AUSTRALIAN PRODUCT INFORMATION

NICABATE MINI LOZENGES (NICOTINE) MINT FLAVOUR

1 NAME OF THE MEDICINE

Nicotine

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: *Nicotine polacrilex*

Nicotine 2 mg lozenge

Nicotine 4 mg lozenge

Excipients: Contains sucralose, mannitol and xylitol. For the full list of excipients, see section 6.1 List of Excipients.

3 PHARMACEUTICAL FORM

NICABATE MINI LOZENGES nicotine 2 mg Mint Flavour

A dual layer oval lozenge with convex surfaces. One side is white to off white, may contain bluish hue and the other side blue with a debossed “2” logo.

NICABATE MINI LOZENGES nicotine 4 mg Mint Flavour

A dual layer oval lozenge with convex surfaces. One side is white to off white, may contain bluish hue and the other side blue with a debossed “4” logo.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For the relief of nicotine withdrawal symptoms including cravings associated with smoking cessation. It may also 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 smoking. It should be used as part of a behavioural support programme.

4.2 DOSE AND METHOD OF ADMINISTRATION

Directions for Use

One lozenge should be placed in the mouth and allowed to dissolve. Periodically, the lozenge should be moved from one side of the mouth to the other and repeated, until the lozenge is

completely dissolved (approximately 10 – 13 minutes). The lozenge should not be chewed or swallowed whole.

Users should not eat or drink while a lozenge is in the mouth.

Adults (18 years and over including the elderly)

Abrupt Cessation of Smoking

Nicabate Mini Lozenges 2 mg are suitable for smokers who smoke less than 20 cigarettes a day.

Nicabate Mini Lozenges 4 mg are suitable for smokers who smoke 20 or more cigarettes a day.

Users should make every effort to stop smoking completely during treatment with Nicabate Mini Lozenges.

Behavioural therapy, advice and support will normally improve the success rate.

Users should follow the schedule of treatment below:

Table 1

Step 1 **Weeks 1 to 6**	**Step 2** **Weeks 7 to 9**	**Step 3** **Weeks 10 to 12**	To help stay smoke free over the next 12 weeks: take a lozenge in situations when strongly tempted to smoke.
Initial treatment period	Step down treatment period	Step down treatment period	
1 lozenge every 1 to 2 hours	1 lozenge every 2 to 4 hours	1 lozenge every 4 to 8 hours	

During weeks 1 to 6 it is recommended that users take at least nine lozenges per day.

Users should not exceed 15 of the 4 mg Mini Lozenges per day or 15 of the 2mg Mini Lozenges per day during weeks 1 to 6.

Users should not use more than 1 lozenge per hour.

Those who use the lozenges beyond 9 months are recommended to seek additional help and advice from a healthcare professional who may consider alternate quit strategies such as combination therapy. Use of Nicabate Lozenges beyond 9 months is only if the potential benefit outweighs the potential risk to the smoker.

Gradual cessation of smoking (Reduce to quit)

For smokers who are unwilling or unable to quit abruptly. Use a lozenge whenever there is a strong urge to smoke in order to reduce the number of cigarettes smoked as far as possible and to refrain from smoking as long as possible. The number of lozenges a day is variable and depends on the patient's needs. Nonetheless it should not exceed 15 of the 4 mg lozenges per day or 15 of the 2 mg lozenges per day.

If a reduction in cigarette consumption has not been achieved after 6 weeks of treatment, a healthcare professional should be consulted. Reduced tobacco consumption may help to lead to complete cessation of smoking. This should be attempted as soon as possible. When the number of cigarettes has been reduced to a level from which the user feels able to quit completely, then start on the schedule for "abrupt cessation" as given above. Nicabate Mini Lozenges should not be used for more than 9 months unless the potential benefit outweighs the potential risk to the smoker.

If an attempt to stop smoking completely has not been started within 6 months after the beginning of treatment, it is recommended to consult a healthcare professional.

Combination therapy

In some instances, it may be beneficial to utilize more than one form of NRT concurrently. For example, combination therapy could be used by smokers who have relapsed with NRT monotherapy in the past, who experience breakthrough cravings or have difficulty controlling cravings for cigarettes using single therapy. This would allow users to identify the combination most appropriate for their individual quit attempt. If required, Nicabate gum 2 mg, or Nicabate Mini Lozenges 2 mg may be combined with Nicabate 21 mg patches. Nicabate 4 mg Mini Lozenges and/or Nicabate 4 mg gum should not be used with Nicabate patches.

