

## Data Sheet

# Nicorette<sup>®</sup> Gum, Nicorette<sup>®</sup> Mint Gum, Nicorette<sup>®</sup> Freshmint Gum and Nicorette<sup>®</sup> Freshfruit Gum

*Chewing Gum containing 2mg or 4mg nicotine*

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## Presentation

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Medicated chewing gum 2mg.  
One gum contains as active ingredient Nicotine-resin complex 20% 10 mg equivalent to nicotine 2 mg.

Medicated chewing gum 4mg.  
One gum contains as active ingredient Nicotine-resin complex 20% 20 mg equivalent to nicotine 4 mg.

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## Uses

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### ***Actions***

Pharmacotherapeutic group: Drug for treatment of nicotine dependence.

ATC code: N07B A01.

Abrupt cessation of the use of tobacco-containing products following a prolonged period of daily use results in a characteristic withdrawal syndrome that includes four or more of the following: dysphoria or depressed mood; insomnia; irritability, frustration or anger; anxiety; difficulty concentrating, restlessness or impatience; decreased heart rate; and increased appetite or weight gain. Nicotine craving, which is recognised as a clinically relevant symptom, is also an important element in nicotine withdrawal.

Clinical studies have shown that nicotine replacement products can help smokers abstain from or reduce their smoking.

### ***Pharmacokinetics***

#### **Pharmacokinetic properties of Nicorette gum**

Nicotine administered in chewing gums is readily absorbed from the oral mucosa membranes. Demonstrable blood levels are obtained within 5-7 minutes after starting chewing and reach a maximum about 5 - 10 minutes after stopping chewing. Blood levels are roughly proportional to the amount of

nicotine released by chewing and are unlikely to exceed those obtained from smoking cigarettes.

The amount of nicotine extracted from one chewing gum depends on how vigorously and for how long it is chewed. The amount of nicotine absorbed depends on the amount extracted and the loss from the oral cavity due to swallowing or expectoration. The systemic availability of swallowed nicotine is lower due to first-pass hepatic metabolism. The high and rapidly rising nicotine concentrations seen after smoking are rarely produced by treatment with the gum. Normally approximately 1.4 mg and 3.4 mg of nicotine will be extracted from the 2 mg and 4 mg gum, respectively.

The volume of distribution following i.v. administration of nicotine is about 2 to 3 L/kg and the half-life is about 2 to 3 hours. The major eliminating organ is the liver, and average plasma clearance is about 70 L/hour. The kidney and lung also metabolise nicotine. More than 20 metabolites of nicotine have been identified, all of which are believed to be less active than the parent compound.

Plasma protein binding of nicotine is less than 5%. Therefore, changes in nicotine binding from use of concomitant drugs or alterations of plasma proteins by disease states would not be expected to have significant effects on nicotine kinetics.

The primary metabolite of nicotine in plasma, cotinine, has a half-life of 15 to 20 hours and concentrations that exceed nicotine by 10-fold.

The primary urinary metabolites are cotinine (15% of the dose) and trans-3-hydroxy-cotinine (45% of the dose). About 10% of nicotine is excreted unchanged in the urine. As much as 30% of nicotine may be excreted unchanged in the urine with high flow rates and acidification of the urine below pH 5.

Progressive severity of renal impairment is associated with decrease total clearance of nicotine. The pharmacokinetics of nicotine is unaffected in cirrhotic patients with mild liver impairment (Child score 5) and decreased in cirrhotic patients with moderate liver impairment (Child score 7). Raised nicotine levels have been seen in smoking patients undergoing hemodialysis.

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

### **Pharmacokinetic properties of the combination of Nicorette patch and Nicorette gum**

The plasma levels of nicotine when combining one 15 mg/16 hours patch and 2 mg chewing gum will depend on the number of gums chewed and the dosing interval.

A simulation of plasma concentrations shows that if one 15 mg/16 hours patch is applied in the morning and five to six 2 mg chewing gums are evenly distributed over the awake hours according to the recommended dosage, a maximum plasma level of about 19 - 20 ng/mL will be reached. The simulation

is based on nicotine pharmacokinetics upon separate use of the 15 mg/16 hours patch and 2 mg gums, respectively.

