Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nicorette 4mg Medicated Chewing-gum

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each piece of medicated chewing gum containing 4 mg nicotine as a resin complex.

Excipients with known effect:
Each piece contains:
0.56mg Butylated hydroxytoluene (E321)
178.97mg of Sorbitol (E420)
Flavour for smoker (contains Cinnamal, Cinnamyl alcohol, Citral, Citronellol, Eugenol, Geraniol, Isoeugenol, Limonene, Linalool) 11 mg/chewing gum.
0.616mg ethanol

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Medicated Chewing-gum
A square, yellow medicated chewing-gum

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of tobacco dependence by relieving nicotine craving and withdrawal symptoms:

- thereby facilitating smoking cessation in smokers motivated to quit.
- Helping smokers temporarily abstain from smoking.

In smokers currently unable or not ready to stop smoking abruptly, Nicorette gum may also be used as part of a programme to reduce smoking prior to stopping completely.

4.2 Posology and method of administration

Nicorette 4mg Gum should be chewed slowly.

Smoking cessation

Adults

The strength of gum to be used will depend on the smoking habit of the individual. In general, if the patient smokes fewer than 20 cigarettes a day, Nicorette 2mg Gum is indicated. If more than 20 cigarettes per day are smoked Nicorette 4mg Gum will be needed to meet the withdrawal of the high serum nicotine levels from heavy smoking. The patient should be urged to stop smoking completely when starting therapy with Nicorette Gum.

The chewing gum should be used whenever there is an urge to smoke according to the "chew and rest" technique described on the pack. After about 30 minutes of such use, the gum will be exhausted. Not more that 15 pieces of the chewing gum may be used each day. Absorption of nicotine is through the buccal mucosa, any nicotine which is swallowed being destroyed by the liver.

Administration of nicotine should be stopped temporarily if any symptoms of nicotine excess occur. Nicotine intake should be decreased by lowering dosing frequency if nicotine excess symptoms persist (see Section 4.9).

Nicorette Gum may be used for up to 3 months during which time the habits associated with smoking will be lost. For those using the 4mg Gum, the 2mg will be helpful during withdrawal.

If not successful after 12 weeks the patient should be encouraged to make a fresh attempt to stop smoking. This may necessitate full or partial re-treatment with an NRT programme.

Temporary Abstinence

During periods of temporary abstinence, the patient should use Nicorette Gum when required to relieve nicotine cravings and withdrawal symptoms.
The strength of gum to be used will depend on the smoking habits of the individual. In general, if the patient smokes fewer than 20 cigarettes a day, Nicorette 2mg Gum is indicated. If more that 20 per day are smoked Nicorette 4mg Gum is indicated. Not more than 15 pieces of the gum should be used per day

Gradual cessation

For smokers who are unwilling or unable to quit abruptly.
Use the gum 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 pieces of gum is variable and depends on the patients needs. Not more than 15 pieces of the gum should be used per day.

If a reduction in number of cigarettes per day has not been achieved after 6 weeks, professional advice should be sought.

Reduced tobacco consumption should lead to complete cessation of smoking. A quit attempt should be made as soon as the number of cigarettes has been reduced to a level whereby the smoker feels ready to quit completely, then start as outlined for "smoking 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.

A minor reduction in total clearance of nicotine has been demonstrated in healthy elderly patients, however, not justifying adjustment of dosage.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Use in non-smokers

4.4 Special warnings and precautions for use

The benefits of quitting smoking outweigh any risks associated with correctly administered nicotine replacement therapy (NRT).

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

- Cardiovascular disease: Dependent smokers with a recent myocardial infarction, unstable or worsening angina including Prinzmetal's angina, severe cardiac arrhythmias, recent cerebrovascular accident, and/or who suffer with uncontrolled hypertension should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). If this fails, Nicorette Gum may be considered but as data on safety in this patient group are limited, initiation should only be under close medical supervision.

- 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
- Gastrointestinal Disease: Nicotine may exacerbate symptoms in patients suffering from oesophagitis, gastric or peptic ulcers and NRT preparations should be used with caution in these conditions
- 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 (see section 4.8).
- Phaeochromocytoma and uncontrolled hyperthyroidism. Nicotine, both from NRT and smoking, causes the release of catecholamines from the adrenal medulla. Therefore, Nicorette should be used with caution in patients with uncontrolled hyperthyroidism or pheochromocytoma.
- Diabetes Mellitus. Patients with diabetes mellitus should be advised to monitor their blood sugar levels more closely than usual when smoking is stopped and NRT is initiated, as reductions in nicotine-induced catecholamine release can affect carbohydrate metabolism. Patients with diabetes mellitus may require lower doses of insulin as a result of smoking cessation.
- Smokers who wear dentures may experience difficulties in chewing Nicorette Gum. The chewing gum may stick to, and may in rare cases damage dentures.

Transferred dependence: Nicotine in any dose form is capable of inducing a dependence syndrome after chronic use and is highly toxic after acute use. However, dependence with Nicorette Gum is a rare side-effect and is both less harmful and easier to break than smoking dependence.

