

## 6.16 VARENICLINE

**Box containing 11 tablets 0.5 mg (as tartrate) and 14 tablets 1 mg (as tartrate) in the first pack and 28 tablets 1 mg (as tartrate) in the second pack;**

**Tablet, 1 mg, 56**

**Champix<sup>®</sup>,**

**Pfizer Australia Pty Ltd.**

### 1 Purpose of Application

- 1.1 The minor submission sought to amend the current listing of varenicline from Authority Required to Authority Required (STREAMLINED).
- 1.2 In March 2015, the PBAC reviewed the restriction level of varenicline as part of the Post market Review of Authority Required PBS listings, and recommended varenicline remain Authority Required (telephone). The PBAC considered the criteria for an Authority Required listing were satisfied, and that an Authority Required listing would enhance the National Medicines Policy objective of safe use of medicines (due to the potential for inappropriate continuous use). At that time, the PBAC noted that the market for smoking cessation aids was not yet stable. In response to a subsequent request from the sponsor, prompted by the February 2016 DUSC analysis of smoking cessation therapies, the PBAC advised that a formal submission would be required to address safety concerns regarding psychiatric adverse events.

### 2 Requested listing

- 2.1 The submission requested a change to the restriction level of all PBS listings of varenicline from Authority Required to Authority Required (STREAMLINED). No other changes to the existing listings were requested. As no other changes to the restriction were requested, the restriction has not been reproduced in full.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
VARENICLINE				
Box containing 11 tablets 0.5 mg (as tartrate) and 14 tablets 1 mg (as tartrate) in the first pack and 28 tablets 1 mg (as tartrate) in the second pack	1	0	\$94.07	Champix <sup>®</sup> Pfizer Australia Pty Ltd
Tablet 1 mg (as tartrate), 56	1	2	\$109.02	
Tablet 1 mg (as tartrate), 56	2	0	\$208.08	
Authority Required (STREAMLINED)				

### 3 Background

- 3.1 Varenicline was TGA registered on 15 February 2007 as an aid for smoking cessation in adults over the age of 18 years.
- 3.2 Varenicline was listed on the PBS on 1 January 2008.
- 3.3 The PBAC has previously considered a number of submissions relating to varenicline. Varenicline was recommended at the July 2007 PBAC meeting. In November 2009, the PBAC recommended a change to listing to allow a further 12 weeks' treatment for responders to therapy. In November 2012, the PBAC rejected a request to permit a further course of treatment for patients who did not cease smoking or relapsed after completing treatment. A resubmission to request an additional course of treatment was recommended by the PBAC in March 2014 on the basis of acceptable cost effectiveness to placebo, bupropion and NRT.
- 3.4 In making its recommendation in March 2014, the PBAC considered that varenicline was superior in terms of efficacy to placebo, bupropion and NRT and no worse in terms of safety to bupropion. The PBAC considered that varenicline was of inferior safety to placebo and NRT.
- 3.5 In March 2015, the PBAC reviewed the restriction level of varenicline as part of the Post market Review of Authority Required PBS listings, and recommended varenicline remain Authority Required (telephone). The PBAC considered in March 2015 that varenicline was a specific instance where the National Medicines Policy objective of safe use of medicines would be enhanced through an Authority Required listing. The PBAC was concerned that amending varenicline to a streamlined authority may create potential for inappropriate continuous use. The PBAC noted that the market for smoking cessation aids had not stabilised at the time the request was considered.
- 3.6 A TGA Safety Update (December 2015) included updates to the Product Information to include reference to psychiatric symptoms that have occurred in patients being treated with varenicline, and advised that patients and families be advised to contact a health care professional if changes in behaviour or thinking, agitation or depressed mood that are not typical for the patient are observed, or if the patient develops suicidal ideation or suicidal behaviour. Further, the update advised clinicians inform patients that alcohol intake may increase the risk of neuropsychiatric events during treatment with varenicline<sup>1</sup>.

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<sup>1</sup> Therapeutic Goods Administration 2015. *Varenicline (Champix) – Safety advisory – risks of psychiatric symptoms and potential interaction with alcohol*. Available online at <https://www.tga.gov.au/alert/varenicline-champix>. Accessed 20 Sep 2016.

- 3.7 The basis of this minor submission’s request was the outcome of the Drug Utilisation Sub-Committee (DUSC) review into smoking cessation therapy in February 2016. The DUSC review found that changes to the restriction level of NRT therapies on 1 December 2013 did not substantially impact the utilisation trends of R/PBS subsidised NRT treatment. The DUSC noted, however, that smoking cessation aids may be being used as smoking reduction tools, outside their PBS intended purpose as an aid to cessation of smoking<sup>2</sup>.

*For more detail on PBAC’s view, see section 5 “PBAC outcome”*

## 4 Consideration of the evidence

### **Sponsor hearing**

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

### **Consumer comments**

- 4.2 The PBAC noted that no consumer comments were received for this item.

