AUSTRALIAN PRODUCT INFORMATION – NICOTINELL (NICOTINE 2MG, 4MG) COATED CHEWING GUM

1 NAME OF THE MEDICINE

Nicotine

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

The active ingredient of Nicotinell Chewing Gum is nicotine.

The Nicotinell Chewing Gum contains 2 mg or 4 mg nicotine per piece of gum. It is available in fruit, mint, liquorice and classic flavours (not all flavours maybe marketed) and is sugar-free.

Each gum contains sorbitol, xylitol and mannitol with a combined total of 0.4g per piece. For the 2mg strength, this is equivalent to 8g per maximum dose of 20 pieces. For the 4mg strength, this is equivalent to 4g per maximum dose of 10 pieces. Please note that products containing these ingredients may have a laxative effect or cause diarrhoea.

Each piece of gum also contains 11.5mg (0.5mmol) sodium which should be taken into account by those on a low sodium diet. For the 2mg strength, this is equivalent to 230mg (10mmol) sodium per maximum dose of 20 pieces. For the 4mg strength, this is equivalent to 115mg (5mmol) sodium per maximum dose of 10 pieces

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

A rectangular white chewing gum with polished surface.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Source of nicotine as an aid for smoking cessation. May be used as part of a smoking reduction strategy by smokers who are unable or not ready to stop smoking abruptly as a step towards stopping completely.

4.2 DOSE AND METHOD OF ADMINISTRATION

The strength of Nicotinell Chewing Gum should be chosen according to the smoker's tobacco dependence. Highly dependent smokers, as well as smokers who have failed to quit when using the 2 mg gum, should use the 4 mg strength. Otherwise, the 2 mg strength should be used.

One piece of gum should be chewed when the user feels the urge to smoke. The amount chewed should normally be 8-12 of the 2 mg pieces or 4-6 of the 4 mg pieces per day, up to a maximum of 20 of the 2 mg pieces or 10 of the 4 mg pieces per day.

Chewing Technique:

1. One piece of gum should be chewed until the taste becomes strong.
2. The chewing gum should be rested between the gum and cheek.

3. When the taste fades, chewing should commence again.
4. The chewing routine should be repeated for 30 minutes.

Concomitant use of acidic beverages such as coffee or soft drinks may interfere with the buccal absorption of nicotine. Acidic beverages should be avoided for 15 minutes prior to chewing the gum.

The patient should be advised to make every effort to completely stop smoking during treatment with Nicotinell Chewing Gum.

After three months, users should gradually cut down the number of pieces chewed each day until only 1-2 pieces of gum per day are required, at which time they should stop using the product. This process may take 6 months from the start of treatment. Counselling may help smokers to quit. Those using NRT for more than 9 months should seek advice from a healthcare professional.

Gradual cessation of smoking

For smokers who are unwilling or unable to suddenly quit, Nicotinell Chewing Gum may be used whenever there is an intense desire to smoke to help reduce the number of cigarettes smoked, before stopping smoking completely. The smoker should attempt a reduction in cigarette consumption as soon as possible. Consult a healthcare professional if the number of cigarettes smoked has not been reduced in 6 weeks. Once the number of cigarettes has been reduced to a point where the smokers can quit completely, then the Nicotinell Chewing Gum program should be followed. Consult a healthcare professional if an attempt to stop smoking completely has not commenced within 6-9 months of beginning treatment.

Combination therapy

If smokers have previously relapsed with use of one form of nicotine replacement therapy (NRT), combination therapy could be beneficial. Smokers who experience breakthrough cravings or have difficulty controlling cravings using one form of NRT alone could combine the use of Nicotinell Patch Step 1 with another form of NRT such as Nicotinell Chewing Gum 2 mg. Nicotinell Chewing Gum 4 mg should not be used with Nicotinell Patches.

When using Nicotinell Patch Step 1 in addition of Nicotinell Chewing Gum 2 mg, it is recommended that 4 to 12 pieces are used each day. Most people will use 5 to 6 pieces. Do not exceed 12 pieces a day.

