SUMMARY OF THE PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

NiQuitin Mint 2 mg lozenge
NiQuitin Mint 4 mg lozenge

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each lozenge contains 2 mg or 4 mg nicotine (as nicotine resinate).

Excipients with known effect (per lozenge):

Aspartame (E951) 6.1 mg

Mannitol (E421) 1028 mg in the 2 mg lozenge, 1015 mg in the 4 mg lozenge

Sodium 15 mg

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Lozenge
2 mg: cream/white biconvex round lozenge, embossed with NL2 on one side.
4 mg: cream/white biconvex round lozenge, embossed with NL4 on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

NiQuitin Mint is indicated for the relief of withdrawal symptoms associated with smoking cessation. If possible, when stopping smoking, NiQuitin Mint should be used in conjunction with a behavioural support programme.

4.2 Posology and method of administration

Adults (including the elderly):
NiQuitin Mint Lozenges 2 mg are suitable for smokers with low nicotine dependency e.g. those smoking their first cigarette of the day more than 30 minutes after waking up.
NiQuitin Mint Lozenges 4 mg are suitable for smokers with high nicotine dependency e.g. those smoking their first cigarette of the day within 30 minutes of waking up.

Users should stop smoking completely during treatment with NiQuitin Mint Lozenges.

Users should follow the schedule of treatment below:

Step 1 Weeks 1 to 6	Step 2 Weeks 7 to 9	Step 3 Weeks 10 to 12	To help stay smoke free

Initial treatment period	Step down treatment period	Step down treatment period	over the next 12 weeks: use 1-2 lozenges per day only on occasions when strongly tempted to smoke
1 lozenge every 1 to 2 hours	1 lozenge every 2 to 4 hours	1 lozenge every 4 to 8 hours	

During weeks 1 to 6 it is recommended that users take a minimum of 9 lozenges per day.
Users should not exceed 15 lozenges per day.
Lozenges should not be used for more than 24 weeks (6 months). If users still feel the need for treatment, a physician should be consulted.

Paediatric population NiQuitin Mint is not recommended for use in children below 12 years of age due to lack of data on safety and efficacy.

NiQuitin Mint Lozenges should only be used in adolescents (12-17 years) with advice from a doctor.
Method of administration One lozenge should be placed in the mouth and allowed to dissolve. Periodically, the lozenge should be moved from one side of the mouth to the other, and repeated, until the lozenge is completely dissolved (approximately 20 – 30 minutes). The lozenge should not be chewed or swallowed whole.
Users should not eat or drink while a lozenge is in the mouth. Liquids which lowers the pH in the mouth such as coffee, juice and soft drinks, can decrease the absorption of nicotine in the mouth. To obtain maximum absorption of nicotine these liquids should be avoided in up to 15 minutes before the lozenge is used.

4.3 Contraindications

NiQuitin Mint Lozenges are contraindicated in:

- those with hypersensitivity to the active substance or any of the excipients listed in section 6.1;
- children below the age of 12 years and non-smokers;
- those with phenylketonuria.

4.4 Special warnings and special precautions for use

NiQuitin Mint should only be used after advice from a doctor in subjects with

- uncontrolled hypertension; cardiovascular disease (e.g. stable angina pectoris, heart failure, cerebrovascular disease, vasospastic diseases, severe peripheral vascular disease).

  Patients hospitalised for MI, severe dysrhythmia or CVA who are considered to be haemodynamically unstable should be encouraged to stop smoking with non pharmacological interventions. If this fails, Nicotine lozenges may be considered by 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 lozenge/ gum / film dose should be reduced or discontinued.

- Gastrointestinal disease: Swallowing 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.

- Renal and hepatic impairment: Use with caution in patients with moderate to severe hepatic impairment and/or moderate to 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

- Diabetes: blood glucose levels may be more variable when stopping smoking, with or without NRT, so it is important for diabetics to closely monitor their blood glucose levels while using this product.

Seizures: Use with caution in subjects taking anti-convulsant therapy or with a history of epilepsy as cases of convulsions have been reported in association with nicotine.

Lozenges should be kept out of the sight and reach of 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.

Aspartame content: Contains aspartame (E951), a source of phenylalanine. May be harmful for those with phenylketonuria.

