# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Nicotinell Fruit 2 mg, medicated chewing-gums

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each piece of medicated chewing-gum contains:
Active substance: 2 mg nicotine (as 10 mg nicotine –polacrilin (1:4)).
Excipient(s) with known effect: sorbitol (0.2 g)and butylhydroxytoluene (E321).
For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Medicated chewing-gum.
Each piece of coated medicated chewing-gum is off-white in colour and rectangular in shape.

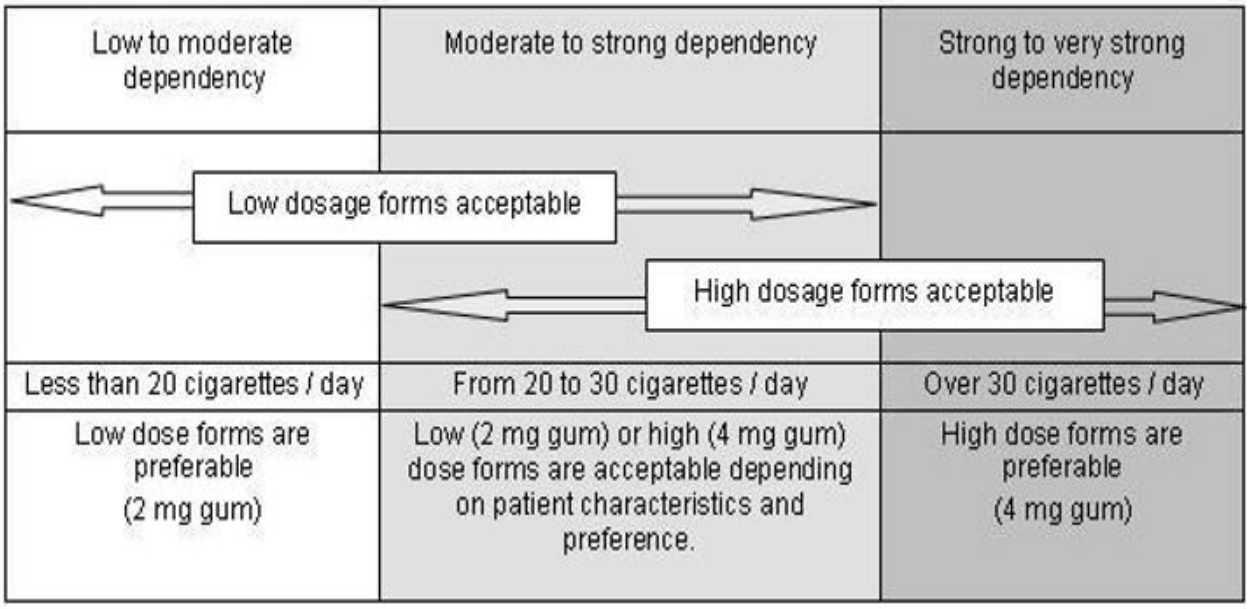
## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

Relief of nicotine withdrawal symptoms, in nicotine dependency as an aid to smoking cessation.
Patient counselling and support normally improve the success rate.

### 4.2 Posology and method of administration

**Posology**
**Adults over 18-years-oldand elderly**
Users should stop smoking completely during treatment with Nicotinell medicated chewing-gum.
The 2 mg medicated chewing-gum is not recommended for smokers with a strong or very strong nicotine dependency.
The optimal dosage form is selected according to the following table:




If an adverse event occurs with the use of the high dose form (4 mg medicated chewing-gum), use of the low dose form (2 mg medicated chewing-gum) should be considered.

The initial dosage should be individualised on the basis of the patients nicotine dependence.
One piece of Nicotinell medicated chewing-gum to be chewed when the user feels the urge to smoke.
If Nicotinell 2 mg medicated chewing-gum is selected, normally use 8-12 pieces per day, up to a maximum of 24 pieces per day.

Do not use more than 1 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.

The treatment durationis individual. Normally, treatment should continue for at least 3 months.
After 3 months, the users should gradually reduce the number of pieces chewed each day until they have stopped using the product.
Treatment should be discontinued when the dose has been reduced to 1-2 pieces of medicated chewing-gum per day. Use of nicotinemedicinalproducts like Nicotinell medicated
chewing-gum beyond 6 months is generally not recommended. Some ex-smokers may need treatment with the medicated chewing-gum for longer to avoid returning to smoking. Patients who have been using oral nicotine replacement therapy beyond 9 months are advised to seek additional help and information from health care professionals.
Counselling may help smokers to quit.

***Paediatric population***

Nicotinell medicated chewing-gum should not be used by people under 18 years of age without recommendation from a physician. There is no experience in treating adolescents under the age of 18 years with Nicotinell medicated chewing-gum.

**Renal impairment**

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

**Hepatic impairment**

Use with caution in patients with 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.

**4.3 Contraindications**

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

**4.4 Special warnings and precautions for use**

Patients with a recent myocardial infarction, unstable or worsening angina including Prinzmetal's angina, severe cardiac arrhythmias, uncontrolled hypertension or recent cerebrovascular accident who are considered to be haemodynamically unstable should be encouraged to stop smoking with non-pharmacological interventions. If this fails, Nicotinell medicated chewing-gums 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 Nicotinell Peppermint gum dose should be reduced or discontinued.
Nicotinell medicated chewing-gums should be used with caution in patients with hypertension, stable angina pectoris, cerebrovascular disease, occlusive peripheral arterial disease, heart failure, moderate to severe hepatic and/or moderate to severe renal impairment, hyperthyroidism or pheochromocytoma, and 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.
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.