### **Clinical trials**

- 4.3 The clinical trials presented in the submission are shown in Table 1:

**Table 1: Trials and associated reports presented in the submission**

Trial ID	Protocol title/ Publication title	Publication citation
<b>Direct randomised trials</b>		
Study A3051123 (EAGLES)	A 24-week, double blind, active (nicotine replacement therapy) and placebo-controlled, multicentre, parallel group study of varenicline and bupropion for smoking cessation in smokers with or without a history of psychiatric disorders  Anthenelli RM, Benowitz NL, West R, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial	29 October 2015  <i>The Lancet</i> , Volume 387, Issue 10037, 18–24 June 2016, Pages 2507-2520, <a href="http://dx.doi.org/10.1016/S0140-6736(16)30272-0">http://dx.doi.org/10.1016/S0140-6736(16)30272-0</a> .

Source: Main body of submission, p 5; Published article identified by the PBAC Secretariat

- 4.4 The key features of the included evidence are included in Table 2:

<sup>2</sup> Drug Utilisation Sub-Committee 2016. *Smoking Cessation Therapy: PBS/RPBS utilisation*. Canberra: Department of Health. Full report available from <http://www.pbs.gov.au/info/industry/listing/participants/public-release-docs/2016-02/smoking-cessation-therapy-2016-02>. Accessed 05 Sep 2016.

**Table 2: Key features of the included evidence**

Trial	N	N (treatment groups)	Design/ duration	Patient population	Outcomes
<b>Individual treatment groups of varenicline, bupropion, nicotine replacement therapy and placebo</b>					
Study A3051123 (EAGLES)	8,144	Varenicline (V): 2,037 Bupropion (B): 2,034 NRT (N): 2,038 Placebo (P): 2,035	MC, R, DB, PG 24 weeks	Male or female cigarette smokers aged 18-75 years, motivated to stop smoking, with or without a history of psychiatric disorders	Continuous abstinence from smoking (CA)  Neuropsychiatric (NPS) adverse events (AEs)  Occurrence of components of NPS AEs endpoint in psychiatric or non-psychiatric history cohorts

Source: Compiled by the PBAC Secretariat

Abbreviations: MC, multi-centre; R, randomised; DB, double blind; PG, parallel group.

4.5 The EAGLES trial screened and allocated participants to cohorts with no history of psychiatric disorders or confirmed history of psychiatric disorders based on Diagnostic and Statistical Manual of Mental Disorders, Version 4 (DSM-IV) criteria based on clinical assessment and structured clinical interview. Patients were included in the psychiatric cohort if they were evaluated to have one of the following (current or past) psychiatric diagnoses:

- Psychotic disorder: schizophrenia, schizoaffective disorder
- Affective disorder: major depression, bipolar I, bipolar II
- Anxiety disorder: panic disorder with or without agoraphobia, post-traumatic stress disorder, obsessive-compulsive disorder, social phobia, generalised anxiety disorder
- Personality disorder: limited to past history of borderline personality disorder

### **Comparative effectiveness**

4.6 The results from the secondary outcome (abstinence from smoking over weeks 9-24) from the EAGLES trial are presented in Table 3.

**Table 3: Continuous abstinence from smoking, weeks 9-24**

Outcome	Overall population	Non-psychiatric cohort	Psychiatric cohort
<b>Continuous abstinence, FAS population n/N (%)</b>			
Varenicline	445/2037 (21.8%)	256/1005 (25.5%)	189/1032 (18.3%)
Bupropion	330/2034 (16.2%)	188/1001 (18.8%)	142/1033 (13.7%)
NRT	320/2038 (15.7%)	187/1013 (18.5%)	133/1025 (13.0%)
Placebo	191/2035 (9.4%)	106/1009 (10.5%)	85/1026 (8.3%)
<b>Treatment comparison, estimated odds ratio in continuous abstinence (95% CI)</b>			
<b>Primary comparison</b>			
Varenicline vs. Placebo	2.74* (2.28, 3.30)	2.99* (2.33, 3.83)	2.50* (1.90, 3.29)
Bupropion vs. Placebo	1.89* (1.56, 2.29)	2.00* (1.54, 2.59)	1.77* (1.33, 2.36)
<b>Secondary comparison</b>			
NRT vs. Placebo	1.81 (1.49, 2.19)	1.96 (1.51, 2.54)	1.65 (1.24, 2.20)
Varenicline vs. Bupropion	1.45 (1.24, 1.70)	1.49 (1.20, 1.85)	1.41 (1.11, 1.79)
Varenicline vs. NRT	1.52 (1.29, 1.78)	1.52 (1.23, 1.89)	1.51 (1.19, 1.93)
Bupropion vs. NRT	1.04 (0.88, 1.24)	1.02 (0.81, 1.28)	1.07 (0.83, 1.39)

Source: Study A3051123 (EAGLES) Clinical Study Report, Section 11, Table 15 p 86

Abbreviations: FAS, full analysis set; CI, confidence interval; N, number of subjects randomised to study treatment; NRT, nicotine replacement therapy.

\*p value <0.001 for primary comparison

- 4.7 The proportion of patients achieving continuous abstinence over weeks 9-24 was statistically significant ( $p < 0.001$ ) for both the primary comparisons of varenicline vs. placebo and bupropion vs. placebo, in both non-psychiatric and psychiatric history groups.
- 4.8 Results for the secondary comparisons showed significantly higher rates of smoking abstinence for varenicline vs. bupropion ( $p < 0.01$ ), and for bupropion and NRT vs. placebo ( $p < 0.001$ ) over weeks 9-24.

