

New Zealand Data Sheet

- 1 HABITROL Step 1 (nicotine 21 mg/24 hours) transdermal patch
- HABITROL Step 2 (nicotine 14 mg/24 hours) transdermal patch
- HABITROL Step 3 (nicotine 7 mg/24 hours) transdermal patch

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Habitrol 7 mg/24 hours

One Habitrol transdermal patch contains 17.5 mg of nicotine in a patch size of 10 cm², releasing a nominal 7 mg of nicotine per 24 hours.

Habitrol 14 mg/24 hours

One Habitrol transdermal patch contains 35.0 mg of nicotine in a patch size of 20 cm², releasing a nominal 14 mg of nicotine per 24 hours.

Habitrol 21 mg/24 hours

One Habitrol transdermal patch contains 52.5 mg of nicotine in a patch size of 30 cm², releasing a nominal 21 mg of nicotine per 24 hours.

To sustain the concentration gradients for diffusion, more nicotine is contained in the Habitrol Patch than is actually delivered over 24 hours. Habitrol Patch releases approximately 0.7 mg/cm²/24 hours of nicotine. Therefore, the average daily dose administered is determined largely by the size of the contact area of the system.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Transdermal patch

Round, flat, matrix patch with yellow-ochre backing foil.

Habitrol 7 mg/24 hours

7 mg/24h is code-marked CWC.

Habitrol 14 mg/24 hours

14 mg/24h is code-marked FEF.

Habitrol 21 mg/24 hours

21 mg/24h is code-marked EME.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of nicotine dependence, as an aid to smoking cessation.

4.2 Dose and method of administration

Dose

The patient should be advised to stop smoking completely when starting treatment with HABITROL Patch.

For those smoking more than 20 cigarettes a day it is recommended that treatment be started with HABITROL Step 1 Patch. Those smoking less than 20 cigarettes a day should start with HABITROL Step 2.

Patients starting on HABITROL Step 1 should use this strength for 3 to 4 weeks, before moving onto Step 2 for 3 to 4 weeks, and finally Step 3 for 3 to 4 weeks.

Patients starting on HABITROL Step 2 may switch to Step 3 after 3 to 4 weeks, or continue to use Step 2 for 6 to 8 weeks before moving onto Step 3 for 3 to 4 weeks.

How quickly the patient moves through the program will vary depending on individual response, and maintaining or increasing the dose may be necessary if abstinence is not achieved or if withdrawal symptoms are experienced.

The treatment duration is about 3 months but may vary as a function of individual response. Intermittent dosing products (such as HABITROL Chewing Gum) may be used beyond 3 months if necessary, but those using NRT for more than 9 months should seek advice from a healthcare professional.

Use in children under 18 years

Children aged 12 to 17 years should only use HABITROL Patch under the advice of a healthcare professional. The use of NRT in children aged 12 to 17 years should only be used when the benefits of abstinence outweigh the risks of continued smoking. Treatment should not exceed 12 weeks without consultation with a healthcare professional, who can reassess the patient for their commitment to quit and the benefits of continued treatment. If treatment is continued, it should not be extended for more than another four weeks.

Children aged 12 to 17 years should not quit with Combination Therapy.

Do not use in children under 12 years.

Use in the elderly

Experience in the use of HABITROL Patch in smokers over the age of 65 years is limited.

Instructions for use

HABITROL should be applied as soon as it has been removed from the see-through child-resistant pouch. The sachet has a pre-cut edge to facilitate removal of the HABITROL Patch contents. Following removal of the metallic backing, the HABITROL Patch should be immediately applied to a clean non-hairy, dry area of intact skin on the trunk or upper arm. Do not apply patch to skin that is red, broken or irritated. The patch should be held in position for 10-20 seconds with the palm of the hand. A different site of application should be chosen each day. One should allow 1 week to elapse before using the same area again, to avoid risk of local irritation.

Hands should be washed thoroughly after application of HABITROL Patch to avoid irritation of the eyes with nicotine from the fingers.

After removal, used patches should be disposed of carefully and kept out of sight and reach of children.

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 HABITROL Patch Step 1 with another form of NRT such as HABITROL Chewing Gum 2 mg or HABITROL Lozenge 1mg. HABITROL Chewing Gum 4 mg and HABITROL Lozenge 2mg should not be used with HABITROL Patches.

Users should stop smoking completely during treatment with combination therapy.

