SUBMISSION TO THE POST-MARKET REVIEW OF MEDICINES FOR SMOKING CESSATION

25-29 Delawney Street
BALCATTA WA 6021

[redacted]

Review terms of Reference

Perrigo Australia welcome opportunity to comment on the Post-Market Review of Medications for Smoking Cessation. Tobacco smoking causes approximately one in every seven deaths. It is the leading preventable cause of disease and death in Australia and linked to the burden of numerous disease including cancers, cardiovascular diseases and respiratory diseases.[1]

Perrigo Australia has seven products that are listed on the Pharmaceutical Benefits Scheme (PBS) for the nicotine dependence: Nicotinell Step 1 Patches, Nicotinell Step 2 Patches, Nicotinell Step 3 Patches, Nicotinell 4mg Gum, Nicotinell 2mg Gum, Nicotinell 4mg Lozenge, and Nicotinell 2mg Lozenge. This submission addresses the Terms of Reference (ToR) of the review by reviewing the recent evidence on the clinical practice, efficacy, safety, cost-effectiveness and the appropriate use of medications for smoking cessation,

Ensuring the accessibility and availability of medications consistent with clinical guidelines is paramount to supporting people to quit smoking and accelerating the decline in prevalence within Australia. Perrigo Australia strongly believe current PBS restrictions should be amended to allow combination nicotine replacement therapy given current evidence indicates it is as effective as varenicline and more effective than monotherapy with NRT.

1. Collate the current clinical guidelines for medicines for smoking cessation and compare these to the Therapeutic Goods Administration (TGA) and PBS restrictions for these medicines.

RACGP Supporting Smoking Cessation: A guide for health professionals (2nd edition) has been developed by a multidisciplinary Expert Advisory Group utilizing the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) process are intended to be relevant to the wider primary care setting. These guidelines provide 16 recommendations for smoking cessation which are summarized in Table 1 below.

Table 1: Summary of recommendations from *RACGP Supporting Smoking Cessation: A Guide for health professionals*[2]

RECOMMENDATION	GRADE
1. All people who smoke should be offered brief advice to quit smoking.	Strong recommendation, high certainty

[1] Whetton S, Tait RJ, Scollo M, Banks E, Chapman J, Dey T et al. Identifying the social costs of tobacco use to Australia in 2015/2016. National Drug Research Institute, Curtin University. 2019. Western Australia: NDRI

[2] The Royal Australian College of General Practitioners. Supporting smoking cessation: A guide for health professionals. 2nd edn. East Melbourne, Vic: RACGP, 2019

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 13a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

2. A system for identifying all people who smoke and documenting tobacco use should be used in every practice or healthcare service.	Strong recommendation, high certainty
3. Offer brief smoking cessation advice in routine consultations and appointments, whenever possible.	Strong recommendation, high certainty
4. Offer follow-up to all people who are attempting to quit smoking.	Strong recommendation, high certainty
5. In the absence of contraindications, pharmacotherapy (nicotine replacement therapy, varenicline or bupropion) is an effective aid when accompanied by behavioural support, and should be recommended to all people who smoke who have evidence of nicotine dependence. Choice of pharmacotherapy is based on efficacy, clinical suitability and patient preference.	Strong recommendation, high certainty
6. Combination nicotine replacement therapy (NRT) (ie patch and oral form) accompanied by behavioural support is more effective than NRT monotherapy accompanied by behavioural support, and should be recommended to people who smoke who have evidence of nicotine dependence.	Strong recommendation, moderate certainty
7. For people who have stopped smoking at the end of a standard course of nicotine replacement therapy (NRT), clinicians may consider recommending an additional course of NRT to reduce relapse.	Conditional recommendation for intervention, low certainty
8. A) Nicotine replacement therapy (NRT) is safe to use in patients with stable cardiovascular disease. B) NRT should be used with caution in patients who have had a recent myocardial infarction, unstable angina, severe arrhythmias or recent cerebrovascular events.	Strong recommendation, high certainty Strong recommendation, moderate certainty
9. For women who are pregnant and unable to quit smoking with behavioural support alone, clinicians might recommend nicotine replacement therapy (NRT), compared with no NRT. Behavioural support and monitoring should also be provided.	Conditional recommendation for intervention, low certainty
10. Varenicline should be recommended to people who smoke and who have been assessed as clinically suitable for this medication; it should be provided in combination with behavioural support.	Strong recommendation, high certainty
11. For people who have abstained from smoking after a standard course of varenicline in combination with behavioural support, clinicians may consider a further course of varenicline to reduce relapse.	Conditional recommendation for intervention, low certainty
12. For people who are attempting to quit smoking using varenicline accompanied by behavioural support, clinicians might recommend the use of varenicline in combination with nicotine replacement therapy, compared with varenicline alone.	Conditional recommendation for intervention, moderate certainty
13. Bupropion sustained release should be recommended to people who smoke and who have been assessed as clinically suitable for this medication; it should be provided in combination with behavioural support. Bupropion is less effective than either varenicline or combination nicotine replacement therapy.	Strong recommendation, high certainty
14. Nortriptyline should be considered as a second-line smoking cessation pharmacotherapy agent because of its adverse effects profile.	Strong recommendation, moderate certainty

