SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

NiQuitin Mint 2 mg Lozenges

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each compressed lozenge contains 2mg Nicotine (as 13.33mg Nicotine Resinate)

Excipients with known effect
Aspartame [E951] 6.10 mg
Mannitol [E421]

Each lozenge contains 15 mg of Sodium

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Compressed Lozenge

Cream/white, biconvex round lozenge, embossed ‘L344’

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Nicotine Perrigo 2mg Lozenges are indicated for the treatment of tobacco dependence by relieving

nicotine withdrawal symptoms including cravings, associated with smoking cessation. Permanent

cessation of tobacco use is the eventual objective.

Nicotine Perrigo 2mg Lozenges should preferably be used in conjunction with a behavioural

support programme.

4.2 Posology and method of administration

Posology

Adults (18 years and over):

Users should make every effort to stop smoking completely during treatment with NiQuitin Mint 2 mg Lozenges
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 lozenge every 1 to 2 hours	1 lozenge every 2 to 4 hours	1 lozenge every 4 to 8 hours

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

To help stay smoke free beyond 12 weeks, users may take 1-2 lozenges per day only on occasions when they are strongly tempted to smoke.
Lozenges should not be used for more than 6 months. If users still feel the need for treatment, a healthcare professional should be consulted.

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

Paediatric population
NiQuitin Mint 2 mg Lozenges should only be used in adolescents (12-17 years) with the advice of a healthcare professional.

NiQuitin Mint 2 mg Lozenges are contraindicated in children under the age of 12 years in the indication of treatment of nicotine dependence (see section 4.3).

Method of Administration

NiQuitin Mint 2 mg Lozenges are suitable for smokers who have their first cigarette of the day more than 30 minutes after waking up.

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 20 – 30 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 lower the pH in the mouth such as coffee, juices and soft drinks, can decrease the absorption of nicotine in the mouth. To obtain maximum absorption of nicotine these liquids should be avoided for up to 15 minutes before the lozenge is used.

4.3 Contraindications

NiQuitin Mint 2 mg Lozenges are contraindicated in:

- hypersensitivity to the active substance (nicotine) or to any of the excipients listed in section 6.1
- children under the age of 12 years and
- non smokers
- those with phenylketonuria
- contains soya-oil. Contraindicated in persons allergic to peanut or soya.

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.

The following patients should be treated only after advice from a doctor: those with cardiovascular disease (also not hospitalised), with uncontrolled hypertension, with insulin dependent diabetes.

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.

Patients with a recent myocardial infarction, unstable or worsening angina pectoris including Prinzmetal angina, or a recent cardiovascular accident should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). If this fails, nicotine lozenges may be considered, but as data on safety in this patient group are limited, initiation should be under medical supervision. If there is a clinically significant increase in cardiovascular or other effects attributable to nicotine, the nicotine lozenge dose should be reduced or discontinued.

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 events

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 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.

Phenylketonuria: Contains aspartame (E951), a source of phenylalanine. May be harmful for people with phenylketonuria.

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

Mannitol: May have a mild laxative effect.

4.5 Interaction with other medicinal products and other forms of interaction

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.

Smoking cessation, with or without nicotine substitutes, may alter the response to concomitant medication in ex-smokers. The following drugs may require adjustment in dose at cessation of smoking:

*May require a **decrease** in dose at cessation of smoking*	*Possible mechanism of action*

Caffeine, theophylline, imipramine, pentazocine, phenacetin, phenylbutazone, tacrine, clomipramine	Reduced induction of CYP1A2
Insulin	Increase in sub-cutaneous insulin absorption
Adrenergic antagonists e.g prazosin, propranolol	Decreases circulating catecholamines
*May require an **increase** in dose at cessation of smoking*	*Possible mechanism of action*
Adrenergic agonists e.g. isoprenaline, salbutamol	Decreases in circulating catecholamines

Paediatric population

Interaction studies have only been performed in adults.

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 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.

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
Smoking increases the risk for infertility in women and men. Both in humans and in animals it has been shown that nicotine can adversely affect sperm quality. In animals reduced fertility has been shown (see section 5.3).

4.7 Effects on ability to drive and use machines

NiQuitin Mint 2 mg Lozenges has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

NRT can cause adverse reactions similar to those associated with nicotine administered in other way, including smoking. These may be attributed to the pharmacological effects of nicotine, which are dose dependent. At recommended doses NiQuitin Mint 2 mg Lozenges have not been found to cause any serious adverse effects. Excessive consumption of NiQuitin Mint 2 mg Lozenges 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 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.

