New Zealand Data Sheet

1 HABITROL 2 mg, 4 mg chewing gum

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Habitrol Chewing Gum contains 2 mg or 4 mg of nicotine as a nicotine resin in a chewing gum formulation.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Chewing gum

Gum pieces are rectangular in shape and white to off-white in colour and are available in fruit and mint flavours.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Habitrol Chewing Gum is indicated for the relief of nicotine withdrawal symptoms in nicotine dependency, as an aid to smoking cessation. Habitrol Chewing Gum 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. Habitrol Chewing Gum may be used by smokers who are unable or not ready to quit on occasions when temporary abstinence from smoking is desired.

4.2 Dose and method of administration

Dose

Quit Now Program

The patient should be advised to stop smoking completely when starting the Habitrol Quit Now Program.

The strength of Habitrol Nicotine Chewing Gum should be chosen according to the smoker's tobacco dependence. Highly dependent smokers (those smoking 20 or more cigarettes per day), 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 slowly when the user feels the urge to smoke. The number chewed should normally be 8-12 pieces of 2 mg gum per day, up to a maximum of 20 per day; or 4-6 pieces of 4 mg gum per day, up to a maximum of 10 per day. Do not use more than one piece of gum per hour.

Use in children under 18 years

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

Adolescents aged 12 to 17 years should only use Habitrol Chewing Gum with the advice of a healthcare professional. Treatment should not exceed 12 weeks without consultation with a healthcare professional. Before recommending the use of NRT beyond 12 weeks in this age group, the healthcare professional should reassess the user's commitment to smoking cessation and the likely benefit of continued treatment; treatment should not be extended by more than a further 4 weeks.

Do not use in children under 12 years.

Instructions for use

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.

Patients should not eat or drink while a gum is in the mouth.

1. Chew one piece of gum until the taste becomes strong
2. Rest the gum between the gum and cheek
3. When the taste fades, recommence chewing
4. The chewing routine should be repeated for 30 minutes.

After 3 months, users should gradually cut down the number of gum pieces chewed each day until only 1-2 pieces of gum per day are required, at which time use of the gum should be stopped. 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.

Reduce to Quit Program (gradual cessation of smoking)

For smokers who are unwilling or unable to suddenly quit smoking, Habitrol Chewing Gum may be used , 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 smoker can quit completely, then the Quit Now 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 a smoker has previously relapsed with use of a single 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 Habitrol Patches Step 1 with Habitrol Chewing Gum 2 mg. Habitrol Chewing Gum 4 mg should not be used with Habitrol Patches.

When using Habitrol Patches Step 1 in addition to Habitrol Chewing Gum 2 mg, it is recommended that 4-12 pieces of gum are used each day. Most people will use 5-6 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 Habitrol Patches and gradually reduce the number of Habitrol Gum used until no longer needed.
2. Continue with Habitrol Patches Step 2 for 3-4 weeks, then Habitrol Patches Step 3 for a further 3-4 weeks while maintaining the number of Habitrol Chewing Gum 2 mg used each day. After use of patches is ceased, gradually reduce the number of gum used until no longer needed.

Users should stop smoking completely during treatment with Habitrol Chewing Gum 2 mg in combination with Habitrol patches.

Temporary abstinence

Smokers who are unable or not ready to quit may use the Habitrol Chewing Gum on occasions when temporary abstinence from smoking is required (for example, in smoke-free areas, at their place of work, on a plane or in other situations where they cannot or choose not to smoke, and there is an urge to smoke). Refer to “Dose” to select the most appropriate Habitrol Chewing Gum strength based on daily cigarette usage.

4.3 Contraindications

Habitrol Chewing Gum should not be used by non-smokers, children under 12 years 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 doses of only milligrams are potentially fatal if rapidly absorbed. For any smoker, with or without concomitant disease or pregnancy, the risk of NRT use in a smoking cessation program should be weighed against the hazard of continued smoking and the likelihood of achieving cessation of smoking without NRT.

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

Therapeutic 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 Overdosage). Habitrol Chewing Gum must be kept out of reach of children at all times.

Nicotine-dependent smokers with a recent myocardial infarction, severe cardiac arrhythmias, or recent cerebrovascular accident should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). If this fails, Habitrol may be considered, but as data on safety in these patient groups are limited, initiation should only be under close medical supervision. If there is a clinically significant increase in cardiovascular or other effects attributable to nicotine, the gum should be reduced or discontinued.