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

15. Nicotine-containing e-cigarettes are not first-line treatments for smoking cessation. The strongest evidence base for efficacy and safety is for currently approved pharmacological therapies combined with behavioural support. The lack of approved nicotine-containing e-cigarettes products creates an uncertain environment for patients and clinicians, as the constituents of the vapour produced have not been tested and standardised. However, for people who have tried to achieve smoking cessation with approved pharmacotherapies but failed, and who are still motivated to quit smoking and have brought up e-cigarette usage with their healthcare practitioner, nicotine-containing e-cigarettes may be a reasonable intervention to recommend. This needs to be preceded by an evidence-informed shared decision-making process, whereby the patient is aware of the following: a. no tested and approved e-cigarette products are available b. the long-term health effects of vaping are unknown c. possession of nicotine-containing e-liquid without a prescription is illegal d. in order to maximise possible benefit and minimise risk of harms, only short-term use is recommended e. dual use (ie with continued tobacco smoking) needs to be avoided.	Conditional recommendation for intervention, low certainty
16. Referral to telephone call-back counselling services should be offered to all people who smoke.	Strong recommendation, high certainty

A variety of other documents that assist with clinical guidance in smoking cessation are available. This includes the *NICE Guidelines [NG92] – Stop smoking interventions and services*[3]*, NSW Health Flowchart of tools to help clinicians manage nicotine dependent clients*[4] *and Queensland Health's Smoking Cessation Pathway*[5]. Much of this guidance aligns with the clinical guidance provided in *RACGP Supporting Smoking Cessation: A guide for health professionals (2nd edition)* however the depth of information regarding pharmacotherapy is limited. As such *RACGP Supporting Smoking Cessation: A guide for health professionals (2nd edition)* provides the most current and in-depth guidance.

The PBS-listings for nicotine replacement therapy, varenicline and bupropion all include the following criteria: '*the treatment must be the sole PBS-subsidised therapy for this condition*.' This is egregiously inconsistent with current best practice guidelines and the body of evidence which recommend use of combination NRT. Consequently, the current PBS restrictions do not allow therapy to be tailored to individual needs. Given cost can be a significant barrier to use of pharmacotherapy in populations in which smoking is more prevalent (e.g. lower socioeconomic groups, Aboriginal and Torres Strait Islanders and people with mental illness) this restriction is likely to result in suboptimal treatment.

[3] Flowchart of tools to help clinicians manage nicotine dependent clients. NSW Health. 2016. Available from: https://www.health.nsw.gov.au/tobacco/Factsheets/tool-1-sc-flowchart.pdf
[4] Smoking Cessation Clinical Pathway. Queensland Government. 2017. Available from: https://www.health.qld.gov.au/__data/assets/pdf_file/0031/435469/smoking-pathway.pdf
[5] National Institute for Health and Care Excellence. Stop Smoking Interventions and Services – NG92. 2018. Available from: https://www.nice.org.uk/guidance/ng92/resources/stop-smoking-interventions-and-services-pdf-1837751801029

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

Given the chronic and relapsing nature of nicotine dependence Perrigo Australia believes it is important to optimize treatment at every opportunity. Removing *'the treatment must be the sole PBS-subsidised therapy for this condition'* would assist in optimizing treatment and allow combination NRT with a *long-acting form (e.g. patch) and a fast acting form (e.g, gum or lozenge)* consistent with the *RACGP Supporting Smoking Cessation: A guide for health professionals (2nd edition)*.

Furthermore the clinical criteria for PBS-listed nicotine replacement therapies also limits patients to not *receive more than 12 weeks of PBS-subsidised nicotine replacement therapy per 12-month period which represents only 1 quit attempt following TGA approved use instructions.* In contrast, the recommendation from the RACGP Guideline states that *for people who have stopped smoking at the end of a standard course of nicotine replacement therapy (NRT), clinicians may consider recommending an additional course of NRT to reduce relapse.* It also does not provide people with the opportunity to commence NRT several weeks before stating smoking cessation to help prepare for quitting. In addition, it is well documented that many people who attempt to quit smoking will require multiple attempts with Chaiton et al[6] estimating that many smoker may require 30 or more quit attempts before being successful. Limiting PBS-subsidised NRT to 12 weeks per 12-month period may discourage and present a barrier for those who are willing to quit but have already received 12 weeks of therapy within a 12-month period.

Perrigo Australia believes that in order to optimise treatment PBS-listings for NRT should be expanded to include up to 24 weeks of PBS-subsidised nicotine replacement therapy per 12-month period to allow people to prepare for quitting, encourage those who have been unsuccessful in the past to continue to make quit attempts and reduce relapse.

Perrigo Australia supports the inclusion of treatment criteria that a patient must be undergoing concurrent counselling for smoking cessation through a comprehensive support and counselling program for all PBS listed drugs used in nicotine dependence.

Perrigo is committed to providing options to quit smoking and included oral forms of NRT on the PBS effective 1st of February 2019. Nicotinell lozenge and chewing gum are the only forms of oral NRT on the PBS. Given the above considerations Perrigo Australia believes the PBS-listings for NRT should be amended to allow combination therapy and extended duration of therapy. This could easily and quickly be achieved by amending the listings of existing PBS-listed NRT to the following:

[6] Chaiton M, Diemert L, Cohen JE, et al. Estimating the number of quit attempts it takes to quit smoking successfully in a longitudinal cohort of smokers. BMJ Open. 2016;6(6):e011045. Published 2016 Jun 9.