Sodium content: This medicinal product contains less than 1 mmol (23 mg) per lozenge that is to say essentially ‘sodium-free’.

Mannitol content: May have a mild laxative effect.

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

During a quit attempt users should not interchange NiQuitin with nicotine gums since pharmacokinetic data indicate a higher availability of nicotine from NiQuitin 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 been established.

However nicotine may possibly enhance the haemodynamic effects of adenosine. i.e. increase in blood pressure and heart rate and also increase pain response (anginapectoris type chest pain) provoked by adenosine administration.

Smoking cessation, with or without nicotine substitutes, may alter the response to concomitant medication in ex-smokers. The following drugs may require adjustment in dose at cessation of smoking:

*May require a **decrease** in dose at cessation of smoking*	*Possible mechanism of action*
Caffeine, theophylline, imipramine, pentazocine, phenacetin, phenylbutazone, tacrine, clomipramine.	Reduced induction of CYP1A2
Insulin	Increase in sub-cutaneous insulin absorption
Adrenergic antagonists e.g. prazosin, propranolol.	Decreases circulating catecholamines
*May require an **increase** in dose at cessation of smoking*	*Possible mechanism of action*
Adrenergic agonists e.g. isoprenaline, salbutamol	Decreases in circulating catecholamines

4.6 Fertility, Pregnancy and lactation

Pregnancy

Smoking during pregnancy is associated with risks 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.

Breast-feeding

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.

Fertility

Studies in male rats have shown that nicotine can decrease testis weight, cause a reversible decrease in Sertoli cell numbers with impairment of spermatogenesis, and result in a variety of changes in the epididymis and vas deferens. However, similar effects have not been reported to occur in humans.

4.7 Effects on ability to drive and use machines

NiQuitin Mint has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

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

Immune system disorders:
- Rare (≥1/10,000 to <1/1,000): Hypersensitivity
- Very rare (<1/10000): Anaphylactic reactions

Nervous system disorders:
- Very common (≥1/10): Dizziness
- Common (≥1/100, <1/10): Headache and Tremor.
- Not known: dysgeusia, paraesthesia mouth, seizures*

Cardiac disorders:
- Uncommon (≥1/1000, <1/100): Palpitations and Tachycardia.
- Not known: Atrial fibrillation.

Respiratory, thoracic and medistinal disorders:
Common (≥1/100, <1/10): Cough, pharyngolaryngeal pain hiccups and Dyspnoea.

Gastrointestinal disorders:
Very common (≥1/10): Nausea and Vomiting.
Common (≥1/100, <1/10): dyspepsia**, abdominal pain upper, diarrhoea, dry mouth, constipation, stomatitis, flatulence and oral discomfort.
Uncommon (≥1/1000, <1/100): Dysphagia
Not known: eructation, salivary hypersecretion

General disorders and adminnstration site conditions:
Common (≥1/100, <1/10): Asthenia, Fatigue, Malaise and Influenza type illness***

Infections and infestations
Common (≥1/100; <1/10): Pharyngitis

Psychiatric disorders:
Very common (≥1/10): Insomnia
Common (≥1/100, </10): Nervousness.
Not known: Abnormal dreams

Skin and subcutaneous tissue disorders
Uncommon: Urticaria, erythema, hyperhidrosis
Not Known: Angioedema, rash, pruritus

Certain symptoms which have been reported such as depression, irritability, anxiety and insomnia may be related to withdrawal symptoms associated with smoking cessation. Subjects quitting smoking by any means could expect to suffer from headache, dizziness, increased coughing or a cold.

** In subjects taking anti-convulsant therapy or with a history of epilepsy.*

***Individuals with a tendency to experience indigestion may suffer initially from minor degrees of indigestion or heartburn if the 4 mg dose is used - slower chewing in the case of gum or the use of the 2 mg dose (if necessary more frequently) will usually overcome this problem.*

**** These events may also be due to withdrawal symptoms following smoking cessation*

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V

4.9 Overdose

Even small quantities of nicotine may be dangerous in children. If poisoning is suspected in a child, a doctor must be consulted immediately.
Overdose with NiQuitin Mint Lozenges may occur if too many lozenges are ingested.
Signs and symptoms of an overdose would be expected to be the same as those of acute nicotine poisoning, including pallor, cold sweat, nausea, salivation, vomiting, abdominal pain, diarrhoea, headache, dizziness, disturbed hearing and vision, tremor, mental confusion and weakness.
Prostration, hypotension, respiratory failure and convulsions may ensue with large overdoses. Lethal doses produce convulsions quickly and death follows as a result of peripheral and central respiratory paralysis or, less frequently, cardiac failure.

