Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nicotinell Spearmint 4 mg medicated chewing-gum

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each piece of medicated chewing-gum contains:

Active substance: 4 mg nicotine (as 20 mg nicotine polacrilin (1:4)).

Excipients with known effect: sorbitol (0.1 g), sodium (11 mg) and butylhydroxytoluene (E321)

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Medicated chewing-gum.
The coated chewing-gum is off-white in colour and rectangular in shape.

4 CLINICAL PARTICULARS

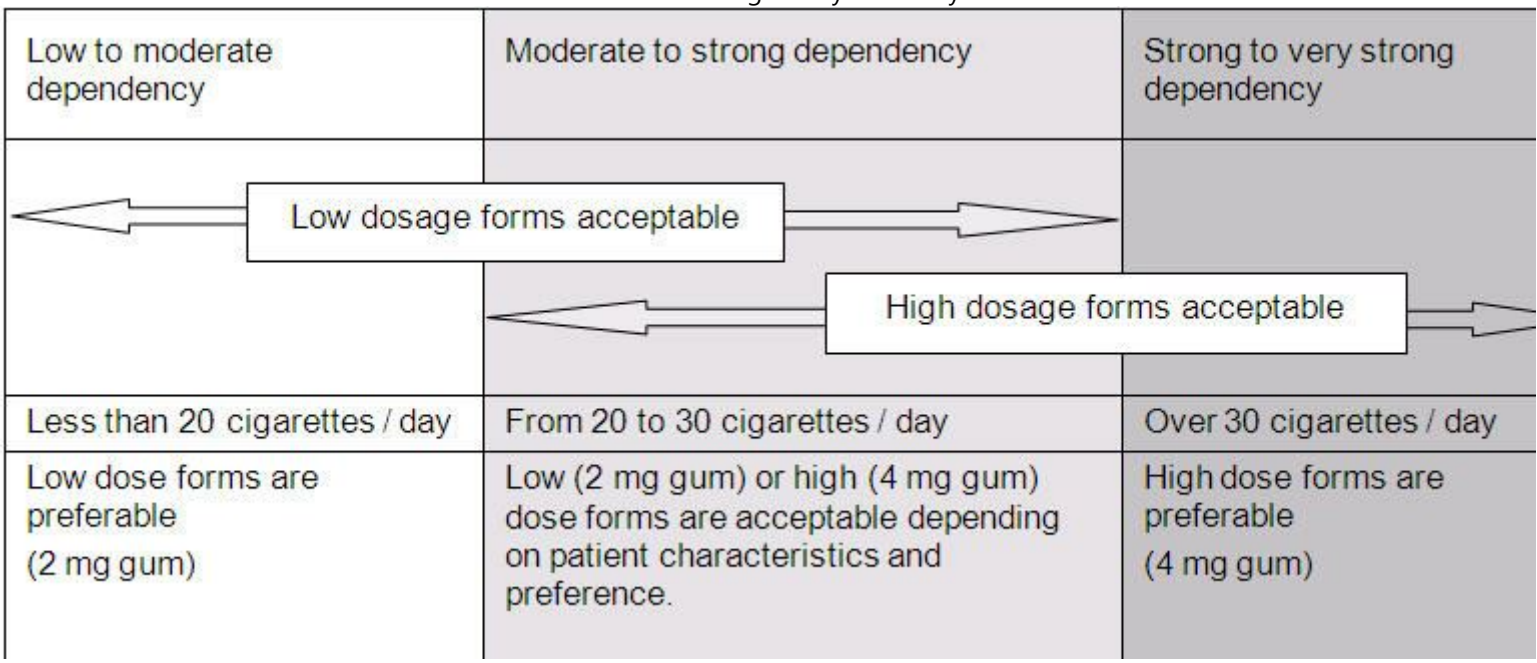
4.1 Therapeutic indications

Treatment of tobacco dependence by providing relief of nicotine craving and nicotine withdrawal symptoms, and by facilitating smoking cessation in smokers motivated to stop smoking or facilitating smoking reduction in smokers who cannot or are reluctant to stop.
Patient counselling and support normally improve the success rate.

