QuitX Coated Chewing Gum

Nicotine

PRODUCT INFORMATION

NAME OF MEDICINE

The active ingredient of QuitX Coated Chewing Gum is nicotine.

Chemical Name: 1-methyl-2-(3-pyridyl)pyrrolidine

Structural Formula:

Molecular Formula: C_{10}H_{14}N_2  
Molecular Weight: 162.26  
CAS Registry No.: 54-11-5

DESCRIPTION

The QuitX Coated Chewing Gum contains 2 mg or 4 mg nicotine per piece of gum. It is available in classic and freshmint flavours and is sugar-free.

QuitX Coated Chewing Gum contains nicotine, chewing gum base (containing butylated hydroxytoluene), acesulfame potassium, calcium carbonate, carnauba wax, gelatin, glycerol, mannitol, menthol, polacrilin, saccharin, saccharin sodium, sodium bicarbonate, sodium carbonate anhydrous, sorbitol, talc, titanium dioxide, water – purified, xylitol. Flavours: Freshmint Gums – eucalyptus oil, peppermint oil; Classic Gums – fruit flavour.

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

Each piece of gum also contains 11.5mg (0.5mmol) sodium which should be taken into account by those on a low sodium diet. For the 2mg strength, this is equivalent to 230mg (10mmol) sodium per maximum dose of 20 pieces. For the 4mg strength, this is equivalent to 115mg (5mmol) sodium per maximum dose of 10 pieces.

PHARMACOLOGY

Pharmacodynamics

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

**Pharmacokinetics**

When the gum is chewed, nicotine is steadily released into the mouth and is rapidly absorbed through the buccal mucosa. By the swallowing of nicotine-containing saliva, a proportion reaches the stomach and intestine where it is inactivated.

The peak plasma concentration after a single dose of the 2 mg chewing gum is approximately 6.4 nanograms per mL. For the 4 mg chewing gum, it has been calculated that the nicotine peak plasma concentration after a single dose is approximately 9.3 nanograms per mL (after approximately 60 minutes). After 45 minutes average plasma concentration of nicotine when smoking a cigarette is 15-30 nanograms per 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 the kidneys. The plasma half-life is approximately three hours.

**INDICATIONS**

Source of nicotine as an aid for smoking cessation.

**CONTRAINDICATIONS**

QuitX Coated Chewing Gum should not be used by non-smokers or children under 12 years of age. Furthermore, people should not use the gum and smoke concomitantly.

Use is contraindicated in patients with known hypersensitivity to nicotine or any of the excipients in the formulation.

**PRECAUTIONS**

Any risks that may be associated with the use of QuitX Coated Chewing Gum are substantially outweighed by the well established dangers of continued smoking.

*Underlying cardiovascular disease.* In stable cardiovascular disease QuitX Coated Chewing Gum presents a lesser hazard than continuing to smoke. However, dependent smokers currently hospitalised as a result of myocardial infarction, severe dysrhythmia or cerebrovascular accident (CVA) and who are considered to be haemodynamically unstable should be encouraged to stop smoking with non-pharmacological interventions. If this fails, QuitX Coated Chewing Gum may be considered, but as data on safety in this patient group are limited, initiation should only be under medical supervision.

*Diabetes mellitus.* Smokers with diabetes mellitus are advised to monitor their blood sugar levels more closely than usual when nicotine replacement therapy (NRT) is initiated because catecholamine release can affect carbohydrate metabolism and vasoconstriction may delay/reduce insulin absorption.
GI disease. Swallowed nicotine may exacerbate symptoms in patients suffering from oesophagitis, gastritis or peptic ulcers and oral NRT preparations should be used with caution in these conditions. Ulcerative stomatitis has been reported.

Renal or hepatic impairment. QuitX Coated Chewing Gum should be used with caution in patients with moderate to severe hepatic impairment and/or severe renal impairment as the clearance of nicotine or its metabolites may be decreased with the potential for increased adverse effects.

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 could be misused, handled or ingested by children. Nicotine gum should be disposed of with care.

Phaeochromocytoma and uncontrolled hyperthyroidism. As nicotine causes release of catecholamines, QuitX Coated Chewing Gum should be used with caution in patients with uncontrolled hyperthyroidism or phaeochromocytoma.

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

Stopping smoking. Polycyclic aromatic hydrocarbons in tobacco smoke induce the metabolism of drugs metabolised by CYP 1A2 (and possible CYP 1A1). When a smoker stops smoking, this may result in slower metabolism and a consequent rise in blood levels of such drugs. This is of potential clinical importance for products with a narrow therapeutic window, e.g. theophylline, clozapine and ropinirole.

Excipients. QuitX Coated Chewing Gum also contains butylated hydroxytoluene; this may cause irritation to the mucous membranes.