Patients should initially be encouraged to stop smoking with non-pharmacological interventions (such as counselling).
Swallowed nicotine may exacerbate symptoms in subjects suffering from active oesophagitis, oral or pharyngeal inflammation, gastritis or peptic ulcer.
Doses of nicotine that are tolerated by adult smokers during treatment may produce severe symptoms of poisoning in small children and may prove fatal (please see Section 4.9).
Nicotine oral products should be kept out of sight and reach of children.
People having problems with the joint of the jawbone and denture wearers may experience difficulty in chewing the medicated chewing-gum. In this case, it is recommended that they use a different pharmaceutical form of nicotine replacement therapy.
Nicotine gum may loosen fillings or dental implants.

***Special warnings about excipients***
Because Nicotinell Fruit medicated chewing-gums contain sorbitol: Patients with rare hereditary conditions of fructose intolerance should not take this medicine.
Nicotinell Fruit 2 mg medicated chewing-gum contains sweeteners, including sorbitol (E420) 0.2 g per medicated chewing-gum, a source of 0.04 g fructose. Calorific value 1.0 kcal/piece of medicated chewing-gum.
Nicotinell Fruit 2 mg medicated chewing-gum contains less than 1 mmol sodium (23 mg) per chewing 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 interactions**

No information is available on clinically relevant interactions between Nicotinell medicated chewing gum and other medicinal products.
Smoking cessation itself may require adjustment of some drug therapy. 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 medicinal products metabolised by CYP1A2, especially drugs with a narrow therapeutic window e.g. theophylline, tacrine, olanzapine and clozapine.
Furthermore, increased subcutaneous absorption of insulin may occurs upon smoking cessation and may necessitate a reduction in insulin dose.

**4.6 Fertility, pregnancy and lactation**

**Pregnancy**
Adverse reproductive and developmental effects have been reported following exposure to tobacco and nicotine during pregnancy. Women who are pregnant should first be advised to stop smoking without the assistance of nicotine replacement therapy. If this fails, the use of oral forms of nicotine replacement therapy may be considered. However, oral forms of nicotine replacement therapy should only be used if the expected benefits to the mother outweigh the potential risks to the foetus.

**Lactation**
Nicotine is excreted in breast milk in quantities that may affect the child even in therapeutic doses. Nicotinell medicated chewing-gum, like smoking itself, should therefore be avoided during breast-feeding. Should smoking withdrawal not be achieved, use of the medicated chewing-gum by breast-feeding smokers should only be initiated after advice from a physician. 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. Oral forms of nicotine replacement therapy should only be used if the expected benefits to the nursing mother outweigh the potential risks to the infant.

**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**

There is no evidence of any risks associated with driving or operating machinery when the medicated chewing-gum is used following the recommended dose. Nevertheless one should take into consideration that smoking cessation can cause behavioural changes.

**4.8 Undesirable effects**

Nicotinell 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, 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 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, <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) |
|---|---|---|---|---|
| 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 diarrhea, dry mouth, constipation. | - | - |
| Respiratory, Thoracic and Mediastinal Disorders | - | Pharyngitis, cough*, pharyngolaryngeal pain | - | - |

* These events may also be due to withdrawal symptoms following smoking cessation.
♦ Individuals with a tendency to experience indigestion may suffer initially from minor degrees of indigestion or heartburn if the 4 mg dose is used - slower chewing in the case of gum or the use of the 2 mg dose (if necessary more frequently) will usually overcome this problem.

**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 medicated chewing-gum may only occur if many pieces are chewed simultaneously. Nicotine toxicity after ingestion will most likely be minimised 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.
Signs and symptoms of nicotine poisoning, of an overdose from nicotine gum would be expected to be the same as those of acute nicotine poisoning and include: weakness, perspiration, pallor, hyperhidrosis, salivation, throat burn, nausea, vomiting, diarrhoea, abdominal pain, hearing and visual disturbances (sensory disturbance), headache, dizziness, tremor, confusional state, and asthenia. Prostration, hypotension, circulatory collapse, coma, respiratory failure and terminal convulsions may ensue with large overdoses.
**Treatment of overdose**
In the event of an overdose (e.g., too many gums ingested) medical attention should be sought immediately. All nicotine intake should cease immediately, and the patient be treated symptomatically, and vital signs monitored.

**5 PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

ATC Code: N07B A01

Pharmacotherapeutic group: Drugs used in nicotine dependence

**Mechanism of action**
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**

**Absorption**
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.
**Distribution**
The nicotine peak plasma mean concentration after a single dose of Nicotinell
2 mg medicated chewing-gum is approximately 6.4 nanograms per ml (after 45 minutes) (average plasma concentration of nicotine when smoking a cigarette is 15-30 nanograms per ml).
**Elimination**
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. Nicotine crosses the blood-brain barrier, the placenta and is detectable in breast milk.

**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 (E 321))
Calcium carbonate
Sorbitol (E420)
Sodium carbonate anhydrous
Sodium hydrogen carbonate
Polacrilin
Glycerol (E422)
Purified water
Levomenthol
Tutti flavour
Saccharin
Sodium saccharin
Acesulfame potassium

Xylitol (E967)
Mannitol (E421)
Gelatin
Titanium dioxide (E171)
Carnauba wax
Talc

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

30 months

**6.4 Special precautions for storage**

Do not store above 25C.

**6.5 Nature and contents of container**

The medicated chewing-gum is packed in PVC/PVdC/aluminium blisters each containing either 2 or 12 pieces of medicated chewing-gum. The blisters are packed in boxes containing 2, 12, 24, 36, 48, 60, 72, 96, 120 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**

GlaxoSmithKline Consumer Healthcare (Ireland) Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

**8 MARKETING AUTHORISATION NUMBER**

PA0678/124/001

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 06 April 2001

Date of last renewal: 25 May 2010

**10 DATE OF REVISION OF THE TEXT**

May 2021