Public Assessment Report

Mutual Recognition Procedure

NICOTINELL FRUIT 2MG CHEWING GUM
NICOTINELL FRUIT 4MG CHEWING GUM
NICOTINELL MINT 2MG CHEWING GUM
NICOTINELL MINT 4MG CHEWING GUM

UK/H/0407-8/001-2/E02
UK Licence No: PL 00030/0162-5

NOVARTIS CONSUMER HEALTH UK LIMITED

LAY SUMMARY

On 16th January 2006, Cyprus, Czech Republic, Estonia, Greece, Hungary, Italy, Lithuania, Latvia, Poland and Slovak Republic granted Novartis Consumer Health UK Limited Marketing Authorisations (licences) for the medicinal products Nicotinell Fruit 2mg and 4mg Chewing Gum (UK/H/0407/001-2/E02) and Nicotinell Mint 2mg and 4mg Chewing Gum (UK/H/0408/001-2/E02). These products have been granted licences by the mutual recognition procedure (MRP), with the UK as reference member state (RMS).

Nicotinell Fruit/Mint 2mg and 4mg Chewing Gum contains nicotine (in the form of nicotine resinate), which is released slowly and absorbed through the lining of the mouth. The nicotine relieves some of the unpleasant symptoms that smokers often feel when they try to give up or when they are in situations where they cannot have a cigarette (such as feeling ill or irritable). The nicotine can reduce your cravings for a cigarette and reduce the urge to smoke.

These products are available on a General Sales Licence (GSL) and are indicated to help people stop smoking, by relieving the withdrawal symptoms that are experienced after stopping. This type of treatment is called Nicotine Replacement Therapy (NRT).

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of taking Nicotinell Fruit/Mint 2mg and 4mg Chewing Gum outweigh the risks, hence Marketing Authorisations have been granted.

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Module 1

Product Name	Nicotinell Fruit 2mg Chewing Gum Nicotinell Fruit 4mg Chewing Gum Nicotinell Mint 2mg Chewing Gum Nicotinell Mint 4mg Chewing Gum
Type of Application	Generic, Article 10.1
Active Substance	Nicotine (as nicotine resinate)
Form	Medicated chewing gum
Strength	2mg and 4mg
MA Holder	Novartis Consumer Health UK Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB
Reference Member State (RMS)	UK
CMS	Cyprus, Czech Republic, Estonia, Greece, Hungary, Italy, Lithuania, Latvia, Poland, Slovak Republic
Procedure Number	UK/H/0407-8/001-2/E02
Timetable	16th January 2006

Module 2
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): sorbitol (0.2 g), sodium (11.50 mg) and butylhydroxytoluene (E321).
For a 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

Adults and 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:

Low to moderate dependency	Moderate to strong dependency	Strong to very strong dependency
← Low dosage forms acceptable →		
	← High dosage forms acceptable →	
Less than 20 cigarettes / day	From 20 to 30 cigarettes / day	Over 30 cigarettes / day
Low dose forms are preferable (2 mg gum)	Low (2 mg gum) or high (4 mg gum) dose forms are acceptable depending on patient characteristics and preference.	High dose forms are preferable (4 mg gum)

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 medicated chewing-gum is selected, normally use 8-12 pieces per day, up to a maximum of 25 pieces per day.

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.

Directions for use:
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.

The treatment duration is 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 nicotine medicinal products 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.

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.

Children and adolescents (< 18 years)
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.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Dependent smokers with a recent myocardial infarction, unstable or worsening angina including Prinzmetal's angina, severe cardiac arrhythmias, uncontrolled hypertensions or recent cerebrovascular accident should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). 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.

Nicotinell medicated chewing-gums should be used with caution in patients with hypertension, stable angina pectoris, cerebrovascular disease, occlusive peripheral arterial disease, heart failure, diabetes mellitus, hyperthyroidism or pheochromocytoma and severe hepatic and/or renal impairment.

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).

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.

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 sodium 11.50 mg per piece.
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 medicated chewing-gum and other medicinal products.

Smoking Cessation: 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. However the clinical significance of this effect for these active substances is unknown.

Smoking may lead to reduced analgesic effects of propoxyphene, reduced diuretic response to furosemide (frusemide), 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 Pregnancy and lactation

Pregnancy
In pregnant women complete cessation of tobacco smoking should always be recommended without nicotine replacement therapy;

Nevertheless, in the case of failure in highly dependent pregnant smokers, tobacco withdrawal via nicotine replacement therapy may be recommended. Indeed, foetal risk is probably lower than that expected with tobacco smoking, due to:
- lower maximal plasma nicotine concentration than with inhaled nicotine
- no additional exposure to polycyclic hydrocarbons and carbon monoxide
- improved chances of quitting smoking by the third trimester.

Smoking continued during the third trimester may lead to intra-uterine growth retardation or even premature birth or stillbirth, depending on the daily amount of tobacco.

Tobacco withdrawal with or without nicotine replacement therapy should not be undertaken alone but as part of a medically supervised smoking cessation program.

In the third trimester nicotine has haemodynamic effects (e.g. changes in foetal heart rate) which could affect the foetus close to delivery. Therefore, after the sixth month of pregnancy, the medicated chewing-gum should only be used under medical supervision in pregnant smokers who have failed to stop smoking by the third trimester.

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.

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, 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 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.

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).

Nervous system disorders:
Common: headache, dizziness

Gastrointestinal disorders:
Common: hiccups, gastric symptoms e.g. nausea, flatulence, vomiting, dyspepsia, salivary hypersecretion, stomatitis, oral pain, or pharyngolaryngeal pain

Musculoskeletal, connective and bone disorders:
Common: jaw muscle ache

Cardiac disorders:
Uncommon: palpitations
Rare: atrial arrhythmia

Skin and subcutaneous tissue disorders:
Uncommon: erythema, urticaria

Immune system disorders:
Rare: hypersensitivity, angioneurotic oedema and anaphylactic reactions

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.

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.