Danger in children: Doses of nicotine tolerated by smokers can produce severe toxicity in children that may be fatal. Products containing nicotine should not be left where they may be handled or ingested by children, see section 4.9 Overdose

Nicorette 4mg Gum contains sorbitol. Patients with hereditary fructose intolerance (HFI) should not take this medicine**.**

This product also contains butylated hydroxy toluene (E321); this may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes.

This product contains 0.616 mg of alcohol (ethanol) in each gum. The amount in each gum is equivalent to less than 1 ml beer or 1 ml wine. The small amount of alcohol in this medicine will not have any noticeable effects.

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

This medicine contains flavour with Cinnamal, Cinnamyl alcohol, Citral, Citronellol, Eugenol, Geraniol, Isoeugenol, Limonene, Linalool. These substances may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

Smoking (but not nicotine) is associated with an increase in CYP1A2 activity. After cessation of smoking, reduced clearance of substrates for this enzyme may occur. This may lead to an increase in plasma levels for some medicinal products of potential clinical importance and for products with a narrow therapeutic window, e.g. theophylline, tacrine, ropinirole and clozapine.

The plasma concentration of other drugs metabolised in part by CYP1A2 e.g. imipramine, olanzapin, 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 is unknown.

Limited data indicate the metabolism of flecainide and pentazocine may also be induced by smoking.

Nicotine may possibly enhance the haemodynamic effects of adenosine i.e. increase in blood pressure and heart rate and also increased pain response (angina-pectoris type chest pain) provoked by adenosine administration.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/ contraception in males and females
In contrast to the well-known adverse effects of tobacco smoking on human conception and pregnancy, the effects of therapeutic nicotine treatment are unknown. Thus, whilst to date no specific advice regarding the need for female

contraception has been found to be necessary, the most prudent state for women intending to become pregnant is to be both non-smoking, and not using NRT.
Whilst smoking may have adverse effects on male fertility, no evidence exists that particular contraceptive measures are required during NRT treatment by males.

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 freely to the foetus and affects its breathing movements and circulation. The effect on the circulation is dose-dependent.

Therefore, the pregnant smoker should always be advised to stop smoking completely without the use of nicotine replacement therapy. The risk of continued smoking may pose a greater hazard to the foetus as compared with the use of nicotine replacement therapy products in a supervised cessation programme. Use of Nicorette should only be initiated after advice from a physician.

Lactation:
Nicotine passes freely into breast milk in quantities that may affect the child even in therapeutic dose. Nicorette should therefore be avoided during breast-feeding. Should smoking cessation not be achieved, use of the Nicorette Gum by breast feeding smokers should only be initiated after advice from a health care professional. Women should take Nicorette Gum just after having breastfed.

Fertility
In females tobacco smoking delays time to conception, decreases in-vitro fertilization success rates, and significantly increases the risk of infertility. In males tobacco smoking reduces sperm production, increases oxidative stress, and DNA damage. Spermatozoa from smokers have reduced fertilizing capacity.

The specific contribution of nicotine to these effects in humans is unknown.

4.7 Effects on ability to drive and use machines

Nicorette Medicated Chewing gum has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Effects of Smoking Cessation
Regardless of the means used, a variety of symptoms are known to be associated with quitting habitual tobacco use. These include emotional or cognitive effects such as dysphoria or depressed mood; insomnia; irritability, frustration or anger; anxiety; difficulty concentrating, and restlessness or impatience. There may also be physical effects such as decreased heart rate; increased appetite or weight gain, dizziness or presyncopal symptoms, cough, constipation, gingival bleeding or aphthous ulceration, or nasopharyngitis. In addition, and of clinical significance, nicotine cravings may result in profound urges to smoke.

Adverse Drug Reactions (ADRs)
Nicorette Gum may cause adverse reactions similar to those associated with nicotine administered by other means and are dose dependent.

Most of the undesirable effects reported by the patient occur during the early phase of treatment and are mainly dose dependent. Irritation in the mouth and throat may be experienced, however most patients adapt to this with ongoing use.

Allergic reactions (including symptoms of anaphylaxis) can occur during the use of this product.

Adverse reactions observed in patients treated with oral nicotine formulations during clinical trials and post-marketing experience are listed below by system organ class (SOC). Frequencies are defined in accordance with current guidance, as: Very common (>1/10); common (>1/100, <1/10); uncommon (>1/1 000, <1/100); rare (>1/10 000, <1/1 000); very rare (<1/10 000), Not known - cannot be estimated from the available data.