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

Nicotine dependence
Treatment Phase:
Commencement of a short-term (12 weeks or 24 weeks) course of treatment.
Clinical criteria:
The treatment must be as an aid to achieving abstinence from smoking,
AND
Treatment may either be:

- *sole PBS-subsidised therapy for this condition; or*
- *in a combination that utilises a long-acting form (e.g. patch) and a fast acting form of nicotine replacement therapy (e.g, gum or lozenge)*

AND
Patient must have indicated they are ready to cease smoking,
AND
Patient must not receive more than 24 weeks of PBS-subsidised nicotine replacement therapy per 12-month period.
Treatment criteria:
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 PBS-subsidised treatment is initiated.

AND

Nicotine dependence
Treatment Phase:
Completion of a short-term (24 weeks) course of treatment
Clinical criteria:
The treatment must be as an aid to achieving abstinence from smoking,
AND
Treatment may either be:

- *sole PBS-subsidised therapy for this condition; or*
- *in a combination that utilises a long-acting form (e.g. patch) and a fast acting form of nicotine replacement therapy (e.g, gum or lozenge)*

AND
Patient must have previously received PBS-subsidised treatment with 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.
AND
Patient must not receive more than 24 weeks of PBS-subsidised nicotine replacement therapy per 12-month period.
***Treatment criteria**:*

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

Patient must be undergoing concurrent counselling for smoking cessation through a comprehensive support and counselling program.

These recommendations would allow people wishing to cease smoking the opportunity to tailor pharmacotherapy to their individual needs. It would make combination NRT readily accessible and affordable and would better recognise the chronic and relapsing nature of smoking cessation providing better support for those who are willing to quit smoking.

2. Review the utilisation of PBS-listed medicines for smoking cessation including but not limited to patient demographics, time on treatment, and the proportion using PBS subsidised combination treatment.

Utilization of medications for smoking cessation is described using publicly available PBS script and benefit paid statistics[7]. These data sources are appropriate because they provide the most accurate and up-to-date representation of medications for smoking cessation usage.

The total PBS cost of medications for smoking cessation over the previous 5 years is presented in Table 2. Total scripts for medications for smoking cessation is presented in Table 3 below.

Table 2: Total cost of medications for smoking cessation to PBS ($m)

	PBS Item Code	2015	2016	2017	2018	2019
Nicotinell Step 1	5571F	$1.30	$0.94	$1.10	$1.26	$1.33
Nicabate P	5465P	$3.53	$3.64	$3.71	$3.90	$3.45
Nicotinell Step 1	3414Q	$0.52	$0.91	$1.01	$1.18	$1.12
Nicotinell Step 2	5572G	$0.82	$0.89	$1.01	$1.17	$1.19
Nicotinell Step 3	5573H	$0.23	$0.26	$0.31	$0.35	$0.34
Nicorette 16 hour Invisipatch	10076H	$0.86	$0.88	$0.95	$1.02	$0.94
Nicotinell 4mg Gum	11612E	-	-	-	-	$0.10
Nicotinell 2mg Lozenge	11617K	-	-	-	-	$0.04
Nicotinell 2mg Gum	11618L	-	-	-	-	$0.12
Nicotinell 4mg Lozenge	11619M	-	-	-	-	$0.06
Cost of NRT to the PBS		**$7.28**	**$7.51**	**$8.10**	**$8.89**	**$8.69**
Growth (%)			**3.25%**	**7.63%**	**9.85%**	**-2.21%**
Champix Initiation Pack		$15.30	$11.69	$11.07	$10.22	$9.18
Champix Continuation Pack (112)	9129L	$21.54	$16.19	$14.10	$12.03	$10.16
Champix Continuation Pack (56)	5469W	$5.28	$4.24	$4.94	$6.38	$6.30
Cost of Champix to the PBS		**$42.11**	**$32.12**	**$30.12**	**$28.63**	**$25.65**
Growth (%)			**-23.72%**	**-6.25%**	**-4.94%**	**-10.40%**
Zyban 30	8465M	$0.45	$0.44	$0.45	$0.47	$0.27

[7] http://medicarestatistics.humanservices.gov.au/statistics/pbs_item.jsp

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

Zyban 90	8710K	$0.91	$1.05	$1.17	$1.36	$0.83
Cost of Zyban to the PBS		**$1.36**	**$1.49**	**$1.62**	**$1.83**	**$1.11**
Growth (%)			**9.61%**	**8.15%**	**13.47%**	**-39.59%**
Cost to PBS		**$50.75**	**$41.13**	**$39.82**	**$39.35**	**$35.45**
Growth (%)			**-18.96%**	**-3.19%**	**-1.18%**	**-9.91%**