When using Nicabate 21 mg patches in addition to Nicabate 2 mg gums, or 2 mg Mini Lozenges, it is recommended that a minimum of 4 pieces of gum/ /4 Mini Lozenges are used daily. Most people will use 4-5 pieces. The maximum number of gum, or Mini Lozenges used in conjunction with the patch is 12 pieces per day.

Combination treatment should be used for 12 weeks after which weaning may be initiated. If required, weaning may be done by either:

1) Using Nicabate 14 mg patch for 2 weeks and then Nicabate 7 mg patch for 2 weeks while maintaining the number of pieces of 2 mg gum or 2 mg Mini Lozenges that have been routinely used. Then, when a patch is no longer used, the number of pieces of gum or 2 mg Mini Lozenges can be gradually reduced. OR
2) Stopping use of Nicabate 21 mg patch and then gradually reducing the number of pieces of 2 mg gum or 2 mg Mini Lozenges that are being used.

Users should stop smoking completely during treatment with Nicabate 2 mg gum or 2 mg Mini Lozenges in combination with Nicabate patches.

Children and adolescents

The use of NRT in adolescents should only be used when the benefits of abstinence outweigh the risks of continued smoking.

Data are limited in relation to the value of NRT use in young people where the demand for cessation products and the motivation to quit is low. NRT should only be used by adolescents in conjunction with a counselling programme. Counselling is needed in this age group because NRT is likely to be ineffective in the absence of counselling.

Adolescents (12-17 years) should follow the schedule of treatment for adults in the table above for steps 1, 2 and 3 but, as data are limited, duration of use of NRT in this age group is restricted to 10 weeks after obtaining medical advice. If longer treatment is required, advice from a healthcare professional should be sought who can then reassess the patient for their commitment to quitting and the benefits of continued treatment. If treatment is continued, it should not be extended for more than another four weeks.

Nicabate Mini Lozenges should not be used by adolescents for gradual cessation of smoking.

Adolescents should not quit with a combination NRT regimen.

Nicabate Mini Lozenges should not be used in children under 12 years of age.

4.3 CONTRAINDICATIONS

Nicabate should not be used by:

- Non-smokers
- Children under 12 years of age
- Those with hypersensitivity to nicotine or any of the excipients

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

The risks associated with the use of NRT (Nicotine replacement therapy) are substantially outweighed in virtually all circumstances by the well-established dangers of continued smoking.

Nicabate Mini Lozenges contains sodium (3.90 mg/lozenge for the 2mg strength, and 3.73 mg/lozenge for the 4mg strength)

Nicabate Mini Lozenges contains sucralose. Nicabate 2 mg Mini Lozenges contains 2.9 g mannitol and 80.3 mg xylitol per 15 lozenges. Nicabate 4 mg Mini Lozenges contains 2.8 g mannitol and 80.3 mg xylitol per 15 lozenges. Products containing mannitol and xylitol may

have a laxative effect or cause diarrhoea. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

Patients hospitalised for or with a recent myocardial infarction, severe dysrhythmia or CVA

Patients hospitalised for or with a recent myocardial infarction, severe dysrhythmia or CVA (cerebrovascular accident) who are considered to be haemodynamically unstable should be encouraged to stop smoking with non-pharmacological interventions. If this fails, Nicabate Mini Lozenges may be considered, but as data on safety in this patient group are limited, initiation should only be under medical supervision. Once patients are discharged from hospital, they can use NRT on medical advice. If there is a clinically significant increase in cardiovascular or other effects attributable to nicotine, the mini lozenges should be reduced or discontinued. Use with caution in patients with recent or unstable cardiovascular disease. In patients with unstable cardiovascular disease, do not continue NRT if patient continues to smoke.

The combination NRT regimen should not be used in people with known cardiovascular disease without evaluation of the risk/benefit by a health care professional.

Diabetes mellitus

Blood glucose levels may be more variable when stopping smoking, with or without NRT, so it is important for patients with diabetes mellitus to monitor their blood glucose levels more closely than usual when NRT is initiated as catecholamines released by nicotine can affect carbohydrate metabolism and vasoconstriction may delay/reduce insulin absorption.

Seizures

Potential risk and benefits of nicotine should be carefully evaluated before use in subjects taking anti-convulsant therapy or with a history of epilepsy as cases of convulsions have been reported in association with nicotine.

Allergic reactions

Susceptibility to angioedema and urticaria. NRT should be used with caution by patients who are susceptible to angioedema and/or urticaria.

