Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

NiQuitin Tropical Fruit 4 mg medictated chewing gum

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewing gum contains 4 mg nicotine (equivalent to 28.40 mg nicotine resinate) Excipients with known effect:
Butylated Hydroxytoluene (E321) 0.4266 mg/piece gum
Sorbitol (E420) 101.48 mg/piece gum

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Medicated Chewing Gum

Off-white rectangular pillow shaped gum and is approximately 20 x 12 mm.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

NiQuitin Tropical Fruit Medicated Gum is 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 Tropical Fruit Medicated Chewing Gum 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 Tropical Fruit Medicated Chewing Gums.

Adults (18 years and over)

NiQuitin Tropical Fruit 4mg Medicated Chewing Gum is suitable for smokers who smoke more than 20 cigarettes a day.

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

The initial dosage should be individualised on the basis of the patients nicotine dependence.

One piece of NiQuitin Tropical Fruit Medicated Chewing Gums should be chewed as directed whenever there is an urge to smoke, to maintain complete abstinence from smoking.

Sufficient gums should be used each day usually 8-12, up to a maximum of 15.

The treatment duration depends on the needs of each smoker. In general the use of the medicated chewing gum is 2-3 months then the use of gums may be reduced gradually. When daily use is 1-2 gums, use should be stopped. Any spare gums should be retained, as cravings may suddenly return.

Paediatric population

NiQuitin Tropical Fruit Medicated Chewing Gums should only be used by adolescents (12 – 17 years inclusive) with advice from a physician. There is only limited experience from the use of NiQuitin Tropical Fruit Medicated Chewing Gums in this age group.

NiQuitin Tropical Fruit Medicated Chewing Gums are contraindicated in children under 12 years old.

Method of administration

The chewing gums should be used whenever there is an urge to smoke according to the "chew and rest" technique: chew slowly until the taste becomes strong (about 1 minute) then stop and rest the gum against the cheek. When the taste fades, chew a few times until the taste gets strong then rest the gum again. After 30 minutes of such use, the gum will be exhausted. Not more than 15 pieces of the chewing gum may be used each day.

The user should not eat or drink while using the chewing-gum. Drinks that lower the pH in the mouth, e.g. coffee, fruit juice or sodas, may reduce the absorption of nicotine from the oral cavity. To achieve the maximum absorption of nicotine, these drinks should be avoided up to 15 minutes prior to using the chewing-gum.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Children under the age of 12 years
- Non-smoker or occasional smoker

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 hypertension or recent cerebrovascular accident should be encouraged to stop smoking with non-pharmacological interventions (such as counseling). If this fails,

NiQuitin Tropical Fruit Medicated Chewing Gum may be considered, but as data on safety in this patient group are limited, initiation should only be under medical supervision. If there is a clinically significant increase in cardiovascular or other effects attributable to nicotine, the dose should be reduced or discontinued

Diabetes: Blood glucose levels may be more variable when stopping smoking, with or without NRT, so it is important for diabetics to continue monitoring blood sugar levels while using this product

Allergic reactions: Susceptibility to angio-oedema and urticaria.

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

- *Renalandhepaticimpairment:* 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.
- *Phaeochromocytomaanduncontrolledhyperthyroidism:*Use with caution in patients with uncontrolled hyperthyroidism or phaeochromocytoma as nicotine causes release of catecholamines.
- *GI disease:* Swallowing of nicotine may exacerbate symptoms in persons suffering from active oesophagitis, oral or pharyngeal inflammation, gastritis, gastric ulcer 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.

Smokers who wear dentures or who have temporomandibular joint disease may experience difficulty in chewing NiQuitin Tropical Fruit Medicated Chewing Gum. Nicotine gum may loosen fillings or dental implants.

Danger in small children: Doses of nicotine that are 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 metabolised by CYP 1A2 (and possibly by CYP 1A1). When a smoker stops smoking this may result in a slower metabolism and a consequent rise in blood levels of such drugs. This is of potential clinical importance for products with a narrow therapeutic window, e.g. theophylline, tacrine, clozapine and ropinirole. The plasma concentration of other medicinal products metabolised in part by CYP1A2 e.g. imipramine, olanzapine, clomipramine and fluvoxamine may also increase on cessation of smoking, although data to support this are lacking and the possible clinical significance of this effect for these drugs is unknown. Limited data indicate that the metabolism of flecainide and pentazocine may also be induced by smoking.

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

Sorbitol (E420) Patients with hereditary fructose intolerance (HFI) should not take/ be given this medicinal product.

Butylated hydroxytoluene (E321): May cause local reactions (e.g. contact dermatitis), or irritation to the mucous membranes.

Sodium: This medicine contains less than 1 mmol sodium (23 mg) per medicated chewing gum, that is to say essentially 'sodium-free'.

