Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Niquitin Mini 2 mg Mint Lozenges

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each lozenge contains nicotine resinate equivalent to 2 mg nicotine.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Compressed Lozenge (lozenge)

Size to the nearest mm: L: 10 mm × W: 5 mm

White to off white oval lozenge with convex surfaces; one surface bearing a debossed "NIC2" logo.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Niquitin is 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 can also be used for gradual cessation for smokers who are unwilling or unable to quit abruptly.

Niquitin should preferably be used in conjunction with a behavioral support programme.

Niquitin Mini 2 mg Mint Lozenges is indicated in adults and adolescents (12-17 years). In adolescents this product should be used only after advice from a healthcare professional.

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 Mini 2 mg Mint Lozenges is suitable for smokers who smoke 20 cigarettes or less a day.

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

Paediatric population
Adolescents (12-17 years) should follow the schedule of treatment for abrupt cessation of smoking as given above, but as data are limited, duration of use of NRT in this age group is restricted to 10 weeks. In adolescents this product should be used only after advice from a healthcare professional. Adolescents should not quit with a Combination NRT Regimen.
Niquitin must not be used in children below the age of 12 due to a lack of data on safety and efficacy, please see section 4.3.

Adults (18 years and over)

Monotherapy

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 patient's 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 Mini 2 mg Mint Lozenges in combination with Niquitin Patch

For smokers who have relapsed after nicotine replacement therapy (NRT), or when monotherapy with one NRT is not sufficient to control cravings, or as first line treatment in smokers with a high level of dependence.

Smokers can combine the transdermal patches and oral nicotine replacement therapy (gum, lozenges, etc.). The combination of transdermal patches and oral nicotine replacement therapy gives better effectiveness than using transdermal patches alone.

The initial treatment should begin with the determination of the dose of the patch, which depends on the previous smoking habit of the patient, in combination with Niquitin Mini 2 mg Mint Lozenges. The recommended daily intake of Niquitin Mini 2 mg Mint Lozenges, when combined with patches, is 5 to 6 pieces. The maximum daily dose for all oral forms is 15 pieces. Only one type of oral Niquitin product (either Niquitin lozenge or Niquitin gum) shall be used in combination with Niquitin patch.

Recommended dosage for combination therapy:

<table>
<tr><td colspan="3">For smokers who smoke more than 10 cigarettes a day</td></tr>
<tr><th>Period</th><th>Transdermal patches</th><th>Niquitin Mini 2 mg Mint Lozenges</th></tr>
<tr><td>For first 6 weeks</td><td>Step 1, Niquitin 21 mg / 24 hours</td><td>5 to 6 pieces per day</td></tr>
<tr><td>Weeks 7 and 8</td><td>Step 2, Niquitin 14 mg / 24 hours</td><td rowspan="2">Continue to use lozenges when necessary</td></tr>
<tr><td>Weeks 9 and 10</td><td>Step 3, Niquitin 7 mg / 24 hours</td></tr>
<tr><td>After 10 weeks</td><td>Stop using Niquitin patches</td><td>Reduce the number of lozenges gradually. When daily use is reduced to 1-2 pieces, treatment should be stopped.</td></tr>
<tr><td colspan="3">Light smokers (those smoking fewer than 10 cigarettes a day)</td></tr>
<tr><th>Period</th><th>Transdermal patches</th><th>Niquitin Mini 2 mg Mint Lozenges</th></tr>
<tr><td>For first 6 weeks</td><td>Step 2, Niquitin 14 mg / 24 hours</td><td>5 to 6 pieces per day</td></tr>
<tr><td>For Weeks 7 and 8</td><td>Step 3, Niquitin 7 mg / 24 hours</td><td>Continue to use lozenges when necessary</td></tr>
</table>

After 8 weeks	Stop using Niquitin patches	Reduce the number of lozenges 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, the use of oral Niquitin preparations is 2 - 3 months, then use may be reduced gradually. When daily use is reduced to 1-2 doses, use should be stopped.

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.

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

- 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 hypertension 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. If there is a clinically significant increase in cardiovascular or other effects attributable to nicotine, the lozenge dose should be reduced or discontinued.

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.

- *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, please see section 4.5 for more details

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

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

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

4.5 Interaction with other medicinal products and other forms of interaction

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. i.e. increase in blood pressure and heart rate and also increase pain response (anginapectoris type chest pain) provoked by adenosine administration.

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, please see section 4.4 above 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.

Nicotine passes into the foetus and affects the breathing pattern and circulation of the foetus. The effect on the circulation of the foetus is dose-dependent. Pregnant smokers should therefore always be recommended to stop smoking without nicotine replacement therapy. The risk of continuous smoking may pose a greater risk for the foetus than the use of nicotine replacement therapy and medical assessment of the risk/benefit ratio of the use of Niquitin should be made. Niquitin should not be used except by pregnant women with high nicotine dependence following advice from a healthcare professional

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 oral forms is not recommended during pregnancy/lactation 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 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.

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
In animal studies, nicotine has been shown to adversely affect both male and female reproductive systems (see section 5.3).

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 behavioral 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 has 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 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 Rare Very rare	 Hypersensitivity Anaphylactic reaction
Psychiatric disorders Very common Common Not known 	 Insomnia** Nervousness Abnormal dreams, depression**, irritability**, anxiety**
Nervous system disorders Common	 Dizziness**, headaches**, tremor

Not Known	Dysgeusia, paresthesia mouth, seizures*
Cardiac Disorders Uncommon	Palpitations, heart rate increased
Respiratory, thoracic and mediastinal disorders Common	Pharyngitis, Cough**, pharyngolaryngeal pain, dyspnoea, hiccups
Gastrointestinal disorders Very common Common	Nausea, vomiting Diarrhoea, abdominal pain upper , flatulence, hiccups, heartburn, dyspepsia, constipation, dry mouth, ulcerative stomatitis, dry mouth, oral discomfort
Uncommon	Dysphagia
Not Known	Eructation, salivary hypersecretion
Skin and Subcutaneous Tissue Disorders Not known	Rash, angioedema, pruritus, erythema, hyperhidrosis, urticaria
General Disorders and Administration Site Conditions Common	Fatigue**, malaise**, Influenza like illness**, asthenia**
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

Paediatric population (12-17 years inclusive)
There are no specific adverse event data for this population. However, the frequency, type and severity of adverse reactions in adolescents are likely to be the same as adults, based upon a pharmacokinetic study demonstrating a similar pharmacokinetic profile in adolescents compared to adults.

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

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, diarrhea, 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 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. 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 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.

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.

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 or carcinogenic in conventional assays. 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 of nicotine replacement therapy on human 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 resulting from the recommended use of Niquitin. Repeated intraperitoneal or oral administration of nicotine to male rats at doses exceeding those resulting from the recommended use of

Niquitin Mini 2 mg Mint Lozenges 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)
Calcium polycarbophil
Sodium carbonate (E500)
Acesulfame potassium (E950)
Mint Flavor (menthol racemic, peppermint oil, acacia)
Magnesium Stearate (E470b)
Sucralose

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 tablet container in order to protect from moisture.

6.5 Nature and contents of container

Child resistant polypropylene tablet container/cap incorporating a desiccant and containing 20 lozenges.

Packs may contain 1 (including 20 lozenges in total), 3 (including 60 lozenges in total) or 5 (including 100 lozenges in total) 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

Chefaro Ireland DAC,
The Sharp Building
Hogan Place
Dublin 2
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1186/018/017

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23rd July 2021

Date of last renewal: 25th February 2026

10 DATE OF REVISION OF THE TEXT

January 2026