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## **Indications**

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

Facilitating smoking cessation in smokers motivated to quit.

Helping smokers to temporarily abstain from smoking.

Facilitating smoking reduction in smokers unable or unwilling to quit.

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## **Dosage and Administration**

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Could be used as a single treatment or in combination with nicotine patch.

Each piece of Nicorette gum should be chewed intermittently for about 30 minutes. Nicorette gum should be chewed until a strong taste or a slight tingling sensation is felt, then stop chewing, place the gum between the cheek and gums until the taste or tingling has disappeared, then chew slowly again and repeat.

### ***Children and Adolescents***

Nicorette chewing gum should not be administered to persons under 18 years of age without recommendation from a health care professional. There is limited experience of treating this age group with Nicorette chewing gum.

### ***Adults and Elderly***

#### **For single use**

Use the gum whenever there is an urge to smoke. The initial dosage should be individualised on the basis of the patient's nicotine dependence. Most smokers require about 8-12 pieces of the 2 mg gum or 4-6 pieces of the 4 mg gum. Not more than 20 pieces of the 2 mg gum or 10 pieces of the 4 mg gum (equivalent to a daily dose of 40 mg) should be chewed in one day. Low dependent smokers (Fagerström Test for Nicotine Dependence (FTND) < 6 or smoking ≤ 20 cigarettes/day) should begin treatment with the 2mg strength and high dependent smokers should receive the 4 mg dosage, initially.

#### **Smoking cessation**

Use the gum for at least 3 months. Gradual weaning from the gum should then be initiated. Treatment should be stopped when the dose is reduced to 1-2 chewing gums per day.

## **Smoking reduction**

Use the gum between smoking episodes whenever there is an urge to smoke, to prolong smoke-free intervals and with the intention to reduce your smoking as much as possible. If a reduction in number of cigarettes per day has not been achieved after 6 weeks it should be considered to seek professional advice.

A quit attempt should be made as soon as you feel ready but not later than 6 months after start of treatment. If it is not possible to make a serious quit attempt within 9 months after start of treatment then seek professional advice.

Regular use of the gum beyond 12 months is generally not recommended. Some ex-smokers may need longer treatment with the gum to avoid returning to smoking. Any spare gum should be retained, as craving may suddenly occur.

Advice and support normally improve the success rate.

## **Temporary abstinence**

Use the gum during smoke-free periods, for example in smoke-free areas or in other situations when you wish to avoid smoking, and there is an urge to smoke.

## **In combination with nicotine patch**

Persons who have failed with single treatment or want to reduce the daily intake of the chewing gum because of local adverse events, can use nicotine patches in addition to the 2 mg chewing gum.

### *Initial treatment:*

The treatment should begin with one 15 mg/16 hours patch daily, applied to an intact area of the skin upon waking up in the morning and removed at bedtime, combined with the 2mg gum. Use a minimum of 4 x 2 mg gums per day; usually 5 to 6 gums will be adequate for effect. The maximum number of gums used in conjunction with the patch is 12 pieces per day. This full dose should be used for 12 weeks whereafter gradual weaning from the products should be initiated.

### *Weaning from combination:*

This can be done in two ways, either by using lower strength patches i.e. 2 weeks on 10 mg/16 hours patches and following 2 weeks on 5 mg/16 hours patches, using the same amount as the initial treatment period of the 2mg gum, and then gradually reduce the amount of gum used up to 12 months. Alternatively stop using the patch and gradually reduce the number of gums used up to 12 months.

*Recommended dosage:*

<b>Initial treatment</b>		
<b>Time period</b>	<b>Patch</b>	<b>Gum 2 mg</b>
First 12 weeks	1 patch 15 mg/16 hours per day	Ad libitum. Recommended 5 to 6 gums per day
<b>Weaning - alternative 1</b>		
Next 2 weeks	1 patch 10 mg/16 hours per day	Continue to use gum as needed
Following 2 weeks	1 patch 5 mg/16 hours per day	Continue to use gum as needed.
Up to 12 months	-----	Gradually wean from gum use
<b>Weaning - alternative 2</b>		
Up to 12 months	-----	Continue to gradually wean from gum use

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## **Contraindications**

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Hypersensitivity to nicotine or any components of the chewing gum.