General symptoms of nicotine poisoning include: weakness, perspiration, salivation, dizziness, 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

Treatment of overdose should be immediate as symptoms may develop rapidly. 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

ATC Code: N07B A01

Pharmacotherapeutic group: Drugs used in nicotine dependence

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 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).

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 (E321))
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

2 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

The chewing-gum is packed in PVC/PVdC/aluminium blisters each containing either 2 or 12 pieces of gum. The blisters are packed in boxes containing 2, 12, 24, 36, 48, 60, 72, 96 and 204 pieces of 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

Novartis Consumer Health (UK) Limited
Trading as Novartis Consumer Health
Wimblehurst Road
Horsham
West Sussex
RH12 5AB
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 00030/0162

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 22-08-2000
Date of last renewal: 15-06-2005

10 DATE OF REVISION OF THE TEXT

09-03-2009

1 NAME OF THE MEDICINAL PRODUCT

Nicotinell Fruit 4 mg, medicated chewing-gums.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each piece of medicated chewing-gum contains:
Active substance: 4 mg nicotine (as 20 mg nicotine - polacrilin (1:4)).
Excipient(s): sorbitol (0.2 g), sodium (11.52 mg) and butylhydroxytoluene (E321).
For a 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.
The 4 mg strength is used when severe withdrawal symptoms are experienced.
Patient counselling and support normally improve the success rate.

4.2 Posology and method of administration

Adults and elderly
Users should stop smoking completely during treatment with Nicotinell medicated chewing-gum.

The 4 mg medicated chewing-gum is intended to be used by smokers with a strong or very strong nicotine dependency and those who have previously failed to stop smoking with the aid of nicotine replacement therapy.

The optimal dosage form is selected according to the following table:

Low to moderate dependency	Moderate to strong dependency	Strong to very strong dependency
Low dosage forms acceptable		
	High dosage forms acceptable	
Less than 20 cigarettes / day	From 20 to 30 cigarettes / day	Over 30 cigarettes / day
Low dose forms are preferable (2 mg gum)	Low (2 mg gum) or high (4 mg gum) dose forms are acceptable depending on patient characteristics and preference.	High dose forms are preferable (4 mg gum)

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 4mg medicated chewing-gum is selected, normally use 8-12 pieces per day, up to a maximum of 15 pieces per day.

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.

Directions for use:
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.

The treatment duration is 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 nicotine medicinal products 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.

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.

Children and adolescents (< 18 years)
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.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Dependent smokers with a recent myocardial infarction, unstable or worsening angina including Prinzmetal's angina, severe cardiac arrhythmias, uncontrolled hypertensions or recent cerebrovascular accident should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). 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.

Nicotinell medicated chewing-gums should be used with caution in patients with hypertension, stable angina pectoris, cerebrovascular disease, occlusive peripheral arterial disease, heart failure, diabetes mellitus, hyperthyroidism or pheochromocytoma and severe hepatic and/or renal impairment.

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).

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.

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 4 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 0.9 kcal/piece of medicated chewing-gum.

Nicotinell Fruit 4 mg medicated chewing-gum contains sodium 11.52 mg per piece.
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 Fruit medicated chewing-gum and other medicinal products.

Smoking Cessation: 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. However the clinical significance of this effect for these active substances is unknown.

Smoking may lead to reduced analgesic effects of propoxyphene, reduced diuretic response to furosemide (frusemide), 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 Pregnancy and lactation

Pregnancy

In pregnant women complete cessation of tobacco smoking should always be recommended without nicotine replacement therapy;

Nevertheless, in the case of failure in highly dependent pregnant smokers, tobacco withdrawal via nicotine replacement therapy may be recommended. Indeed, foetal risk is probably lower than that expected with tobacco smoking, due to:
- lower maximal plasma nicotine concentration than with inhaled nicotine
- no additional exposure to polycyclic hydrocarbons and carbon monoxide
- improved chances of quitting smoking by the third trimester.

Smoking continued during the third trimester may lead to intra-uterine growth retardation or even premature birth or stillbirth, depending on the daily amount of tobacco.

Tobacco withdrawal with or without nicotine replacement therapy should not be undertaken alone but as part of a medically supervised smoking cessation program.

In the third trimester nicotine has haemodynamic effects (e.g. changes in foetal heart rate) which could affect the foetus close to delivery. Therefore, after the sixth month of pregnancy, the medicated chewing-gum should only be used under medical supervision in pregnant smokers who have failed to stop smoking by the third trimester.

Lactation

Nicotine is excreted in breast milk in quantities that may affect the child even in therapeutic doses. Nicotinell Fruit 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.

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 Fruit 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 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.

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).

Nervous system disorders:
Common: headache, dizziness

Gastrointestinal disorders:
Common: hiccups, gastric symptoms e.g. nausea, flatulence, vomiting, dyspepsia, salivary hypersecretion, stomatitis, oral pain, or pharyngolaryngeal pain

Musculoskeletal, connective and bone disorders:
Common: jaw muscle ache

Cardiac disorders:
Uncommon: palpitations
Rare: atrial arrhythmia

Skin and subcutaneous tissue disorders:
Uncommon: erythema, urticaria

Immune system disorders:
Rare: hypersensitivity, angioneurotic oedema and anaphylactic reactions

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.

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 Fruit 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.

General symptoms of nicotine poisoning include: weakness, perspiration, salivation, dizziness, 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

Treatment of overdose should be immediate as symptoms may develop rapidly. 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

ATC Code: N07B A01

Pharmacotherapeutic group: Drugs used in nicotine dependence

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 Nicotinell Fruit 4 mg medicated chewing-gum is approximately 9.3 nanograms per ml (after approximately 60 minutes) (average plasma concentration of nicotine when smoking a cigarette is 15-30 nanograms per ml).