Table 3: Total scripts for medications for smoking cessation

	PBS Item Code	2015	2016	2017	2018	2019
Nicotinell Step 1	5571F	29,953	22,918	27,375	31,867	35,665
Nicabate P	5465P	80,346	87,321	89,734	94,339	89,107
Nicotinell Step 1	3414Q	11,681	21,683	24,122	28,407	28,793
Nicotinell Step 2	5572G	18,903	21,136	24,591	28,385	30,829
Nicotinell Step 3	5573H	5,181	5,894	7,182	8,059	8,620
Nicorette 16 hour Invisipatch	10076H	19,762	21,103	23,067	24,766	24,513
Nicotinell 4mg Gum	11612E	-	-	-	-	2,293
Nicotinell 2mg Lozenge	11617K	-	-	-	-	963
Nicotinell 2mg Gum	11618L	-	-	-	-	1,995
Nicotinell 4mg Lozenge	11619M	-	-	-	-	1,296
Total NRT scripts		**165,826**	**180,055**	**196,071**	**215,823**	**224,074**
Growth (%)			**8.58%**	**8.90%**	**10.07%**	**3.82%**
Champix Initiation Pack		195,302	162,363	156,799	156,868	150,545
Champix Continuation Pack (112)	9129L	107,867	87,805	77,494	69,837	62,458
Champix Continuation Pack (56)	5469W	51,109	44,221	55,009	78,065	81,926
Total Champix scripts		354,278	294,389	289,302	304,770	294,929
Growth (%)			**-16.90%**	**-1.73%**	**5.35%**	**-3.23%**
Zyban 30	8465M	10,973	11,003	11,191	11,790	6,882
Zyban 90	8710K	6,153	7,443	8,276	9,680	5,981
Total Zyban scripts		**17,126**	**18,446**	**19,467**	**21,470**	**12,863**
Growth (%)			**7.71%**	**5.34%**	**10.29%**	**-40.09%**
Total Scripts		**537,230**	**492,890**	**504,840**	**542,063**	**531,866**
Growth (%)			**-8.25%**	**2.42%**	**7.37%**	**-1.88%**

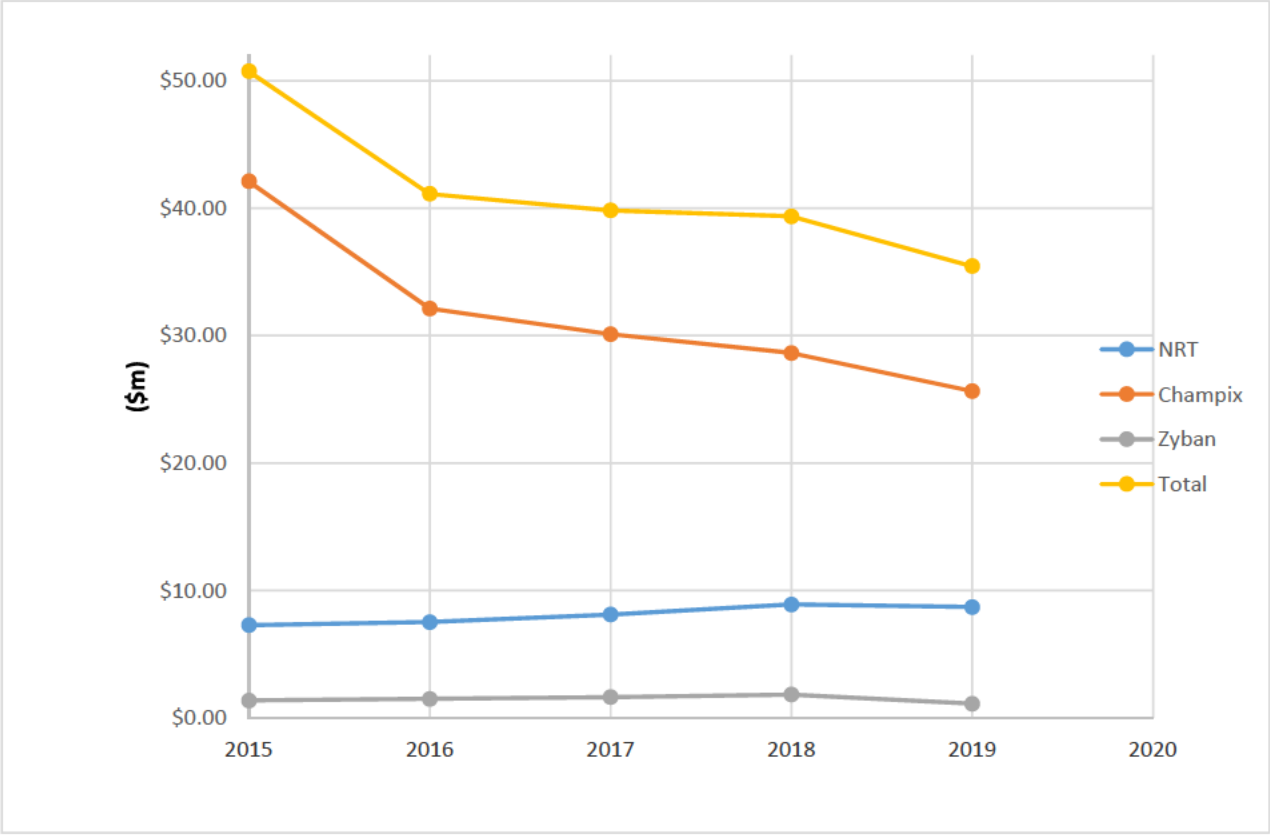
There has been negative growth in cost across all medications for smoking cessation since 2015. In contrast, the growth in PBS script volume across all medications for smoking cessation peaked in the 2018 calendar year.