Denture warning. Smokers who wear dentures may experience difficulty in chewing QuitX Coated Chewing Gum. The chewing gum may stick to, and may in rare cases damage dentures.

Note. Precautions for the combination use of QuitX Patches with QuitX 2mg Coated Chewing Gum are the same as those for each treatment alone.

Use in Pregnancy (Category 'D')

The use of QuitX Coated Chewing Gum is not contraindicated in pregnancy. However, nicotine is harmful to the foetus. The decision to use QuitX Coated Chewing Gum should be made on a risk-benefit assessment as early on in the pregnancy as possible with the aim of discontinuing use as soon as possible.

Smoking during pregnancy is associated with risks such as intra-uterine growth retardation, premature birth and still birth. 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 the use of nicotine replacement therapy. However for women unable to quit on their own, QuitX Coated Chewing Gum may be recommended to assist attempts to quit.

Nicotine passes to the foetus affecting breathing movements and has a dose-dependent effect on placental/foetal circulation. However, the risk of using QuitX Coated Chewing Gum 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.

Intermittent dosing products may be preferable 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**

The use of QuitX Coated Chewing Gum is not contraindicated in lactation. Nicotine from smoking and nicotine replacement products is found in breast milk. However, the amount of nicotine the infant is exposed to is relatively small and less hazardous than the second-hand smoke they would otherwise be exposed to.

Using intermittent dose NRT preparations such as QuitX Coated Chewing Gum, compared with patches, may minimise the amount of nicotine in the breast milk as the time between administrations of coated gum and feeding may be more easily prolonged. Women should breastfeed just before using the product.

**Use in Children (under 12 years of age)**

Not to be used by children under 12 years of age. Medicines should be kept out of the reach of children.

**Effects on Ability to Drive or Use Machines**

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

**Interactions with Other Medicines**

No information is available on interactions between QuitX Coated Chewing Gum and other medicines.

**Cessation of smoking**

Cessation of smoking may alter the individual’s response to some medications. Smoking increases the metabolism of some drugs through enzyme induction, thought to be due mainly to the polycyclic aromatic hydrocarbons contained in the smoke. This results in lower blood concentrations of drugs such as theophylline, warfarin, caffeine, paracetamol, phenylbutazone, pentazocine, lignocaine, benzodiazepines, imipramine, oestrogen and vitamin B12. Cessation of smoking may be expected to slow down or normalise the metabolism of these drugs, resulting in an increase in their blood concentrations. Therefore, a possible dose adjustment should be considered.

Other reported effects of smoking include a reduction in the analgesic effects of propoxyphene, a reduced diuretic response to frusemide, a change in the pharmacological effect of propranolol and altered response rates in ulcer healing with H2-antagonists.

Smoking and nicotine may raise the blood levels of cortisol and catecholamines. Dose adjustment of nifedipine, adrenergic agonists or adrenergic antagonists may be necessary.

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

In principle, QuitX Coated Chewing Gum can cause adverse effects similar to those associated with nicotine administered by smoking.

The most common side effects are dizziness, headaches and insomnia. These could also be withdrawal symptoms associated with giving up smoking and could be the result of too little nicotine.

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 hiccupping. Those people with a tendency to indigestion may suffer initially from minor indigestion or heartburn. Slower chewing will usually overcome this problem. Excessive consumption of chewing gum by people who have not been in the habit of inhaling tobacco smoke could possibly lead to nausea, faintness or headaches. Less common side effects include palpitations, redness and rashes.

DOSAGE AND ADMINISTRATION

Users of QuitX Coated Chewing Gum should stop smoking completely during treatment.

The strength of QuitX Coated Chewing Gum should be chosen according to the smoker's tobacco dependence. Highly dependent smokers who smoke more than 20 cigarettes per day, as well as smokers who have failed to quit when using the 2 mg gum, should use the 4 mg strength to meet the withdrawal of the high serum nicotine levels from heavy smoking. If the patient smokes 20 or less cigarettes a day, the 2 mg strength should be used.

One piece of gum should be chewed when the user feels the urge to smoke. The amount chewed should normally be 8-12 of the 2 mg pieces or 4-6 of the 4 mg pieces per day, up to a maximum of 20 of the 2 mg pieces or 10 of the 4 mg pieces per day.

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.

Directions for use:
1. One piece of gum should be chewed until the taste becomes strong.
2. The chewing gum should be rested between the gum and cheek.
3. When the taste fades, chewing should commence again.
4. The chewing 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 pieces of gum 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. Patients who use nicotine replacement therapy beyond nine months are recommended to seek additional help and advice from a healthcare professional.