### **Comparative harms**

- 4.9 The results from the primary outcome (estimation of the NPS AE endpoint) in the safety population of the EAGLES trial are presented in Table 4.

Table 4: Estimation of NPS AE primary endpoint

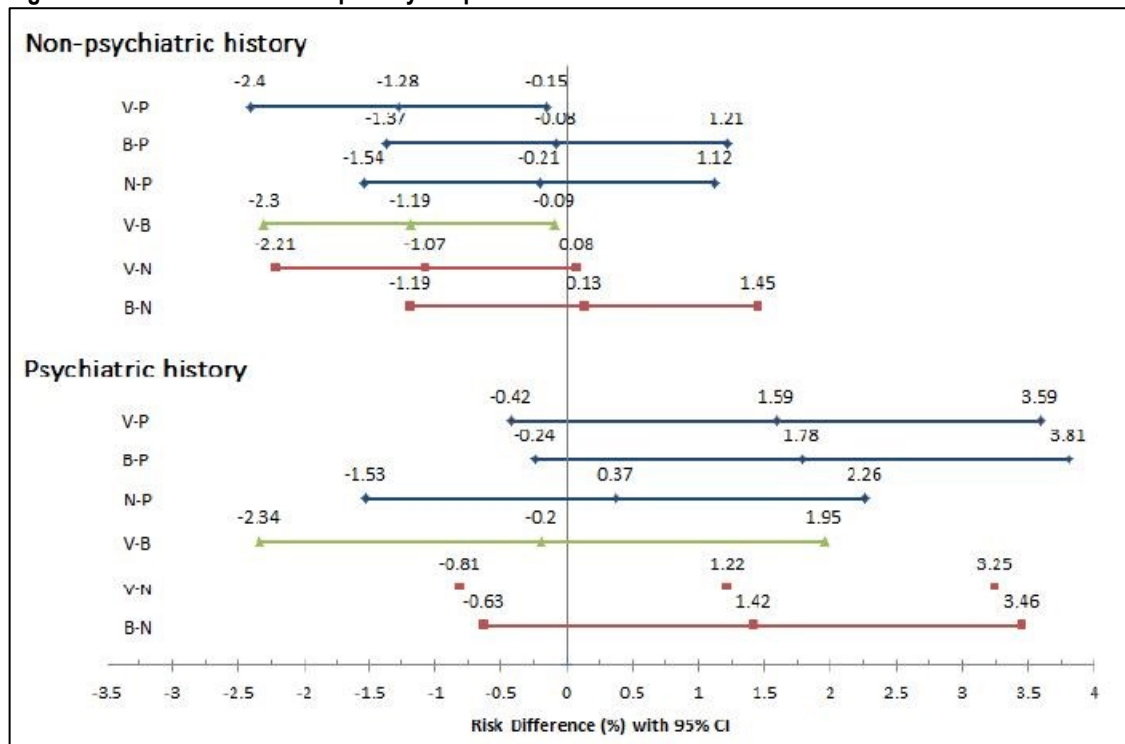
Outcome	Non-psychiatric history	Psychiatric history
<b>Treatment group</b>	<b>Estimated NPS AE risk % (95% CI)</b>	
Varenicline	1.25 (0.60, 1.90)	6.42 (4.91, 7.93)
Bupropion	2.44 (1.52, 3.36)	6.62 (5.09, 8.15)
NRT	2.31 (1.37, 3.25)	5.20 (3.84, 6.56)
Placebo	2.52 (1.58, 3.46)	4.83 (3.51, 6.16)
<b>Treatment comparisons</b>	<b>Estimated risk difference in NPS AE % (95% CI)</b>	
<b>Primary comparison</b>		
Varenicline vs. Placebo	-1.28 (-2.40, -0.15)	1.59 (-0.42, 3.59)
Bupropion vs. Placebo	-0.08 (-1.37, 1.21)	1.78 (-0.24, 3.81)
<b>Secondary comparison</b>		
NRT vs. Placebo	-0.21 (-1.54, 1.12)	0.37 (-1.53, 2.26)
Varenicline vs. Bupropion	-1.19 (-2.30, -0.09)	-0.20 (-2.34, 1.95)
Varenicline vs. NRT	-1.07 (-2.21, 0.08)	1.22 (-0.81, 3.25)
Bupropion vs. NRT	0.13 (-1.19, 1.45)	1.42 (-0.63, 3.46)

Source: Study A3051123 (EAGLES) Clinical Study Report, Section 12, Table 25 p 100

Abbreviations: CI, confidence interval; NPS AE, neuropsychiatric adverse event; NRT, nicotine replacement therapy.

- 4.10 The estimated risk difference (95% CI) in the NPS AE primary endpoint, by treatment group and psychiatric history cohorts is presented in Figure 1.

Figure 1: Estimation of NPS AE primary endpoint



Source: Figure 1, p 11 of the submission.

Abbreviations: V, Varenicline; P, Placebo; B, Bupropion; N, Nicotine Replacement Therapy; CI, confidence interval.

- 4.11 The incidence of all NPS AEs was not significantly different with for either varenicline or bupropion, relative to either NRT or placebo, in either the non-psychiatric or psychiatric history cohorts.

- 4.12 A summary of deaths for all cohorts and the reported cause of death is presented in Table 5.

