and counselling program during the consultation at which this authority is requested. Details of the program must be specified in the authority application.

NOTE:
A follow-up visit to the requesting doctor is recommended within 2 to 3 weeks of the original prescription being requested.

Authority required
Completion of short-term treatment to aid the goal of achieving abstinence for adults who have indicated that they are ready to cease smoking and who are enrolled in a comprehensive support and counselling program. Details of the program must be specified in the original authority application.

For PBAC's view, see Recommendation and Reasons.

5. Clinical Place for the Proposed Therapy

Smoking related illnesses are a significant public health problem. Smoking and nicotine addiction are strongly interrelated and it is therefore important to treat them as such when

attempting to reduce smoking prevalence. Varenicline may assist those patients who are ready to quit smoking to do so, together with appropriate support mechanisms.

6. Comparator

Appropriately, the submission nominated bupropion as the main comparator.

7. Clinical Trials

The submission presented a meta-analysis of results from two double-blind randomised trials (A3051028 and A3051036) comparing varenicline (1 mg twice daily after initial titration), bupropion (150 mg twice daily after initial titration) and placebo in smokers over 52 weeks. Subjects received 12 weeks of treatment with either varenicline or bupropion, with follow up to 52 weeks.

These trials had been published at the time of submission, as follows:

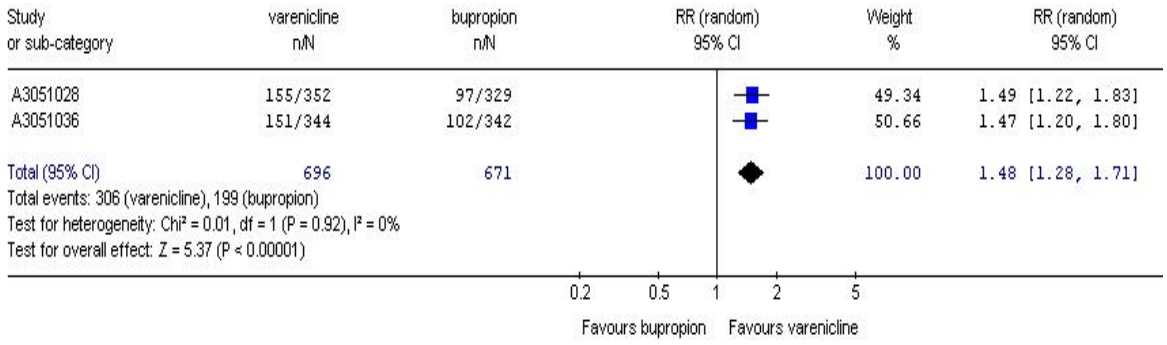
Trial/First author	Protocol title/Publication title	Publication citation
A3051028 Gonzales D et al, 2006	Varenicline, an α4β2 nicotinic acetylcholine receptor partial agonist, vs. sustained-release bupropion and placebo for smoking cessation: a randomized controlled trial.	Journal of the American Medical Association. 296(1):47-55.
A3051036 Jorenby D et al, 2006	Efficacy of varenicline, an α4β2 nicotinic acetylcholine receptor partial agonist, vs. placebo or sustained-release bupropion for smoking cessation: a randomized controlled trial.	Journal of the American Medical Association. 296(1):56-63.

8. Results of Trials

The results of the individual trials and the meta-analyses are summarised below.

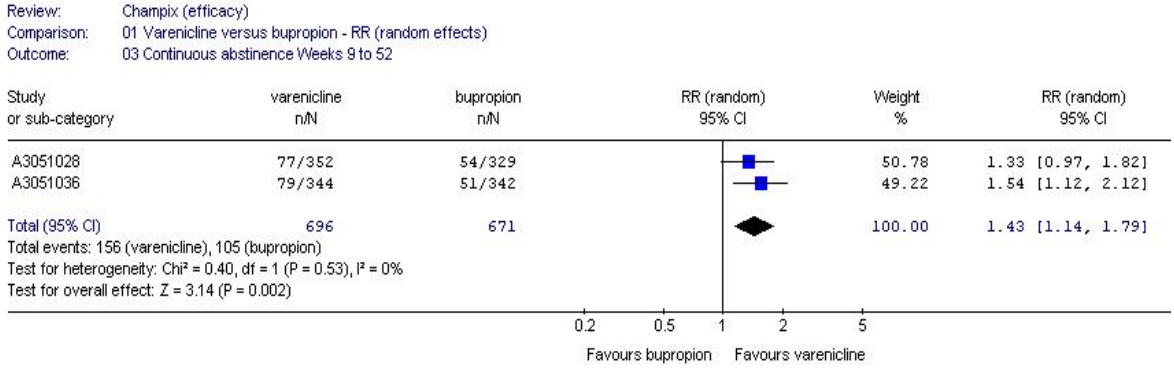
Results of the primary outcome of four-week continuous quit rate from Weeks 9 to 12 for varenicline versus bupropion

Review: Champix (efficacy)
Comparison: 01 Varenicline versus bupropion - RR (random effects)
Outcome: 01 Four-week CQR Weeks 9 to 12



The result for the primary outcome of four-week continuous quit rate from Weeks 9 to 12 was significant for both Trial A3051036 and Trial A3051028. The result of the meta-analyses of the two trials was also significant for the primary outcome.

