Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Niquitin mini 4mg mint lozenges

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Excipient with known effect:
Each lozenge contains 4 mg sodium.
For a full list of excipients, see section 6.1.

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 Minis 4mg are to be used for the treatment of tobacco dependence by relief of nicotine withdrawal symptoms and cravings. Permanent cessation of tobacco use is the eventual objective.
NiQuitin Minis 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 Minis 4mg.

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

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

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

In heavy smokers, or those who have relapsed after NRT before, or when one NRT is not enough to control cravings, it may also be beneficial to use NiQuitin Minis 4 mg in combination with NiQuitin patches to support sudden cravings.

NiQuitin Minis 4 mg may be used alone or in combination with NiQuitin patches.

Adults (18 years and over)

Abrupt cessation of smoking:

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.

Gradual cessation of smoking:

For smokers who are unwilling or unable to quit abruptly.

Use a lozenge 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 lozenges a day is variable and depends on the patients needs. Nonetheless it should not exceed 15 lozenges 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 the 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.

Combination therapy: Treatment with NiQuitin Minis 4 mg and NiQuitin Minis 1.5 mg in combination with NiQuitin patches
The initial treatment should begin with the determination of the dose of the patch in combination with NiQuitin Minis 4 mg. The daily intake of NiQuitin Minis 4 mg when combined with patches, is recommended to be around 5 to 6 pieces. When used in combination with patches, the maximum daily dose for NiQuitin Minis 4 mg is 10 pieces and for NiQuitin Minis 1.5 mg is 15 pieces.

Recommended dosage for combination therapy:

Period	**Patches**	**NiQuitin Minis**
Step 1: 6 weeks	NiQuitin 21 mg / 24 hours	5 to 6 pieces of NiQuitin Minis 4 mg per day
Step 2: 2 weeks	NiQuitin 14 mg / 24 hours	Continue to use NiQuitin Minis 1.5 mg when necessary
Step 3: 2 weeks	NiQuitin 7 mg / 24 hours	
After 10 weeks	Stop using NiQuitin patches	Reduce the number of NiQuitin Minis 1.5 mg gradually. When daily use is reduced to 1-2 pieces, treatment should be stopped.

The treatment duration depends on the needs of each smoker. In general, when used in combination, the use of oral NiQuitin Minis 4 mg and NiQuitin Minis 1.5 mg preparations is 2 - 3 months, then use may be reduced gradually. When daily use is reduced to 1-2 doses, use should be stopped.

Paediatric population:

NiQuitin Minis should only be used by adolescents (12-17 years inclusive) with advice from a healthcare professional. Adolescents should not quit with a combination NRT regimen.

NiQuitin Minis 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 Minis 4mg may be considered but as data on safety in this patient group are limited, initiation should only be under close medical supervision.

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

- Stable cardiovascular diseases such as hypertension, stable angina pectoris, cerebrovascular disease, occlusive peripheral arterial disease, and heart failure.
- *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.
- *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.
- *Seizure*s: 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 say essentially sodium-free. During a quit attempt users should not interchange NiQuitin Minis with nicotine gums since pharmacokinetic data indicate a higher availability of nicotine from NiQuitin Minis in comparison to the gum. Special warnings and precautions for use for combined treatment with NiQuitin Minis 4 mg and NiQuitin transdermal patches are the same as for each treatment alone (see SmPC for respective patch preparation used in combination). The combination NRT regimen should not be used in people with known cardiovascular disease without evaluation of the risk/benefit by a healthcare professional.

4.5 Interaction with other medicinal products and other forms of interactions

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

Aromatic hydrocarbons in tobacco smoke induce cytochrome P450 (CYP) 1A2 activity. At cessation of smoking CYP1A2 activity decreases which can lead to increased blood concentrations of medicinal products metabolised via CYP1A2, such as caffeine, theophylline, flecainide, clozapine, olanzapine, ropinirole and pentazocine. The dose may need to be adjusted, and for medicinal products with a narrow therapeutic margin, such as theophylline, smoking cessation should be accompanied by close clinical and even laboratory monitoring and the patient should be informed about the risks of overdose. 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.

Due to an absence of specific studies, combination therapy with patches and NiQuitin Mini 4 mg is not recommended during pregnancy unless the healthcare professional considers it necessary to ensure abstinence.

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.

Due to an absence of specific studies, combination therapy with patches and NiQuitin Mini 4 mg is not recommended during lactation unless the healthcare professional considers it necessary to ensure abstinence.

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

There are no known effects of NiQuitin Minis 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 Minis have not been found to cause any serious adverse effects. Excessive consumption of NiQuitin Minis by those who have not been in the habit of inhaling tobacco smoke could possible 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	Anaphylactic reactions
Not Known	Hypersensitivity
Psychiatric disorders	
Common	Irritability, anxiety, sleep disorders incl. abnormal dreams
Uncommon	Nervousness, depression
Nervous system disorders	
Common	Dizziness, headaches
Not Known	Tremor, dysgeusia, paresthesia mouth, seizures*
Cardiac Disorders	
Uncommon	Palpitations, heart rate increased
Respiratory, thoracic and mediastinal disorders	
Common	Cough, sore throat
Not Known	Dyspnoea
Gastrointestinal disorders	
Very common	Nausea, mouth/throat and tongue irritation
Common	Vomiting, diarrhoea, gastro-intestinal discomfort, flatulence, hiccups, heartburn, dyspepsia, dry mouth, constipation, ulcerative stomatitis, oral discomfort
Not Known	Dysphagia, eructation, salivary hypersecretion
Skin and Subcutaneous Tissue Disorders	
Uncommon	Rash
Not Known	Angioedema, pruritus, erythema, hyperhidrosis
General Disorders and Administration Site Conditions	
Uncommon	Fatigue, malaise, chest pain
Not Known	Influenza like illness**
Infections and infestations	
Common	Pharyngitis

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

***these events may also be due to withdrawalsymptoms 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 HPRA Pharmacovigilance. Website: www.hpra.ie.

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 small 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 lozenges 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 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 gastro-intestinal 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. The lozenges 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
NiQuitin Minis 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 Minis is typically achieved in 10 minutes. The mean peak plasma concentration of nicotine achieved after single 4 mg dose is approximately 9.1 ng/ml.

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 foetal 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 Minis. 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 Minis indicate that the potential risk is low and outweighed by the demonstrable benefit of nicotine therapy in smoking cessation. However, NiQuitin Minis 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 (E950)

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 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

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Chefaro Ireland DAC
The Sharp Building
Hogan Place
Dublin 2
Ireland

8 MARKETING AUTHORISATION NUMBER

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 8th May 2009
Date of last renewal: 17th March 2013

10 DATE OF REVISION OF THE TEXT

April 2021