Adolescents (12 to 18 years)

The patient should make every effort to stop smoking completely during treatment with QuitX Coated Chewing Gum. NRT should only be used in adolescents in conjunction with a counseling program.
One piece of gum should be chewed when the user feels the urge to smoke. The amount chewed should normally be 8-12 of the 2 mg pieces or 4-6 of the 4 mg pieces per day, up to a maximum of 20 of the 2 mg pieces or 10 of the 4 mg pieces per day.

Continue use for up to 8 weeks to break the habit of smoking, then gradually reduce gum use over a 4 week period. When daily use is down to 1-2 gums, use should be stopped. For those using the 4mg nicotine gum, the 2mg strength will be helpful during withdrawal from treatment.

As data are limited in this age group, the recommended duration of treatment is 12 weeks. If longer treatment is required, advice from a healthcare professional should be sought. The healthcare professional 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 four weeks in this case.

**In Combination with QuitX Patches**

The use of combination therapy may be appropriate for smokers who have previously relapsed or experienced cravings using NRT monotherapy, or who experience breakthrough craving or have difficulty in controlling cravings for cigarettes with NRT monotherapy.

**Initial treatment:**

The treatment should begin with one 21 mg/day patch (Step 1) daily applied to an intact area of the skin upon waking up in the morning and removed the next morning, combined with the 2mg gum. Use a minimum of 4 x 2mg gums/day with a maximum recommended dose of 12 gums/day. Usually 5 to 6 gums will be adequate for effect.

This full dose should be used for 12 weeks. Gradual weaning from the products should then be initiated.

**Weaning from combination use:**

This can be done in two ways:

- By using lower strength patches i.e. 3 to 4 weeks on 14mg/day patches (Step 2) and then 3 to 4 weeks on 7 mg/day (Step 3), using the same amount of QuitX 2mg coated chewing gum as per the initial treatment period, and then gradually reduce the amount of gums until only 1 – 2 gums are required each day, at which the therapy should be stopped, or alternatively,

- Stop using the patch and gradually reduce the number of gums up to 9 months. Those who use nicotine replacement therapy beyond 9 months are recommended to seek additional help and advice from a healthcare professional.
Recommended dosage:

<table>
<thead>
<tr>
<th>Initial treatment</th>
<th>QuitX patch</th>
<th>QuitX 2mg coated chewing gum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time period</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 weeks</td>
<td>1 x 21mg/day (Step 1) patch per day</td>
<td>Minimum 4 gums per day and maximum 12 gums per day. To be used as needed.</td>
</tr>
<tr>
<td>Weaning – alternative 1</td>
<td></td>
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</tr>
<tr>
<td>Next 3 to 4 weeks</td>
<td>1 x 14mg/day (Step 2) patch per day</td>
<td>Continue to use gum as needed</td>
</tr>
<tr>
<td>Following 3 to 4 weeks</td>
<td>1 x 7mg/day (Step 3) patch per day</td>
<td>Continue to use gum as needed</td>
</tr>
<tr>
<td>Up to 9 months</td>
<td>-----------------------------</td>
<td>Gradually wean from gum use</td>
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<tr>
<td>Weaning – alternative 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Up to 9 months</td>
<td>-----------------------------</td>
<td>Continue to gradually wean from gum use</td>
</tr>
</tbody>
</table>

OVERDOSAGE

Symptoms:

In overdose, symptoms corresponding to heavy smoking may be seen. General symptoms of nicotine poisoning include: pallor, sweating, burning throat, salivation, nausea, vomiting, abdominal cramps, diarrhoea, headache, dizziness, hearing and vision disturbances, tremor, mental confusion, muscle weakness, palpitations, dilated pupils, tachycardia, cardiac arrhythmias, dyspnoea, circulatory disturbance, convulsions, prostration, absence of neurological reaction, respiratory failure.

Lethal doses may produce convulsions, and death follows as a result of peripheral or central respiratory paralysis or, less frequently, cardiac failure. The acute lethal oral dose is approximately 0.5-0.75 mg per kg body weight, corresponding in an adult to 40-60 mg. Doses of nicotine that are tolerated by adult smokers during treatment 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.

Overdose with QuitX Coated 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. Any that is absorbed will be inactivated by the liver.

Treatment:

In the event of overdosage, a suspension of activated charcoal should then be passed through a wide bore 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 and supportive.

Contact the Poisons Information Centre on 131126 (Australia) for advice on the management of an overdose.
PRESENTATION AND STORAGE CONDITIONS

QuitX Coated Chewing Gum is available in classic or freshmint flavour, containing 2 mg or 4 mg nicotine per piece; packed in blister packs each containing 12 pieces of gum, in boxes of 24 and 96.

Store below 25 degrees Celsius.

POISONS SCHEDULE OF MEDICINE

Unscheduled.

NAME AND ADDRESS OF THE SPONSOR

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DATE OF APPROVAL

Approved by the Therapeutic Goods Administration on 28 July 2008.