

Executive summary

This submission is made by a consortium of four not-for-profit organisations committed to reducing Australian smoking rates: the Cancer Council Australia, National Heart Foundation of Australia, Australian Council on Smoking and Health and Quit Victoria.

We seek extension of the existing PBS nicotine patch listing (for Aboriginal and Torres Strait Islander people) to other disadvantaged Australians.

We believe that the fact that nicotine replacement therapy (NRT) is not subsidised more broadly is an unfortunate anomaly. The very limited current subsidy is inconsistent with the recommendations of expert guidelines, and does not correspond with practice in countries such as New Zealand, the United Kingdom and the United States. It is imperative that this anomaly be rectified as soon as possible because enhanced tobacco control programs are likely to be implemented in Australia in 2010. Proposals by the Preventative Health Taskforce for intensive anti-smoking media campaigns and tobacco tax increases are receiving serious, sympathetic consideration by government.

Media campaigns and tax increases will prompt more smokers to attempt to quit, but their attempts will be thwarted by a lack of affordable access to the full range of effective, cost-effective smoking cessation pharmacotherapies, in particular because smoking is now strongly associated with low socioeconomic status. The National Prescribing Service recommends NRT as first-line therapy for smoking cessation and other expert guidelines recommend that the choice of pharmacotherapy be based on clinical factors and patient preference. None of the expert guidelines recommend any one pharmacotherapy over another.

The smoking cessation pharmacotherapies currently PBS-subsidised (bupropion and varenicline) are not suitable for all smokers. The cost of a four-week course of nicotine patches, purchased OTC in a pharmacy or from a grocery store is at least \$100, and can be as high as \$140, and the smallest available pack of nicotine patches costs two to three times as much as a pack of cigarettes. The price of NRT is a major deterrent to its use by people with low incomes.

In March 2008, the PBAC recommended PBS listing of nicotine patch 15 mg/16 hours for Aboriginal and Torres Strait Islander people. The consortium supports this initiative, but we argue that other Australian smokers have a similar need for subsidised NRT. The data

presented in this submission show that Australians receiving government income support have smoking rates that are much higher than average. Around 50% of 25 to 34 year olds receiving income support are smokers, a rate as high as that seen among Indigenous Australians.

We propose extending the existing PBS subsidy to two additional groups: (i) concessional patients, as concessional status is the only practical surrogate for low socioeconomic status and is highly correlated with receipt of government income support; and (ii) people for whom other smoking cessation pharmacotherapies should not be prescribed because of contraindications, precautions or adverse reactions. However, we would have no objection if the PBAC recommended extending the existing PBS subsidy for nicotine patch to all Australians, consistent with listings for bupropion and varenicline.

We are cognisant of the fact that previous submissions for broad PBS subsidy of NRT products, most recently in 2003, have been rejected. The following developments support a re-examination of the proposition that nicotine patch be subsidised more broadly:

- Nicotine patch was compared to bupropion in the 2003 submission, using data from one head-to-head randomised trial (Jorenby et al. *N Engl J Med* 1999;340:685-691), and the PBAC concluded that nicotine patch was less effective than bupropion. However, a 2009 Cochrane Collaboration review (Hughes et al. *Cochrane Database Syst Rev* 2009; (4):CD000031), which pooled data from the three trials of bupropion versus nicotine patch now available, concluded that ‘The efficacy of bupropion ... appears to be similar to that of nicotine replacement’. It is also noteworthy that in the Jorenby et al. trial, reviewed by the PBAC in 2003, nicotine patch was NOT found to be more effective than placebo. This finding contrasts starkly with the findings of another Cochrane Collaboration review, published in 2008, (Stead et al. *Cochrane Database Syst Rev* 2008;(1):CD000146) of 41 RCTs of nicotine patch versus placebo or a no-NRT control, which found that nicotine patch significantly increases the rate of cessation compared to placebo or no-NRT (risk ratio = 1.66; 95%CI: 1.53 to 1.81).
- Varenicline is now PBS-subsidised and meets the criteria for ‘main comparator’ for nicotine patch. In 2008, there were 228,216 ‘first’ prescriptions for varenicline (9128K) and 100,852 ‘second’ prescriptions (9129L). The cost to government was over \$40 million. An intention-to-treat analysis of the one trial comparing varenicline with nicotine patch (Aubin et al. *Thorax* 2008;63(8):717-724) found only a marginally

statistically significant benefit of varenicline in the continuous smoking abstinence rate at 52 weeks.