Treatment of overdose:
In the event of overdosage, 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in nicotine dependence
ATC Code: N07BA01
Nicotine, the main alkaloid in tobacco products and a naturally occurring autonomic substance, 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 upon cessation craving and withdrawal symptoms occur. 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 lozenges replace some of the nicotine provided by tobacco and help reduce the severity of these nicotine craving and withdrawal symptoms.
Six week smoking cessation rates for Nicotine Lozenge 2 mg were 46.0% and 29.7% in active and placebo groups respectively. Rates at six months were 24.2% and 14.4 % in active and placebo groups respectively. Odds ratios, adjusted for centre effects, at six weeks and six months were calculated as 2.10 and 1.96 respectively.
Six week smoking cessation rates for Nicotine Mint Lozenge 4 mg were 48.7% and 20.8% in active and placebo groups respectively. Rates at six months were 23.6% and 10.2 % in active and placebo groups respectively. Odds ratios, adjusted for centre effects, at six weeks and six months were calculated as 3.69 and 2.76 respectively.

5.2 Pharmacokinetic properties

Absorption
NiQuitin Mint Lozenges completely dissolve in the oral cavity, and the entire amount of nicotine contained in the lozenge becomes available for buccal absorption or ingestion (swallowing). Complete dissolution of NiQuitin Mint Lozenge is typically achieved in 20-30 minutes. Concurrent consumption of liquids which lower pH in the mouth, such as coffee, juice and carbonated drinks, can drastically reduce the absorption of nicotine.
For the 2 mg lozenge the peak plasma concentration of nicotine achieved after a single dose is approximately 4.4 ng/ml. When dosed every 1.5 hours, the steady state peak and trough concentrations are 12.7 and 9.4 ng/ml respectively.
For the 4 mg lozenge the peak plasma concentration of nicotine achieved after single dose is approximately 10.8 ng/ml. When dosed every 1.5 hours, the steady state peak and trough concentrations are 26.0 and 19.7 ng/ml respectively.
Ingestion of NiQuitin Mint Lozenges not following dosing instructions (chewed, retained in the mouth and swallowed; chewed and immediately swallowed) gives a slower and a somewhat reduced absorption of nicotine.

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.

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 for 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.

Elimination
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 documented. Nicotine was not mutagenic or carciogenic in conventional assays. In studies in pregnant animals, at exposure levels resulting in maternal toxicity (in excess of those that will be obtained with the recommended use of NiQuitin Mint), a mild foetal toxicity was seen. Other effects included pre- and postnatal growth retardation and delays and changes in postnatal CNS development. Effects on fertility have not been established.

Nicotine has been reported to induce changes to the ovary and uterus of female rats and mice following repeated oral or intraperitoneal administration of doses exceeding those that result from the recommended use of NiQuitin Mint Lozenge. Repeated intraperitoneal or oral administration of nicotine to male rats at doses exceeding those resulting from the recommended use of NiQuitin Mint Lozenge was reported to cause a decrease in testis weight, changes in the epididymis and vas deferens, and a reversible decrease in Sertoli cell numbers with impairment of spermatogenesis.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol (E421)
Sodium alginate (E401)
Xanthan gum (E415)
Potassium hydrogen carbonate (E501)
Sodium carbonate anhydrous
Aspartame (E951)
Magnesium stearate (E407b)
Peppermint Flavour (contains maltodextrin and modified starch)

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

2 Years

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package in order to protect from moisture.

6.5 Nature and content of container

Clear PCTFE/PVC/aluminium or Clear PVC/PVdC/PVC/aluminium blister packs of 12, 24, 36 and 72.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

To be completed nationally.

8 MARKETING AUTHORISATION NUMBER(S)

To be completed nationally.

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

2002-11-01/2007-11-01

10 DATE OF REVISION OF THE TEXT

2025-11-06