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 (E321))
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

2 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

The chewing-gum is packed in PVC/PVdC/aluminium blisters each containing either 2 or 12 pieces of gum. The blisters are packed in boxes containing 2, 12, 24, 36, 48, 60, 72, 96 and 204 pieces of gum.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Novartis Consumer Health (UK) Limited
Trading as Novartis Consumer Health
Wimblehurst Road
Horsham
West Sussex
RH12 5AB
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 00030/0163

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 22-08-2000
Date of last renewal: 15-06-2005

10 DATE OF REVISION OF THE TEXT

09-03-2009

1 NAME OF THE MEDICINAL PRODUCT

Nicotinell Mint 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): sorbitol (0.2 g), sodium (11.50 mg) and butylhydroxytoluene (E321).
For a 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.

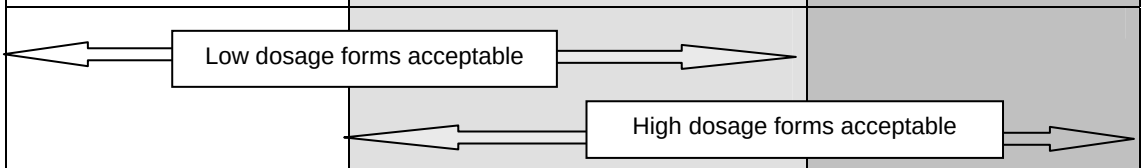
4.2 Posology and method of administration

Adults and 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:

Low to moderate dependency	Moderate to strong dependency	Strong to very strong dependency
		
Less than 20 cigarettes / day	From 20 to 30 cigarettes / day	Over 30 cigarettes / day
Low dose forms are preferable (2 mg gum)	Low (2 mg gum) or high (4 mg gum) dose forms are acceptable depending on patient characteristics and preference.	High dose forms are preferable (4 mg gum)

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 2mg chewing-gum is selected, normally use 8-12 pieces per day, up to a maximum of 25 pieces per day.

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.

Directions for use:
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.

The treatment duration is 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 nicotine medicinal products 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.

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.

Children and adolescents (< 18 years)
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.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Dependent smokers with a recent myocardial infarction, unstable or worsening angina including Prinzmetal's angina, severe cardiac arrhythmias, uncontrolled hypertensions or recent cerebrovascular accident should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). 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.

Nicotinell medicated chewing-gums should be used with caution in patients with hypertension, stable angina pectoris, cerebrovascular disease, occlusive peripheral arterial disease, heart failure, diabetes mellitus, hyperthyroidism or pheochromocytoma and severe hepatic and/or renal impairment.

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).

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.

Special warnings about excipients
Because Nicotinell Mint medicated chewing-gums contain sorbitol: Patients with rare hereditary conditions of fructose intolerance should not take this medicine.

Nicotinell Mint 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 Mint 2 mg medicated chewing-gum contains sodium 11.50 mg per piece.
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 medicated chewing-gum and other medicinal products.

Smoking Cessation: 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. However the clinical significance of this effect for these active substances is unknown.

Smoking may lead to reduced analgesic effects of propoxyphene, reduced diuretic response to furosemide (frusemide), 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 Pregnancy and lactation

Pregnancy

In pregnant women complete cessation of tobacco smoking should always be recommended without nicotine replacement therapy;

Nevertheless, in the case of failure in highly dependent pregnant smokers, tobacco withdrawal via nicotine replacement therapy may be recommended. Indeed, foetal risk is probably lower than that expected with tobacco smoking, due to:
- lower maximal plasma nicotine concentration than with inhaled nicotine
- no additional exposure to polycyclic hydrocarbons and carbon monoxide
- improved chances of quitting smoking by the third trimester.

Smoking continued during the third trimester may lead to intra-uterine growth retardation or even premature birth or stillbirth, depending on the daily amount of tobacco.

Tobacco withdrawal with or without nicotine replacement therapy should not be undertaken alone but as part of a medically supervised smoking cessation program.

In the third trimester nicotine has haemodynamic effects (e.g. changes in foetal heart rate) which could affect the foetus close to delivery. Therefore, after the sixth month of pregnancy, the medicated chewing-gum should only be used under medical supervision in pregnant smokers who have failed to stop smoking by the third trimester.

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.

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, 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 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.

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).

Nervous system disorders:
Common: headache, dizziness

Gastrointestinal disorders:
Common: hiccups, gastric symptoms e.g. nausea, flatulence, vomiting, dyspepsia, salivary hypersecretion, stomatitis, oral pain, or pharyngolaryngeal pain

Musculoskeletal, connective and bone disorders:
Common: jaw muscle ache

Cardiac disorders:
Uncommon: palpitations
Rare: atrial arrhythmia

Skin and subcutaneous tissue disorders:
Uncommon: erythema, urticaria

Immune system disorders:
Rare: hypersensitivity, angioneurotic oedema and anaphylactic reactions

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.

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.

General symptoms of nicotine poisoning include: weakness, perspiration, salivation, dizziness, 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

Treatment of overdose should be immediate as symptoms may develop rapidly. 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

ATC Code: N07B A01

Pharmacotherapeutic group: Drugs used in nicotine dependence

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 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).

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 (E321))
Calcium carbonate
Sorbitol (E420)
Sodium carbonate anhydrous
Sodium hydrogen carbonate
Polacrilin
Glycerol (E422)
Purified water
Levomenthol
Peppermint oil
Eucalyptus oil
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

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 either 2 or 12 pieces of medicated chewing-gum. The blisters are packed in boxes containing 2, 12, 24, 36, 48, 60, 72, 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

Novartis Consumer Health (UK) Limited
Trading as Novartis Consumer Health
Wimblehurst Road
Horsham
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RH12 5AB
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 00030/0164

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 22-08-2000
Date of last renewal: 15-06-2005

10 DATE OF REVISION OF THE TEXT

09-03-2009

1 NAME OF THE MEDICINAL PRODUCT

Nicotinell Mint 4 mg, medicated chewing-gums.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each piece of medicated chewing-gum contains:
Active substance: 4 mg nicotine (as 20 mg nicotine - polacrilin (1:4)).
Excipient(s): sorbitol (0.2 g), sodium (11.52 mg) and butylhydroxytoluene (E321).
For a 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.
The 4 mg strength is used when severe withdrawal symptoms are experienced.
Patient counselling and support normally improve the success rate.