**Table 5: Deaths reported – all treatment groups, non-psychiatric and psychiatric cohorts**

Cohort n/N (%)	Varenicline	Bupropion	NRT	Placebo
Non-psychiatric	0/990	1/989 (0.1) <i>Heroin overdose</i>	1/1006 (0.1) <i>Prostate cancer</i>	3/999 (0.3) <i>Completed suicide</i> <i>Myocardial infarction</i> <i>Car accident</i>
Psychiatric	0/1026	1/1017 (0.2) <i>Cardiorespiratory arrest</i> <i>Lung cancer</i>	1/1016 (0.1) <i>Oesophageal cancer</i>	1/1015 (0.1) <i>Pulmonary embolism and cocaine abuse</i>

Source: Table 4, p 12 of the submission.

Abbreviations: N, number of patients treated; NRT, nicotine replacement therapy.

- 4.13 One death, in the placebo group, was reported as a completed suicide. An additional two deaths were associated with illicit drug abuse. No deaths were reported in either the psychiatric or non-psychiatric cohorts of patients who received varenicline.
- 4.14 Summaries of severe NPS AEs reported in in the trial are presented in Table 6 (non-psychiatric cohort) and Table 7 (psychiatric cohort).

**Table 6: Severe component NPS AEs, non-psychiatric cohort**

Component NPS AE	Number (%) of subjects			
	Varenicline (N = 990)	Bupropion (N = 989)	NRT (N = 1006)	Placebo (N = 999)
Anxiety	0	1 (0.1)	0	3 (0.3)
Depression	1 (0.1)	0	0	0
Feeling abnormal	0	0	0	0
Hostility	0	1 (0.1)	1 (0.1)	0
Agitation	10 (1.0)	11 (1.1)	19 (1.9)	11 (1.1)
Aggression	3 (0.3)	3 (0.3)	2 (0.2)	3 (0.3)
Delusions	0	0	1 (0.1)	0
Hallucination	1 (0.1)	0	0	0
Mania	0	1 (0.1)	2 (0.2)	2 (0.2)
Panic	0	4 (0.4)	1 (0.1)	3 (0.3)
Paranoia	0	1 (0.1)	0	0
Psychosis	0	0	1 (0.1)	0
Homicidal ideation	0	0	1 (0.1)	0
Suicidal behaviour	0	1 (0.1)	1 (0.1)	0
Suicidal ideation	0	1 (0.1)	2 (0.2)	3 (0.3)
Completed suicide	0	0	0	1 (0.1)

Source: Study A3051123 (EAGLES) Clinical Study Report, Section 12, Table 26 p 102

Table 7: Severe component NPS AEs, psychiatric cohort

Component NPS AE	Number (%) of subjects			
	Varenicline (N = 1026)	Bupropion (N = 1017)	NRT (N = 1016)	Placebo (N = 1015)
Anxiety	5 (0.5)	4 (0.4)	6 (0.6)	2 (0.2)
Depression	6 (0.6)	4 (0.4)	7 (0.7)	6 (0.6)
Feeling abnormal	0	1 (0.1)	0	0
Hostility	0	0	0	0
Agitation	25 (2.4)	29 (2.9)	21 (2.1)	22 (2.2)
Aggression	14 (1.4)	9 (0.9)	7 (0.7)	8 (0.8)
Delusions	1 (0.1)	1 (0.1)	1 (0.1)	0
Hallucination	5 (0.5)	4 (0.4)	2 (0.2)	2 (0.2)
Mania	7 (0.7)	9 (0.9)	3 (0.3)	6 (0.6)
Panic	7 (0.7)	16 (1.6)	13 (1.3)	7 (0.7)
Paranoia	1 (0.1)	0	0	2 (0.2)
Psychosis	4 (0.4)	2 (0.2)	3 (0.3)	1 (0.1)
Homicidal ideation	0	0	0	0
Suicidal behaviour	1 (0.1)	1 (0.1)	0	1 (0.1)
Suicidal ideation	5 (0.5)	2 (0.2)	3 (0.3)	2 (0.2)
Completed suicide	0	0	0	0

Source: Study A3051123 (EAGLES) Clinical Study Report, Section 12, Table 27 p 102

- 4.15 The results showed substantially more NPS AEs in the psychiatric cohort than the non-psychiatric cohort, however they did not show significant differences between treatments within the psychiatric and non-psychiatric cohorts.

### **Clinical Claim**

- 4.16 The submission claimed the presented evidence addressed the safety concerns raised by the PBAC in its consideration of the submission to the Post Market Review of Authority Required PBS listings, and claimed the risk-benefit profile of varenicline was favourable.
- 4.17 The PBAC reaffirmed its previous consideration that varenicline was superior in regards to comparative effectiveness compared to bupropion, NRT and placebo.
- 4.18 The PBAC has previously considered that varenicline was non-inferior to bupropion, and inferior to NRT and placebo with regards to safety. The PBAC considered, based on the evidence presented, that varenicline was non-inferior to bupropion with regards to comparative safety, and likely to be non-inferior to NRT and placebo. The PBAC noted that for patients with a history of neuropsychiatric disorders, attempting to quit smoking was associated with an increase in neuropsychiatric events.
- 4.19 The EAGLES trial did not differentiate between participants who were symptomatically stable and treated or who had previous psychiatric disorders that were in remission. The trial also excluded participants with current drug/substance abuse or who were at imminent risk of suicide<sup>3</sup>, which may limit the generalisability of

