

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

NiQuitin CQ 4 mg Mint Gum

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewing gum contains 4 mg nicotine (equivalent to 21.80 mg of nicotine resinate).

Excipients (per gum):

Sorbitol (E420) 144.41 mg
Maltitol liquid (E965) 25 mg
Sodium 11.4 mg

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Medicated chewing gum.

Yellow rectangular pillow-shaped gum.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

NiQuitin CQ 4 mg Mint Gum is for the relief of nicotine withdrawal symptoms as an aid to smoking cessation.

It should preferably be used in conjunction with a behavioural support programme, as this normally improves the success rate.

4.2 Posology and method of administration

Directions for use:

NiQuitin CQ Mint Gum should be chewed slowly according to the instructions.

NiQuitin CQ 4 mg Mint Gum is suitable for smokers who smoke more than 20 cigarettes a day.

Behavioural therapy, advice and support will normally improve the success rate.

The chewing gums should be used whenever there is an urge to smoke according to the “chew and rest” technique described on the pack. After about 30 minutes of such use, the gum will be exhausted. Not more than 15 pieces of the chewing gum may be used each day.

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

Adults (18 years and over)

Abrupt cessation of smoking:

Users should make every effort to stop smoking completely during treatment with NiQuitin CQ Mint Gum.

NiQuitin CQ Mint Gum should be chewed as directed whenever there is an urge to smoke to maintain complete abstinence from smoking.

Sufficient gums should be used each day, usually 8-12, up to a maximum of 15.

Continue use for up to three months to break the habit of smoking, then gradually reduce gum use. When daily use is 1-2 gums, use should be stopped. Any spare gum should be retained, as craving may suddenly return.

Those who use the gum beyond 9 months are recommended to seek additional help and advice from a healthcare professional.

For those using the 4 mg gum, the 2 mg gum will be helpful during withdrawal from treatment.

Children and adolescents

Adolescents (12 to 17 years) should follow the above usage advice for abrupt cessation of smoking, but as data are limited, duration of NRT in this age group is restricted to 12 weeks. If longer treatment is required, or where adolescents are unwilling or unable to quit smoking abruptly, advice from a healthcare professional should be sought.

NiQuitin CQ Mint Gum is not recommended for use in children under 12 years of age.

4.3 Contraindications

- people with hypersensitivity to the active substance or to any of the excipients;
- children under the age of 12 years
- non-smokers.

4.4 Special warnings and precautions for use

The risks associated with the use of NRT are substantially outweighed in virtually all circumstances by the well established dangers of continued smoking.

Dependent smokers with a recent myocardial infarction, unstable or worsening angina 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 counseling). If this fails, NiQuitin CQ Mint Gum may be considered, but as data on safety in this patient group are limited, initiation should only be under medical supervision.

Diabetes Mellitus: Patients with diabetes mellitus should be advised to monitor their blood sugar levels more closely than usual when NRT is initiated as catecholamines released by nicotine can affect carbohydrate metabolism.

Allergic reactions: Susceptibility to angioedema and urticaria.

A risk-benefit assessment should be made by an appropriate healthcare professional for patients with the following conditions:

- *Renal and hepatic impairment:* Use 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 events.
- *Phaeochromocytoma and uncontrolled hyperthyroidism:* Use with caution in patients with uncontrolled hyperthyroidism or phaeochromocytoma as nicotine causes release of catecholamines.

- *GI disease:* Swallowed nicotine may exacerbate symptoms in patients suffering from oesophagitis, gastric or peptic ulcers and oral NRT preparations should be used with caution in these conditions. Ulcerative stomatitis has been reported.

Smokers who wear dentures or who have temporomandibular joint disease may experience difficulty in chewing NiQuitin CQ 4 mg Mint Gum.

Danger in small children: Doses of nicotine that are tolerated by adult and adolescent smokers can produce severe toxicity in small children that maybe fatal. Products containing nicotine should not be left where they may be misused, handled or ingested by children.

Stopping smoking: Polycyclic aromatic hydrocarbons in tobacco smoke induce the metabolism of drugs catalysed by CYP 1A2 (and possibly by CYP 1A1). When a smoker stops this may result in a slower metabolism and a consequent rise in blood levels of such drugs

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

Sorbitol (E420) and Maltitol Liquid (E965): Patients with rare hereditary problems of fructose intolerance should not take this medicine.

Butylated hydroxytoluene (E321): May cause irritation of mucous membranes.

Sodium: Each piece of NiQuitin CQ Mint Gum contains 11.4 mg of sodium. People on a low sodium diet should take this into account.