Usage of NRT continues to grow, however the cost to the PBS for NRT decreased in the 2019 calendar year due to the impact of pricing events that occurred recently. The price reductions have ensured that NRT remains a very cost-effective treatment option given smoking cessation has a flow-on effect in terms of reducing disease burden from smoking related illness. As can be seen from in Figure 1 below NRT is a small contributor to PBS costs with Champix accounting for the majority of the cost relating to medications for smoking cessation. In 2019, the volume of Champix was 1.3 times

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 13a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

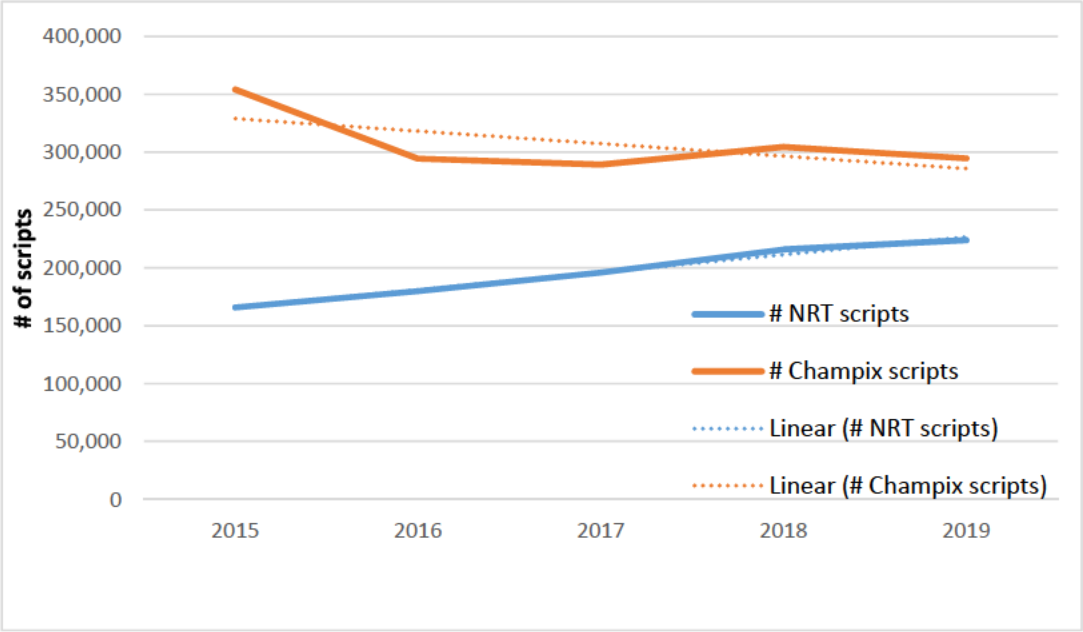
higher than all NRT while the cost is 2.24 times higher demonstrating from a cost perspective it is over indexing compared to NRT. Over the past 3 years, NRT has represented 20 – 25 % of total PBS costs for smoking cessation while making up 39 to 42% of the total scripts of the same period. This is illustrated in Figure 2.

Figure 1: Cost of Smoking Cessation to the PBS



Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

Figure 2: Script numbers of Champix vs NRT



Zyban has declined significantly. This is to be expected based upon evidence that combination NRT and varenicline are the most effective forms of pharmacotherapy. As per the RACGP guidelines, Zyban is predominantly considered when NRT or varenicline are not suitable. While more varenicline was prescribed on the PBS in 2019 it showed negative growth in contrast to NRT which has shown year on year growth and growth of 3.8% in 2019. This reflects a changing preference towards NRT. The availability of combination NRT could further strengthen and encourage uptake of NRT leading to increased rates of smoking cessation.

In 2019, there was 531,866 prescriptions across all medications for smoking cessation. We estimated that this represents approximately 250,000 people. This is based on the following assumptions:

- Patients using varenicline as pharmacotherapy are commenced on the initiation pack (PBS code 9128K - varenicline 0.5mg tablets [11] + varenicline 1mg tablets [42]) and each patient only accesses PBS-subsidised Champix once in a 12-month period as per PBS restrictions. Therefore, the 150,545 prescriptions filled for PBS Item code 9128K represents 150,545 people who attempted to quit smoking using varenicline in 2019.
- Patients using bupropion as pharmacotherapy are commenced on the initiation pack (PBS code 8465M – bupropion 150mg tablet [30]) and each patient only accesses PBS-subsidised bupropion once in a 12-month period as per PBS restrictions. Therefore, the 6,882 prescriptions filled for PBS Item code 8465M

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

represents 6,882 people who attempted to quit smoking using bupropion in 2019.

- Unlike varenicline and bupropion there is no need to titrate therapy so it is more challenging to estimate how many people attempted to quit smoking using NRT. 224,074 PBS prescriptions for NRT were filled in 2019. Assuming every person who received PBS-subsidised therapy completed a full 12-week course of treatment this would represent 74,691 people who attempted to quit smoking. Given studies have shown that smokers who use medication for nicotine dependence do so at lower than the recommended dose and cease treatment prior to the recommended treatment course[8] we believe that 100,000 people would be a better estimate of the number of people who attempted to quit smoking in 2019.

Given the latest statistics from the Australian Bureau of Statistics (ABS)[9] suggest that 2.6 million adults are daily smokers the proportion of smokers accessing PBS-subsidised therapy is low (<10%). This is consistent with evidence that suggests although behavioural and pharmacological treatments can improve cessation rates these treatments are under-utilised[10] and many people who attempt to quit do so without support. Ensuring access and availability of combination NRT on the PBS is vital particularly for lower socioeconomic smokers who are already less likely to be interested in quitting and less likely to make a quit attempt.[11]

3. Review the efficacy and safety of nicotine replacement therapy, varenicline and bupropion for smoking cessation including combination therapies not currently PBS subsidised.

Monotherapy with NRT

Efficacy[2,12,15]

Nicotine Replacement Therapy (NRT) is designed to provide nicotine to reduce withdrawal symptoms associated with the transition from cigarette smoking to abstinence. Monotherapy with NRT almost doubles the odds of quitting. Nicotine

[8] Shiffman S, Hughes JR, Pillitteri JL, Burton SL. Persistent use of nicotine replacement therapy: an analysis of actual purchase patterns in a population based sample. Tob Control. 2003;12(3):310–316.