Phaeochromocytoma and uncontrolled hyperthyroidism

Use with caution in patients with uncontrolled hyperthyroidism or phaeochromocytoma as nicotine causes release of catecholamines. A risk-benefit assessment should be made by an appropriate healthcare professional.

GI disease

Swallowed nicotine may exacerbate symptoms in patients suffering from active oesophagitis, oral or pharyngeal inflammation, gastritis and gastric or peptic ulcers. Oral NRT preparations

should be used with caution in these conditions. Ulcerative stomatitis has been reported. A risk-benefit assessment should be made by an appropriate healthcare professional.

Danger in small children

Doses of nicotine tolerated by adult and adolescent smokers can produce severe toxicity in small children that may be fatal. Products containing nicotine should not be left where they may be misused, handled or ingested by children.
Nicabate products should be kept out of the sight and reach of children.

Transferred dependence

Transferred dependence is rare and is both less harmful and easier to break than smoking dependence.

Combination Nicabate therapy should not be used in people with known cardiovascular disease without evaluation of the risk/benefit by a health professional.

Use in hepatic impairment

Use with caution in patients with moderate to severe hepatic impairment as the clearance of nicotine or its metabolites may be decreased with the potential for increased adverse effects. A risk-benefit assessment should be made by an appropriate healthcare professional.

Use in renal impairment

Use with caution in patients with moderate to severe renal impairment as the clearance of nicotine or its metabolites may be decreased with the potential for increased adverse effects. A risk-benefit assessment should be made by an appropriate healthcare professional.

Use in the elderly

No data available.

Paediatric use

Do not use in children under 12 years of age.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No clinically relevant interactions between nicotine replacement therapy and other drugs have definitely been established, however nicotine may possibly enhance the haemodynamic effects of adenosine.

Smoking cessation, with or without nicotine replacement, may alter the individual's response to concomitant medication and may require adjustment of dose.

Polycyclic aromatic hydrocarbons in tobacco smoke induce the metabolism of drugs metabolised by CYP 1A2 (and possibly by CYP 1A1). When a smoker stops this may result in a slower metabolism and a consequent rise in blood levels of such drugs.

The following drugs may require adjustment in dose at cessation of smoking:

Caffeine, theophylline, imipramine, pentazocine, tacrine, clomipramine, insulin, clozapine, olanzapine and fluvoxamine. In particular, anticonvulsants may require special monitoring and/or dosage adjustment.

Other reported effects of smoking include reduced analgesic efficacy of propoxyphene, reduced diuretic response to frusemide and altered pharmacological response to propranolol, as well as altered rates of ulcer healing with H2 antagonists. Both smoking and nicotine can increase levels of circulating cortisol and catecholamines. Dosages of nifedipine, adrenergic agonists or adrenergic blocking agents may need to be adjusted.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

In rats and rabbits, implantation can be delayed or inhibited by a reduction DNA synthesis that appears to be caused by nicotine. Studies have shown a decrease in litter size in rats treated with nicotine during gestation.

Use in pregnancy – Pregnancy Category D

Adverse reproductive and developmental effects have been reported following exposure to tobacco and nicotine during pregnancy. Smoking during pregnancy is associated with risks such as intra-uterine growth retardation, premature birth or stillbirth. Stopping smoking is the single most effective intervention for improving the health of both pregnant smoker and her baby. The earlier abstinence is achieved the better.

Ideally smoking cessation during pregnancy should be achieved without NRT. However for women unable to quit on their own, oral forms of NRT should only be used on the advice of a health care professional. Oral forms of NRT should only be used if the expected benefits to the mother outweigh the potential risks to the foetus. Nicotine is harmful to the foetus. However, the risk of using NRT to the foetus is lower than that expected with tobacco smoking, due to lower maximal plasma nicotine concentration and no additional exposure to polycyclic hydrocarbons and carbon monoxide. However, as nicotine passes to the foetus affecting breathing movements and has a dose dependent effect on placental/foetal circulation, the decision to use NRT should be made as early on in the pregnancy as possible. The aim should be to use NRT for only 2-3 months.

While no data exist to support one form of NRT over another, it may be prudent to use intermittent dosing products as these usually provide a lower daily dose of nicotine than patches. However, patches may be preferred if the woman is suffering from nausea during pregnancy. If patches are used they should be removed before going to bed.

Use in lactation.

