Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

NiQuitin Strips Mint 2.5mg orodispersible film

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each orodispersible film contains 2.5 mg nicotine.
Contains ethanol, not more than 3.9 mg per film.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Orodispersible Film
Transparent film approximately 20 mm by 30 mm.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

NiQuitin Films are to be used for the treatment of tobacco dependence by relief of nicotine withdrawal symptoms, including cravings, during a quit attempt (See section 5.1). Permanent cessation of tobacco use is the eventual objective.

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

4.2 Posology and method of administration

Posology

NiQuitin Films are suitable for smokers who have their first cigarette of the day more than 30 minutes after waking up.

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

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

Adults (18 years and over)

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

Recommended treatment schedule:

Step 1 **Weeks 1 to 6**	**Step 2** **Weeks 7 to 9**	**Step 3** **Weeks 10 to 12**
Initial treatment period	Step down treatment period	Step down treatment period
1 nicotine film every 1 to 2 hours	1 nicotine film every 2 to 4 hours	1 nicotine film every 4 to 8 hours

During weeks 1 to 6 it is recommended that users take a minimum of 9 nicotine films per day. Users should not exceed 15 nicotine films per day.

To help stay smoke free beyond 12 weeks, users may take 1-2 nicotine films per day only on occasions when they are strongly tempted to smoke.

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

Paediatric population

NiQuitin Films should only be used by adolescents (12-17 years inclusive) with advice from a physician.

Nicotine films are contraindicated for use in children under 12 years of age due to the lack of data on safety and efficacy. See section 4.3. There is no experience in treating adolescents under the age of 18 with NiQuitin films.

Method of administration

Place one nicotine film on the tongue. Close the mouth and press the tongue gently to the roof of the mouth until the nicotine film dissolves (approximately 3 minutes). The nicotine film should not be chewed or swallowed whole. Do not use if nicotine film is damaged.

4.3 Contraindications

- people with 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 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 Films 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 film dose should be reduced or discontinued.

Diabetes: Blood glucose levels may be more variable when stopping smoking,

with or without NRT, so it important for diabetics to continue monitoring blood sugar levels 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.

- *Gastrointestinal 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.

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**.**

Ethanol (alcohol): This medicinal product contains small amounts of ethanol (alcohol), less than 100 mg per nicotine film.

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. 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 breastfeeding 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 minimise 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 use the nicotine films.

Fertility

There are no relevant data available.
See section 5.3

4.7 Effects on ability to drive and use machines

NiQuitin Film has no known effects 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

Adults
Nicotine films can cause adverse reactions similar to those associated with nicotine from tobacco. Many of the observed adverse reactions are consistent with the pharmacological effects of nicotine, which are dose dependent. The following undesirable effects detailed in Table 1 are nicotine related adverse events for all oral dosage forms.

Events were identified from:

- a double-blind, randomised, placebo controlled lozenge clinical study involving 1818 patients. Adverse events reported in this study have been considered for inclusion, where the incidence in the 2 mg or 4 mg nicotine arm was higher than the corresponding placebo arm. Frequencies are calculated from the study safety data.
- post-marketing experience of oral nicotine products. Frequencies for these events cannot be estimated for oral nicotine dosage forms from the available data.

Table 1

Cardiac Disorders	
Frequency: Unknown	palpitations, tachycardia
Gastrointestinal Disorders	
Very common ≥1/10	nausea
Common ≥1/100 to<1/10	vomiting, dyspepsia, abdominal pain upper, diarrhoea, dry mouth, constipation, hiccups, stomatitis, flatulence, oral discomfort
Frequency: Unknown	dysphagia, eructation, salivary hypersecretion
General Disorders and Administration Site Conditions	
Frequency: Unknown	asthenia*, fatigue*, malaise*, influenza type illness*
Immune System Disorders	
Frequency: Unknown	hypersensitivity, angioedema, urticaria, ulcerative stomatitis, and very rare anaphylactic reactions
Nervous System Disorders	
Common ≥1/100 to <1/10	headache*, dizziness*
Frequency: Unknown	tremor
Psychiatric Disorders	
Common ≥1/100 to <1/10	insomnia*
Frequency: Unknown	nervousness*
Respiratory, Thoracic and Mediastinal Disorders	
Common ≥1/100 to <1/10	pharyngitis, cough*, pharyngolaryngeal pain
Frequency: Unknown	dyspnoea

***** 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: hprapharmacovigilance@hpra.ie

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 expected to be the same as adults, based upon a pharmacokinetic study demonstrating a similar pharmacokinetic profile in the adolescent age group compared to adults.

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 films 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 films 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: N07BA01

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 nicotine films replace some of the nicotine provided by tobacco. Clinical studies for the bioequivalent 2 mg lozenge have shown a reduction in intensity of cravings.

5.2 Pharmacokinetic properties

Absorption

Nicotine films completely dissolve in the oral cavity, and the entire amount of nicotine contained in the nicotine film becomes available for buccal absorption or ingestion (swallowing). The complete dissolution of a nicotine film is typically achieved in approximately 3 minutes. The peak plasma concentrations of nicotine achieved after a single dose are approximately 4.13 ng/ml.

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 metabolised 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 metabolised primarily to cotinine but is also metabolised 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 oxidised 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 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 of Niquitin films. Effects on fertility have not been established.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methacrylic Acid - Ethyl Acrylate Copolymer (1:1), Type A
Triethyl Citrate (E1505)
Peppermint Flavour TAK - 032230
Sucralose (E955)
Sodium Hydrogen Carbonate (E500 ii)
Ethanol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 30°C. Store in the original package to protect from light and moisture.

6.5 Nature and contents of container

Each Niquitin film is contained in a polyethyleneterephthalate (PET)/aluminium/polyacrylnitrile (PAN) laminate sachet.
Each pack contains 10, 15, 30 or 60 sachets. Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

7 MARKETING AUTHORISATION HOLDER

Chefaro Ireland Limited
First Floor
Block A
The Crescent Building
Northwood Office Park
Dublin 9
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1186/018/013

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12 August 2011

10 DATE OF REVISION OF THE TEXT

November 2015