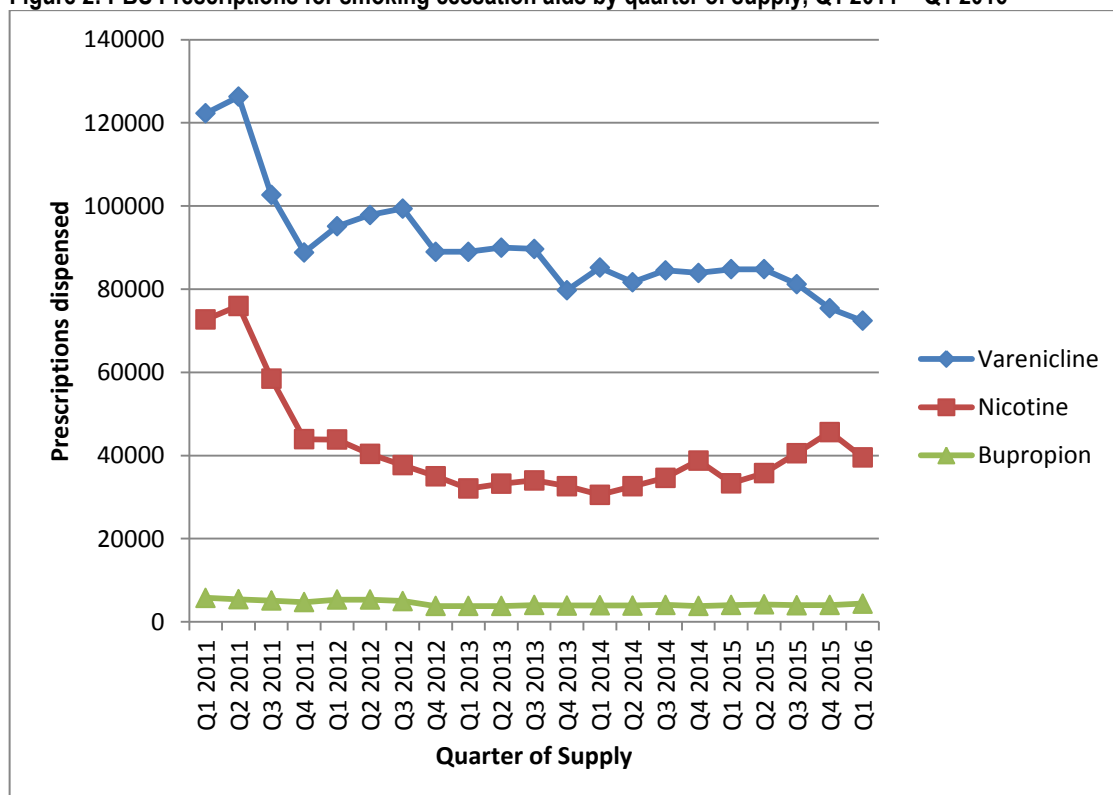
<sup>3</sup> Anthenelli, Robert M, et al, 2016. *Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-*

the trial to some sub-populations, such as those with untreated or symptomatically unstable psychiatric illness.

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

- 4.20 The minor submission estimated there to be no significant financial implications to the PBS.
- 4.21 The DUSC did not consider that the change of NRT to a streamlined authority had a substantial impact on utilisation trends (paragraph 3.7 refers).
- 4.22 The PBAC considered that the market for smoking cessation aids was unstable when it previously considered this request in March 2015. The DUSC review provided utilisation data to 30 September 2015. As additional data were available to 31 March 2016, utilisation data on PBS subsidised varenicline, NRT and bupropion to that date were collected from the DUSC database.
- 4.23 Input was sought from the Drug Utilisation Sub-Committee secretariat on the utilisation of varenicline, NRT and bupropion for the period quarter 1 (Q1), 2011 to Q1, 2016, representing an additional 12 months' data since prior consideration by the PBAC. Prescription counts are presented, based on quarter of supply, in Figure 2.

Figure 2: PBS Prescriptions for smoking cessation aids by quarter of supply, Q1 2011 – Q1 2016



Source: DUSC Database

- 4.24 The use of both PBS subsidised NRT and varenicline peaked in Q2 2011, and declined substantially until Q4 2011. Since then, the market for varenicline and NRT has fluctuated, but not to the same extent. During 2015 and early 2016, the use of varenicline has declined, while the use of NRT has increased. Bupropion use has remained low and stable between Q1 2011 and Q1 2016.
- 4.25 The DUSC review of smoking cessation therapies in October 2015 found a substantial increase in the number of prescriptions for varenicline and NRT following the Australian Government announcing a tobacco tax increase in April 2010<sup>4</sup>. This tax increase may have contributed to the high use of smoking cessation aids in early 2011.
- 4.26 Further, the DUSC considered in its October 2015 review that it was difficult to interpret utilisation trends in terms of cause and effect, as there are multiple contributing factors to the overall use of smoking cessation aids.
- 4.27 The Department of Human Services (DHS) provided data on authority approvals and rejections for varenicline. In the period 1 September 2015 to 31 August 2016, DHS received 301,085 authority requests, of which 2,350 were rejected.