System Organ Class	Reported Adverse Event	Incidence
Immune System Disorders	Hypersensitivity [a] Anaphylactic reaction [a]	Common Not known

Psychiatric disorders	Abnormal dreams*	Uncommon
Nervous System Disorders	Headache [a#]	Very Common
	Burning sensation [c]	Common
	Dysgeusia	Common
	Paraesthesia [a]	Common
	Seizure*****	Not known
Eye Disorders	Blurred Vision	Not known
	Lacrimation increased	Not known
Cardiac Disorders	Palpitations [a]	Uncommon
	Tachycardia [a]	Uncommon
	Atrial fibrillation	Not known
Vascular Disorders	Flushing [a]	Uncommon
	Hypertension [a]	Uncommon
Respiratory, Thoracic and Mediastinal Disorders	Throat irritation**	Very common
	Cough**	Common
	Bronchospasm	Uncommon
	Dysphonia	Uncommon
	Dyspnoea [a]	Uncommon
	Nasal Congestion	Uncommon
	Sneezing	Uncommon
	Throat tightness	Uncommon
Gastrointestinal Disorders	Hiccups****	Very common
	Nausea [a]	Very common
	Abdominal pain	Common
	Diarrhoea ***	Common
	Dry mouth	Common
	Dyspepsia	Common
	Flatulence	Common
	Salivary hypersecretion	Common
	Stomatitis	Common
	Vomiting [a]	Common
	Eructation	Uncommon
	Glossitis	Uncommon
	Oral mucosal blistering and exfoliation	Uncommon
	Paraesthesia oral ***	Uncommon
	Dysphagia	Rare
	Hypoaesthesia oral ***	Rare
	Retching	Rare
	Dry throat	Not known
	Gastrointestinal discomfort [a]	Not known
	Lip pain	Not known
Skin and Subcutaneous Tissue Disorders	Hyperhidrosis [a]	Uncommon
	Pruritus [a]	Uncommon
	Rash [a]	Uncommon
	Urticaria [a]	Uncommon
	Erythema [a]	Not known
Musculoskeletal and Connective Tissue Disorders	Pain in jaw [b]	Uncommon
	Muscle tightness[b]	Not known
General Disorders and Administration Site Conditions	Fatigue [a]	Common
	Asthenia [a]	Uncommon
	Chest discomfort and pain [a]	Uncommon
	Malaise[a]	Uncommon
	Allergic reactions including angioedema	Rare

[a] Systemic effects;
[b] Tightness of jaw and pain in jaw with nicotine gum formulation
[c] At the application site

*Identified only for formulations applied during the night
**Higher frequency observed in clinical studies with inhaler formulation.
***Reported the same or less frequently than placebo
**** Higher frequency observed in clinical studies with mouth spray formulation
# Although the frequency in the active group is less than that of the placebo group, the frequency in the specific formulation in which the PT was identified as a systemic ADR was greater in the active group than the placebo group.
***** Cases of seizures have been reported 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 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

Excessive use of nicotine from either NRT and/or smoking might cause symptoms of an overdose. Symptoms of an overdose are those of acute nicotine poisoning and include nausea, salivation, abdominal pain, diarrhoea, sweating, headache, dizziness, disturbed hearing and marked weakness. At high doses, these symptoms may be followed by hypotension, weak and irregular pulse, breathing difficulties, prostration, circulatory collapse and general convulsions.

Doses of nicotine that are tolerated by adult smokers during treatment may produce severe symptoms of poisoning in small children and may prove fatal. Suspected nicotine poisoning in a child should be considered a medical emergency and treated immediately.

Management of overdose:
The administration of nicotine must be stopped immediately and the patient should be treated symptomatically.If excessive amount of nicotine is swallowed, activated charcoal reduces the gastrointestinal absorption of nicotine.Tachycardia causing circulatory impairment may require treatment with a β-blocker. Excitation and convulsions may be treated with diazepam. Mechanically assisted ventilation should be instituted if necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Drug for treatment of addiction
ATC Code: NO7B A01

The pharmacological effects of nicotine are well documented. Those resulting from chewing Nicorette 4mg Gum are comparatively small. The response at any one time represents a summation of stimulation and depressant actions from direct, reflex and chemical mediator influences on several organs. The main pharmacological actions are central stimulation and/or depression; transient hyperpnoea; peripheral vasoconstriction (usually associated with a rise in systolic pressure); suppression of appetite and stimulation of peristalsis.

5.2 Pharmacokinetic properties

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 proportioned to the amount of nicotine chewed and are unlikely to exceed those obtained from smoking cigarettes.

5.3 Preclinical safety data

There are no findings derived from preclinical testing of relevance to the prescriber in determining the safety of the product which have not been considered in other relevant sections of this Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Chewing gum base (contains Butylated hydroxytoluene (E321))
Sorbitol (E420)
Sorbitol, liquid crystallising (E420)
Sodium carbonate, anhydrous
Flavour for smoker (contains traces of ethanol, Cinnamal, Cinnamyl alcohol, Citral, Citronellol, Eugenol, Geraniol, Isoeugenol, Limonene, Linalool)
Haverstroo flavour
Talc
Glycerol (E422)
Quinoline Yellow E104

6.2 Incompatibilities

None known.

6.3 Shelf life

30 months.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Blister (PVC/PDC/AL) packed strips each containing 15 pieces supplied in packs of 15, 30,105 and 210 pieces. Pack containing blister strip of 6 pieces.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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