Combination therapy should be used for 12 weeks, after which one of the two following programs should be followed:

1. Stop use of Nicotinell Patch and gradually reduce the number of gums used until they are no longer needed.
2. Continue with Nicotinell Patch Step 2 for 3-4 weeks, then Nicotinell Patch Step 3 for a further 3-4 weeks while maintaining the number of Nicotinell Chewing Gum 2 mg that is used each day. After use of patches is ceased, gradually reduce the number of gums used until they are no longer needed.

Use in children under 18 years

Children aged 12 to 17 years should only use Nicotinell Chewing Gum under the advice of a healthcare professional. Treatment should not exceed 12 weeks without consultation with a healthcare professional, who should reassess the person for their commitment to quitting smoking and the likely benefit of continued treatment, before recommending use of NRT in this

age group beyond 12 weeks. Treatment should not be extended by more than a further 4 weeks in this case. Do not use in children under 12 years.

4.3 CONTRAINDICATIONS

Nicotinell Chewing Gum should not be used by non-smokers, children under 12 years, occasional smokers or those with known hypersensitivity to nicotine or any of the excipients in the formulation.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Nicotine is a toxic and addictive drug and milligram doses are potentially fatal if rapidly absorbed. For any smoker, with or without concomitant disease or pregnancy, the risk of nicotine replacement in a smoking cessation program should be weighed against the hazard of continued smoking and the likelihood of achieving cessation of smoking without nicotine replacement.

Treatment with Nicotinell Chewing Gum should be discontinued if symptoms of nicotine overdose appear. Mild intoxication produces nausea, vomiting, abdominal pain, diarrhoea, headache, sweating, and pallor (see 4.9 Overdose).

Doses of nicotine that are tolerated by adult smokers during treatment can produce severe symptoms of poisoning in small children and may prove fatal (see 4.9 Overdose).

Nicotinell Chewing Gum must be kept out of reach of children at all times.

Occasional smokers are not expected to benefit from the use of Nicotinell Chewing Gum.

Dependent smokers with a recent myocardial infarction, unstable or worsening angina pectoris including Prinzmetal's angina, severe cardiac arrhythmias, uncontrolled hypertension or recent cerebrovascular accident should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). If this fails, Nicotinell Chewing Gum may be considered but as data on safety in these patient groups are limited, initiation should only be under close medical supervision.

Nicotinell Chewing Gum should be used with caution in patients with:
- severe hypertension, stable angina pectoris, cerebrovascular disease, occlusive peripheral arterial disease, heart failure,
- hyperthyroidism or pheochromocytoma,
- moderate to severe hepatic and/or severe renal impairment, active peptic ulcer.

Smokers with diabetes mellitus should be advised to monitor their blood sugar levels more closely than usual when NRT is initiated because catecholamine release can affect carbohydrate metabolism and vasoconstriction may delay or reduce insulin absorption.

Swallowed nicotine may exacerbate symptoms in subjects suffering from active oesophagitis, gastritis or peptic ulcer. Avoid use of Nicotinell Chewing Gum if oral or pharyngeal inflammation is present.

There is the possibility that, as with other gums, Nicotinell Chewing Gum may stick to dentures, dental caps or partial bridges and may damage dental work.

Transfer Dependence: Nicotine transferred dependence can occur.

Use in the elderly

No data available.

Paediatric Use

Data on the use of NRT in treating adolescents under the age of 18 years are limited.

NRT should only be used in adolescents 12 to 17 years after consultation with a healthcare professional and use should be restricted to 12 weeks. If treatment is required for longer than 12 weeks, this should be discussed with a healthcare professional.

Do not use in children under 12 years.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No clinically relevant interactions between NRT and other drugs have definitely been established. However nicotine may enhance the haemodynamic effects of adenosine.

Smoking but not nicotine is associated with increased CYP1A2, and possibly CYP1A1, activity. After cessation of smoking there may be reduced clearance of substrates for these enzymes and increased plasma levels of some medicinal products. This is of potential clinical importance in products with a narrow therapeutic window e.g. theophylline, ropinirole, clozapine and olanzapine.