4.2 Posology and method of administration

Adults and elderly

Users should stop smoking completely during treatment with Nicotinell medicated chewing-gum.

The 4 mg medicated chewing-gum is intended to be used by smokers with a strong or very strong nicotine dependency and those who have previously failed to stop smoking with the aid of nicotine replacement therapy.

The optimal dosage form is selected according to the following table:

Low to moderate dependency	Moderate to strong dependency	Strong to very strong dependency
← Low dosage forms acceptable →		
	← High dosage forms acceptable →	
Less than 20 cigarettes / day	From 20 to 30 cigarettes / day	Over 30 cigarettes / day
Low dose forms are preferable (2 mg gum)	Low (2 mg gum) or high (4 mg gum) dose forms are acceptable depending on patient characteristics and preference.	High dose forms are preferable (4 mg gum)

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 4mg chewing-gum is selected, normally use 8-12 pieces per day, up to a maximum of 15 pieces per day.

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.

Directions for use:
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.

The treatment duration is 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 nicotine medicinal products 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.

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.

Children and adolescents (< 18 years)
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.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Dependent smokers with a recent myocardial infarction, unstable or worsening angina including Prinzmetal's angina, severe cardiac arrhythmias, uncontrolled hypertensions or recent cerebrovascular accident should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). 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.

Nicotinell medicated chewing-gums should be used with caution in patients with hypertension, stable angina pectoris, cerebrovascular disease, occlusive peripheral arterial disease, heart failure, diabetes mellitus, hyperthyroidism or pheochromocytoma and severe hepatic and/or renal impairment.

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).

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.

Special warnings about excipients
Because Nicotinell Mint medicated chewing-gums contain sorbitol: Patients with rare hereditary conditions of fructose intolerance should not take this medicine.

Nicotinell Mint 4 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 0.9 kcal/piece of medicated chewing-gum.

Nicotinell Mint 4 mg medicated chewing-gum contains sodium 11.52 mg per piece.
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 medicated chewing-gum and other medicinal products.

Smoking Cessation: 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. However the clinical significance of this effect for these active substances is unknown.

Smoking may lead to reduced analgesic effects of propoxyphene, reduced diuretic response to furosemide (frusemide), 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 Pregnancy and lactation

Pregnancy

In pregnant women complete cessation of tobacco smoking should always be recommended without nicotine replacement therapy;

Nevertheless, in the case of failure in highly dependent pregnant smokers, tobacco withdrawal via nicotine replacement therapy may be recommended. Indeed, foetal risk is probably lower than that expected with tobacco smoking, due to:
- lower maximal plasma nicotine concentration than with inhaled nicotine
- no additional exposure to polycyclic hydrocarbons and carbon monoxide
- improved chances of quitting smoking by the third trimester.

Smoking continued during the third trimester may lead to intra-uterine growth retardation or even premature birth or stillbirth, depending on the daily amount of tobacco.

Tobacco withdrawal with or without nicotine replacement therapy should not be undertaken alone but as part of a medically supervised smoking cessation program.

In the third trimester nicotine has haemodynamic effects (e.g. changes in foetal heart rate) which could affect the foetus close to delivery. Therefore, after the sixth month of pregnancy, the medicated chewing-gum should only be used under medical supervision in pregnant smokers who have failed to stop smoking by the third trimester.

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.

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, 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 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.

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).

Nervous system disorders:
Common: headache, dizziness

Gastrointestinal disorders:
Common: hiccups, gastric symptoms e.g. nausea, flatulence, vomiting, dyspepsia, salivary hypersecretion, stomatitis, oral pain, or pharyngolaryngeal pain

Musculoskeletal, connective and bone disorders:
Common: jaw muscle ache

Cardiac disorders:
Uncommon: palpitations
Rare: atrial arrhythmia

Skin and subcutaneous tissue disorders:
Uncommon: erythema, urticaria

Immune system disorders:
Rare: hypersensitivity, angioneurotic oedema and anaphylactic reactions

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.

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.

General symptoms of nicotine poisoning include: weakness, perspiration, salivation, dizziness, 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

Treatment of overdose should be immediate as symptoms may develop rapidly. 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

ATC Code: N07B A01

Pharmacotherapeutic group: Drugs used in nicotine dependence

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 Nicotinell 4 mg medicated chewing-gum is approximately 9.3 nanograms per ml (after approximately 60 minutes) (average plasma concentration of nicotine when smoking a cigarette is 15-30 nanograms per ml).

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 (E321))
Calcium carbonate
Sorbitol (E420)
Sodium carbonate anhydrous
Sodium hydrogen carbonate
Polacrilin
Glycerol (E422)
Purified water
Levomenthol
Peppermint oil
Eucalyptus oil
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

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 either 2 or 12 pieces of medicated chewing-gum. The blisters are packed in boxes containing 2, 12, 24, 36, 48, 60, 72, 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

Novartis Consumer Health (UK) Limited
Trading as Novartis Consumer Health
Wimblehurst Road
Horsham
West Sussex
RH12 5AB
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 00030/0165

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 22-08-2000
Date of last renewal: 15-06-2005

10 DATE OF REVISION OF THE TEXT

09-03-2009

Module 3
Patient Information Leaflet

Please note that the Patient Information Leaflets submitted are the text versions submitted to the UK only and may differ from those submitted to other member states. The marketing authorisation holder has committed to submitting mock-ups to the regulatory authorities for approval before marketing any products.

Nicotinell Fruit 2 mg medicated chewing-gum

Nicotine

Read all of this leaflet carefully because it contains important information for you.

This medicine is available without prescription. However, you still need to use Nicotinell Fruit 2 mg medicated chewing-gum carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if you still need to use Nicotinell after 9 months.
- If any of the side effects gets serious, or if you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Nicotinell medicated chewing-gum is and what it is used for
2. Before you take Nicotinell medicated chewing-gum
3. How to take Nicotinell medicated chewing-gum
4. Possible side effects
5. How to store Nicotinell medicated chewing-gum
6. Further information

1. WHAT NICOTINELL MEDICATED CHEWING-GUM IS AND WHAT IT IS USED FOR

Nicotinell belongs to a group of medicines which are used to help you to stop smoking.

