SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

NiQuitin Extra Fresh Mint 4 mg Medicated Chewing Gum.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each medicated chewing gum contains 4 mg nicotine (equivalent to 28.40 mg nicotine resinate).

Excipients with known effect:

Sorbitol (E420) 137.55 mg/piece gum

Sodium 15.19 mg/piece gum

Xylitol (E967) 353.89 mg/piece gum

For full list of excipients see 6.1.

3 PHARMACEUTICAL FORM

Medicated chewing gum.

Off-white rectangular pillow shaped gum.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

NiQuitin Extra Fresh Mint Gum relieves and/or prevents craving and nicotine withdrawal symptoms associated with tobacco dependence. It is indicated to aid smokers wishing to quit or reduce prior to quitting, to assist smokers who are unwilling or unable to smoke, and as a safer alternative to smoking for smokers and those around them.

This product is indicated in pregnant and lactating women making a quit attempt.

NiQuitin Extra Fresh Mint Gum should preferably be used in conjunction with a behavioural support programme.

4.2 Posology and method of administration

Directions for use:
NiQuitin Extra Fresh Mint Gum should be chewed slowly according to the instructions.

NiQuitin Extra Fresh Mint 4 mg Gum is suitable for smokers who have their first cigarette of the day within 30 minutes of waking up.

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. Absorption of nicotine is through the buccal mucosa, any nicotine which is swallowed being destroyed by the liver.

Adults (18 years and over)

Abrupt cessation of smoking:
Users should make every effort to stop smoking completely during treatment with NiQuitin Extra Fresh Mint Gum.

This product 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 have quit smoking but are having difficulty discontinuing using the gum 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.

Gradual cessation of smoking:

For smokers who are unwilling or unable to quit abruptly. Use a piece of gum whenever there is a strong urge to smoke in order to reduce the number of cigarettes smoked as far as possible and to refrain from smoking as long as possible. The number of pieces of gum a day is variable and depends on the patients needs. Nonetheless it should not exceed 15 pieces per day.

If a reduction in cigarette consumption has not been achieved after 6 weeks of treatment, a healthcare professional should be consulted.

Reduced tobacco consumption should lead to complete cessation of smoking. This should be attempted as soon as possible. When the number of cigarettes has been reduced to a level from which the user feels able to quit completely, then start on the schedule for "abrupt cessation" as given above.

If an attempt to stop smoking completely has not been started within 6 months after the beginning of treatment, it is recommended to consult a healthcare professional.

Reduction in smoking:
For smokers who wish to cut down with no immediate plans to quit.

Use a piece of gum whenever there is a strong urge to smoke in order to reduce the number of cigarettes smoked as far as possible and to refrain from smoking as long as possible. Users should be encouraged to stop smoking completely as soon as possible.

The number of pieces of gum a day is variable and depends on the patients needs. Nonetheless it should not exceed 15 pieces per day.

If users are still feeling the need to use the gum on a regular basis 6 months after the start of treatment and have still been unable to undertake a permanent quit attempt, then it is recommended to seek additional help and advice from a healthcare professional.

Temporary abstinence:
Use a piece of gum whenever there is a strong urge to smoke to control troublesome withdrawal symptoms including cravings. Users should not take more than 15 pieces of gum per day.

Users should be encouraged to stop smoking completely as soon as possible. If users are still feeling the need to use gum on a regular basis 6 months after the start of treatment and have still been unable to undertake a permanent quit attempt, then it is recommended to seek additional help and advice from a healthcare professional.

Adolescents and children
Adolescents (12 to 17 years) should follow the above usage advice for abrupt cessation of smoking. Where adolescents are unwilling or unable to quit smoking abruptly, advice from a healthcare professional should be sought.

Safety and effectiveness in children who smoke has not been evaluated. NiQuitin Extra Fresh Mint Gum is not recommended for use in children under 12 years of age.

4.3 Contraindications

Hypersensitivity to nicotine or any of the other ingredients in this product.

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.

Patients hospitalised for MI, severe dysrhythmia or CVA who are considered to be haemadynamically unstable should be encouraged to stop smoking with non-pharmacological interventions. If this fails, NiQuitin Extra Fresh Mint Gum may be considered, but as data on safety in this patient group are limited, initiation should only be under medical supervision. Once patients are discharged from hospital they can use NRT as normal. If there is a clinically significant increase in cardiovascular or other effects attributable to nicotine, the gum dose should be reduced or discontinued.

Diabetes: Blood glucose levels may be more variable when stopping smoking, with or without NRT as catecholamines released by nicotine can affect carbohydrate metabolism, so it is important for diabetics to monitor their blood glucose levels more closely than usual while using this product.

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

- *GI Disease:* Swallowing of nicotine may exacerbate symptoms in persons suffering from active oesophagitis, oral or pharyngeal inflammation, gastritis, gastric ulcer or peptic ulcer and oral NRT preparations should be used with caution in these conditions. Ulcerative stomatitis has been reported.

- *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.

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 may be misused, handled or ingested by children. NiQuitin Extra Fresh Mint Gum should be disposed of with care.

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.

Smokers who wear dentures may experience difficulty in chewing NiQuitin Extra Fresh Mint Gum.