During a quit attempt users should not interchange nicotine gums with nicotine lozenges since pharmacokinetic data indicate a higher availability of nicotine from some nicotine lozenges in comparison to the gum.

4.5 Interaction with other medicinal products and other forms of interaction

No clinically relevant interactions between nicotine replacement therapy and other drugs have definitely been established; however nicotine may possibly enhance the haemodynamic effects of adenosine.

4.6 Fertility, pregnancy and lactation

Pregnancy

Smoking during pregnancy is associated with risks such as intra-uterine growth retardation, premature birth or stillbirth. 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 NRT. However for women unable to quit on their own, NRT may be recommended by a healthcare professional to assist a quit attempt. The risk of using NRT 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.

However, as nicotine passes to the foetus affecting breathing movements and has a dose dependent effect on placental/foetal circulation, the decision to use NRT should be made as early on in the pregnancy as possible. The aim should be to use NRT for only 2-3 months.

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.

Lactation

Nicotine from smoking and NRT is found in breast milk. However the amount of nicotine the infant is exposed to from NRT is relatively small and less hazardous than the second-hand smoke they would otherwise be exposed to.

Ideally smoking cessation during lactation should be achieved without NRT. However for women unable to quit on their own, NRT may be recommended by a healthcare professional to assist a quit attempt.

Using intermittent dose NRT preparations, compared with patches, may minimize the amount of nicotine in the breast milk as the time between administrations of NRT and feeding can be made as long as possible. Women should try to breastfeed just before they take the product.

4.7 Effects on ability to drive and use machines

There are no known effects of NiQuitin CQ Mint Gum on the ability to drive and use machines. However, users of nicotine replacement products should be aware that smoking cessation can cause behavioural changes.

4.8 Undesirable effects

Nicotine from the gum may sometimes cause a slight irritation of the throat at the start of treatment and may also cause increased salivation. Excessive swallowing of dissolved nicotine may, at first, cause hiccups.

Excessive consumption of NiQuitin CQ 4 mg Mint Gum by those who have not been in the habit of inhaling tobacco smoke could possibly lead to nausea, faintness or headache (as may be experienced by such a patient if tobacco smoke is inhaled).

Psychiatric disorders

Common ($\geq 1\%$ - $< 10\%$): insomnia, irritability

Central and Peripheral Nervous System Disorders

Common ($\geq 1\%$ - $< 10\%$): dizziness; headache

Uncommon ($\geq 0.1\%$ - $< 1\%$): lightheadedness; tremor

Gastro-intestinal system disorders

Common ($\geq 1\%$ - $< 10\%$): nausea; gastro-intestinal discomfort; sore mouth; vomiting; indigestion; mouth irritation; mouth ulceration.

Uncommon ($\geq 0.1\%$ - $< 1\%$): stomatitis

Respiratory, thoracic and mediastinal disorders

Common ($\geq 1\%$ - $< 10\%$): hiccups; sore throat; pharyngitis; cough

Uncommon ($\geq 0.1\%$ - $< 1\%$): dyspnoea

Musculoskeletal and connective tissue disorders

Common ($\geq 1\%$ - $< 10\%$): jaw pain

Cardiac disorders

Uncommon ($\geq 0.1\%$ - $< 1\%$): palpitation; tachycardia

Rare ($\geq 0.01\%$ - $< 0.1\%$): atrial fibrillation

Skin and subcutaneous tissue disorders

Uncommon ($\geq 0.1\%$ - $< 1\%$): erythema; urticaria; increased sweating

Immune system disorders

Rare ($\geq 0.01\%$ - $< 0.1\%$): allergic reactions such as angio-oedema

Very rare ($< 0.0001\%$): anaphylactic reactions

Special senses other, disorders

Uncommon ($\geq 0.1\%$ - $< 1\%$): parageusia; metallic taste; taste perversion

General disorders and administration site conditions.

Uncommon ($\geq 0.1\%$ - $< 1\%$): chest pain; arthralgia; myalgia; malaise

Some reported symptoms, such as dizziness, headache and sleep disturbances may be related to withdrawal symptoms associated with abstinence from smoking. Increased frequency of aphthous ulcer may occur after abstinence from smoking.

Those with a tendency to indigestion may suffer initially from minor degrees of indigestion or heartburn if the 4 mg nicotine gum is used; slower chewing and the use of the 2 mg nicotine gum (if necessary more frequently) will usually overcome this problem.