Nicotinell contains nicotine, which is one of the substances contained in tobacco.

When chewed, nicotine is released slowly and absorbed through the lining of the mouth.

This medicinal product is used to relieve the nicotine withdrawal symptoms in nicotine dependency, as an aid to smoking cessation.

Patient counselling and support normally improve the success rate.

2. BEFORE YOU TAKE NICOTINELL MEDICATED CHEWING-GUM

Do not take Nicotinell medicated chewing-gum

- If you are allergic (hypersensitive) to nicotine or any of the other ingredients of Nicotinell
- If you are a non-smoker.

Take special care with Nicotinell medicated chewing-gum

Please check with your doctor or pharmacist before taking Nicotinell if you have:

- heart disease, e.g. heart attack, heart failure, angina, Prinzmetal's angina or abnormalities in heart beat rhythm,
- had a "stroke" (cerebrovascular accident),
- high blood pressure (uncontrolled hypertension),
- problems with your circulation,
- diabetes (monitor your blood sugar levels more often when starting to use Nicotinell as you may find your insulin or medication requirements alter)
- overactive thyroid glands (hyperthyroidism),
- overactive adrenal glands (pheochromocytoma),
- kidney or liver disease,
- oesophagitis, inflammation in the mouth or throat, gastritis or peptic ulcer,
- fructose intolerance.

Even small quantities of nicotine are dangerous in children and may result in severe symptoms or death. It is therefore essential that you keep Nicotinell out of reach and sight of children at all times

People having problems with the joint of the jawbone and some denture wearers may experience difficulty in chewing the gum. If you do, it is recommended that you use a different pharmaceutical form of nicotine replacement therapy. Ask your doctor or pharmacist for advice.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. If you stop smoking and if you are using other medicines, your doctor may want to adjust the dose.

No information is available on interactions between Nicotinell and other medicines. However, apart from nicotine, other substances in cigarettes may have an effect on certain medicine.

Stopping smoking can affect the action of certain medicines e.g.:

- theophyllin (a medicine used for the treatment of bronchial asthma)
- tacrine (medicine used to treat Alzheimer's disease)
- olanzapine and clozapine (for the treatment of schizophrenia)
- Insulin dose (medicine used for the treatment of diabetes) may need to be adjusted

Taking Nicotinell medicated chewing-gum with food and drink

Coffee, acidic drinks (e.g. fruit juice) and soft drinks may decrease the absorption of nicotine and should be avoided for 15 minutes before chewing Nicotinell.

Pregnancy and breast-feeding

It is very important to stop smoking during pregnancy because it can result in poor growth of your baby. It can also lead to premature births and even stillbirths. Ideally you should try to give up smoking without the use of medicines. If you cannot manage this, Nicotinell may be recommended to help as the risk to the developing baby is less than that expected from continued smoking. Nicotine in any form may cause harm to your unborn baby. Nicotinell should only be used after consulting the healthcare professional who is managing your pregnancy, or a doctor that is specialised in helping people quit smoking.

Nicotinell like smoking itself should be avoided during breast-feeding as nicotine may be found in breast milk. If your doctor has recommended that you should take this medicinal product, the medicated chewing-gum should be taken just after breast-feeding and not during the two hours before breast-feeding.

Driving and using machines

There is no evidence of risk associated with driving or operating machinery if Nicotinell is taken according to the recommended dose but remember that smoking cessation can cause behavioural changes.

Important information about some of the ingredients of Nicotinell medicated chewing-gum

Because Nicotinell Fruit contains sorbitol: if you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

The gum base contains butylhydroxytoluene (E321) which may cause local irritation to mucous membranes.

Each piece of Nicotinell Fruit 2 mg contains sweeteners, including sorbitol (E420) 0.2 g, a source of 0.04 g fructose. Calorific value 1.0 kcal/piece.

Nicotinell Fruit 2 mg contains 11.50 mg of sodium per piece. To be taken into consideration by patients on a controlled sodium diet.

3. HOW TO TAKE NICOTINELL MEDICATED CHEWING-GUM

Always take Nicotinell exactly as stated in this package leaflet. You should check with your doctor or pharmacist if you are not sure.

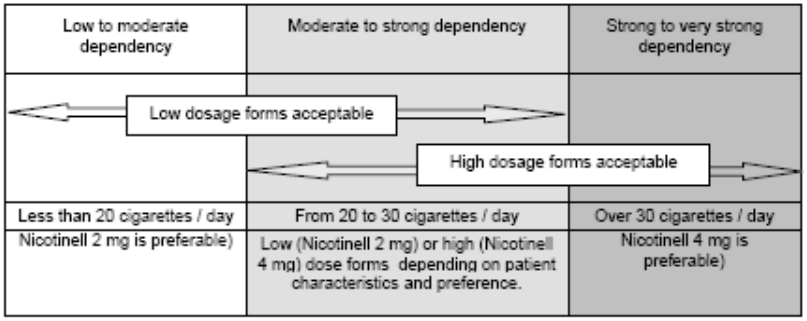
To improve your chances of giving up smoking you should stop smoking completely when you start to use Nicotinell and for the whole treatment duration.

Nicotinell is available in two strengths: 2 and 4 mg. The appropriate dose will depend on your previous smoking habits. You should use Nicotinell 4 mg if:

- you are a smoker with a strong or very strong nicotine dependency,
- you have previously failed to stop smoking with Nicotinell 2 mg,
- your withdrawal symptoms remain so strong as to threaten relapse.

Otherwise Nicotinell 2 mg should be used.

Select your optimal dosage from the following table:



If an adverse event occurs with the use of the high dose (Nicotinell 4 mg), use of the low dose (Nicotinell 2 mg) should be considered.

Instructions for use:

1. Chew one piece of Nicotinell slowly until the taste becomes strong.
2. Allow Nicotinell to rest between your gum and cheek.
3. Chew again when taste has faded.
4. Repeat this routine for about 30 minutes, to get a gradual release of nicotine.

