

Data Sheet

HABITROL LOZENGE

Nicotine lozenge 1 mg, 2 mg

Presentation

HABITROL lozenge contains 1 mg or 2 mg of nicotine in a lozenge formulation. Lozenges are white and round in shape and available in mint flavour.

Uses

Actions

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

Pharmacokinetics

The absorbed amount of nicotine depends on the amount released into the mouth and absorbed through the buccal mucosa.

The main part of nicotine in HABITROL Lozenges are absorbed through the buccal mucosa. A proportion, by the swallowing of nicotine containing saliva, reaches the stomach and intestine where it is inactivated. Due to the first-pass effect in the liver, the systemic bioavailability of nicotine is low. Consequently, in the treatment with HABITROL Lozenges the high and quick systemic nicotine concentration, as seen when smoking, is rarely obtained.

Distribution volume after intravenous administration of nicotine is approximately (2-3) L/kg and the half-life is 2 hours. Nicotine is metabolised principally in the liver and the plasma clearance is approximately 1.2 L/min; nicotine also metabolises in the kidney and lungs. Nicotine crosses the blood-brain barrier.

More than 20 metabolites have been identified, all believed to be less active than nicotine. The main metabolite is cotinine, which has a half-life of 15-20 hours and with approximately 10 times higher plasma concentration than nicotine. Nicotine's plasma-protein binding is less than 5%. Changes in nicotine binding from the use of concomitant drugs or due to altered disease state are not expected to have significant effect on nicotine kinetics. The main metabolite in urine is cotinine (15% of the dose) and trans-3-hydroxy cotinine (45% of the dose).

About 10% of the nicotine is excreted unchanged. Up to 30% may be excreted with urine in increased diuresis and acidity (under pH 5).

The peak value for the plasma concentration of the 1mg lozenge after a single dose is approximately 4 nanogram per mL and the maximal concentration at steady state is approximately 10.6 nanogram per mL (average plasma concentration of nicotine after smoking one cigarette is 15-30 nanogram per mL). Peak plasma concentration is reached after about 45 minutes following sucking of a single lozenge and after about 30 minutes at steady state.

The peak value for the plasma concentration of the 2mg lozenge after a single dose is approximately 7 nanogram per mL and the maximal concentration at steady state is approximately 22.5 nanogram per mL (average plasma concentration of nicotine after smoking one cigarette is 15-30 nanogram per mL). Peak plasma concentration is reached after about 48 minutes following sucking of a single lozenge and after about 30 minutes at steady state.

Indications

HABITROL Lozenge treatment is indicated for the relief of nicotine withdrawal symptoms, in nicotine dependency as an aid to smoking cessation. May be used as part of a smoking reduction strategy by smokers who are unable or not ready to stop smoking abruptly as a step towards stopping completely. May be used by smokers who are unable or not ready to quit on occasions when they want to temporarily abstain from smoking.

Dosage and Administration

The strength of HABITROL Lozenge should be chosen according to the smoker's tobacco dependence. Highly dependent smokers, as well as smokers who have failed to quit when using the 1 mg lozenge, should use the 2 mg lozenge. Otherwise, the 1 mg strength should be used.

One lozenge should be sucked slowly when the user feels the urge to smoke. The amount chewed should normally be 8-12 per day, up to a maximum of 25 of the 1 mg lozenge or 15 of the 2 mg lozenge per day.

Directions 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 sucking the lozenge.

1. One lozenge should be sucked slowly until the taste becomes strong.
2. The lozenge should be rested between the gum and cheek.
3. When the taste fades, sucking should commence again.
4. This routine should be repeated for 30 minutes.

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

Gradual cessation of smoking

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

Combination therapy

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

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:

1. Stop use of HABITROL Patch and gradually reduce the number of lozenges used until they are no longer needed.
2. 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.

Use in children under 18 years

Children aged 12 to 17 years should only use HABITROL Lozenges under the advice of a healthcare professional. Treatment should not exceed 12 weeks without consultation with a healthcare professional, who should reassess the person for their commitment to quitting smoking and the likely benefit of continued treatment, before recommending use of NRT in this age group beyond 12 weeks. Treatment should not be extended by more than a further 4 weeks in this case. Do not use in children under 12 years.

Temporary Abstinence

Smokers who are unable or not ready to quit may use HABITROL lozenges on occasions when they want to temporarily abstain from smoking. 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 'Dosage and Administration' to select the most appropriate gum strength based on daily cigarette consumption.

Contraindications

Do not use HABITROL Lozenges if:

- you are hypersensitive to nicotine or any other excipients of the lozenge.
- you are a non-smoker
- you are under 12 years of age.

Warnings and Precautions

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

Treatment with HABITROL Lozenges should be discontinued if symptoms of nicotine overdose appear. Mild intoxication produces nausea, vomiting, abdominal pain, diarrhoea, headache, sweating, and pallor (see "Overdosage").

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 Lozenges must be kept out of reach of children at all times.

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 Lozenges 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 severe renal impairment or active peptic ulcer.

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

Swallowed nicotine may exacerbate symptoms in patients suffering from active oesophagitis, gastritis or peptic ulcer. Avoid use of HABITROL Lozenge if oral or pharyngeal inflammation is present.

HABITROL Lozenges contain aspartame, which metabolises to phenylalanine, which is of relevance for patients with phenylketonuria.

Use in 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, HABITROL Lozenge should preferably be used while pregnant as they usually provide a lower daily dose of nicotine than patches. However, if the woman suffers from nausea and/or vomiting, the patch may be preferred but should be removed before going to bed.

Use in Lactation

Nicotine is excreted in breast milk in quantities that may affect the child even in therapeutic doses.