Nicotine from smoking and NRT is found in breast milk. However the amount of nicotine the infant is exposed to from NRT is relatively small and less hazardous than the second-hand smoke they would otherwise be exposed to. Nicabate patches should not be used and NRT should be avoided while breastfeeding. Should smoking withdrawal not be achieved, Intermittent dosing products such as Nicabate gums or mini lozenges, may be considered and women should breast feed just before they use the product to allow as long a time as possible between NRT use and feeding. Nicabate Gums or Mini Lozenges should only be used if the expected benefits to the nursing mother outweigh the potential risks to the infant.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Used as recommended there are minimal risks associated with the use of Nicabate Mini Lozenges in driving vehicles or operating machinery. Nevertheless, one should take into consideration that smoking cessation can cause behavioural changes.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Nicotine lozenges can cause adverse reactions similar to those associated with nicotine from tobacco. Many of the observed adverse reactions are consistent with the pharmacological effects of nicotine, which are dose dependent.

Clinical Trial Data

The following undesirable effects detailed in Tables 2 and 3 are nicotine related adverse events for all oral dosage forms.

Table 2 shows events which were identified from a double-blind, randomised, placebo-controlled lozenge clinical study involving 1818 patients. Adverse events reported in this study have been considered for inclusion, where the incidence in the 2 mg or 4 mg nicotine arm was higher than the corresponding placebo arm. Frequencies calculated from the study safety data.

Table 2

Gastrointestinal Disorder	
Very common ≥1/10	Nausea
Common ≥1/100;<1/10	vomiting, dyspepsia**, abdominal pain upper, diarrhoea, dry mouth, constipation, hiccups, stomatitis, flatulence, oral discomfort
Nervous System Disorders	
Common ≥1/100;<1/10	headache*, dizziness*
Psychiatric Disorders	
Common ≥1/100;<1/10	insomnia*
Respiratory, Thoracic and Mediastinal Disorders	
Common ≥1/100;<1/10	pharyngitis, cough*, pharyngolaryngeal pain

*These events may also be due to withdrawal symptoms following smoking cessation.

**Individuals with a tendency to experience indigestion may suffer initially from minor degrees of indigestion or heartburn if the 4 mg dose is used. The use of the 2 mg dose (if necessary more frequently) will usually overcome this problem.

Post Marketing

Table 3 shows events which have been identified from post-marketing experience of oral nicotine products. Frequencies for these events cannot be estimated for oral nicotine dosage forms from the available data.

Table 3

Cardiac Disorders
palpitations, tachycardia, reversible atrial fibrillation or arrhythmias
Gastrointestinal Disorder
dysphagia, eructation, salivary hypersecretion
General Disorders and Administration Site Conditions
asthenia*, fatigue*, malaise*, influenza type illness*
Immune System Disorders
hypersensitivity, angioedema, urticaria, ulcerative stomatitis, and very rarely anaphylactic reactions
Nervous System Disorders
Tremor
Psychiatric Disorders
nervousness*
Respiratory, Thoracic and Mediastinal Disorders
dyspnoea

*These events may also be due to withdrawal symptoms following smoking cessation.

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

Nicotine doses that are tolerated by adult smokers during treatment, and even small quantities of nicotine are dangerous in children, and may produce severe symptoms of poisoning in small children and may be fatal.

Signs and symptoms of an overdose from nicotine mini lozenges would be expected to be the same as those of acute nicotine poisoning, including pallor, hyperhidrosis cold sweat, salivation, nausea, vomiting, abdominal pain, diarrhoea, headache, dizziness, sensory disturbances such as disturbed hearing and vision, tremor, mental confusion and weakness.

Prostration, hypotension, circulatory collapse, respiratory failure and convulsions may ensue with large overdoses.

Treatment of overdose

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

In the event of an overdose, medical attention should be sought immediately. All nicotine intake should stop immediately and the patient should be treated symptomatically, and vital signs monitored. Activated charcoal may reduce absorption of the medicine if given within one or two hours after ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via a nasogastric tube, once the airway is protected.

5 PHARMACOLOGICAL PROPERTIES

Nicotine, the chief alkaloid in tobacco products, binds stereoselectively to acetylcholine receptors at the autonomic ganglia, in the adrenal medulla, at neuromuscular junctions and in the brain. Two types of central nervous system effects are believed to be the basis of nicotine's positively reinforcing properties. A stimulating effect exerted mainly in the cortex via the locus ceruleus, produces increased alertness and cognitive performance. A "reward" effect via the "pleasure system" in the brain is exerted in the limbic system. At low doses the stimulant effects predominate, while at high doses the reward effects predominate. Intermittent intravenous administration of nicotine activates neurohormonal pathways, releasing acetylcholine, noradrenaline, dopamine, serotonin, vasopressin, beta-endorphin, growth hormone and ACTH.