Do not swallow.

Dosage for adults over 18 years:

Chew one piece of Nicotinell when you feel the urge to smoke. In general one piece should be chewed every one or two hours. Normally 8-12 pieces per day are sufficient. If you still experience an urge to smoke, you can chew additional pieces of Nicotinell. Do not exceed 25 pieces a day of Nicotinell 2 mg.

The treatment duration is individual. Normally, treatment should continue for at least 3 months. After 3 months, you should gradually reduce the number of pieces of Nicotinell chewed each day. Treatment should be stopped when you have reduced your use of Nicotinell to 1-2 pieces per day. It is generally not recommended to use Nicotinell for longer than 6 months. However, some ex-smokers may need treatment with Nicotinell for longer to avoid returning to smoking.

If you are still using Nicotinell after 9 months, you should speak to your doctor or pharmacist.

Counselling may improve your chances of giving up smoking.

Children and adolescents(< 18 yrs)

Nicotinell should **not** be used by people under 18 years of age without recommendation from a doctor.

If you take more Nicotinell medicated chewing-gums than you should

Chewing too many Nicotinell pieces can result in the same symptoms as smoking too much. The general symptoms of nicotine overdose include weakness, sweating, increased production of saliva, dizziness, throat burn, nausea, vomiting, diarrhoea, pain in the abdomen, disturbance of hearing and vision, headache, fast or other disturbance in heart beat (tachycardia and cardiac arrhyhtmia), shortness of breath, prostration, circulatory problems, coma and terminal convulsions.

You should consult your doctor or pharmacist if you experience any problems.

If poisoning is suspected in a child, a doctor must be consulted immediately. Even small quantities of nicotine are dangerous in children and may result in severe symptoms or death.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Nicotinell can cause side effects, although not everybody gets them.

Some effects you may notice in the first few days are dizziness, headache and sleep disturbances. These may be withdrawal symptoms in connection with smoking cessation and may be caused by insufficient administration of nicotine.

Common side effects (occur in 1 to 10 users in 100)

- dizziness and headache.
- Hiccups, stomach trouble such as nausea, flatulence, vomiting, heartburn, increased saliva production, irritation of the mouth and throat and jaw muscle ache may also occur, especially as a result of intense chewing.
  Slower chewing will usually overcome these problems.

Uncommon side effects (occur in 1 to 10 users in 1,000)

- palpitations.
- red skin rash (erythema) and itching of raised bumps of the skin (urticaria). .

Rare side effects (occur in 1 to 10 users in 10,000)

- disturbances in heart beat rhythm and allergic reactions. These reactions may in very few cases be serious and include swelling of the skin, swelling of the face and mouth, low blood pressure and difficulty in breathing.

Mouth ulcers may be related to quitting smoking and not to your treatment.

Nicotinell can stick to and very rarely damage dentures or other dental work.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE NICOTINELL MEDICATED CHEWING-GUM

Keep out of the reach and sight of children.

Do not use Nicotinell after the expiry date which is stated on the label after "EXP". The expiry date refers to the last day of that month.

Do not store above 25°C.

Used Nicotinell should be disposed of with care.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Nicotinell medicated chewing-gum contains

The **active substance** is nicotine.

Each piece of Nicotinell medicated chewing-gum contains 2 mg of nicotine (as 10 mg nicotine-polacrilin).

The **other ingredients** are

- gum base (containing butylhydroxytoluene (E321)), 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 and talc.

What Nicotinell medicated chewing-gum looks like and contents of the pack

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

Nicotinell medicated chewing-gum is available in two strengths (2 and 4 mg) and four flavours (Fruit, Mint, Liquorice and Classic). This package leaflet deals with Nicotinell Fruit 2 mg medicated chewing-gums.

The blisters are packed in boxes containing 2, 12, 24, 36, 48, 60, 72, 96 or 204 pieces of medicated chewing-gum. Not all pack sizes may be marketed.

Marketing Authorisation Holder

Novartis Consumer Health, Horsham, RH12 5AB.

Manufacturer

Novartis Consumer Health, Alfreton Trading Estate, Wimsey Way, Somercotes, Derbyshire DE55 4PT, United Kingdom.

FAMAR S.A., 48th km National Road Athens-Lamia, 19011, Avlonas, Attiki, Greece.

This medicinal product is authorised in the Member States of the EEA under the following names:

AT	Nicotinell Fruit 2 mg - Kaugummi
BE	Nicotinell Fruit, 2 mg, kauwgom
BG	NICOTINELL FRUIT 2 mg Medicated chewing-gum
CY	Nicotinell Fruit 2mg medicated chewing-gum
CZ	Nicotinell Fruit gum 2mg
DE	Nicotinell Kaugummi 2 mg Fruit
DK	Nicotinell Fruit
EE	Nicotinell Fruit
EL	Nicotinell Fruit
ES	Nicotinell fruit 2 mg chicle medicamentoso
FI	Nicotinell Fruit 2 mg lääkepurukumi
FR	NICOTINELL FRUIT 2 mg SANS SUCRE, gomme à mâcher médicamenteuse
HU	Nicotinell Fruit 2 mg gyógyszeres rágógumi
IE	Nicotinell Fruit 2mg Medicated Chewing Gum.
IS	Nicotinell Fruit 2 mg lyfjatyggigúmmí
IT	Nicotinell Frutta 2 mg gomma da masticare medicata
LT	Nicotinell Fruit
LU	Nicotinell Fruit, 2 mg, gomme à mâcher médicamenteuse
LV	Nicotinell Fruit 2 mg medicated chewing gum
NL	Nicotinell Fruit, 2 mg, kauwgom
NO	Nicotinell medisinsk tyggegummi med fruktsmak
PL	Nicotinell Fruit
PT	Nicotinell Fruit 2 mg
RO	NICOTINELL FRUIT, guma medicamentoasa masticabila 2 mg
SE	Nicotinell Fruit 2 mg.
SK	Nicotinell Fruit gum 2 mg
UK	Nicotinell Fruit 2mg Medicated Chewing Gum.