Cessation of smoking, with or without NRT, may alter the individual's response to concomitant medication and may require adjustment of dose. In particular, anticonvulsants may require special monitoring and/or dosage adjustment.

Dose reduction may be required for:

- caffeine, oestrogens, imipramine, lignocaine, oxazepam, pentazocine, theophylline, warfarin, possibly due to reversal of hepatic enzyme induction on smoking cessation
- insulin, possibly due to increase in subcutaneous absorption on smoking cessation
- adrenergic antagonists (e.g. prazosin, labetalol), possibly due to reduction in circulating catecholamines on smoking cessation

Dose increase may be required for:

- adrenergic agonists (e.g. isoprenaline, phenylephrine), possibly due to reduction in circulating catecholamines on smoking cessation

Smoking may lead to reduced analgesic effects of opioids (e.g. dextropropoxyphene, pentazocine), reduced diuretic response to furosemide, reduced effect of beta-adrenergic blockers (e.g. propranolol) on blood pressure and heart rate decrease and reduced responder rates in ulcer healing with H_2-antagonists.

Both smoking and nicotine may raise the blood levels of cortisol and catecholamines. Dosages of nifedipine, adrenergic antagonists and adrenergic agonists may need to be adjusted.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

No data available.

Use in pregnancy – Pregnancy Category D

In pregnant women, complete cessation of tobacco consumption should always be recommended without nicotine replacement therapy (NRT). However, for women unable to quit on their own, NRT may be recommended to assist a quit attempt. Nicotine is harmful to the foetus. However, the risk for the foetus is probably less than to be expected with continued smoking due to:

- Lower maximal plasma concentrations compared to inhaled nicotine, resulting in a nicotine exposure less or not more than associated with smoking.

- No exposure to polycyclic hydrocarbons and carbon monoxide.

As nicotine does pass to the foetus, the decision to use NRT should be made as early on in pregnancy as possible with the aim of discontinuing after use for two to three months.

If NRT is used during pregnancy, Nicotinell Chewing Gum should preferably be used while pregnant as they usually provide a lower daily dose of nicotine than patches. However, if the woman suffers from nausea and/or vomiting, the patch may be preferred but should be removed before going to bed.

Due to an absence of specific studies, combination therapy with patches and oral forms is not recommended during pregnancy unless the healthcare professional considers it necessary to ensure abstinence.

Use in lactation

Nicotine is excreted in breast milk in quantities that may affect the child even in therapeutic doses. Like smoking, nicotine replacement therapy should be avoided during breast-feeding. However Nicotinell Chewing Gum may be used if necessary. Women should breastfeed just before they use the product to allow time between NRT use and feeding to be as long as possible.

Due to an absence of specific studies, combination therapy with patches and oral forms is not recommended during lactation unless the healthcare professional considers it necessary to ensure abstinence.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Smoking cessation can cause behavioural changes. Any risks associated with driving vehicles or operating machinery are considered minimal when the gum is used according to the recommended dose.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

In principle, Nicotinell Chewing Gum can cause adverse effects similar to those associated with nicotine administered by smoking.

The most common side effects are dizziness, headaches and insomnia. These could also be withdrawal symptoms associated with giving up smoking and could be the result of too little nicotine.

Nicotine from chewing gum may sometimes cause a slight irritation of the mouth and throat and increase salivation at the start of treatment. Excessive swallowing of dissolved nicotine may, at first, cause hiccupping. Those people with a tendency to indigestion may suffer initially from minor indigestion or heartburn. Slower chewing will usually overcome this problem. Excessive consumption of chewing gum by people who have not been in the habit of inhaling tobacco smoke

could possibly lead to nausea, faintness or headaches. Less common side effects include palpitations, redness and rashes.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Symptoms

In overdose, symptoms corresponding to heavy smoking may be seen. General symptoms of nicotine poisoning include: pallor, sweating, burning throat, salivation, nausea, vomiting, abdominal cramps, diarrhoea, headache, dizziness, hearing and vision disturbances, tremor, mental confusion, muscle weakness, palpitations, dilated pupils, tachycardia, cardiac arrhythmias, dyspnoea, circulatory disturbance, convulsions, prostration, absence of neurological reaction, respiratory failure.