- In July 2009, the FDA issued warnings about the risk of serious neuropsychiatric symptoms, including the potential to commit suicide, with bupropion and varenicline. Varenicline was the subject of an Australian Adverse Drug Reactions bulletin in December 2008. Prescribers were reminded to advise patients about these symptoms. Patients who develop these symptoms are advised to seek urgent medical help.
- When nicotine patch was PBS-subsidised in 2008, its price-to-pharmacists reduced by about 42%. Under the PBS, the price of a course of nicotine patch is now substantially lower than the price of a course of bupropion or a course of varenicline.

Meeting all the PBAC submission requirements is beyond our consortium’s operational and budgetary capacity, but we have attempted to provide key information. However, we note that in listing nicotine patch for Aboriginal and Torres Strait Islander people, the PBAC have presumably already accepted that the medicine is effective, and that its cost and cost-effectiveness are acceptable. If these parameters have already been judged acceptable for Indigenous people, we argue that they should be judged acceptable for other Australians.

Table ES.1 Details of drug proposed for listing (from <i>Product Information</i>)	
Australian approved name	Nicotine patch
Brand name	Nicorette Patch (Transdermal Patches) 15 mg/16 hours
Marketing status	Registered on the Australian Register of Therapeutic Good
Principal pharmacological action	A natural alkaloid with ganglion stimulating properties that produces a wide range of pharmacological actions. ATC code N07BA01 (Drugs used in nicotine dependence).
TGA –approved indication	Treatment of tobacco dependence by relieving nicotine craving and withdrawal symptoms, thereby facilitating smoking cessation in smokers motivated to quit
Recommended course of treatment	Apply one patch to nonhairy, clean, dry, intact skin for 16 hours daily. Begin with 15 mg/16 hour patches for 8 weeks, then 10 mg/16 hour patches for 2 weeks then 5 mg/16 hour patches for 2 weeks.

Table ES.2 Proposed PBS listing for nicotine patch						
<p>Authority required. Nicotine dependence in concessional patients, or patients for whom other smoking cessation pharmacotherapies should not be prescribed because of contraindications, precautions or adverse reactions, or an Aboriginal or a Torres Strait Islander person, as the sole PBS-subsidised therapy.</p> <p>Note: Only 2 courses of PBS-subsidised nicotine replacement therapy will be authorised per year. No applications for increased maximum quantities and/or repeats will be authorised. Benefit is improved if used in conjunction with a comprehensive support and counselling program.</p>						
Item code	Name, manner of administration and form & strength	Brand name & manufacturer	Max quantity	No. of repeats	Pack size	DPMQ
9198D	NICOTINE Transdermal patch releasing approximately 15 mg per 16 hours	Nicorette Patch Johnson & Johnson Pacific Pty Limited	28	2	28	\$55.22

Note that our proposal specifies the Johnson & Johnson brand, Nicorette Patch (Tables ES.1 and ES.2). This reflects the current listing, not any preference by the consortium for that brand. The Cochrane Collaboration (Stead et al. Cochrane Database Syst Rev 2008;(1):CD000146) concluded that: ‘Wearing the [nicotine] patch only during waking hours (16 hours a day) is as effective as wearing it for 24 hours a day’ and we therefore assume that the PBAC would regard the 21 mg/24 hour nicotine patches (manufactured by Alphapharm, GlaxoSmithKline, Novartis and Sigma) as equivalent to the Nicorette Patch 15 mg/16 hour, and would view favourably any applications by these companies to list such products.

Note also that the *Product Information* for Nicorette specifies a reducing dosage regimen, but only one strength of patch is currently listed on the PBS. Neither the 10 mg/16 hour nor the 5 mg/16 hour Nicorette Patch (nor the corresponding 7 mg/day and 14 mg/day products made by other manufacturers) are PBS-subsidised. The consortium encourages the PBAC to view favourably any applications to have these different strengths listed, although we note that the Cochrane Collaboration (Stead et al. Cochrane Database Syst Rev 2008;(1):CD000146) concluded that: ‘Eight weeks of patch therapy is as effective as longer courses and there is no evidence that tapered therapy is better than abrupt withdrawal’.

Rationale for extending listing

There are two key reasons to extend the listing as we propose. **First**, Australians receiving government income support have smoking rates up to two-and-a-half fold higher than Australians not receiving income support. In the 25 to 34 year age-group, smoking rates for Indigenous people and for Australians on income support are approximately the same (see Table ES.3).