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## **Warnings and Precautions**

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Smokers who wear dentures may experience difficulty in chewing Nicorette gum. The chewing gum may stick to, and may in rare cases damage dentures.

Nicorette gum should only be used after consulting a physician by particular cardiovascular patient groups: those who have experienced a serious cardiovascular event, or hospitalisation for a cardiovascular complaint, in the previous 4 weeks (e.g. stroke, myocardial infarction, unstable angina, cardiac arrhythmia, coronary artery bypass graft and angioplasty) or where they suffer with uncontrolled hypertension. The risk of using nicotine replacement therapy should be weighed against the risk of continued smoking.

Nicorette chewing gum should be used with caution in patients with severe or moderate hepatic impairment, severe renal impairment, active duodenal and gastric ulcers.

Nicotine, both from nicotine replacement products and smoking, causes the release of catecholamines from the adrenal medulla. Therefore Nicorette chewing gum should also be used with caution in patients with uncontrolled hyperthyroidism or pheochromocytoma.

Patients with diabetes mellitus may require lower doses of insulin as a result of smoking cessation.

Some users may continue to use Nicorette gum after the recommended period, but the potential risk of longer term use is far less than those associated with resuming to smoking.

Special warnings and precautions for the combination of nicotine gum with nicotine patch are the same as those for each treatment alone.

### ***Pregnancy and Lactation***

Nicotine passes to the foetus and affects its breathing movements and circulation. The effect on the circulation is dose dependent. Smoking can seriously harm the foetus or infant and should be stopped. Pregnant or breast-feeding smokers should only use Nicorette chewing gum after consulting a health care professional. The risks for the foetus from Nicorette chewing gum are not fully known. The benefits of nicotine replacement therapy in pregnant women who cannot abstain without such therapy substantially outweigh the risk of continued smoking.

Nicotine passes into breast milk in small quantities that may affect the infant, even at therapeutic doses. To reduce the exposition to the child the Nicorette chewing gum should be used just after breast-feeding.

### ***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.

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## **Interactions**

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Smoking (but not nicotine) is associated with 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 for products with a narrow therapeutic window, e.g. theophylline, tacrine, clozapine and ropinirole.

The plasma concentration of other drugs 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.

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## **Adverse Effects**

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Nicorette chewing gum may cause adverse reactions similar to those associated with nicotine administered by other means and are mainly dose-dependent.

Most of the undesirable effects reported by the patients occur during the first 3-4 weeks after start of treatment.

Some symptoms, such as dizziness, headache and sleeplessness may be related to withdrawal symptoms associated with abstinence from smoking. Increased frequency of aphthous ulcers may occur after abstinence from smoking. The causality is unclear.

The chewing gum may stick to, and may in rare cases damage dentures.

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), including isolated reports

<b>Nervous system disorders:</b>	Very common:	Headache
	Common:	Dizziness
<b>Cardiac disorders:</b>	Uncommon:	Palpitations
	Very rare:	Reversible atrial fibrillation
<b>Gastrointestinal disorders:</b>	Very common:	Gastrointestinal discomfort, hiccups, nausea,
	Common:	Vomiting
<b>Skin and subcutaneous tissue disorders</b>	Uncommon:	Erythrema, urticaria
<b>General disorders and administration site conditions:</b>	Very common:	Sore mouth or throat, jaw-muscle ache
	Rare:	Allergic reactions such as angiooedema

Adverse reactions that may occur when using the combination treatment (patch and gum) only differ from each treatment alone in terms of local adverse events associated with the formulations. The frequencies of these adverse events are comparable to those reported for each product respectively.

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## Overdosage

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Excessive use of nicotine from either nicotine replacement therapy and/or smoking might cause symptoms of an overdose. The risk of poisoning as a result of swallowing the gum is very small, as absorption in the absence of chewing is slow and incomplete.

Symptoms of overdosage 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.