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

The actions of nicotine in man are complex, depending on dose, rate of delivery, prevalent autonomic tone, individual variation and prior exposure (tolerance).

The cardiovascular effects of nicotine include peripheral vasoconstriction, tachycardia and elevated blood pressure. Acute and chronic tolerance to nicotine develops from smoking tobacco or ingesting nicotine preparations. Acute tolerance (a reduction in response for a given dose) develops rapidly (less than 1 hour), but at distinct rates for different physiological effects (skin temperature, heart rate, subjective effects). Withdrawal symptoms, such as cigarette craving, can be reduced in some individuals by plasma nicotine levels lower than those for smoking.

Withdrawal from nicotine in addicted individuals is characterised by craving, nervousness, restlessness, irritability, mood lability, anxiety, drowsiness, sleep disturbances, impaired concentration, increase appetite, minor somatic complaints (headache, myalgia, constipation, fatigue) and weight gain. Nicotine toxicity is characterised by nausea, abdominal pain, vomiting, diarrhoea, diaphoresis, flushing, dizziness, disturbed hearing and vision, confusion, weakness, palpitations, altered respiration, and hypotension.

Clinical trials

A multicentre, double-blind, placebo-controlled, randomised, parallel group study assessed the efficacy of nicotine lozenges 2 mg and 4 mg in smokers wanting to quit. These lozenges had a different formulation to that of the Nicabate Minis. Treatment allocation was based on time to first cigarette (TTFC). Those smoking within 30 minutes of waking were allocated to the 4 mg group (or matching placebo) and those smoking more than 30 minutes after waking were allocated to the 2 mg group (or matching placebo).

The study was undertaken in both the USA and the UK. A total of 1,818 smokers motivated to stop and aged over 18 years were randomised; 459 in the 2 mg active group, 458 in the 2 mg placebo, 450 in the 4 mg active and 451 in the 4 mg placebo.

Subjects were given clear instructions on how to suck the lozenge. Treatment instructions were to use one lozenge every 1-2 hours for the first 6 weeks, one lozenge every 2-4 hours for weeks 7-9, and one lozenge every 4-8 hours for weeks 10-12. Thereafter subjects were advised to use 1-2 lozenges per day as needed to remain abstinent. During the first six weeks, subjects were advised to use a minimum of 9 lozenges daily. At the end of 6 months subjects were told to abstain from taking the lozenge.

Six week, 3 month and 6 month, continuous, biochemically-confirmed smoking cessation rates presented by treatment group are tabulated below.

Table 4

	2 mg lozenge		4 mg lozenge	
	Active n=459	Placebo n=458	Active n=450	Placebo n=451
6 weeks	46.0%	29.7%	48.7%	20.8%
3 months	34.4%	21.6%	35.3%	14.0%
6 months	24.2%	14.4%	23.6%	10.2%

In a single clinical study, Nicabate 4 mg lozenge has been shown to attenuate cessation-related weight gain in high dependency smokers during the 12 weeks treatment period. Weight gain was reduced from a mean of 2.30 kg (range -3.6 to 7.3 kg) in placebo lozenge users to 1.27 kg (range -3.7 to 9.9 kg) in 4 mg lozenge users after 6 weeks lozenge use, and reduced from 3.40 kg (range -2.2 to 10.9 kg) in placebo users to 2.67 kg (range -4.2 to 14.5 kg) in 4 mg lozenge users after 3 months lozenge use. Weight gain rebounded to at least placebo levels after cessation of use of the lozenges in subjects continuing to abstain from smoking.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Nicabate Minis dissolve completely in the oral cavity and the entire amount of nicotine contained in the lozenge becomes available for buccal absorption or ingestion (swallowing). The complete dissolution of Nicabate Minis is typically achieved in approximately 10 - 13 minutes. The mean peak plasma concentrations of nicotine achieved after a single 4 mg dose are approximately 9.1 ng/mL.

Distribution

The plasma protein binding of nicotine is low (4.9%), and the volume of distribution of nicotine is large (2.5 L/kg). The distribution of nicotine to tissue is pH dependent, with the highest concentrations of nicotine found in the brain, stomach, kidney and liver.