Lethal doses may produce convulsions, and death follows as a result of peripheral or central respiratory paralysis or, less frequently, cardiac failure. The acute lethal oral dose is approximately 0.5-0.75 mg per kg body weight, corresponding in an adult to 40-60 mg. Doses of nicotine that are tolerated by adult smokers during treatment can produce severe symptoms of poisoning in small children and may prove fatal. If poisoning is suspected in a child, a doctor must be consulted immediately.

Overdose with Nicotinell Chewing Gum could occur if many pieces are chewed simultaneously. Risk of overdose is small as nausea and vomiting usually occurs at an early stage. Risk of poisoning by swallowing the gum is small. Since the release of nicotine from the gum is slow, very little nicotine is absorbed from the stomach and intestine. Any that is absorbed will be inactivated by the liver.

Treatment

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Nicotinell Chewing Gum mimics the pharmacological effects of nicotine from smoking and may, therefore, be used to help provide relief from nicotine withdrawal symptoms. In addition to its effects on the central nervous system, nicotine produces haemodynamic effects such as increased heart rate and systolic blood pressure.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

When the gum is chewed, nicotine is steadily released into the mouth and is rapidly absorbed through the buccal mucosa. By the swallowing of nicotine-containing saliva, a proportion reaches the stomach and intestine where it is inactivated.

Distribution

The peak plasma concentration after a single dose of the 2 mg chewing gum is approximately 6.4 nanograms per mL. For the 4 mg chewing gum, it has been calculated that the nicotine peak plasma concentration after a single dose is approximately 9.3 nanograms per mL (after approximately 60 minutes). After 45 minutes average plasma concentration of nicotine when smoking a cigarette is 15-30 nanograms per mL.

Nicotine crosses the blood-brain barrier, the placenta and is detectable in breast milk.

Metabolism

The plasma half-life is approximately three hours.

Excretion

Nicotine is eliminated mainly via hepatic metabolism, small amounts being eliminated in unchanged form via the kidneys.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Nicotinell Chewing Gum contains nicotine, chewing gum base (containing butylated hydroxytoluene), calcium carbonate, carnauba wax, gelatin, glycerol, mannitol, menthol, polacrilin, sodium bicarbonate, sodium carbonate anhydrous, sorbitol, talc, titanium dioxide, water – purified, xylitol.

Classic Nicotinell Chewing Gum contains maltitol solution.

Fruit, Mint and Liquorice Nicotinell Chewing Gums contain saccharin, saccharin sodium, acesulfame potassium.

Flavours: Fruit – fruit flavour. Mint – eucalyptus oil, peppermint oil. Liquorice – eucalyptus oil, anise oil, liquorice root extract. Classic – fruit flavour.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C.

6.5 NATURE AND CONTENTS OF CONTAINER

Nicotinell Chewing Gum is available in fruit, mint, liquorice and classic flavour, containing 2 mg or 4 mg nicotine per piece; packed in blister packs then boxed. Nicotinell Chewing Gum is available in packs of 24, 96, 144, 216 and 384 (not all sizes maybe marketed).

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

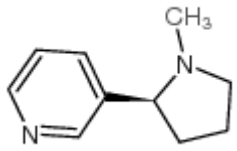
6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

Chemical name: 1-methyl-2-(3-pyridyl) pyrrolidine

Molecular formula: C10-H14-N2

Molecular weight: 162.26



CAS number

54-11-5

7 MEDICINE SCHEDULE (POISONS STANDARD)

Not scheduled

8 SPONSOR

Perrigo Australia
25-29 Delawney Street,
WA, 6021, Australia

Contact: 1800 805 546

9 DATE OF FIRST APPROVAL

28 April 2009

10 DATE OF REVISION

4th October 2018

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	Updated to new format
4.4	Additional warnings added.