Use of HABITROL Patch Step 1 with HABITROL Chewing Gum 2mg

When using HABITROL Patch Step 1 in addition to HABITROL 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:

- Stop use of HABITROL Patch and gradually reduce the number of gums used until they are no longer needed.
- Continue with HABITROL Patch Step 2 for 3-4 weeks, then HABITROL Patch Step 3 for a further 3-4 weeks while maintaining the number of HABITROL 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 of HABITROL Patch Step 1 with HABITROL Lozenge 1mg

When using HABITROL Patch Step 1 in addition to HABITROL Lozenge 1 mg, it is recommended that 4 to 12 lozenges are used each day. Most people will use 5 to 6 lozenges. Do not exceed 12 lozenges a day.

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

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

4.3 Contraindications

HABITROL Patch should not be used for non-smokers or occasional smokers, children under 12 years of age, those with diseases of the skin (which may complicate patch therapy) or known hypersensitivity to nicotine or to any of the components of the therapeutic system.

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 while using HABITROL and the likelihood of achieving cessation of smoking without nicotine replacement.

Treatment with HABITROL Patch should be discontinued if symptoms of nicotine overdose appear. Mild intoxication produces nausea, vomiting, abdominal pain, diarrhoea, headache, sweating, and weakness (see "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. Both before and after use, HABITROL Patch contains a significant amount of nicotine. Keep patches out of sight and reach of children. Patients must be cautioned that the patches are not to be handled casually or left where they might be inadvertently misused or consumed by children. Care must be exercised in the handling and disposal of both the fresh and the used patches so that they do not fall into the hands of children under any circumstances.

As soon as a patch is removed from the skin, it should be folded firmly in half, with the sticky sides together, and disposed of with utmost care. Similarly, the patches should not be stored or disposed of where they might be consumed by pets.

Occasional smokers are not expected to benefit from the use of HABITROL.

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, HABITROL may be considered but as data on safety in these patient groups are limited, initiation should only be under close medical supervision.

Combination therapy should not be used in people with known cardiovascular disease unless the benefits outweigh the risks.

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 and/or moderate to severe renal impairment,
- gastric ulcer or peptic ulcer, active oesophagitis, oral and pharyngeal inflammation or gastritis.

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. Blood sugar levels may be more variable during smoking cessation, with or without NRT.

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.

HABITROL patch should be used with caution in patients who are susceptible to angioedema and/or urticaria. Patients with a history of dermatitis, or with generalised dermatological disorders such as psoriasis or chronic dermatitis should not use the patch (see “Contraindications”).

In the event of a severe or persistent skin reaction, discontinue treatment and use another pharmaceutical form.

HABITROL Patch contains aluminum. The patch should be removed prior to undergoing any MRI (Magnetic Resonance Imaging) procedures.

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 cessation itself may require adjustment of some drug therapy.

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.

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 H2-antagonists.

Both smoking and nicotine may raise the blood levels of cortisol and catecholamines, i.e. may lead to a reduced effect of nifedipine or adrenergic antagonist and to an increased effect of adrenergic agonists.

Increased subcutaneous absorption of insulin which occurs upon smoking cessation may necessitate a reduction in insulin dose.

4.6 Pregnancy and lactation

Pregnancy

Adverse reproductive and developmental effects have been reported following exposure to tobacco and nicotine during pregnancy. 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, if the expected benefits to the mother outweigh the potential risks to the foetus. 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, intermittent dosing products (such as HABITROL Chewing Gum or Lozenge) should preferably be used while pregnant as the gums 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.

Breast-feeding

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. HABITROL Patch should not be used while breastfeeding. Should smoking withdrawal not be achieved, intermittent NRT products such as HABITROL Chewing Gum may be used rather than Habitrol patches. However the use of any form of NRT in breastfeeding women should be initiated only if the expected benefits to the nursing mother outweigh the potential risks to the

infant. 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

When HABITROL Patch is used as recommended there are minimal risks for driving vehicles or operating machinery. Nevertheless one should take into consideration that smoking cessation can cause behavioural changes.

4.8 Undesirable effects

In principle, HABITROL Patch can cause adverse reactions similar to those associated with nicotine administered by smoking. Since the maximum plasma concentrations of nicotine that are produced by HABITROL Patch are lower than those produced by smoking and fluctuate less, nicotine-related adverse reactions occurring during treatment with HABITROL Patch can be expected to be less marked than during smoking.