[9] Australian Bureau of Statistics. 4364.0.55.001 - National Health Survey: First results, 2017-18 ABS, 2018. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/4364.0.55.001~2017-18~Main%20Features~Smoking~85

[10] Shiffman S, Brockwell SE, Pillitteri JL, and Gitchell JG. Use of smoking-cessation treatments in the United States. American Journal of Preventive Medicine, 2008; 34(2):102–11. Available from: http://www.sciencedirect.com/science/journal/07493797

[11] Hughes J and Callas P. Definition of a quit attempt: a replication test. Nicotine & Tobacco Research, 2010; 12(11):1176–9. Available from: http://ntr.oxfordjournals.org/content/12/11/1176.long

[12] Australian Medicines Handbook. Adelaide: Australian Medicines Handbook Pty Ltd; 2020

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

Replacement Therapy is available in a variety of dosage forms. This includes patches, gum, and lozenges. These different types of NRT are generally considered to be equally effective. Patches deliver a steady-dose of nicotine via the skin and adherence is simple. In contrast, other forms such as gum and lozenges provide fast-acting relief for general cravings and breakthrough cravings. As monotherapy, all forms of NRT (at equivalent doses) are considered to have similar efficacy. Stead et al[13] showed that although additional support was beneficial in facilitating the likelihood of quitting smoking it was not essential to the success of NRT.

Safety[2,13,15]

NRT is generally well tolerated. Adverse effects are often related to the dosage form being used. For example, the most common side effects reported with nicotine gum include hiccoughs, gastrointestinal disturbances, jaw pain and orodental problems. Patch users reported skin sensitivity and irritation however this rarely lead to discontinuation. Despite concerns regarding the safety of NRT use in people with cardiovascular disease a number of reviews and trials have found no excess or increase in risk. Similarly, studies investigating the use of NRT in pregnant women have not detect serious increases in adverse events amongst the treatment groups.

Combination NRT

Efficacy[2,13,15]

Combination NRT uses a long-acting form of nicotine such as a patch to provide a steady-dose of nicotine with a fast acting oral form to provide relief from breakthrough cravings. Because of the differing profiles of nicotine delivery, there are considerable advantages of allowing flexibility to use more than one form of NRT to match the need of the quitting smoker – providing background level of NRT support produced by a patch, supplemented by an oral format for immediate craving relief. Using combination NRT almost triples the odds of quitting and is comparable in efficacy to Varenicline.

Safety[2,13,15]

Combination NRT is well tolerate and consistent with those anticipated with those of each form alone. Studies have not observed an increased risk of nicotine toxicity with combination therapy.

Bupropion

Efficacy[2,13,15]

Although the exact mechanism of action is unknown, it is thought it may assist in nicotine dependence by inhibition of neuronal reuptake of dopamine and noradrenaline. Monotherapy with Bupropion almost doubles the odds of quitting.

[13] Stead LF, Buitrago D, Preciado N, Sanchez G, Hartmann-Boyce J, et al. Physician advice for smoking cessation. Cochrane Database of Systematic Reviews, 2013

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

Safety[2,13,15]

The most frequently experienced adverse event in patients using buproprion was insomnia which was experienced by 30-40% of user followed by dry mouth (10%) and nausea. Drop-out rates in studies as a result of adverse events ranged from 7% to 12%. Trials have also reported allergic reactions (uritus, hives, angioedema and dyspnoea) in about 1 to 3 per 1000. There has been reports of arthralgia, myalgia, fever with rash, and other symptoms suggestive of delayed hypersensitivity in national surveillances schemes.

Seizures are the main serious adverse event which may occur at a rate of about 1:1000 users. As a result of this risk bupropion is not recommended in people with a history of seizures.

A follow-up study regarding the use of bupropion in the first-trimetser of pregnancy did not report an increase in the major malformations but did report a significant increase in the risk of spontaneous abortion.

Varenicline

Efficacy[2,13,15]

Varenicline is a partial agonist at a subtype of neuronal nicotinic acetylcholine receptors. It blocks nicotine binding to these receptors, preventing the pleasurable effects of smoking, while its partial agonist activity reduces symptoms of nicotine withdrawal. Varenicline is superior to monotherapy with NRT and bupropion. Varenicline almost triple the odds of quitting and is comparable in efficacy to combination NRT.

Safety[2,13,15]

The most frequent adverse event in patients being treated with varenicline is nausea which was generally mild to moderate and improved with time. To assist with nausea the dose of varenicline can be titrated, self-regulated or lowered. Discontinuation due to nausea ranged from 0.6% to 7.6%. Other adverse events reported include insomnia, abnormal dreams and headache.

Post-marketing surveillance has raised concerns regarding neuropsychiatric events however prescription event monitoring studies in the UK and NZ have not detected a significantly raised incidence rates of depression or of suicidal ideation or behavior.

A summary of PBS-listed pharmacotherapy is provided in Table 4 below.