Like smoking, nicotine replacement therapy should be avoided during breast-feeding. However HABITROL Lozenges 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.

Use in children and adolescents

Data on the use of NRT in treating adolescents under the age of 18 years are limited. NRT should only be used in adolescents 12 to 17 years after consultation with a healthcare professional and use should be restricted to 12 weeks. If treatment is required for longer than 12 weeks, this should be discussed with a healthcare professional.

Do not use in children under 12 years.

Effects on ability to drive and use machines

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

Adverse Events

HABITROL Lozenges can cause adverse reactions similar to those associated with nicotine administered in other ways. These can be attributed to the pharmacological effects of nicotine, which are dose-dependent.

Most of the side effects which are reported by patients occur generally during the first 3-4 weeks after initiation of therapy.

Nicotine from lozenges may sometimes cause a slight irritation of the throat and increase salivation at the start of the treatment. Excessive swallowing of nicotine which is released in the saliva may, at first, cause hiccups. Those with a tendency to indigestion may suffer initially from slight dyspepsia or heartburn.

Slower sucking will usually overcome this problem.

Excessive consumption of lozenges by subjects who have not been in the habit of inhaling tobacco smoke, could possibly lead to nausea, faintness and headache.

Common (>1%)

General: Dizziness, headache

GI: Nausea, flatulence, hiccups, epigastritis, dryness of the mouth and irritation of the oral cavity and oesophagus.

Less common (0.1% - 1%)

Circ.: Palpitation

Rare (<0.1%)

Circ: Atrium arrhythmia.

Certain symptoms which have been reported such as dizziness, headache and insomnia may be ascribed to withdrawal symptoms in connection with smoking cessation and may be due to insufficient administration of nicotine.

Cold sores may develop in connection with smoking cessation, but any relation with the nicotine treatment is unclear. The patient may still experience nicotine dependence after smoking cessation.

Interactions

No information is available on interactions between HABITROL lozenge and other medicines

Smoking Cessation

Smoking is associated with increase in CYP1A2 activity. After cessation of smoking, reduced clearance of substrates for this enzyme may occur. This may lead to an increase in plasma levels for some medicinal products of potential clinical importance for products with a narrow therapeutic window, e.g. theophylline, tacrine and clozapine.

The plasma concentration of other drugs metabolised in part by CYP1A2 e.g. caffeine, paracetamol, phenazone, phenylbutazone, pentazocine, lidocaine, benzodiazepines, warafin, oestrogen and vitamin B12 may also increase on cessation of smoking, although data to support this are lacking and the possible clinical significance of this effect for these drugs is unknown.

Smoking may lead to reduced analgesic effects of propoxyphene, reduced diuretic response to furosemide (frusemide), reduced effect of propranolol on blood pressure and heart rate and reduced responder rates in ulcer healing with H2-antagonists.

Smoking and nicotine may raise the blood levels of cortisol and catecholamines, i.e. may lead to a reduced effect of nifedipine or adrenergic antagonists 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.

Overdosage

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 Lozenges may only occur if many lozenges are sucked simultaneously. Risk of overdose is small as nausea or vomiting usually occurs at an early stage.

General symptoms of nicotine poisoning include: weakness, perspiration, salivation, throat burn, nausea, vomiting, diarrhoea, abdominal pain, hearing and visual disturbances, headache, tachycardia and cardiac arrhythmia, dyspnoea, prostration, circulatory collapse, coma and terminal convulsions.

Treatment of overdose:

Seek immediate medical advice or contact the Poisons Information Centre (Telephone 0800 764 766). In the event of overdose, vomiting should be induced

with syrup of ipecac or gastric lavage carried out (wide bore tube). A suspension of activated charcoal should then be passed through the tube and left in the stomach. Artificial respiration with oxygen should be instituted if needed and continued for as long as necessary. Other therapy, including treatment of shock, is purely symptomatic.

Pharmaceutical Precautions

- Store below 25°C.
- Store in the original package.
- Medicines should be kept out of reach of children.

Medicine Classification

General Sale Medicine

Package Quantities

Boxes containing 36 lozenges (12 lozenges per blister platform)

Further Information

Each 1 mg lozenge contains 3.072 mg nicotine bitartrate dehydrate (equivalent to 1 mg nicotine)

Each 2 mg lozenge contains 6.144 mg nicotine bitartrate dehydrate (equivalent to 2 mg nicotine)

Each lozenge contains the following excipients: maltitol, sodium carbonate anhydrous, sodium hydrogen carbonate, polyacrylate dispersion 30%, silica – colloidal anhydrous, xanthan gum, menthol, peppermint oil, aspartame, magnesium stearate.

Each Lozenge contains 9.8 mg sodium per lozenge (equivalent to 245 mg/ maximum dose of 25 of HABITROL Lozenge 1 mg or equivalent to 147 mg / maximum dose of 15 of HABITROL lozenge 2 mg), which should be taken into account by those on a low sodium diet.

Each lozenge also contains 0.88 g maltitol per lozenge (equivalent to 22 g /maximum dose of the 25 of HABITROL Lozenge 1mg, or equivalent to 13.2g/maximum dose of the 15 of HABITROL Lozenge 2mg). Products containing maltitol may have a laxative effect or cause diarrhoea.

Each 1 mg and 2 mg lozenge contains 0.01 g aspartame, a source of phenylalanine, which may be harmful for people with phenylketonuria.

HABITROL Lozenges are sugar-free.

Name and Address

Novartis Consumer Health Australasia Pty Ltd
54 Carbine Rd
Mount Wellington
Auckland 7
Phone: 0800 700 222

Date of Preparation

20 May 2009