Metabolism

Nicotine is extensively metabolised to a number of metabolites, all of which are less active than the parent compound. The metabolism of nicotine primarily occurs in the liver, but also in the lung and kidney. Nicotine is metabolised primarily to cotinine but is also metabolised to nicotine N'-oxide. Cotinine has a half-life of 15-20 hours and its blood levels are 10 times higher than nicotine. Cotinine is further oxidised to trans-3'-hydroxycotinine, which is the most abundant metabolite of nicotine in the urine. Both nicotine and cotinine undergo glucuronidation.

Excretion

The elimination half-life of nicotine is approximately 2 hours (range 1 - 4 hours). Total clearance for nicotine ranges from approximately 62 to 89 l/hr. Non-renal clearance for nicotine is estimated to be about 75% of total clearance. Nicotine and its metabolites are excreted almost exclusively in the urine. The renal excretion of unchanged nicotine is highly dependent on urinary pH, with greater excretion occurring at acidic pH.

5.3 PRECLINICAL SAFETY DATA

The general toxicity of nicotine is well known and taken into account in the recommended posology. Nicotine was not mutagenic in appropriate assays. The results of carcinogenicity assays did not provide any clear evidence of a tumorigenic effect of nicotine. In studies in pregnant animals, nicotine showed maternal toxicity and consequential mild foetal toxicity. Additional effects included pre- and postnatal growth retardation and delays and changes in postnatal CNS development.

Effects were only noted following exposure to nicotine at levels in excess of those which will result from recommended use of Nicabate Mini Lozenges. Effects on fertility have not been established.

Comparison of the systemic exposure necessary to elicit these adverse responses from preclinical test systems with that associated with the recommended use of Nicabate Mini Lozenges indicate that the potential risk is low and outweighed by the demonstrable benefit of nicotine therapy in smoking cessation. However, Nicabate Mini Lozenges should only be used by pregnant women on medical advice if other forms of treatment have failed.

Genotoxicity

Nicotine and cotinine were not mutagenic in the Ames *Salmonella* test. Nicotine induced repairable DNA damage in an *E.coli* test system. Nicotine was shown to be genotoxic in a test system using Chinese hamster ovary cells.

Carcinogenicity

Nicotine itself does not appear to be a carcinogen in laboratory animals. However, nicotine and its metabolites increased the incidence of tumours in the cheek pouches of hamsters and forestomach of F344 rats, respectively, when given in combination with tumour initiators. One study, which could not be replicated, suggested that cotinine, the primary metabolite of nicotine, may cause lymphoreticular sarcoma in the large intestine in rats.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Mannitol, Sucralose, Acesulfame Potassium, Magnesium Stearate, Hypromellose, Sodium Carbonate, Xanthan Gum, Sodium Bicarbonate, F-Melt Type C, Sweet Mint Flavour 516152 AP0504, Indigo Carmine Aluminium Lake.

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 30°C.

6.5 NATURE AND CONTENTS OF CONTAINER

Nicabate Mini Lozenges are presented in a polypropylene tube containing 20 lozenges with a reclosable flip top lid. Pack sizes include 20, 60 and 120 lozenges. Not all pack sizes may be marketed.

Not all pack sizes may be marketed.

All presentations contain information on Nicabate and how to use it.

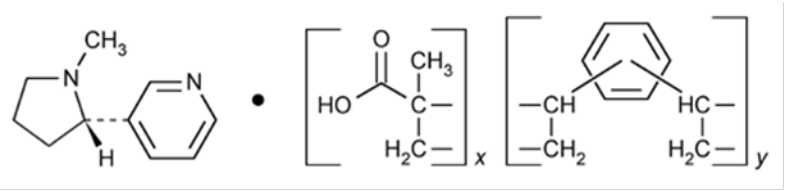
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

Nicotine polacrilex



CAS number : 96055-45-7

7 MEDICINE SCHEDULE (POISONS STANDARD)

Unscheduled

8 SPONSOR

Haleon

Sydney, NSW, Australia

Telephone: 1800 028 533

www.haleon.com

9 DATE OF FIRST APPROVAL

NICABATE MINI LOZENGES nicotine 2 mg Mint Flavour

(AUST R 392045) 31 October 2022

NICABATE MINI LOZENGES nicotine 4 mg Mint Flavour

(AUST R 392046) 31 October 2022

10 DATE OF REVISION

9 May 2024

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	Updates to multiple sections and statements, change to sponsor and contact details, removal of discontinued products.