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

Table 4: Summary of Pharmacotherapy for smoking cessation[2,13,15]

NICOTINE REPLACEMENT THERAPY	VARENICLINE	BUPROPION
• Few, minor and transient AEs when used by people with moderate to severe nicotine dependence • Fast acting products useful for cravings and may be used by patients using bupropion or varenicline • Can be used to cut-down • Suitable for adolescents • May be used in pregnancy under medical supervision • Variety of dosage forms	• Nausea in 30% of patients • Not recommended in pregnancy, childhood • Dose adjustment required in renal impairment • Lack of drug interactions	• >40% of patients experience insomnia • Potential to cause seizures • Interacts with MAOIs • Not recommended in pregnancy

Based on the information provided about combination NRT provides a suitable option in a wide variety of clinical scenarios. It is as effective as the varenicline and has a favourable safety profile. The addition of combination therapy to the PBS would allow patients greater choice both format and in dosing which can have a positive impact on patient success.

In addition to pharmacotherapy, behavioural and advised-based support can increase the chances of prolonged abstinence. Health care professionals should offer brief cessation advice in routine consultations and appointments whenever possible however often face barriers when offering smoking cessation advice. Barriers may include limited time, lack of interest from patients, perception that people will be offended and lack of awareness of options available through the PBS.[2] As such it is important that health care professionals are provided with increased support and are aware of current evidence based treatment options.

Perrigo Australia has invested significantly in educational promotion of smoking cessation products. This includes allocating a significant amount of resources to education of health professionals resulting in increased awareness of the various formats of NRT available on the PBS.

4. Subject to the findings of Terms of Reference 1, 2 and 3, review the cost-effectiveness of medicines for smoking cessation.

It has been estimated that tobacco smoking causes approximately one in every seven deaths. It is the leading preventable cause of disease and death in Australia and linked to the burden of numerous disease including cancers, cardiovascular diseases and respiratory diseases. In 2015 tobacco use resulted in 443,235 years of healthy life lost

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

('disability-adjusted life years', or DALYs) from death and illness with an estimated social cost in 2015-16 of $136.9 billion including $6.8 billion of healthcare expenses.[14]

Nicotine replacement therapy is considered very cost effective ($0 to $10,000 per DALY) as an intervention.[15] This was reflected at the PBAC meeting in November 2016[16] where NRT was considered to be safer and cheaper than bupropion and viewed the two drugs as having comparable efficacy. Furthermore although PBAC considered varenicline to be of superior efficacy to bupropion, NRT and placebo and comparable in safety, however given NRT is considerable cheaper it has been included on the PBS.

Interventions that address smoking among lower socioeconomic groups are an important clinical and economic priority to reduce health inequalities, improve life expectancies and reduce the financial burden of smoking. Since 2014, more prescriptions have been provided to concessional patients than general patients, with substantially higher proportion of NRT prescription recipients being concessional. In 2018, for example, 78% of all NRT prescriptions were for concession patients.

Given that combination NRT and varenicline are considered to be of equal efficacy consideration should be given to the comparative cost of these treatments.

The RACGP guidelines recommends the following combination NRT for those who smoke within 30 minutes of waking and smoke 10 or more a day:

Nicotine 21mg/24-hour patch
PLUS
4mg gum
OR
4mg lozenge
OR
1mg spray
OR
15mg inhalator

If PBS-listed treatments were used the cost for a 12-week course of treatment with combination NRT is outlined in Table 5 below.

---

[14] Whetton S, Tait RJ, Scollo M, Banks E, Chapman J, Dey T et al. Identifying the social costs of tobacco use to Australia in 2015/2016. National Drug Research Institute, Curtin University. 2019. Western Australia: NDRI

[15] Vos T, Carter R, Barendregt J, Mihalopoulos C, Veerman JL, Magnus A, Cobiac L, Bertram MY, Wallace AL, ACE–Prevention Team (2010). Assessing Cost-Effectiveness in Prevention (ACE–Prevention): Final Report. University of Queensland, Brisbane and Deakin University, Melbourne.

[16] Pharmaceutical Benefits Advisory Committee. November 2016 pbac meeting - pbs. 2016. Available from: https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2016-11/files/varenicline-psd-november-2016.docx

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

Table 5: Potential cost for 12 weeks of PBS-subsidised combination NRT

PRODUCT	PACK QTY	#UNITS FOR 12 WEEKS	DPMQ/UNIT	TOTAL COST FOR 12 WEEKS
Nicotine 21mg/24 hour patch	28	3	$49.36	$148.08
Nicotine 4mg Gum OR Lozenge	216	3*	$49.36	$148.08
TOTAL FOR COMBINED NRT				**$296.16**

* Usage rates taken from PBAC Public Summary March 2018 PBAC Meeting 4.06 Nicotine, Gum 2mg, Gum 4mg, Lozenge 2mg, Lozenge 4mg, Nicotinell, Orion Laboratories

Directions for varenicline therapy for 12-weeks are as follows:

> *Take 0.5 mg once daily for 3 days, then 0.5 mg twice daily for 4 days, then 1 mg twice daily for 11–23 weeks, as tolerated.*[17]

If PBS-listed treatments were used the cost for treatment with varenicline in weeks 0-12 is outlined in Table 6 below.

Table 6: Cost of PBS-subsidised Varenicline for 0-12 weeks

PRODUCT	PACK QTY	#UNITS FOR 12 WEEKS	DPMQ/UNIT	TOTAL COST FOR 12 WEEKS
Champix Initiation Pack	11+42	1	$86.64	$86.64
Champix Continuation Pack	56	2	$100.09	$200.18
TOTAL FOR VARENICLINE				**$286.82**

Although the total cost is marginally higher for combination NRT the patient would be required to pay the patient contribution fee ($41 for general patients and $6.60 for concession patients) for both the long-acting form of NRT and short-acting form of NRT which offsets the higher cost. This is outlined in table 7 below.