4.2 Posology and method of administration

Posology
Adults and elderly
Users should stop smoking completely during treatment with Nicotinell Spearmint medicated chewing-gum.
The dosage should be chosen on the basis of the patient's nicotine dependence. The 4 mg medicated chewing-gum is intended to be used by smokers with a strong nicotine dependency and by those who have previously failed to stop smoking with the 2 mg gum. In other cases, the 2 mg gum shall be used.

The optimal strength is selected according to the following table:



If an adverse event occurs with the use of the high dose form, use of the low dose form should be considered.
The initial dosage should be individualized on the basis of the patient's nicotine dependence.
One piece of Nicotinell Spearmint medicated chewing-gum to be chewed when the user feels the urge to smoke.
Normal use is 8-12 pieces per day, up to a maximum of 15 pieces a day for the 4 mg gum. Do not use more than one gum per hour.

The characteristics of medicated chewing-gum as a pharmaceutical form are such that individually different nicotine levels can result in the blood. Therefore, dosage frequency should be adjusted according to individual requirements within the stated maximum limit.

Smoking cessation
The treatment durationis individual. Normally, treatment should continue for at least 3 months. After 3 months, the users should gradually reduce the nicotine dose. Treatment should be discontinued when the dose has been reduced to 1-2 pieces of medicated chewing-gum per day. Regular use of Nicotinell Spearmint medicated chewing-gum should not be used for more than 12 months unless the potential benefit outweighs the potential risk to the smokers.
Counselling may improve the chance for smokers to quit.

Smoking reduction:
Nicotinell Spearmint medicated chewing-gum should be used between periods of smoking in order to prolong smoke-free intervals and with the intention of reducing smoking as much as possible. If a reduction in the number of cigarettes per day has not been achieved after 6 weeks, professional advice should be sought. A quit attempt should be made as soon as the smoker feels ready, but not later than 6 months after start of treatment. If a quit attempt cannot be made within 9 months after starting treatment, professional advice should be sought. Regular use of Nicotinell Spearmint medicated chewing-gum should not be used for more than 12 months unless the potential benefit outweighs the potential risk to the smokers.

Counselling may improve the chance for smokers to quit.

Paediatric population
Nicotinell Spearmint medicated chewing-gum should not be used by adolescents 12-17 years of age without prescription from a healthcare professional. There is no experience in treating adolescents under the age of 18 years with Nicotinell Spearmint medicated chewing-gum.

Children below 12 years of age
Nicotine gum are not recommended for use in children under 12 years.

Renal and hepatic impairment
Use with caution in patients with moderate to severe renal impairment and/or moderate to severe hepatic impairment as the clearance of nicotine or its metabolites maybe decreased with the potential for increased adverse effects.

Method of administration
1. One piece of medicated chewing-gum should be chewed until the taste becomes strong.
2. The medicated chewing-gum should be rested between the gum and cheek.
3. When the taste fades, chewing should commence again.
4. The chewing routine should be repeated for 30 minutes.

Concomitant use of acidic beverages such as coffee or soda may decrease the buccal absorption of nicotine. Acidic beverages should be avoided for 15 minutes prior to chewing the medicated chewing-gum. Users should not eat or drink while a gum is in the mouth.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Nicotinell Spearmint medicated chewing-gum should not be used by non-smokers.