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

Habitrol should be used with caution in patients with:

- severe hypertension, stable angina pectoris, cerebrovascular disease, occlusive peripheral arterial disease, heart failure
- hyperthyroidism or phaeochromocytoma,
- moderate to severe hepatic impairment and/or severe renal impairment; active peptic ulcer.

Seizures: Potential risks 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.
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 patients with active oesophagitis, gastritis, gastric ulcer or peptic ulcer. Avoid use of Habitrol Chewing Gum if oral or pharyngeal inflammation is present.

As with other gums, Habitrol Chewing Gum may stick to dentures, dental caps or partial bridges and may damage dental work.

Special warnings about excipients
Because Habitrol Chewing Gum contains sorbitol, patients with rare hereditary conditions of fructose intolerance should not take this medicine.

The gum base contains butylated hydroxytoluene (E321) which may cause local irritation to the mucous membranes.

Habitrol Gums contain saccharin, saccharin sodium, phenylalanine and sulfites. Habitrol Gum Fruit flavour also contains benzoates.

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

Each gum also contains 11.4 mg sodium, which should be taken into account by those on a low sodium diet. For the 2 mg strength, this is equivalent to 228.6 mg sodium per maximum dose of 20 pieces. For the 4 mg strength, this is equivalent to 114.3 mg sodium per maximum dose of 10 pieces.

Paediatric population
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.

4.5 Interaction with other medicines and other forms of interaction

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 reduced clearance of substrates for these enzymes may occur. This may lead to an increased plasma levels for some medicinal products that may be 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 and warfarin, possibly due to reversal of hepatic enzyme induction on smoking cessation
- insulin, possibly due to increased subcutaneous absorption of insulin 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 blood pressure and heart rate reduction effect of beta-adrenergic blockers (e.g. propranolol) and reduced responder rates in ulcer healing with H_2 antagonists.

Both smoking and nicotine administration may raise the blood levels of cortisol and catecholamines. Dosages of nifedipine, adrenergic antagonists and adrenergic agonists may require adjustment.

4.6 Pregnancy and lactation

Pregnancy (Category D)

In pregnant women, complete cessation of tobacco consumption should always be recommended, without NRT use. 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 foetal risk is expected to be less than that of continued smoking due to:

- Lower maximal plasma concentrations with NRT compared with inhaled nicotine, resulting in nicotine exposure lower or no more than associated with smoking.
- No exposure to polycyclic hydrocarbons and carbon monoxide with NRT.

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 2-3 months.

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

Breast-feeding

Even in therapeutic doses, nicotine is excreted in breast milk in quantities that may affect the child. Like smoking, NRT should be avoided during breast-feeding. However HABITROL Chewing Gum or Lozenge 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.

4.7 Effects on ability to drive and use machines

Smoking cessation can cause behavioural changes. Any risks associated with driving a vehicle or operating machinery are considered minimal if Habitrol Chewing Gum is used according to the recommended dose.

4.8 Undesirable effects

Habitrol Chewing Gum can cause adverse reactions similar to those associated with nicotine administered in other ways.

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 hiccups. Those people with a tendency to indigestion may suffer initially from slight dyspepsia or heartburn. Slower chewing will usually overcome this problem.

Excessive consumption of nicotine chewing gum by non-smokers may lead to nausea, faintness or headache.

Increased frequency of aphthous ulcer may occur after abstinence from smoking.

The chewing gum may stick to and, in rare cases, damage dentures and dental appliances.

Adverse reactions are listed below, by system organ class and frequency. Frequencies are defined as: *very common* (≥1/10), *common* (≥1/100 to <1/10), *uncommon* (≥1/1,000 to <1/100), *rare* (≥1/10,000 to <1/1,000) or *very rare* (<1/10,000).

Nervous system disorders:	Common: headache, dizziness
Gastrointestinal disorders:	Very common: nausea Common: salivary hypersecretion, stomatitis, oral pain, pharyngolaryngeal pain, hiccups, vomiting, dyspepsia and flatulence
Musculoskeletal, connective and bone disorders:	Common: jaw muscle ache
Cardiac disorders:	Uncommon: palpitations Rare: atrial arrhythmia
Skin and subcutaneous tissue disorders:	Uncommon: erythema, urticaria
Immune system disorders:	Rare: hypersensitivity, angioneurotic oedema and anaphylactic reactions

Certain symptoms such as dizziness, headaches and insomnia may be ascribed to withdrawal symptoms from smoking cessation and may be due to insufficient administration of NRT.
Cold sores may develop in association with smoking cessation, but any relationship with NRT is unclear.