Clinical trial experience has shown that skin reactions at the application sites are the most frequent adverse reactions. This led to premature discontinuation of HABITROL Patch in about 6% of clinical trial participants. These reactions include application site erythema, pruritus, oedema, burning sensation, rash, irritation, urticaria and vesicles. Most of the skin reactions resolved within 48h, but in more severe cases they lasted from 1 to 3 weeks. The onset of significant skin reactions occurred between 3 and 8 weeks from the start of therapy. Upper respiratory tract infection and cough reported as adverse reactions may be linked to a chronic bronchitis induced by long term smoking in the past.

If there is a clinically significant increase in cardiovascular or other effects attributable to nicotine, the Habitrol patch dose should be reduced or discontinued.

Aphthous stomatitis may develop in connection with smoking cessation, but any relation with the nicotine treatment is unclear.

Certain symptoms which have been reported such as depression, irritability, nervousness, restlessness, mood lability, anxiety, drowsiness, impaired concentration, insomnia and sleep disturbances may be related to withdrawal symptoms associated with smoking cessation. Subjects quitting smoking by any means could expect to suffer from asthenia, headache, dizziness, coughing or influenza-like illness.

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$), or not known (can not be estimated from available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

SYSTEM ORGAN CLASS	VERY COMMON ($\geq 1/10$)	COMMON ($\geq 1/100$ to $< 1/10$)	UNCOMMON ($\geq 1/1,000$ to $< 1/100$)	RARE ($\geq 1/10,000$ to $< 1/1,000$)	VERY RARE ($< 1/10,000$)
Immune system disorders			hypersensitivity*		anaphylactic reactions
Psychiatric disorders	sleep disorders including abnormal dreams and insomnia	nervousness			
Nervous system disorders	dizziness, headache	tremor			
Cardiac disorders		palpitations	tachycardia	arrythmia	
Respiratory, thoracic and mediastinal disorders		cough, dyspnoea, pharyngitis			
Gastrointestinal disorders	nausea, vomiting	abdominal pain upper, dyspepsia, diarrhoea, dry mouth, constipation			
Skin and subcutaneous tissue disorders		hyperhidrosis			dermatitis allergic*, dermatitis contact*, photosensitivity
Musculoskeletal, connective tissue and bone disorders		myalgia, arthralgia			
General disorders and administration site conditions	application site reactions*	application site pain, asthenia, fatigue	malaise, influenza type illness		

*The majority of topical reactions are minor and resolve quickly following removal of the patch. Pain or sensation of heaviness in the area around which the patch is applied (e.g. chest, limbs) may be reported.

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 to <https://pophealth.my.site.com/carmreportnz/s/>.

4.9 Overdose

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

The acute lethal oral dose of nicotine is about 0.5 - 0.75 mg per kg body weight, corresponding in an adult to 40 - 60 mg. Even small quantities of nicotine are dangerous in children, and may result in severe symptoms of poisoning which may prove fatal. If poisoning is suspected in a child, a doctor must be consulted immediately.

Overdose with HABITROL Patch may occur when many patches are applied simultaneously on the skin.

Signs and symptoms of an overdose from a nicotine patch would be expected to be the same as those of acute nicotine poisoning, including pallor, hyperhidrosis, salivation, vomiting, abdominal pain, diarrhoea, headache, dizziness, 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

Overdose from Topical Exposure

The nicotine patches should be removed immediately in the event of an overdose or if the patient shows signs of overdosage. The skin surface may be flushed with water and dried. No soap should be used, since it may increase nicotine absorption. Nicotine will continue to be delivered into the bloodstream for several hours after removal of the system because of a depot of nicotine in the skin.

Overdose from Ingestion

All nicotine intake should stop immediately and the patient treated symptomatically and all vital signs monitored.

General considerations

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Mechanism of action

Nicotine acts primarily on cholinergic receptors of the nicotine type in the peripheral and in the central nervous system. Nicotine 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.

Pharmacodynamic effects

Nicotine, the primary alkaloid in tobacco products and a naturally occurring autonomous substance, is a nicotine receptor agonist in the peripheral and central nervous systems. On consumption of tobacco products, nicotine has proven to be addictive.

Quitting smoking abruptly after prolonged, daily consumption induces a withdrawal syndrome consisting of at least four of the following symptoms: dysphoria or depressive mood, insomnia, irritability, feelings of frustration or anger, anxiety, difficulty concentrating, agitation or impatience, slowed cardiac rhythm, increased appetite and weight gain. The craving for nicotine is considered as a recognized clinical symptom of the withdrawal syndrome.