### ***Management of overdose***

Administration of nicotine must be stopped immediately and the patient should be treated symptomatically. Activated charcoal reduces gastrointestinal absorption of nicotine.

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## **Pharmaceutical Precautions**

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### ***Shelf-life and Special Precautions for Storage***

Nicorette gum 30 months stored at or below 25°C.

Nicorette Mint gum 30 months stored at or below 25°C.

Nicorette Freshmint Gum 24 months stored at or below 25°C.

Nicorette Freshfruit Gum 24 months stored at or below 25°C.

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## **Medicine Classification**

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General Sale Medicine.

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## **Package Quantities**

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Nicorette Gum 2mg and 4mg: 15, 30 and 105 pieces.

Nicorette Mint Gum 2mg and 4mg: 15, 30 and 105 pieces.

Nicorette Freshmint Gum 2mg and 4mg: 15, 30 and 105 pieces

Nicorette Freshfruit Gum 2mg and 4mg: 15, 30, 60 and 105 pieces

The chewing gums are packed in press through packages (blister packages) held together within a cardboard box.

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## **Further Information**

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### ***List of excipients***

**Nicorette 2 mg**  
Chewing gum base  
Sorbitol powder  
Sorbitol 70%

Flavour for smoker  
Haverstroo flavour  
Sodium carbonate anhydrous  
Sodium hydrogen carbonate  
Glycerol 85%.

**Nicorette 2 mg Mint**

Chewing gum base  
Xylitol  
Peppermint oil  
Menthol  
Sodium carbonate anhydrous  
Sodium hydrogen carbonate  
Magnesium oxide, light.

**Nicorette 2mg Freshmint**

Chewing gum base  
Xylitol  
Peppermint Oil  
Sodium carbonate anhydrous  
Sodium hydrogen carbonate  
Acesulfame K  
Levomenthol  
Magnesium oxide, light  
Acaciae gummi  
Titanium dioxide  
Carnauba wax

**Nicorette 2mg Freshfruit**

Chewing gum base  
Xylitol  
Peppermint Oil  
Sodium carbonate anhydrous  
Sodium hydrogen carbonate  
Acesulfame K  
Levomenthol  
Magnesium oxide, light  
Tutti-fruitti QL84441  
Hyromellose  
Sucralose  
Polysorbate 80  
Acacia  
Titanium dioxide  
Carnauba wax

**Nicorette 4 mg**

Chewing gum base  
Sorbitol powder  
Sorbitol 70%  
Flavour for smoker  
Haverstroo flavour  
Sodium carbonate anhydrous

Quinoline Yellow  
Glycerol 85%.

**Nicorette 4 mg Mint**

Chewing gum base  
Xylitol  
Peppermint oil  
Menthol  
Sodium carbonate anhydrous  
Quinoline Yellow Al-lake E 104  
Magnesium oxide, light.

**Nicorette 4mg Freshmint**

Chewing gum base  
Xylitol  
Peppermint Oil  
Sodium carbonate anhydrous  
Acesulfame K  
Levomenthol  
Magnesium oxide, light  
Acaciae gummi  
Titanium dioxide  
Carnauba wax  
Quinoline yellow E104 AL-Lake

**Nicorette 4mg Freshfruit**

Chewing gum base  
Xylitol  
Peppermint Oil  
Sodium carbonate anhydrous  
Acesulfame K  
Levomenthol  
Magnesium oxide, light  
Tutti-fruitti QL84441  
Hypromellose  
Sucralose  
Polysorbate 80  
Acacia  
Titanium dioxide  
Carnauba wax  
Quinoline yellow E104 Al-Lake

***Preclinical safety data***

There are no pre-clinical data on the safety of Nicorette chewing gum.

The toxicity of nicotine as a component of tobacco is, however, well documented. Typical symptoms of acute poisoning are weak and irregular pulse, breathing difficulties, and general convulsions.

There are no clear evidence of nicotine being genotoxic or mutagenic. The well established carcinogenicity of tobacco smoke is mainly related to

substances formed by the pyrolysis of tobacco. None of these occur in Nicorette chewing gum.

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## **Name and Address**

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## **Date of Preparation**

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31 July 2007