4.4 Special warnings and precautions for use

Cardiovascular disease: 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, Nicotinell Spearmint medicated chewing-gums may be considered. 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 Nicotinell Spearmint gum dose should be reduced or discontinued.
Nicotinell Spearmint medicated chewing-gums should be used with caution in patients with: hypertension, stable angina pectoris, cerebrovascular disease, occlusive peripheral arterial disease, heart failure, hyperthyroidism or pheochromocytoma.
Diabetes mellitus: blood glucose levels may be more variable during smoking cessation, with or without nicotine replacement therapy. So, it is important for diabetics to closely monitor their blood glucose levels while using this product.
Renal or hepatic impairment: moderate to severe hepatic and/or renal impairment
Seizures: potential risks and benefits of nicotine should be carefully evaluated before use in subjects taking anti-convulsant therapy or with a history of epilepsy as cases of convulsions have been reported in association with nicotine.
Patients should initially be encouraged to stop smoking with non-pharmacological interventions (such as counselling).
Gastrointestinal disease: swallowed nicotine may exacerbate symptoms in subjects suffering from active oesophagitis, oral or pharyngeal inflammation, gastritis or peptic ulcer.
Danger in small children: doses of nicotine that are tolerated by adult smokers during treatment may produce severe symptoms of poisoning in small children and may prove fatal (see section 4.9).
Nicotine oral products should be kept out of sight and reach of children.
Smokers who wear dentures or who have temporomandibular joint disease may experience difficulty in chewing Nicotinell Spearmint. In this case, it is recommended that they use a different pharmaceutical form of nicotine replacement therapy.
Nicotinell Spearmint may loosen fillings or dental implants.

Special warnings about excipients
Patients with rare hereditary conditions of fructose intolerance should not take this medicine.
Nicotinell Spearmint medicated chewing-gum contains sugar substitutes, including 0,1 g sorbitol (E420) per medicated chewing-gum, a source of 0.02 g fructose. Calorific value 1.0 kcal/piece of medicated chewing-gum and 0.9 kcal/piece respectively (Nicotinell Spearmint 2 mg and Nicotinell Spearmint 4 mg respectively).
This medicinal product contains less than 1 mmol (23 mg) per gum, that is to say essentially 'sodium-free'.
The gum base contains butylhydroxytoluene (E321) which may cause local irritation to mucous membranes.

4.5 Interaction with other medicinal products and other forms of interaction

Drug Interactions: No information is available on interactions between Nicotinell Spearmint medicated chewing-gum and other medicinal products.
Smoking but not nicotine is associated with increased CYP1A2 activity. After stopping smoking there may be reduced clearance of substrates for this enzyme and increased plasma levels of some medicinal products of potential clinical importance because of their narrow therapeutic window e.g. theophylline, tacrine**,** olanzapine and clozapine.
The plasma concentrations of other active substances metabolised by CYP1A2 e.g. caffeine, paracetamol, phenazone, phenylbutazone, pentazocine, lidocaine, benzodiazepines, warfarin, oestrogen and vitamin B12 may also increase after stopping smoking. However the clinical significance of this effect is unknown.

Smoking may lead to reduced analgesic effects of propoxyphene, reduced diuretic response to furosemide, reduced effect of propranolol on blood pressure and heart rate and reduced responder rates in ulcer healing with H2-antagonists.
Smoking and nicotine may raise the blood levels of cortisol and catecholamines, i.e. may lead to a reduced effect of nifedipine or adrenergic antagonists and to an increased effect of adrenergic agonists.
Increased subcutaneous absorption of insulin which occurs upon smoking cessation may necessitate a reduction in insulin dose.

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 the pregnant smoker and her baby. The earlier abstinence is achieved the better. Nicotine passes to the foetus and affects its breathing movements and circulation. The effect on the circulation is dose-dependent.
Women who are pregnant should first be advised to stop smoking without the assistance of nicotine replacement therapy. If this fails, the use of nicotine replacement therapy should only be used after advice from a health care professional.

Breast-feeding
Nicotine is excreted in breast milk in quantities that may affect the child even in therapeutic doses. Nicotine replacement therapy should therefore be avoided during breast-feeding. Should smoking withdrawal not be achieved, use of the medicated chewing-gum should only be initiated after advice from a healthcare professional. Where nicotine replacement therapy is used whilst breast-feeding, the medicated chewing-gum should be taken just after breast-feeding and not during the two hours before breast-feeding.

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.

4.7 Effects on ability to drive and use machines

Smoking cessation can cause behavioral changes. There is no evidence of any risks associated with driving or operating machinery when the medicated chewing-gum is used following the recommended dose.