Clinical trials have shown that nicotine replacement products may help smokers refrain from smoking or reduce their smoking habits by decreasing the withdrawal symptoms.

5.2 Pharmacokinetic properties

Absorption

Nicotine is readily absorbed through the skin into the systemic circulation. The absorption profile after single application of HABITROL Patch to healthy abstinent smokers (patients undergoing a course of smoking cessation therapy with the patch) shows an initial 1-2 hours delay followed by a progressive rise in plasma concentrations, plateaus being attained at about 8-10 hours after application.

After the patch is removed, plasma concentrations decline more slowly than would be predicted by the 2-hour elimination half-life for this agent after an intravenous infusion.

About 10% of the total amount of nicotine that reaches the circulation is delivered from the skin after HABITROL Step 1 Patch is removed. This is likely due to the existence of a cutaneous deposit of nicotine. The absolute bioavailability of the patch, compared to intravenous nicotine perfusion, is about 77%.

The area under the plasma concentration curve (0-24h) increases in proportion to the dose of nicotine delivered by the patches: HABITROL Patch 7mg, 14mg and 21mg per 24h. With repeated application of HABITROL Patch 14mg/24h and 21mg/24h, mean minimum and maximum plasma concentrations at steady state were 7.1 ng/mL to 12.0 ng/mL and 10.3 ng/mL to 17.7 ng/mL respectively.

Distribution

Nicotine is distributed widely in the body with a volume of distribution between 1 and 3 L/kg. It crosses the blood-brain barrier and the placenta. Plasma protein binding of nicotine is

negligible, less than 5%. Therefore changes in nicotine binding from use of concomitant drugs or alternations of plasma proteins by disease states would not be expected to have significant consequences.

Elimination

The major eliminating organ is the liver and the main metabolites are cotinine and nicotine 1'-N-oxide. Renal excretion of unchanged nicotine is pH-dependent and minimal under alkaline conditions.

Nicotine is excreted in breast milk.

5.3 Preclinical safety data

Nicotine was positive in some in vitro genotoxicity tests but there are also negative results with the same test systems. Nicotine was negative in standard in vivo tests.

Animal experiments have shown that nicotine induces post-implantation loss and reduces the growth of fetuses.

The results of carcinogenicity assays did not provide any clear evidence of a tumorigenic effect of nicotine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Drug solution:

Basic butylated methacrylate copolymer

External layer:

Aluminium coated polyester foil

Matrix layer:

Acrylate-vinylacetate copolymer

Triglycerides, medium-chain

Basic butylated methacrylate copolymer

Non-woven backing:

Paper 26g/m²

Adhesive layer:

Acrylate-vinylacetate copolymer

Triglycerides, medium-chain

Detachable protective film:

Siliconised aluminized polyester film

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store at or below 30°C.

6.5 Nature and contents of container

One transdermal patch per sachet.

Boxes containing 7 or 28 patches.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

The transdermal patch should be folded in half sticky side inwards before being discarded.

7 MEDICINE SCHEDULE

General Sale Medicine

8 SPONSOR

Haleon New Zealand ULC

Private Bag 106600

Downtown

Auckland 1143

New Zealand

FREECALL NZ: 0800 540 144

9 DATE OF FIRST APPROVAL

30 August 1990

10 DATE OF REVISION OF THE TEXT

17 January 2024

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
4.2	Dose – Use in children under 18 years <ol style="list-style-type: none">Added: The use of NRT in children aged 12 to 17 years should only be used when the benefits of abstinence outweigh the risks of continued smoking Instructions for Use <ol style="list-style-type: none">Multiple updates to application instructionsMultiple updates to combination therapy section
4.4	<ol style="list-style-type: none">Addition of more restrictive safety related statements

	2. Addition of further warnings for diabetic users
4.5	1. Added: Smoking cessation itself may require adjustment of some drug therapy.
4.6	1. Updates to usage while pregnant or breastfeeding
4.8	1. Added: If there is a clinically significant increase in cardiovascular or other effects attributable to nicotine, the Habitrol patch dose should be reduced or discontinued. 2. Minor typographical corrections 3. Update to adverse reactions email address
4.9	1. Addition of header 'General considerations'
5.1	1. Minor typographical corrections
6.1	1. Removal of printing ink excipients
8	1. Update to sponsor details