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

4.5 Interaction with other medicinal products and other forms of interactions

No clinically relevant interactions between nicotine replacement therapy and other drugs 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, (see section 4.4).

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 recommendedby a healthcare professionalto 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.

Breastfeeding
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 take breast-feeding hours into account 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.
See section 5.3.

4.7 Effects on ability to drive and use machines

NiQuitin Tropical Fruit Medicated Chewing Gums have 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. Excessive consumption of NiQuitin Tropical Fruit Medicated Chewing Gum 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 available data.)

System Organ Class and Frequency	Adverse Reaction /Events
Immune system disorders	
Very rare	anaphylactic reactions
Not known	Hypersensitivity
Psychiatric disorders	
Common	insomnia, irritability
Not known	Abnormal dreams
Nervous System Disorders	
Common	dizziness; headache
Uncommon	tremor parageusia, metallic taste
Not Known	taste perversion seizures*, paresthesia mouth
Cardiac disorders	
Uncommon Rare	palpitation; tachycardia atrial fibrillation
Respiratory, thoracic and mediastinal disorders	
Common	hiccups; sore throat; cough; pharyngolaryngeal pain
Uncommon	dyspnoea
Gastro-intestinal system disorders	Nausea
Very common	gastro-intestinal discomfort; sore mouth; vomiting; indigestion; mouth irritation; mouth ulceration; dyspepsia; abdominal pain upper; diarrhoea; dry mouth; constipation; hiccups; flatulence; oral discomfort
Common	
Uncommon	stomatitis
Not known	dysphagia, eructation, salivary hypersecretion
Skin and subcutaneous tissue disorders	
Uncommon	erythema; urticaria; increased sweating

Not known	Angioedema, rash, pruritus
Musculoskeletal and connective tissue disorders Common	 jaw pain
General disorders and administration site conditions Uncommon Not known	 chest pain; arthralgia; myalgia; malaise asthenia**, fatigue**, influenza type illness**
Infections and infestations Common ≥/100; <1/10	 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 HPRA Pharmacovigilance, Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

Paediatric Population (12-17 years inclusive)
There are no specific adverse events for this population.

4.9 Overdose

Symptoms: 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.
Signs and symptoms of an overdose from nicotine gums 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 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 gums ingested) the user should seek medical attention 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. The gums 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

Nicotine administered in chewing gums is readily absorbed from the buccal mucous membranes. Demonstrable blood levels are obtained within 5 - 7 minutes and reach a maximum about 30 minutes after the start of chewing. Blood levels are roughly proportional to the amount of nicotine chewed and have been shown never to exceed those obtained from smoking cigarettes.

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. Nicotine crosses the blood-brain barrier, the placenta and is detectable in breast milk.

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 post-natal growth retardation and delays and changes in post-natal CNS development.

Studies in female rodents have shown that nicotine can decrease the number of oocytes in the fallopian tubes, decrease the concentration of serum estradiol, and result in a number of changes to the ovaries and uterus. 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.

Effects were only noted following exposure to nicotine at levels in excess of those which will result from recommended use of NiQuitin Tropical Fruit Medicated Chewing Gum. There are no other pre-clinical data of relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gum core
Gum Base 25048 (incl. 0.09 %w/w Butylated hydroxytoluene (E321)
Sorbitol (E420)
Xylitol (E967)
Calcium Carbonate (E170)
Sodium Carbonate Anhydrous (E500)
Optamint Tropical Flavour (incl.glyceryl triacetate (E1518), alpha-Tocopherol (E307))
Glycerol (E422)
Levomenthol
Optamint Tropical SD Flavour (incl. gum arabic (E414) and sorbitol (E420))
Microcandy Fruit Cocktail Flavour (incl. mannitol (E421), glyceryl triacetate (E1518) & mono and digylycerides of fatty acids (E471))
Optacool Flavour
Acesulfame Potassium (E950)
Sucralose (E955)
Gum Coating
Xylitol (E967) Mannitol (E421)
Acacia (E414)
Titanium Dioxide (E171)

Optamint Grapefruit Aroma
Optacool Flavour
Sucralose (E955)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

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

6.5 Nature and contents of container

20 micron aluminium blister film. The blister film is a clear thermoformable blister film, consisting either of 250 micron polyvinyl chloride (PVC) and 90 g/m^2 polyvinylidene chloride (PVdC) (duplex) or of 250 micron polyvinyl chloride (PVC), 30 micron polyethylene (PE) and 90 g/m^2 polyvinylidene chloride (PVdC) (triplex).

The aluminium sealing side of the aluminium foil is coated with a vinyl based lacquer which seals to the PVdC side of the blister film.
NiQuitin Tropical Fruit Medicated Chewing Gum is available in packs of 4, 10, 30, 100 and 200.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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

7 MARKETING AUTHORISATION HOLDER

Chefaro Ireland DAC
The Sharp Building
Hogan Place
Dublin 2
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1186/019/004

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

April 2021