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. 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.

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. 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 several days to elapse before using the same area again.

*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.

**Use of HABITROL Patch Step 1 with HABITROL Chewing Gum 2mg**
When using HABITROL Patch Step 1 in addition of 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 of 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 overdosage 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. 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.

HABITROL 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.

HABITROL patch should be used with caution in patients who are susceptible to angioedema and/or urticaria. Patients 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 2 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 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
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, 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. Intermittent NRT products such as HABITROL Chewing Gum may be used. 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 the erythema and infiltration 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.

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

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); very rare (< 1/10,000), or not known (can not to be
estimated from available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

<table>
<thead>
<tr>
<th>SYSTEM ORGAN CLASS</th>
<th>VERY COMMON (≥1/10)</th>
<th>COMMON (≥1/100 to &lt;1/10)</th>
<th>UNCOMMON (≥1/1,000 to &lt;1/100)</th>
<th>RARE (≥1/10,000 &lt;1/1,000)</th>
<th>NOT KNOWN (cannot be estimated from available data)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune system disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Allergic reactions such as urticaria, rash and pruritus; angioedema and anaphylactoid reaction</td>
</tr>
<tr>
<td>Psychiatric disorders*</td>
<td>agitation, anxiety, nervousness, insomnia, abnormal dreams</td>
<td>disturbance in attention, somnolence, effect lability, irritability, depressed mood and confusional state</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nervous system disorders*</td>
<td>headache, dizziness, motor dysfunction</td>
<td>paraesthesia, dysgeusia and blurred vision</td>
<td></td>
<td>tremor</td>
<td></td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>chest pain, dyspnea and arrhythmia</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td></td>
<td></td>
<td>hypertension and hot flush</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>cough</td>
<td>upper respiratory tract infections</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorders*</td>
<td>nausea, abdominal pain, dyspepsia</td>
<td>vomiting, constipation, diarrhea, flatulence, dry mouth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
<td></td>
<td>hyperhidrosis</td>
<td></td>
<td>skin discoloration, cutaneous vasculitis</td>
</tr>
<tr>
<td>Musculoskeletal, connective tissue and bone disorders</td>
<td>myalgia, arthritis</td>
<td>arthralgia, muscle cramp and back pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>application site reactions</td>
<td>asthenic conditions, pain and discomfort</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Symptoms may be ascribed also to withdrawal symptoms in connection with smoking cessation and may be due to insufficient replacement of nicotine.
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.

General symptoms of nicotine poisoning may include: weakness, sweating, nausea, salivation, vomiting, abdominal pain, diarrhoea, headache, hearing and vision disturbances, tachycardia and cardiac arrhythmia, dyspnea, prostration, circulatory collapse, coma and terminal convulsions.

Treatment of Overdose
Treatment of overdose should be immediate as symptoms may develop rapidly. Immediately discontinue nicotine administration and institute symptomatic treatment. Monitor vital signs.

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 stereoslectively 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
Printing ink:
Brown ink

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years

6.4 Special precautions for storage
Store at or below 30ºC.

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**  
GlaxoSmithKline Consumer Healthcare  
Level 11 Zurich House  
21 Queen Street  
Auckland 1010  
New Zealand  
FREECALL NZ: 0800 540 144

9 **DATE OF FIRST APPROVAL**  
30 August 1990

10 **DATE OF REVISION OF THE TEXT**  
03 April 2017

**SUMMARY TABLE OF CHANGES**

<table>
<thead>
<tr>
<th>Section changed</th>
<th>Summary of new information</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.4</td>
<td>Use with caution in patients with active peptic ulcer added</td>
</tr>
<tr>
<td>All</td>
<td>Transferred to new data sheet template</td>
</tr>
</tbody>
</table>