The **second** reason to extend the subsidy for nicotine patches is that bupropion and varenicline have different contraindication/precaution/adverse reaction profiles to NRT. In particular both bupropion and varenicline are associated with the development of serious neuropsychiatric symptoms. Bupropion, and possibly also varenicline, are associated with seizures. Patients who cannot, or should not, take bupropion and varenicline because of these problems should have access to subsidised NRT.

Table ES.3 Smoking rates for Australians on income support and Indigenous people.*					
HILDA survey data				Indigenous people	
Age group	Smoking prevalence		RR of smoking†	Age group	Smoking prevalence
	Not on income support (N= 8435)	On income support (N=3122)			
15–19	9.6%	24.6%	2.5	18-24	50%
20–24	22.6%	31.4%	1.38		
25–29	24.1%	56.4%	2.34	25-34	55%
30–34	23.2%	47%	2.02		
35–39	21.9%	31.8%	1.45	35-44	55%
40–44	21.1%	37.9%	1.79		
45–49	21.2%	34.4%	1.62	45-54	50%
50–54	18.6%	27.3%	1.46		
55–59	13.0%	25.6%	1.96	55+	30%

Sources: Household, Income and Labour Dynamics in Australia (HILDA) survey data for 2006, and National Aboriginal and Torres Strait Islander Health Survey, 2004–05.

†Our calculations, relative risk (RR) for those on income support relative to those not on income support.

Comparator and clinical management algorithm

The main comparator is **varenicline**. Over 200,000 patients were prescribed varenicline in 2008, at a cost to the PBS of over \$40 million. If doctors follow the NPS recommendations and the Australian *Smoking Cessation Guidelines for General Practice*, and if our proposal to extend the PBS subsidy is accepted, the clinical algorithm for prescribers assisting smokers to quit through pharmacotherapy would be along the lines summarised in Table ES.4. Without

extension to the subsidy, prescribers may be inclined to offer bupropion or varenicline as first-line therapy because these medicines are cheaper for patients than purchasing NRT OTC.

Table ES.4 Clinical management algorithm based on expert guidelines and NPS recommendations
<p>Is the patient a smoker, ready to quit and dependent on tobacco-delivered nicotine? If yes, offer pharmacotherapy.</p> <p>Is NRT contraindicated, do precautions preclude use or is the smoker opposed to using a patch? If No, offer nicotine patch.</p> <p>If Yes, offer bupropion or varenicline, provided they are not contraindicated, or precautions preclude use.</p>

Key clinical evidence

The key clinical evidence comes from a single open-label randomised trial comparing nicotine patch to varenicline, and the main results are summarised in Table ES.5. Only 62.2% of patients randomised to NRT and 65.7% of patients randomised to varenicline completed the study. The CAR at 52 weeks was about 20% lower for patients assigned to nicotine patch than for patients assigned to varenicline. This difference was only marginally statistically significant. The absolute difference in CARs was 6.1%.

Two of the 378 patients randomised to varenicline (0.5%) experienced neuropsychiatric symptoms attributed by the investigators to varenicline.

Table ES.5 Key results of Aubin et al. trial. 'All randomised' (intention-to-treat) analysis				
Outcome	Proposed drug (NRT)	Main comparator (varenicline)	Relative risk (95% CI) NRT to varenicline	Risk difference (95% CI)* NRT versus varenicline
CAR through week 52	75 non-smokers /379 (19.8%)	98 non-smokers/378 (25.9%)	0.76 (95% CI: 0.59 to 0.995) chi2(1)=4.04, Pr>chi2=0.0444	-0.0614 (95% CI: -0.121 to -0.0017)
*Continuous smoking abstinence rate (CAR) at week 52 after randomisation Aubin et al. Varenicline versus transdermal nicotine patch for smoking cessation: Results from a randomised, open-label trial Thorax. 2008;63:717-24				

Therapeutic conclusions

The comparative effectiveness of nicotine patch relative to no pharmacological treatment is ‘Superior’. The comparative effectiveness of nicotine patch relative to bupropion is ‘Noninferior’. The comparative effectiveness of nicotine patch relative to **varenicline** is ‘Uncertain’; nicotine patch maybe ‘Noninferior’ or ‘Inferior’. The comparative safety of nicotine patch relative to bupropion and to varenicline is ‘Superior’.

Cost analysis

The cost of a course of nicotine patch is about \$170 less (50% lower) than a course of varenicline. A more comprehensive cost analysis taking into account management of adverse effects would be likely to increase this cost differential.