This leaflet was last approved in 03/2009.

NCH Fruit B 4 mg medicated chewing-gum

Nicotine

Read all of this leaflet carefully because it contains important information for you.

This medicine is available without prescription. However, you still need to use NCH Fruit B 4 mg medicated chewing-gum carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if you still need to use NCH after 9 months.
- If any of the side effects gets serious, or if you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What NCH medicated chewing-gum is and what it is used for
2. Before you take NCH medicated chewing-gum
3. How to take NCH medicated chewing-gum
4. Possible side effects
5. How to store NCH medicated chewing-gum
6. Further information

1. WHAT NCH MEDICATED CHEWING-GUM IS AND WHAT IT IS USED FOR

NCH belongs to a group of medicines which are used to help you to stop smoking.

NCH contains nicotine, which is one of the substances contained in tobacco.

When chewed, nicotine is released slowly and absorbed through the lining of the mouth.

This medicinal product is used to relieve the nicotine withdrawal symptoms in nicotine dependency, as an aid to smoking cessation.

Patient counselling and support normally improve the success rate.

2. BEFORE YOU TAKE NCH MEDICATED CHEWING-GUM

Do not take NCH medicated chewing-gum

- If you are allergic (hypersensitive) to nicotine or any of the other ingredients of NCH
- If you are a non-smoker.

Take special care with NCH medicated chewing-gum

Please check with your doctor or pharmacist before taking NCH if you have:

- heart disease, e.g. heart attack, heart failure, angina, Prinzmetal's angina or abnormalities in heart beat rhythm,
- had a "stroke" (cerebrovascular accident),
- high blood pressure (uncontrolled hypertension),
- problems with your circulation,
- diabetes (monitor your blood sugar levels more often when starting to use NCH as you may find your insulin or medication requirements alter)
- overactive thyroid glands (hyperthyroidism),
- overactive adrenal glands (pheochromocytoma),
- kidney or liver disease,
- oesophagitis, inflammation in the mouth or throat, gastritis or peptic ulcer,
- fructose intolerance.

Even small quantities of nicotine are dangerous in children and may result in severe symptoms or death. It is therefore essential that you keep NCH out of reach and sight of children at all times

People having problems with the joint of the jawbone and some denture wearers may experience difficulty in chewing the gum. If you do, it is recommended that you use a different pharmaceutical form of nicotine replacement therapy. Ask your doctor or pharmacist for advice.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. If you stop smoking and if you are using other medicines, your doctor may want to adjust the dose.

No information is available on interactions between NCH and other medicines. However, apart from nicotine, other substances in cigarettes may have an effect on certain medicine.

Stopping smoking can affect the action of certain medicines e.g.:

- theophyllin (a medicine used for the treatment of bronchial asthma)
- tacrine (medicine used to treat Alzheimer's disease)
- olanzapine and clozapine (for the treatment of schizophrenia)
- Insulin dose (medicine used for the treatment of diabetes) may need to be adjusted

Taking NCH medicated chewing-gum with food and drink

Coffee, acidic drinks (e.g. fruit juice) and soft drinks may decrease the absorption of nicotine and should be avoided for 15 minutes before chewing NCH.

Pregnancy and breast-feeding

It is very important to stop smoking during pregnancy because it can result in poor growth of your baby. It can also lead to premature births and even stillbirths. Ideally you should try to give up smoking without the use of medicines. If you cannot manage this, NCH may be recommended to help as the risk to the developing baby is less than that expected from continued smoking. Nicotine in any form may cause harm to your unborn baby. NCH should only be used after consulting the healthcare professional who is managing your pregnancy, or a doctor that is specialised in helping people quit smoking.

NCH like smoking itself should be avoided during breast-feeding as nicotine may be found in breast milk. If your doctor has recommended that you should take this medicinal product, the medicated chewing-gum should be taken just after breast-feeding and not during the two hours before breast-feeding.

Driving and using machines

There is no evidence of risk associated with driving or operating machinery if NCH is taken according to the recommended dose but remember that smoking cessation can cause behavioural changes.

Important information about some of the ingredients of NCH medicated chewing-gum

Because NCH Fruit B contains sorbitol: if you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

The gum base contains butylhydroxytoluene (E321) which may cause local irritation to mucous membranes.

Each piece of NCH Fruit B 4 mg contains sweeteners, including sorbitol (E420) 0.2 g, a source of 0.04 g fructose. Calorific value 0.9 kcal/piece.

NCH Fruit B 4 mg contains 11.52 mg of sodium per piece. To be taken into consideration by patients on a controlled sodium diet.

3. HOW TO TAKE NCH MEDICATED CHEWING-GUM

Always take NCH exactly as stated in this package leaflet. You should check with your doctor or pharmacist if you are not sure.

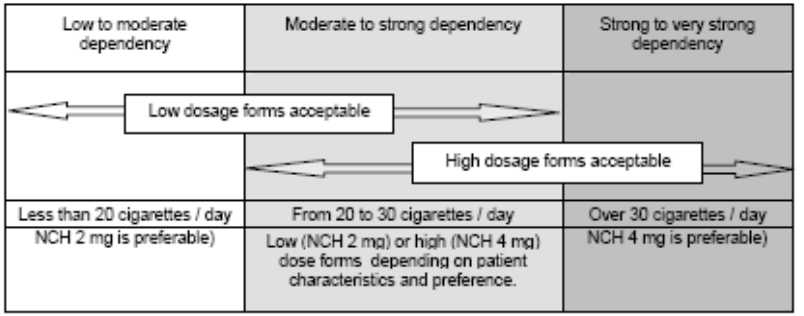
To improve your chances of giving up smoking you should stop smoking completely when you start to use NCH and for the whole treatment duration.

NCH is available in two strengths: 2 and 4 mg. The appropriate dose will depend on your previous smoking habits. You should use NCH 4 mg if:

- you are a smoker with a strong or very strong nicotine dependency,
- you have previously failed to stop smoking with NCH 2 mg,
- your withdrawal symptoms remain so strong as to threaten relapse.