4.8 Undesirable effects

Nicotinell Spearmint medicated chewing-gum can cause adverse reactions similar to those associated with nicotine administered by smoking. These can be attributed to the pharmacological effects of nicotine, which are dose-dependent.
Non dose-dependent adverse reactions are as follows: jaw muscle ache, erythema, urticaria, hypersensitivity, angioneurotic oedema and anaphylactic reactions.
Most of the side effects which are reported by patients occur generally during the first
3-4 weeks after initiation of therapy.
Nicotine from gums may sometimes cause a slight irritation of the throat and increase salivation at the start of the treatment.
Excessive swallowing of nicotine which is released in the saliva may, at first, cause hiccups. Those who are prone to indigestion may suffer initially from minor degrees of dyspepsia or heartburn; slower chewing will usually overcome this problem.
Excessive consumption of nicotine medicated chewing-gums by subjects who have not been in the habit of inhaling tobacco smoke, could possibly lead to nausea, faintness and headache.
Increased frequency of aphthous ulcer may occur after abstinence from smoking.
The medicated chewing-gum may stick to and in rare cases damage dentures and dental appliances.

The following undesirable effects detailed in Table 1 are nicotine related adverse events for all oral dosage forms.

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) or very rare (<1/10,000).

Table 1 shows events which 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 safety data of the study.

Table 1: Adverse Reactions from clinical trial data

System Organ Class	**Very Common** (≥1/10)	**Common** (≥1/100 to <1/10)	**Uncommon** (≥1/1,000 to <1/100)	**Rare** (≥1/10,000 to <1/1000)
Immune system disorders	-	-	-	Hypersensitivity, angioneurotic oedema and anaphylactic reactions
Psychiatric Disorders	-	Insomnia*	-	-
Nervous system disorders	-	Headache*, dizziness*	-	-
Gastrointestinal disorders	Nausea	Hiccups, gastric symptoms e.g. flatulence, vomiting, dyspepsia, stomatitis, oral discomfort, abdominal pain upper, diarrhoea, dry mouth, constipation.	-	-
Respiratory, thoracic and mediastinal disorders	-	Pharyngitis, cough*, pharyngolaryngeal pain	-	-
Musculoskeletal and connective tissue disorders	-	Jaw muscle ache	-	-
Cardiac disorders		-	Palpitations	Atrial arrhythmia (e.g. atrial fibrillation)
Skin and subcutaneous tissue disorders	-	-	Erythema, urticaria	-

* These events may also be due to withdrawal symptoms following smoking cessation.

Post Marketing Data

Table 2 shows events which were identified from post-marketing experience of nicotine oral forms. As these reactions are reported voluntarily from a population of uncertain size, the frequency of these reactions is unknown, but considered likely to be rare or very rare.

Table 2: Adverse Reactions from post-marketing data

System Organ Class	**Adverse Reactions**
Immune System Disorders	Hypersensitivity, angioedema, urticaria, ulcerative stomatitis, and very rare anaphylactic reactions.
Nervous System Disorders	Tremor
Cardiac Disorders	Palpitations, tachycardia, arrhythmias
Respiratory, Thoracic and Mediastinal Disorders	Dyspnoea
Gastrointestinal Disorders	Dysphagia, eructation, salivary hypersecretion
General Disorders and Administration Site Conditions	Asthenia**, fatigue**, malaise**, influenza type illness**

** These events may also be due to withdrawal symptoms following smoking cessation.

Certain symptoms which have been reported such as dizziness, headache and insomnia may be ascribed to withdrawal symptoms in connection with smoking cessation and may be due to insufficient administration of nicotine.
Cold sores may develop in connection with smoking cessation, but any relation with the nicotine treatment is unclear.
The patient may still experience nicotine dependence after 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