Description of selected adverse reactions

Immune system disorders

Very rare (<1/10,000)>: anaphylactic reactions, platelet bleeding and clotting disorders

Uncommon (≥1/1,000 to <1/100)>: gingival bleeding; nosebleed

Rare (≥1/10,000 to <1/1,000)>: hypersensitivity

Psychiatric disorders

Common (≥1/100 to <1/10)>: insomnia; anxiety; irritability; increased appetite

Uncommon (≥1/1,000 to <1/100)>: anger; aggravated anxiety; abnormal dreaming; abnormal hunger; mood swings; wakefulness

Nervous system disorders

Very common (≥1/10)>: headache, dizziness*

Uncommon (≥1/1,000 to <1/100)>: localised numbness, parageusia, metallic taste; taste perversion

Not known: dysgeusia, paraesthesia mouth, seizures**

Cardiac disorders

Uncommon (≥1/1,000 to <1/100)>: aggravated palpitations; palpitations; tachycardia

Vascular disorders

Uncommon (≥1/1,000 to <1/100)>: vascular disorder; flushing; skin flushed

Respiratory, thoracic and mediastinal disorders

Common (≥1/100 to <1/10)>: cough*, pharyngolaryngeal pain, hiccups, dyspnoea

Uncommon (≥1/1,000 to <1/100)>: laryngismus; aggravated asthma; lower respiratory tract infection; nasal irritation; throat irritation; nasal congestion

Gastrointestinal disorders

Very common (≥1/10)>: nausea

Common (≥1/100 to <1/10)>: vomiting; dyspepsia, heartburn, indigestion; hiccup; mouth irritation, mouth ulceration; tongue ulceration; diarrhoea; belching; flatulence, abdominal pain upper, constipation, dry mouth, oral discomfort

Uncommon (≥1/1,000 to <1/100)>: peptic ulcer; dysphagia; aggravated dyspepsia; gastroesophageal reflux; hiatus hernia; oesophagitis; eructation; buccal mucosa ulceration; borborygmus; dry lips; dry throat; tongue disorder; tooth ache

Not known: salivary hypersecretion

Skin and subcutaneous tissue disorders

Uncommon (≥1/1,000 to <1/100)>: erythema; itching; rash; skin reaction localised; increased sweating, urticaria

Not known: angioedema

Musculoskeletal and connective tissue disorders

Uncommon (≥1/1,000 to <1/100)>: jaw pain

Renal and urinary disorders

Uncommon (≥1/1,000 to <1/100)>: nocturia

General disorders and administration site conditions

Common (≥1/100 to <1/10)>: asthenia*, fatigue*, malaise*, influenza like illness*

Uncommon (≥1/1,000 to <1/100)>: overdose effect; pain; leg pain; oedema legs

Infections and infestations
Common (>1/100; <1/10): pharyngitis

**These events may also be due to withdrawal symptoms following smoking cessation.*
*** In subjects taking anti-convulsant therapy or with a history of epilepsy*

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the risk/benefit balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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: The minimum lethal dose of nicotine in a non-tolerant man has been estimated to be 40 to 60mg. Symptoms of acute nicotine poisoning include pallor,

cold sweat, nausea, salivation, vomiting, abdominal pain, diarrhoea, sweating headache, dizziness, disturbed hearing and vision, tremor, mental confusion and marked weakness. In extreme cases, these symptoms may be followed by hypotension, rapid or weak or irregular pulse, breathing difficulties, prostration, respiratory failure, circulatory collapse and terminal convulsions.

Management of an overdose: All nicotine intake should stop immediately and the patient should be treated symptomatically. Artificial respiration should be instituted if necessary. Activated charcoal reduces the gastro-intestinal absorption of nicotine.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drug in nicotine dependence, ATC Code: NO 7B A01

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 Mint 2 mg Lozenges completely dissolve 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 Mint 2 mg Lozenges is typically achieved in 20-30 minutes. The peak plasma concentrations of nicotine achieved after a single dose are approximately 4.4 ng/ml. When dosed every 1.5 hours, the steady state peak and trough concentrations are 12.7 and 9.4 ng/ml respectively. Ingestion of NiQuitin Mint 2 mg Lozenges not following dosing instructions (chewed, retained in the mouth, and swallowed; chewed and immediately swallowed) does not result in faster or higher absorption, but a substantial amount of nicotine (80-93%) is still absorbed.

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 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.

Studies in male rats have shown that nicotine can decrease testis weight, cause a reversible decreased 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 Mint 2mg Lozenges.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol

Magnesium stearate

Sodium alginate

Xanthan gum

Potassium bicarbonate

Sodium carbonate anhydrous

Aspartame

Peppermint flavour

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months in ACLAR/PVC/AL blisters

21 months in COC/PVdC/AL blisters

21 months in PVC/PVdC/PVC/AL blisters

6.4 Special precautions for storage

Do not store above 25°C. Store in the original packaging in order to protect from light.

6.5 Nature and contents of container

Clear, Colourless Laminate comprising: 76 micron UltRx3000 ACLAR / Adhesive / 254 micron PVC blister pack comprising of 20 micron Aluminium Foil with heat seal lacquer.

Clear, Colourless Laminate comprising: 60 micron PVC/240 micron COC (Cyclic Olefin Copolymer) / 90gsm PVdC blister pack comprising of 20 micron Aluminium Foil with heat seal lacquer.

Clear Colourless Laminate comprising: 127 micron PVC/120 g/m2 PVdC/127 micron PVC blister pack comprising of 20 micron Aluminium Foil with heat seal lacquer.

Clear Colourless Laminate comprising: 127 micron PVC/180 g/m2 PVdC/127 micron PVC blister pack comprising of 20 micron Aluminium Foil with heat seal lacquer.

Each pack contains 12, 36, 72, 132, 144 and 204 lozenges in a cardboard carton.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Omega Pharma Limited
32 Vauxhall Bridge Road
London
SW1V 2SA
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 02855/0332

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

15/02/2013

10 DATE OF REVISION OF THE TEXT

18/03/2022