<sup>4</sup> Drug Utilisation Sub-Committee 2016. Smoking Cessation Therapy: PBS/RPBS utilisation. Canberra: Department of Health. Full report available from <http://www.pbs.gov.au/info/industry/listing/participants/public-release-docs/2016-02/smoking-cessation-therapy-2016-02>. Accessed 05 Sep 2016.

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

## **5 PBAC Outcome**

- 5.1 The PBAC recommended amending the listings of varenicline from Authority Required to Authority Required (STREAMLINED).
- 5.2 The PBAC considered that the results of the EAGLES trial supported the comparative safety of varenicline, bupropion, NRT and placebo, and noted that changes to the authority level of bupropion and NRT had not resulted in substantial impacts on utilisation trends.
- 5.3 The PBAC reaffirmed its previous consideration that varenicline was superior to bupropion, NRT and placebo concerning comparative efficacy.
- 5.4 The PBAC considered the results of the EAGLES study, a large randomised head-to-head clinical trial comparing the efficacy and safety of varenicline with bupropion, NRT and placebo. The EAGLES study divided patients into cohorts based on treatment group and previous history of psychiatric disorders, and found differences between the non-psychiatric history and psychiatric history cohorts, but no difference in safety outcomes between treatments within these two cohorts. The PBAC considered that varenicline may be non-inferior to NRT and placebo with regards to comparative safety.
- 5.5 The PBAC noted the latest update to the TGA Periodic Safety Update Report and Risk Management Plans, where no new or increased safety signals with varenicline were identified.
- 5.6 The PBAC considered whether a caution, that clinicians should monitor patients with a history of psychiatric disorders or alcohol/drug use while being treated with varenicline, was appropriate and decided that a caution was not required. The risks of neuropsychiatric adverse events were well documented in the approved Product Information, and other mechanisms such as practice software already correlate medical records and prescribing history.
- 5.7 The PBAC noted there were differences in the wording of current restrictions for varenicline, bupropion and NRT, such as wording related to patient participation in counselling programs, the purpose of treatment and maximum treatment duration per course, and recommended it was appropriate to align them. The PBAC noted this would have flow-on restriction changes to bupropion and NRT.
- 5.8 The PBAC noted the previous outcomes of the DUSC analysis of smoking cessation therapies in February 2016, and considered that changing the authority level of varenicline was unlikely to have a significant impact on utilisation trends. The PBAC further noted that in the period 1 September 2015 to 31 August 2016 that only 2,350 of 301,085 (0.8%) of authority requests for varenicline were rejected.
- 5.9 The PBAC advised that varenicline remains suitable for prescribing by nurse practitioners.

5.10 The PBAC recommended no change to varenicline concerning the Early Supply Rule.

5.11 The PBAC noted that this submission was not eligible for an Independent Review as it received a positive recommendation.

**Outcome:**

Recommended

**6 Recommended listing**

6.1 Amend existing/recommended listings of varenicline, bupropion and nicotine as follows:

Additions are in italics and deletions are in strikethrough.

**Varenicline initial restriction (PBS item 9128K)**

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
VARENICLINE varenicline 500 microgram tablet [11 1 tablets] (& varenicline 1 mg tablet [42 tablets], 53		0	Champix® Pfizer Australia Pty Ltd

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<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>PBS Indication:</b>	Nicotine dependence
<b>Treatment phase:</b>	Treatment Phase: Commencement of a short-term (12 weeks or 24 weeks) course of treatment
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
<b>Treatment criteria:</b>	Patient must be undergoing concurrent counselling for smoking cessation through a comprehensive support and counselling program or is about to enter such a program at the time the Authority application is requested.

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<p><b>Clinical criteria:</b></p>	<p>The treatment must be as an aid to achieving abstinence from smoking, AND The treatment must be the sole PBS-subsidised therapy for this condition, AND <del>Patient must have entered a comprehensive support and counselling program,</del> AND Patient must have indicated they are ready to cease smoking, AND <i>Patient must not receive more than 24 weeks of PBS-subsidised treatment with this drug per 12-month period.</i></p>
<p><b>Prescriber Instructions</b></p>	<p>Details of the support and counselling program must be documented in the patient's medical records at the time treatment is initiated.  Clinical review is recommended within 2 to 3 weeks of the initial prescription being requested.</p>
<p><b>Administrative Advice</b></p>	<p>No increase in the maximum quantity or number of units may be authorised.  Note No increase in the maximum number of repeats may be authorised.  Note A course of treatment with this drug is 12 weeks or up to 24 weeks, if initial treatment of 12 weeks has been successful.  Note The period between commencing varenicline and bupropion or a new course of varenicline must be at least 6 months.  Note A patient may only qualify for PBS-subsidised treatment under this treatment phase restriction once during a short-term course of treatment.</p>

**Varenicline continuing restriction (PBS item, 9129L)**

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
VARENICLINE varenicline 1 mg tablet, 56	2	0	Champix®	Pfizer Australia Pty Ltd