Table ES.6 Cost-minimisation analysis based on equi-effective doses		
	Nicotine patch 15 mg/16 hours	Varenicline 0.5 mg and 1 mg tablets
Dosage	One patch daily	Day 1 to 3: 0.5 mg daily Day 4 to 7: 0.5 mg twice daily Then: 1mg twice daily
Course duration*	12 weeks	11 weeks
Cost for economic evaluation	\$165.66 Based on current (October 2009) DPMQ of \$55.22 for one prescription of 28 patches. One prescription and two repeats are required to obtain 12 weeks therapy	\$336.82 Based on current (October 2009) DPMQ of \$103.76 for a prescription for the first 5 weeks (11 tablets 0.5 mg and 28 tablets 1 mg) and \$233.06 for a prescription for the next 8 weeks (112 tablets 1 mg)

Estimated extent of use and financial implications

We provide estimates for a typical, or average, year. Providing estimates for each of five years is beyond the operational and budgetary capacity of our consortium. Our estimates are summarised in Table ES.7. We estimate that almost one million Australians receiving income support are smokers. We assume that doctors would not prescribe bupropion or varenicline for people with a '12-month mental disorder', as defined in the Australian Bureau of Statistics National Survey of Mental Health and Well-Being (diagnosed anxiety disorder, affective disorder or substance use disorder and symptoms in the 12 months before interview). This is almost certainly an overestimate of the number of people for whom other smoking cessation pharmacotherapies would not be prescribed, and so we are overestimating potential prescribing of nicotine patch.

We estimate that around 570,000 additional patients are likely to be treated with NRT each year as a consequence of our proposed listing. The annual cost to the government for the additional 620,000 prescriptions for nicotine patch would be about \$24.8 million. This would be offset by savings of approximately \$21 million in prescriptions for varenicline, giving an estimated net annual cost to the PBS of \$3.7 million. Additional consultations would cost the government a further \$6.3 million each year.

Table ES.7 Annual estimates of number of patients treated, number of prescriptions dispensed and costs to the PBS and government		
Data	Numbers and costs	Source/assumptions
No. of smokers eligible		
with concessional status	997,651	4,506,269 adults with concessional status, excluding Indigenous Australians and holders of Repatriation Benefit cards (nicotine patch already funded for these groups) and excluding Safety Net Card holders (request to Medicare for numbers refused) . See: 'Health care card data.xls' Age-specific smoking rates for people on income support applied to estimate number of smokers. See: 'Smoking rates HILDA.xls'
for whom other smoking pharmacotherapies should not be prescribed	591,500	2,366,000 adults with mental disorder in the last 12 months and not on income support. (ABS National Survey of Health and Well-Being, 2007). See 'ABS survey of mental health.pdf' Smoking rate 25%
TOTAL	1,589,151	
No. of patients likely to be treated	572,094	30% of eligible patients will get a prescription. In 2006, ~19% of Australian smokers used NRT in an attempt to quit
No. of prescriptions per year	619,769	Average duration of actual use of NRT is 4 weeks, so assume 80% get one prescription, 10% get two prescriptions, and 10% get three prescriptions, i.e. 1.3 prescriptions per person.
Cost to PBS of additional nicotine patch prescriptions		
unit cost of nicotine patch	\$40.05	DPMQ (\$55.22) less average patient co-payment (\$15.17)
Total cost	\$24,819,698	
Savings to PBS through reduced use of varenicline	\$21,097,549	Assume 100,000 fewer patients (one third of current number) don't get first varenicline prescription (9128K; DPMQ = \$103.76) and that 49% of these patients would have filled second varenicline prescription (9129L; DPMQ=\$233.06). Average patient co-payment = \$22.08
Net cost to PBS	\$3,722,149	
Cost to government from MBS changes	\$6,319,902	188,373 additional consultations, item 23 Level B @\$33.55
Total cost to government	\$10,042,051.26	

Equity issues

Two equity arguments provide further support for our proposal. First, Australians aged 25 to 34 years receiving income support have smoking rates as high as those of Indigenous people. Second, the government provides substantial PBS subsidies for two drugs for opiate dependence (buprenorphine and methadone). People addicted to nicotine are also entitled to have the available, safe, effective, cost-effective medicines to aid quitting subsidised.

Summary

Our proposal to extend the existing subsidy for nicotine patches to concessional patients and people for whom currently subsidised pharmacotherapies should not be prescribed is supported by the evidence-based reviews of the Cochrane Collaboration, the recommendations of the National Prescribing Service and smoking cessation guidelines published by Australian and international expert groups. It is underpinned by equity principles: the patients who would benefit by this listing have smoking rates that are in many instances as high as those of Indigenous people who are eligible for PBS-subsidised NRT.

The estimated net annual cost to the PBS of \$3.7 million is modest.