Table 7: Cost to the government of combination NRT vs Varenicline for 0-12 weeks

	TOTAL COST	#UNITS	COST TO GOVERNMENT AFTER PATIENT CONTRIBUTION		
			General	Concession	Safety Net
Combination NRT	$296.16	6	$50.16	$256.56	$296.16
Varenicline	$286.82	3	$163.82	$267.02	$286.82

As recommended in the RACGP Guidelines an additional course of NRT may be considered for those who have stopped smoking at the end of a standard course of NRT to reduce relapse. Similarly, it is recommended that for people who have abstained from smoking after a standard course of varenicline a further course of varenicline may be considered to reduce relapse. The cost of an addition 12-weeks (weeks 12-24) of combination NRT would be the same as the first 12 weeks (illustrated above in Table 5). There is a slight increase in the total cost for weeks 12-24 of varenicline due the initial titration and pack quantities. This is outlined in Table 8.

[17] Australian Medicines Handbook. Adelaide: Australian Medicines Handbook Pty Ltd; 2020.

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

Table 8: Cost of PBS-subsidised Varenicline for 12-24 weeks

PRODUCT	PACK QTY	#UNITS FOR 12 WEEKS	DPMQ/UNIT	TOTAL COST FOR 12 WEEKS
Champix Continuation Pack	56	1	$100.09	$100.09
Champix Continuation Pack	112	1	$188.71	$188.78
TOTAL FOR VARENICLINE				**$288.87**

The flow-on effect in terms of costs to the government are outlined in Table 9.

Table 9: Cost to the government of combination NRT vs Varenicline for 12-24 weeks

	TOTAL COST	#UNITS	COST TO GOVERNMENT AFTER PATIENT CONTRIBUTION		
			General	Concession	Safety Net
Combination NRT	$296.16	6	$50.16	$256.56	$296.16
Varenicline	$288.87	2	$206.87	$275.67	$288.87

Again, the total cost is marginally higher for combination NRT however the cost to the government is offset by the patient contribution fee. It should be noted that due to the PBS-listing quantities for varenicline the patient contribution fee may only be paid twice during the 12-24 week period which results in a higher cost to the government for varenicline during the 12-24 week period than during the initial 0-12 week period.

The potential impact of subsidising combination NRT via the PBS is outlined in Table 10.

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

Table 10: Potential implications of including combination NRT on the PBS

Currently prescribed	Potential impact of subsidising combination NRT	Cost-implications
Prescribed monotherapy with PBS-listed NRT	Prescribed PBS-listed combination NRT	Although the cost of pharmacotherapy will be increased, combination NRT is more effective than monotherapy with NRT. If more people quit successfully fewer quit attempts may be needed reducing pharmacotherapy costs longer term. Increased quit rates would also improve individual health and have a flow-on effects in terms of reducing the overall cost to the healthcare system.
	Prescribed combination NRT with a PBS-listed and non-PBS listed product. Although this is already an option for prescribers and patients, the availability of PBS-listed combination NRT may lead to more prescribers engaging in discussions about combination NRT options.	Negligible impact
	Continue to be prescribed monotherapy. Monotherapy with NRT is recommended for certain patient groups such as: • those who smoke 10 or less a day AND smoke more than 30 minutes after waking. • women who are unable to quit on their own with intermittent dosing products preferable as these provide a lower daily dose of nicotine than patches	Negligible impact
Prescribed varenicline	Prescribed combination NRT instead of varenicline.	As demonstrated in Table 7 and 9 this will reduce the cost to the government for general and concessional patients. The cost for safety net patients would be slightly higher however this would be offset by the reduction in cost for general and concessional patients
	Continue to be prescribed varenicline	Negligible impact
Prescribed bupropion	Given RACGP Guidelines recommend use of bupropion when NRT or varenicline is not suitable we anticipate the availability of combination NRT would be unlikely to have an impact on this area.	Negligible impact

Although NRT, is available as an over-the-counter (OTC) medicine the provision via the PBS significantly reduces the cost for concession cardholders to $6.60. This is in contrast to general patients for whom the patient contribution is $41. As such, we believe the real value to public health and reducing total cost to the health system is for the lower socioeconomic group in which smoking is more prevalent. As a prescription is required to receive PBS subsidised therapy, consultation with a prescriber such as a GP is required and this in itself this increases the likelihood a smoker will successfully quit and remain a non-smoker 12 months later. Given smokers of lower socioeconomic status were generally more likely to seek help from a doctor and to use prescription

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au

medication than higher socioeconomic status smokers ensuring the availability of combination therapy on the PBS should be considered a priority.

Perrigo Australia | | www.perrigo.com.au | | ABN 56 009 293 136
Head Office, Perth: 25-29 Delawney Street, Balcatta WA 6021, Australia I Phone: +61 8 9441 7800 I Fax: +61 8 9441 7888
Sales, Marketing and Distribution, Sydney: Suite 14, Level 1 | 3a Narabang Way Belrose, NSW 2085, Australia I Phone: +61 2 8850 9555 I Fax: +61 2 8850 9599
Sales Office, Brisbane: PO Box 2504, Fortitude Valley, Qld, 4006, Australia
Customer Service: Toll Free Phone: 1800 805 546 I Toll Free Fax: 1800 004 110 I Email: customerservice@perrigo.com.au