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<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>PBS Indication:</b>	Nicotine dependence
<b>Treatment phase:</b>	Treatment Phase: Continuation of a short-term (12 weeks or 24 weeks) course of treatment
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
<b>Treatment criteria:</b>	Patient must be undergoing concurrent counselling for smoking cessation through a comprehensive support and counselling program.
<b>Clinical criteria:</b>	The treatment must be as an aid to achieving abstinence from smoking,  AND  The treatment must be the sole PBS-subsidised therapy for this condition,  AND  Patient must have previously <del>been issued with an authority prescription</del> received PBS-subsidised treatment with for this drug during this current course of treatment.
<b>Administrative Advice</b>	No increase in the maximum quantity or number of units may be authorised.  Note No increase in the maximum number of repeats may be authorised.  Note A course of treatment with this drug is 12 weeks or up to 24 weeks, if initial treatment of 12 weeks has been successful.  Note A patient may only qualify for PBS-subsidised treatment under this treatment phase restriction once during a short-term course of treatment.

**Varenicline continuing restriction (PBS item 5469W)**

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
VARENICLINE varenicline 1 mg tablet, 56	1	2	Champix®	Pfizer Australia Pty Ltd

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<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>PBS Indication:</b>	Nicotine dependence
<b>Treatment phase:</b>	Treatment Phase: Completion of a short-term (24 weeks) course of treatment.
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
<b>Treatment criteria:</b>	Patient must be undergoing concurrent counselling for smoking cessation through a comprehensive support and counselling program.
<b>Clinical criteria:</b>	The treatment must be as an aid to achieving abstinence from smoking,  AND  The treatment must be the sole PBS-subsidised therapy for this condition,  AND  Patient must have previously <del>been issued with an authority prescription</del> received PBS-subsidised treatment with <del>for</del> this drug during this current course of treatment,  AND  Patient must have ceased smoking in the process of completing an initial 12-weeks or ceased smoking following an initial 12-weeks of PBS-subsidised treatment with this drug in the current course of treatment.
<b>Administrative Advice</b>	No increase in the maximum quantity or number of units may be authorised.  Note No increase in the maximum number of repeats may be authorised.  Note A course of treatment with this drug is 12 weeks or up to 24 weeks, if initial treatment of 12 weeks has been successful.  Note A patient may only qualify for PBS-subsidised treatment under this treatment phase restriction once during a short-term course of treatment.

Minor flow-on changes to align the restrictions between nicotine dependence therapies outlined below.

**Bupropion initial restriction (PBS item 8465M)**

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
BUPROPION bupropion hydrochloride 150 mg modified release tablet, 30	1	0	Zyban® Aspen Pharmacare Australia Pty Ltd

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<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>PBS Indication:</b>	Nicotine dependence
<b>Treatment phase:</b>	Treatment Phase: Commencement of a short-term (9 weeks) course of treatment
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
<b>Treatment criteria:</b>	<i>Patient must be undergoing concurrent counselling for smoking cessation through a comprehensive support and counselling program or is about to enter such a program at the time the Authority application is requested.</i>
<b>Clinical criteria:</b>	<i>The treatment must be as an aid to achieving abstinence from smoking, AND The treatment must be the sole PBS-subsidised therapy for this condition, AND Patient must have entered a comprehensive support and counselling program, AND Patient must have indicated they are ready to cease smoking, AND Patient must not receive more than 9 weeks of PBS-subsidised treatment with this drug per 12-month period.</i>
<b>Prescriber Instructions</b>	Details of the support and counselling program must be documented in the patient's medical records at the time treatment is initiated.  <i>Clinical review is recommended within 2 to 3 weeks of the original prescription being requested.</i>

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<b>Administrative Advice</b>	<p>No increase in the maximum quantity or number of units may be authorised.</p> <p>Note No increase in the maximum number of repeats may be authorised.</p> <p>Note The period between commencing a course of bupropion hydrochloride and varenicline tartrate must be at least 6 months.</p> <p>Note <i>A patient may only qualify for PBS-subsidised treatment under this treatment phase restriction once during a short-term course of treatment.</i></p>
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<b>Treatment phase:</b>	Treatment Phase: Commencement of a short-term (9 weeks) course of treatment
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
<b>Treatment criteria:</b>	<i>Patient must be undergoing concurrent counselling for smoking cessation through a comprehensive support and counselling program or is about to enter such a program at the time the Authority application is requested.</i>
<b>Clinical criteria:</b>	<p><i>The treatment must be as an aid to achieving abstinence from smoking,</i></p> <p>AND</p> <p><i>The treatment must be the sole PBS-subsidised therapy for this condition,</i></p> <p>AND</p> <p><i>Patient must have indicated they are ready to cease smoking,</i></p> <p>AND</p> <p><del><i>Patient must be entering a comprehensive support and counselling program during the consultation at which this prescription is written,</i></del></p> <p>AND</p> <p><i>Patient must not receive more than 9 weeks of PBS-subsidised treatment with this drug per 12-month period.</i></p>
<b>Prescriber Instructions</b>	<p>Details of the support and counselling program must be documented in the patient's medical records at the time treatment is initiated.</p> <p><i>Clinical review is recommended within 2 to 3 weeks of the original prescription being requested.</i></p>
<b>Administrative Advice</b>	<p>No increase in the maximum quantity or number of units may be authorised.</p> <p>Note No increase in the maximum number of repeats may be authorised.</p> <p>Note The period between commencing a course of bupropion hydrochloride and varenicline tartrate must be at least 6 months.</p> <p>Note <i>A patient may only qualify for PBS-subsidised treatment under this treatment phase restriction once during a short-term course of treatment.</i></p>