Results for the secondary outcome of continuous abstinence from Weeks 9 to 52 for varenicline versus bupropion



The trials were also powered for the key secondary outcome, continuous abstinence from Weeks 9 to 52. The results for the key secondary outcome of continuous abstinence from Weeks 9 to 52 was significant for Trial A3051036 but not for Trial A3051028. However, the result of the meta-analyses of the two trials was significant for continuous abstinence from Weeks 9 to 52.

The submission presented the results of safety outcomes from the randomised trials A3051028 and A3051036. Smokers receiving varenicline reported higher incidences of nausea, abnormal dreams and headache compared to smokers randomised to bupropion. Smokers receiving varenicline reported lower incidences of insomnia than smokers receiving bupropion. These four adverse events may be clinically relevant as they could influence patients' compliance to continued therapy.

While the PBAC noted that significantly more patients on varenicline treatment experienced nausea, abnormal dreams and headache compared with patients on bupropion, the Committee accepted that the pooled rate of discontinuations due to adverse events was lower with varenicline compared to bupropion (9.5% vs 13.9%; RR= 0.69 (0.47, 1.00)).

9. Clinical Claim

The submission described varenicline as having significant advantages in effectiveness over bupropion and having similar or less toxicity.

See Recommendation and Reasons for the PBAC's view.

10. Economic Analysis

The submission presented a stepped economic evaluation that progressed from a trial-based analysis to a modelled analysis. The choice of the cost-effectiveness and cost-utility approaches were considered appropriate. The resources included were drug costs and GP costs.

Both the incremental cost-effectiveness ratios per additional life year gained and per additional quality adjusted life year (QALY) versus bupropion were less than $15,000.

11. Estimated PBS Usage and Financial Implications

The submission estimated that in Year 1 of listing the likely number of patients per year would be > 200,000 and the likely financial cost per year to the PBS (excluding co-payments)

minus any savings in use of other drugs would be in the range $60 - $100 million. The PBAC noted that the submission may have overestimated usage.

12. Recommendation and Reasons

The PBAC recommended listing on the PBS of varenicline as a short-term treatment to aid smoking cessation on the basis of an acceptable cost-effectiveness compared with bupropion. The PBAC considered that the incremental cost-effectiveness ratio of <$15,000 was acceptable for the higher quit and continuous abstinence rates demonstrated in the meta-analyses of two head-to-head trials comparing varenicline to bupropion.

While the PBAC noted that significantly more patients on varenicline treatment experienced nausea, abnormal dreams and headache compared with patients on bupropion, the Committee accepted the sponsor's comment that the pooled rate of discontinuations due to adverse events was lower with varenicline compared to bupropion (9.5% vs 13.9%; RR= 0.69 (0.47, 1.00)).

The PBAC recommended that treatment is initiated with a four week course of varenicline, with a further two months of treatment made available on a second authority prescription. Further, concurrent treatment with bupropion should not be approved, and only one course of either varenicline or bupropion per patient per 12 months should be approved. The recommendation in the TGA approved Product Information that an additional 12 weeks treatment be undertaken by patients who have successfully stopped smoking during the first 12 weeks of treatment was noted, however, the PBAC considered a further major submission would be required to justify this additional treatment period (which had not been sought by the sponsor in its application).

The PBAC noted that the sponsor's estimates may have overestimated usage, and requested usage be monitored. The actions being undertaken by the sponsor in regard to the appropriate use of varenicline, including the provision of counselling support via a sponsor-provided Behavioural Modification Program were noted. However, the PBAC considered similar requirements for counselling to those for bupropion should apply to varenicline, ie. a specific counselling and support program is not mandated in the wording of the listing.

The PBAC recommended the 20 day safety rule should not apply.

Recommendation

VARENICLINE TARTRATE, tablets, 0.5 mg, 11 and 1 mg, 14 and 1 mg, 28 and tablets 1 mg, 56

NOTE:
Only one course of PBS-subsidised smoking cessation therapy (bupropion hydrochloride or varenicline tartrate) will be authorised per year. A course of treatment with varenicline is 12 weeks. No increased maximum quantities or repeats will be authorised. Clinical review is recommended within 2 to 3 weeks of the original prescription being requested.

Restriction: Authority required

	Commencement of short-term, sole PBS-subsidised, therapy as an aid to achieving abstinence in a patient who has indicated they are ready to cease smoking and: (c) who has entered a comprehensive support and counselling program; or (d) who is entering a comprehensive support and counselling program during the consultation at which this authority is requested. Details of the program must be specified in the authority application.
Maximum Quantity: Repeats:	1 initiation pack (11 x 0.5mg, 14 x 1mg, 28 x 1mg) Nil
Restriction:	<u>Authority required</u> Completion of short-term, sole PBS-subsidised, therapy as an aid to achieving abstinence in a patient who has previously been issued with an authority prescription for this drug and who is enrolled in a comprehensive support and counselling program.
Maximum Quantity: Repeats:	2 (56 x 1mg) Nil

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

Pfizer Australia (the Sponsor) welcomes the PBAC recommendation to list varenicline (Champix) on the PBS for smoking cessation. The Sponsor believes the availability of Champix with its superior cessation rates will help to reduce the significant health and economic burden associated with smoking in Australia.