4.9 Overdose

Symptoms: The minimum lethal dose of nicotine in a non-tolerant man has been estimated to be 40 to 60 mg. Symptoms of acute nicotine poisoning include nausea, salivation, abdominal pain, diarrhea, sweating, headache, dizziness, disturbed hearing and marked weakness. In extreme cases, these symptoms may be followed by hypotension, rapid or weak or irregular pulse, breathing difficulties, prostration, circulatory collapse and terminal convulsions.

Management of an overdose: All nicotine intake should stop immediately and the patient should be treated symptomatically. Artificial respiration with oxygen should be instituted if necessary. Activated charcoal reduces the gastro-intestinal absorption of the nicotine.

5 PHARMACOLOGICAL PROPERTIES**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Drugs used in nicotine dependence

ATC Code: N07B A01

Nicotine is an agonist at nicotine receptors in the peripheral and central nervous system and has pronounced CNS and cardiovascular effects. When consumed in tobacco products, it has been shown to be addictive and abstinence is linked to craving and withdrawal symptoms. These craving and withdrawal symptoms include urge to smoke, depressed

mood, insomnia, irritability, frustration or anger, anxiety, difficulty in concentrating, restlessness and increased appetite or weight gain. The gums replace some of the nicotine provided by tobacco and help reduce the severity of these nicotine craving and withdrawal symptoms.

5.2 Pharmacokinetic properties

Absorption

Nicotine administered in chewing gums is readily absorbed from the buccal mucous membranes. Demonstrable blood levels are obtained within 5 - 7 minutes and reach a maximum about 30 minutes after the start of chewing. Blood levels are roughly proportional to the amount of nicotine chewed and have been shown never to exceed those obtained from smoking cigarettes.

Distribution

As the plasma protein binding of nicotine is low (4.9% - 20%), the volume of distribution of nicotine is large (2.5 l/kg). The distribution of nicotine to tissue is pH dependent, with the highest concentrations of nicotine found in the brain, stomach, kidney and liver. Nicotine crosses the blood-brain barrier, the placenta and is detectable in breast milk.

Metabolism

Nicotine is extensively metabolized to a number of metabolites, all of which are less active than the parent compound. The metabolism of nicotine primarily occurs in the liver, but also in the lung and kidney. Nicotine is metabolized primarily to cotinine but is also metabolized to nicotine N'-oxide. Cotinine has a half-life of 15-20 hours and its blood levels are 10 times higher than nicotine. Cotinine is further oxidized to trans-3'-hydroxycotinine, which is the most abundant metabolite of nicotine in the urine. Both nicotine and cotinine undergo glucuronidation.

Excretion

The elimination half-life of nicotine is approximately 2 hours (range 1 - 4 hours). Total clearance for nicotine ranges from approximately 62 to 89 l/hr. Non-renal clearance for nicotine is estimated to be about 75% of total clearance. Nicotine and its metabolites are excreted almost exclusively in the urine. The renal excretion of unchanged nicotine is highly dependent on urinary pH, with greater excretion occurring at acidic pH.

5.3 Preclinical safety data

The general toxicity of nicotine is well known and taken into account in the recommended posology. Nicotine was not mutagenic in appropriate assays. The results of carcinogenicity assays did not provide any clear evidence of a tumorigenic effect of nicotine. In studies in pregnant animals, nicotine showed maternal toxicity, and consequential mild fetal toxicity. Additional effects included pre-and post natal growth retardation and delays and changes in post-natal CNS development. Effects were only noted following exposure to nicotine at levels in excess of those which will result from recommended use of NiQuitin CQ Mint Gum. Effects on fertility have not been established. There are no other pre-clinical data of relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Chewing gum base 2890106
Calcium carbonate
Butylhydroxytoluene E321
Sorbitol E420
Maltitol liquid E965
Glycerol

Acesulfame potassium
Mint Flavour 295920
Mannitol E421
Sodium Carbonate, Anhydrous
Sodium Hydrogen Carbonate
Eurolake Quinoline Yellow, E104
Carnauba wax
Talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C. Keep gum in the carton in the blister pack.

6.5 Nature and contents of container

NiQuitin CQ 4 mg Mint Gum is available in packs of 12, 24, 48 and 96 gums. Not all pack sizes may be marketed.

Gums are packed 12 to a clear or opaque polyvinyl chloride/ polyethylene/ polyvinylidene chloride/ aluminium blister in 3 rows of 4 gums. The blister is part-perforated, splitting the blister into 2 sections of 6 gum pieces each.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Consumer Healthcare (Ireland) Ltd.,
Stonemasons Way,
Rathfarnham,
Dublin 16

8 MARKETING AUTHORISATION NUMBER

PA 678/99/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18 March 2005

Date of last renewal: 24 February 2008

10 DATE OF REVISION OF THE TEXT

June 2011