Sorbitol content: Patients with rare hereditary problems of fructose intolerance should not take this medicine**.**

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

Sodium content: Each piece of NiQuitin Extra Fresh Mint Gum contains 10.42 mg of sodium per piece of gum. To be taken into consideration by patients on a controlled sodium diet.

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. Smoking cessation itself may require the adjustment of some drug therapy.

4.6 Fertility, Pregnancy and lactation

Pregnancy

Stopping smoking is the single most effective intervention for improving the health of both the pregnant smoker and her baby, and the earlier abstinence is achieved the better. However, if the mother cannot (or is considered unlikely to) quit without pharmacological support, NRT may be used as the risk to the foetus is lower than that expected with smoking tobacco. Stopping completely is by far the best option but NRT may be used in pregnancy as a safer alternative to smoking. Because of the potential for nicotine-free periods, intermittent dose forms are preferable, but patches may be necessary if there is significant nausea and/or vomiting. If patches are used they should, if possible, be removed at night when the foetus would not normally be exposed to nicotine.

Lactation

The relatively small amounts of nicotine found in breast milk during NRT use are less hazardous to the infant than second-hand smoke. Intermittent dose forms would minimize the amount of nicotine in breast milk and permit feeding when levels were at their lowest.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

NRT may cause adverse reactions similar to those associated with nicotine administered by other means, including smoking. These may be attributable to the pharmacological effects of nicotine, some of which are dose dependent. In relation to this 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.

NiQuitin Extra Fresh Mint Gum in the recommended dose has not been found to cause any serious adverse effects. Excessive consumption of NiQuitin Extra Fresh 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). 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 hiccuping.

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.

Common	Nervous System disorders	Dizziness, headache
	Gastro-intestinal disorders	Nausea, gastro-intestinal

(≥1/100 to <1/10)		discomfort, hiccups, sore mouth or throat.
	General disorders and administration site conditions	Jaw-muscle ache. The gum may stick to, and may in rare cases, damage dentures.
Uncommon (≥1/1,000 to <1/100)	Cardiac disorders	Palpitation
	Skin and subcutaneous tissue disorders	Erythema, urticaria
	Gastrointestinal disorders	Stomatitis
Rare (≥1/10,000 to <1/1,000)	Cardiac disorders	Atrial fibrillation
	Immune system disorders	Allergic reactions such as angio-oedema
Very Rare (<1/10,000)	Immune system disorders	Anaphylactic reactions
Not known (cannot be estimated from the available data)	Nervous System disorders	Seizures

4.9 Overdose

The minimum lethal dose of nicotine in a non tolerant man has been estimated to be 40 to 60 mg. Even small quantities of nicotine may be dangerous in children and may prove fatal. Suspected nicotine poisoning in a child should be considered a medical emergency and treated immediately.

Symptoms

Signs and symptoms of an overdose from nicotine lozenges would be expected to be the same as those of acute nicotine poisoning, including pallor, cold sweat, salivation, nausea, vomiting, abdominal pain, diarrhoea, headache, dizziness, disturbed hearing and vision, tremor, mental confusion and weakness. Prostration, hypotension, respiratory failure, rapid or weak or irregular pulse, circulatory collapse and convulsions (including terminal convulsions) may ensue with large overdoses.

Management

In the event of an overdose (e.g. too many gum pieces chewed) the user should seek medical attention immediately. All nicotine intake should cease immediately and the patient be treated symptomatically. Artificial respiration with oxygen should be instituted if necessary. Activated charcoal reduces the gastrointestinal absorption of nicotine.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: N07B A01

The pharmacological effects of nicotine are well documented. Those resulting from chewing NiQuitin Extra Fresh Mint Gum are comparatively small. The response at any one time represents a summation of stimulant and depressant actions from direct, reflex and chemical mediator influences on several organs.

The main pharmacological actions are central stimulation and/or depression; transient hyperpnoea; peripheral vasoconstriction (usually associated with a rise in systolic pressure); suppression of appetite and stimulation of peristalsis.

5.2 Pharmacokinetic properties

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.

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 Extra Fresh 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

Gum Base 25048 (incl. 0.09%w/w Butylated hydroxytoluene (E321)
Sorbitol (E420)

Xylitol (E967)
Calcium Carbonate (E227)
Sodium Carbonate Anhydrous (E500)
Eucamenthol Flavour
Glycerol (E422)
L-Menthol
Optacool Flavour
Acesulfame Potassium (E950)
Sucralose (E955)
Talc

Gum Coating
Xylitol (E967)
Mannitol (E421)
Acacia (E414)
Titanium Dioxide
L-Menthol
Eucamenthol Flavour
Optacool Flavour
Sucralose (E955)
Carnauba Wax (E903)
Talc

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 25ºC. Store in the original package.

6.5 Nature and contents of container

NiQuitin Extra Fresh Mint 4 mg Medicated Chewing Gums are available is available in packs of 4, 10, 30, 100 and 200.
Not all pack sizes may be marketed.
20 micron aluminium blister film. The blister film is a clear thermoformable blister film, consisting either of 250 micron polyvinyl chloride (PVC) and 90 g/m^2 polyvinylidene chloride (PVdC) (duplex) or of 250 micron polyvinyl chloride (PVC), 30 micron polyethylene (PE) and 90 g/m^2 polyvinylidene chloride (PVdC) (triplex).
The aluminium sealing side of the aluminium foil is coated with a vinyl based lacquer which seals to the PVdC side of the blister film.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

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