In overdose, symptoms corresponding to heavy smoking may be seen.
The acute lethal oral dose of nicotine is about 0.5 - 0.75 mg per kg bodyweight, corresponding in an adult to 40 - 60 mg. Even small quantities of nicotine are dangerous in children, and may result in severe symptoms of poisoning which may prove fatal. If poisoning is suspected in a child, a doctor must be consulted immediately.
Overdose with Nicotinell Spearmint medicated chewing-gum may only occur if many pieces are chewed simultaneously. Nicotine toxicity after ingestion will most likely be minimized as a result of early nausea and vomiting that occur following excessive nicotine exposure. Risk of poisoning by swallowing the medicated chewing-gum is small. Since the release of nicotine from the medicated chewing-gum is slow, very little nicotine is absorbed from the stomach and intestine, and if any is, it will be inactivated in the liver.
General symptoms of nicotine poisoning include: weakness, perspiration, salivation, throat burn, nausea, vomiting, diarrhoea, abdominal pain, hearing and visual disturbances, headache, tachycardia and cardiac arrhythmia, dyspnoea, prostration, circulatory collapse, coma and terminal convulsions.
Treatment of overdose
Symptoms of overdose may develop rapidly, especially in children.Emesis is usually spontaneous. Administration of oral activated charcoal and gastric lavage should be considered as soon as possible and within 1 hour of ingestion. Monitor vital signs and treat symptomatically.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in nicotine dependence
ATC Code: N07BA01
Nicotine, the primary alkaloid in tobacco products and a naturally occurring autonomous substance, is a nicotine receptor agonist in the peripheral and central nervous systems and has pronounced CNS and cardiovascular effects. On consumption of tobacco products, nicotine has proven to be addictive, resulting in craving and other withdrawal symptoms when administration is stopped. This craving and these withdrawal symptoms include a strong urge to smoke, dysphoria, insomnia, irritability, frustration or anger, anxiety, concentration difficulties, agitation and increased appetite or weight gain. The medicated chewing-gum replaces part of the nicotine that would have been administrated via tobacco and reduces the intensity of the withdrawal symptoms and smoking urge.

5.2 Pharmacokinetic properties

When the medicated chewing-gum is chewed, nicotine is steadily released into the mouth and is rapidly absorbed through the buccal mucosa. A proportion, by the swallowing of nicotine containing saliva, reaches the stomach and intestine where it is inactivated.
The nicotine peak plasma mean concentration after a single dose of a 2 mg medicated chewing-gum is approximately 6.4 nanograms per ml (after approximately 45 minutes). The nicotine peak plasma mean concentration after a single dose of a 4 mg medicated chewing-gum is approximately 9.3 nanograms per ml (after approximately 60 minutes). (The average plasma concentration of nicotine when smoking a cigarette is 15-30 nanograms per ml). Nicotine crosses the blood-brain barrier, the placenta and is detectable in breast milk.
Nicotine is eliminated mainly via hepatic metabolism. Small amounts of nicotine are eliminated in unchanged form via the kidneys. The plasma half-life is approximately three hours.

5.3 Preclinical safety data

Nicotine was positive in some in vitro genotoxicity tests but there are also negative results with the same test systems. Nicotine was negative in standard in-vivo tests.
Animal experiments have shown that nicotine induces post-implantation loss and reduces the growth of foetuses.
The results of carcinogenicity assays did not provide any clear evidence of a tumorigenic effect of nicotine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gum base (containing butylhydroxytoluene (E321))
Xylitol

Calcium carbonate (E170)
Sorbitol (E420)
Mannitol (E421)
Sodium carbonate anhydrous
Sodium hydrogen carbonate
Natural mint flavouring
Novamint Spearmint
Polacrilin
Glycerol (E422)
Levomenthol
Sucralose
Gelatine
Titanium dioxide (E171)
Acesulfame potassium (E950)
Carnauba wax
Talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

The medicated chewing-gum is packed in PVC/PVdC/aluminium blisters each containing 12 pieces of medicated chewing-gum. The blisters are packed in boxes containing 12, 24, 48, 84, 96 and 204 pieces of medicated chewing-gum.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Used Nicotinell medicated chewing-gum should be disposed of with care.

7 MARKETING AUTHORISATION HOLDER

Haleon Ireland Limited>
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0678/134/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10th February 2012
Date of last renewal: 17th April 2014

10 DATE OF REVISION OF THE TEXT

April 2023