SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

NiQuitin 4 mg Compressed Lozenges

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each lozenge contains 4 mg nicotine (as nicotine resinate). For a full list of excipients, see section 6.1.

Excipient with known effect

Each lozenge contains 4 mg sodium

3 PHARMACEUTICAL FORM

Compressed Lozenge (lozenge)

White to off white oval lozenge with convex surfaces; one surface bearing a debossed "NIC4" logo.

Dimensions of approximately 10 mm length × 5 mm width

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

NiQuitin are to be used for the treatment of tobacco dependence by relief of nicotine withdrawal symptoms (see section 5.1) including cravings. Permanent cessation of tobacco use is the eventual objective.

NiQuitin should preferably be used in conjunction with a behavioural support programme.

4.2 Posology and method of administration

Posology:

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

The strength of lozenge to be used will depend on the smoking habits of the individual.

NiQuitin 4 mg are suitable for smokers who smoke more than 20 cigarettes a day.

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

Adults (18 years and over)

Use the lozenges whenever there is an urge to smoke.
Sufficient lozenges should be used each day, usually 8-12, up to a maximum of 15.

Continue use for up to six weeks to break the habit of smoking, then gradually reduce lozenge use. When daily use is 1-2 lozenges, use should be stopped.
To help stay smoke free after treatment, users may take a lozenge in situations when they are strongly tempted to smoke.

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

Paediatric population:

NiQuitin should only be used by adolescents (12-17 years inclusive) with advice from a healthcare professional.
NiQuitin are not recommended for use in children below the age of 12 due to a lack of data on safety and efficacy.

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 10 minutes). The lozenge should not be chewed or swallowed whole.

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

4.3 Contraindications

- hypersensitivity to nicotine or any of the excipients listed in section 6.1
- children under the age of 12 years
- non-smokers.

4.4 Special warnings and precautions for use

The risks associated with the use of nicotine replacement therapy (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 hypertensions or recent cerebrovascular accident should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). If this fails, NiQuitin may be considered but as data on safety in this patient group are limited, initiation should only be under close 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 effects.

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

- *Gastrointestinal 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.

- *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

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.

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.

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

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 interaction studies have been performed. 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

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 fetus 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 fetus affecting breathing movements and has a dose dependent effect on placental/fetal 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 has no or negligible influence 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

NRT can cause adverse reactions similar to those associated with nicotine administered in other ways, including smoking. These may be attributed to the pharmacological effects of nicotine, some of which are dose dependent. At recommended doses NiQuitin have not been found to cause any serious adverse effects. Excessive consumption of NiQuitin by those who have not been in the habit of inhaling tobacco smoke could possibly lead to nausea, faintness or headaches.

Certain symptoms which have been reported such as depression, irritability, anxiety, increased appetite 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, sleep disturbance, increased coughing or a cold.

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: Very common (≥1/10), common (≥1/100 to 1/<10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000) and very rare (<1/10,000), not known (cannot be estimated from the available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

System Organ Class and Frequency	Adverse Reaction /Events
Immune System Disorder Very rare Not Known	 Anaphylactic reactions Hypersensitivity
Psychiatric disorders Common Uncommon	 Irritability, anxiety, sleep disorders incl. abnormal dreams Nervousness, depression
Nervous system disorders Common Not Known	 Dizziness, headaches Tremor, dysgeusia, paresthesia mouth, seizures*
Cardiac Disorders Uncommon	 Palpitations, heart rate increased
Respiratory, thoracic and mediastinal disorders Common Not Known	 Cough, sore throat Dyspnoea
Gastrointestinal disorders Very common Common Not Known	 Nausea, mouth/throat and tongue irritation Vomiting, diarrhoea, gastro-intestinal discomfort, flatulence, hiccups, heartburn, dyspepsia Dysphagia, eructation, salivary hypersecretion
Skin and Subcutaneous Tissue Disorders Uncommon Not Known	 Rash Angioedema, pruritus, erythema, hyperhidrosis
General Disorders and Administration Site Conditions Uncommon Not Known	 Fatigue, malaise, chest pain Influenza like illness**
Infections and infestations Common	 Pharyngitis

**observed in users taking anti-convulsant therapy or with a history of epilepsy.*

***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

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 lozenges ingested). The user should seek medical attentions immediately. All nicotine intake should cease immediately and the patient should 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

Pharmacotherapeutic group: Drugs used in nicotine dependence. ATC Code: N07B A01

Mechanism of Action

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.

Cravings and other symptoms of nicotine withdrawal are at their most intense during the first few weeks of a quit attempt, diminishing thereafter. The lozenges replace some of the nicotine provided by tobacco and clinical studies measuring intensity of cravings and other withdrawal symptoms have been shown to alleviate these symptoms when they are at their most intense

5.2 Pharmacokinetic properties

Absorption

NiQuitin dissolve completely in the oral cavity, and the entire amount of nicotine contained in the lozenge becomes available for buccal absorption or ingestion (swallowing). The complete dissolution of NiQuitin is typically achieved in 10 minutes. When dosed every hour, the steady state mean c_{max} and c_{min} concentrations are 18.4 and 15.0 ng/ml respectively.

Distribution

As the plasma protein binding of nicotine is low (4.9%), 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.

Biotransformation
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.

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 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 postnatal growth retardation and delays and changes in postnatal CNS development.

Effects were only noted following exposure to nicotine at levels in excess of those which will result from recommended use NiQuitin. Effects on fertility have not been established.

Comparison of the systemic exposure necessary to elicit these adverse responses from preclinical test systems with that associated with the recommended use of NiQuitin indicate that the potential risk is low and outweighed by the demonstrable benefit of nicotine therapy in smoking cessation. However, NiQuitin should only be used by pregnant women on medical advice if other forms of treatment have failed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol (E421)
Sodium alginate (E401)
Xanthan gum (E415)
Potassium bicarbonate (E501)
Calcium polycarbophil
Sodium carbonate anhydrous E500)
Acesulfame potassium (E 950)
Mint Flavour Powder
Sucralose (E955)

Magnesium Stearate (E470b)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

30 months

6.4 Special precautions for storage

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

6.5 Nature and contents of container

Child resistant polypropylene tablet container/cap incorporating a molecular sieve desiccant (sodium aluminosilicate) and containing 20 lozenges

Packs may contain 1, 3 or 5 tablet containers.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirement.

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

To be completed nationally.

10 DATE OF REVISION OF THE TEXT

2021-03-31