The patient may continue to experience nicotine dependence after smoking cessation.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https//nzphvc.otago.ac.nz/reporting/

4.9 Overdose

In overdose, symptoms corresponding to those with heavy smoking may be seen.

The acute lethal oral dose is about 0.5 - 0.75 mg/kg body weight, or 40-60 mg in an adult. Therapeutic doses of nicotine that are tolerated by adult smokers 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.

Signs and symptoms of an overdose from Habitrol Chewing Gum would be expected to be the same as those of acute nicotine poisoning, including pallor, salivation, hyperhidrosis, vomiting, abdominal pain, diarrhoea, headache, dizziness, sensory disturbance, tremor, confusional state and asthenia.

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

Overdose with Habitrol 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 and any that is absorbed will be inactivated by the liver.

Treatment of Overdose

In the event of overdose or suspected overdose, seek immediate medical advice or contact the Poisons Information Centre (Telephone: New Zealand 0800 764 766)

Treatment of overdose should be immediate as symptoms may develop rapidly. Emesis is usually spontaneous. Administration of oral activated charcoal and gastric lavage should be considered as soon as possible and within 1 hour of ingestion. Monitor vital signs and treat symptomatically.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: drugs used in nicotine dependence, ATC code: N07BA01

<u>Mechanism of action</u>

Nicotine Chewing Gum mimics the pharmacological effects of nicotine from smoking and therefore may be used to help provide relief from nicotine withdrawal symptoms.

5.2 Pharmacokinetic properties

When Habitrol Chewing Gum is chewed, nicotine is steadily released into the mouth and is rapidly absorbed across the buccal mucosa. A proportion of nicotine reaches the stomach and intestine, by the swallowing of nicotine containing saliva, where it is inactivated.

The peak plasma nicotine concentration following a single dose of 2 mg gum is approximately 6.4 ng/mL (at approximately 45 minutes). The peak plasma nicotine concentration following a single dose of 4 mg gum is approximately 9.3 ng/mL (at approximately 60 minutes). The average plasma nicotine concentration 45 minutes after smoking a cigarette is 15-30 ng/mL.

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

Nicotine is eliminated mainly via hepatic metabolism; small amounts being eliminated in unchanged form, via renal excretion. The plasma half-life is approximately 3 hours.

5.3 Preclinical safety data

No animal studies have been undertaken on Habitrol Chewing Gum. The toxicity of nicotine as a constituent of tobacco has been well documented. Acute toxic effects include convulsions, cardiac insufficiency, and paralysis of the respiratory system. In cats and dogs, nicotine at high doses has been shown to potentiate histamine-induced peptic ulcer. Nicotine has no genotoxic activity in most of the mutagenicity test systems. The well-known carcinogenicity of tobacco smoking is predominantly caused by pyrolysis products. However, use of nicotine chewing gum avoids the high temperature required for the formation of these carcinogenic products.

Reproductive toxicity studies with nicotine in several animal species have demonstrated non-specific retardation of foetal growth. Studies in rats produced evidence of decreased fertility, prolonged pregnancy, and behavioural disorders in the offspring. In mice, the offspring of animals exposed to very high doses of nicotine showed skeletal defects in the peripheral limbs. Overall, there is no clear-cut evidence that nicotine at the concentrations produced with nicotine gum treatment has teratogenic potential and/or inhibitory effects on fertility.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Habitrol Chewing Gum contains the following excipients:

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)
Saccharin
Saccharin sodium
Acesulfame potassium
Xylitol

Flavours: Fruit – fruit flavour. Mint – eucalyptus oil, peppermint oil.

6.2 Incompatibilities
Not applicable

6.3 Shelf life
30 Months

6.4 Special precautions for storage
Store below 25ºC. Store in the original package.

6.5 Nature and contents of container
Boxes containing 96 or 204 pieces of gum (12 pieces of gum per blister pack).
Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements.

7 MEDICINE SCHEDULE
General Sale Medicine

8 SPONSOR
Haleon
12 Madden Street
Wynyard Quarter
Auckland 1010
New Zealand
FREECALL NZ: 0800 540 144

9 DATE OF FIRST APPROVAL
10 April 2008

10 DATE OF REVISION OF THE TEXT

22 May 2023

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
	-
4.4	Sodium and allergen content in product
8	Sponsor details