**Bupropion continuing restriction (PBS item 8710K)**

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
BUPROPION bupropion hydrochloride 150 mg modified release tablet, 90	1	0	Zyban®	Aspen Pharmacare Australia Pty Ltd

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<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>PBS Indication:</b>	Nicotine dependence
<b>Treatment phase:</b>	Treatment Phase: Completion of a short-term (9 weeks) course of treatment
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
<b>Treatment Criteria</b>	<i>Patient must be undergoing concurrent counselling for smoking cessation through a comprehensive support and counselling program.</i>
<b>Clinical criteria:</b>	<i>The treatment must be as an aid to achieving abstinence from smoking,</i>  <i>AND</i>  <i>The treatment must be the sole PBS-subsidised therapy for this condition,</i>  <i>AND</i>  <i>Patient must have previously been issued with an authority prescription received PBS-subsidised treatment with for this drug during this current course of treatment.</i>  <i>AND</i>  <i>Patient must be enrolled in a comprehensive support and counselling program,</i>  <i>AND</i>  <i>Patient must not receive more than 9 weeks of PBS-subsidised treatment with this drug per 12-month period.</i>
<b>Administrative Advice</b>	No increase in the maximum quantity or number of units may be authorised.  Note No increase in the maximum number of repeats may be authorised.  Note The period between commencing a course of bupropion hydrochloride and varenicline tartrate must be at least 6 months.  Note Clinical review is recommended within 2 to 3 weeks of the original prescription being requested.

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**Nicotine replacement therapies (PBS items 3414Q, 5465P 5572G, 5573H, 10076H)**

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
NICOTINE				
nicotine 21 mg/24 hours patch, 28	1	2	Nicotinell® Step 1	Orion Laboratories Pty Ltd
nicotine 14 mg/24 hours patch, 28	1	2	Nicotinell® Step 2	Orion Laboratories Pty Ltd
nicotine 7mg/ 24 hours patch, 28	1	2	Nicotinell® Step 3	Orion Laboratories Pty Ltd
nicotine 25 mg/16 hours patch, 28	1	2	Nicorette 16hr Invisipatch	Johnson & Johnson Pacific Pty Limited
nicotine 21 mg/24 hours patch, 28	1	2	Nicabate P	GlaxoSmithKline Australia Pty Ltd

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<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>PBS Indication:</b>	Nicotine dependence
<b>Restriction Level / Method:</b>	<input checked="" type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
<b>Treatment criteria:</b>	<i>Patient must be undergoing concurrent counselling for smoking cessation through a comprehensive support and counselling program or is about to enter such a program at the time the Authority application is requested.</i>
<b>Clinical criteria:</b>	<i>The treatment must be as an aid to achieving abstinence from smoking,</i>  <i>AND</i>  <i>The treatment must be the sole PBS-subsidised therapy for this condition,</i>  <i>AND</i>  <i>Patient must have indicated they are ready to cease smoking,</i>  <i>AND</i>  <i>Patient must have entered a comprehensive support and counselling program,</i>  <i>AND</i>  <i>Patient must not receive more than 12 weeks of PBS-subsidised nicotine replacement therapy per 12-month period.</i>
<b>Prescriber Instructions</b>	Details of the support and counselling program must be documented in the patient's medical records at the time treatment is initiated.
<b>Administrative Advice</b>	No increase in the maximum quantity or number of units may be authorised.  Note No increase in the maximum number of repeats may be authorised.

<b>PBS Indication:</b>	Nicotine dependence
<b>Restriction Level / Method:</b>	<input checked="" type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
<b>Treatment criteria:</b>	<i>Patient must be undergoing concurrent counselling for smoking cessation through a comprehensive support and counselling program or is about to enter such a program at the time the Authority application is requested.</i>
<b>Clinical criteria:</b>	<p><i>The treatment must be as an aid to achieving abstinence from smoking,</i></p> <p>AND</p> <p><i>The treatment must be the sole PBS-subsidised therapy for this condition,</i></p> <p>AND</p> <p><i>Patient must have indicated they are ready to cease smoking,</i></p> <p>AND</p> <p><i>Patient must be entering a comprehensive support and counselling program during the consultation at which this prescription is written,</i></p> <p>AND</p> <p><i>Patient must not receive more than 12 weeks of PBS-subsidised nicotine replacement therapy per 12-month period.</i></p>
<b>Prescriber Instructions</b>	Details of the support and counselling program must be documented in the patient's medical records at the time treatment is initiated.
<b>Administrative Advice</b>	<p>No increase in the maximum quantity or number of units may be authorised.</p> <p>Note</p> <p>No increase in the maximum number of repeats may be authorised.</p>

## 7 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.

**8 Sponsor's Comment**

Pfizer Australia welcomes the PBAC's recommendation to change the Authority Required Restriction of Champix (varenicline) to Streamlined. The change in restriction will allow clinicians more time to support, counsel and monitor their patients. This is likely to increase adherence and consequently the chance of a successful smoking cessation attempt for patients.