Otherwise NCH 2 mg should be used.

Select your optimal dosage from the following table:



If an adverse event occurs with the use of the high dose (NCH 4 mg), use of the low dose (NCH 2 mg) should be considered.

Instructions for use:

1. Chew one piece of NCH slowly until the taste becomes strong.
2. Allow NCH to rest between your gum and cheek.
3. Chew again when taste has faded.
4. Repeat this routine for about 30 minutes, to get a gradual release of nicotine.

Do not swallow.

Dosage for adults over 18 years:

Chew one piece of NCH when you feel the urge to smoke. In general one piece should be chewed every one or two hours. Normally 8-12 pieces per day are sufficient. If you still experience an urge to smoke, you can chew additional pieces of NCH. Do not exceed 15 pieces per day of NCH 4mg.

The treatment duration is individual. Normally, treatment should continue for at least 3 months. After 3 months, you should gradually reduce the number of pieces of NCH chewed each day. Treatment should be stopped when you have reduced your use of NCH to 1-2 pieces per day. It is generally not recommended to use NCH for longer than 6 months. However, some ex-smokers may need treatment with NCH for longer to avoid returning to smoking.

If you are still using NCH after 9 months, you should speak to your doctor or pharmacist.

Counselling may improve your chances of giving up smoking.

Children and adolescents(< 18 yrs)

NCH should **not** be used by people under 18 years of age without recommendation from a doctor.

If you take more NCH medicated chewing-gums than you should

Chewing too many NCH pieces can result in the same symptoms as smoking too much. The general symptoms of nicotine overdose include weakness, sweating, increased production of saliva, dizziness, throat burn, nausea, vomiting, diarrhoea, pain in the abdomen, disturbance of hearing and vision, headache, fast or other disturbance in heart beat (tachycardia and cardiac arrhyhtmia), shortness of breath, prostration, circulatory problems, coma and terminal convulsions.

You should consult your doctor or pharmacist if you experience any problems.

If poisoning is suspected in a child, a doctor must be consulted immediately. Even small quantities of nicotine are dangerous in children and may result in severe symptoms or death.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, NCH can cause side effects, although not everybody gets them.

Some effects you may notice in the first few days are dizziness, headache and sleep disturbances. These may be withdrawal symptoms in connection with smoking cessation and may be caused by insufficient administration of nicotine.

Common side effects (occur in 1 to 10 users in 100)

- dizziness and headache.
- Hiccups, stomach trouble such as nausea, flatulence, vomiting, heartburn, increased saliva production, irritation of the mouth and throat and jaw muscle ache may also occur, especially as a result of intense chewing.
  Slower chewing will usually overcome these problems.

Uncommon side effects (occur in 1 to 10 users in 1,000)

- palpitations.
- red skin rash (erythema) and itching of raised bumps of the skin (urticaria). .

Rare side effects (occur in 1 to 10 users in 10,000)

- disturbances in heart beat rhythm and allergic reactions. These reactions may in very few cases be serious and include swelling of the skin, swelling of the face and mouth, low blood pressure and difficulty in breathing.

Mouth ulcers may be related to quitting smoking and not to your treatment.

NCH can stick to and very rarely damage dentures or other dental work.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE NCH MEDICATED CHEWING-GUM

Keep out of the reach and sight of children.

Do not use NCH after the expiry date which is stated on the label after "EXP". The expiry date refers to the last day of that month.

Do not store above 25°C.

Used NCH should be disposed of with care.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What NCH medicated chewing-gum contains

The **active substance** is nicotine.

Each piece of NCH medicated chewing-gum contains 4 mg of nicotine (as 20 mg nicotine-polacrilin).

The **other ingredients** are

- gum base (containing butylhydroxytoluene (E321)), 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 and talc.

What NCH medicated chewing-gum looks like and contents of the pack

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

NCH medicated chewing-gum is available in two strengths (2 and 4 mg) and four flavours (Fruit, Mint, Liquorice and Classic). This package leaflet deals with NCH Fruit B 4 mg medicated chewing-gums.

The blisters are packed in boxes containing 2, 12, 24, 36, 48, 60, 72, 96 or 204 pieces of medicated chewing-gum. Not all pack sizes may be marketed.

Marketing Authorisation Holder

Novartis Consumer Health, Horsham, RH12 5AB.

Manufacturer

Novartis Consumer Health, Alfreton Trading Estate, Wimsey Way, Somercotes, Derbyshire DE55 4PT, United Kingdom.

FAMAR S.A., 48th km National Road Athens-Lamia, 19011, Avlonas, Attiki, Greece.

This medicinal product is authorised in the Member States of the EEA under the following names:

AT	Nicotinell Fruit 4 mg - Kaugummi
BE	Nicotinell Fruit, 4 mg, kauwgom
CY	Nicotinell Fruit 4mg medicated chewing-gum
CZ	Nicotinell Fruit gum 4mg
DE	Nicotinell Kaugummi 4 mg Fruit
DK	Nicotinell Fruit
EE	Nicotinell Fruit
EL	Nicotinell Fruit
ES	Nicotinell fruit 4 mg chicle medicamentoso
FI	Nicotinell Fruit 4 mg lääkepurukumi
FR	NICOTINELL FRUIT 4 mg SANS SUCRE, gomme à mâcher médicamenteuse
IE	Nicotinell Fruit 4mg Medicated Chewing Gum
IS	Nicotinell Fruit 4 mg lyfjatyggigúmmí
IT	Nicotinell Frutta 4 mg gomma da masticare medicata
LT	Nicotinell Fruit
LU	Nicotinell Fruit, 4 mg, gomme à mâcher médicamenteuse
LV	Nicotinell Fruit 4 mg medicated chewing gum
NL	Nicotinell Fruit, 4 mg, kauwgom
NO	Nicotinell medisinsk tyggegummi med fruktsmak
PL	Nicotinell Fruit
PT	Nicotinell Fruit 4 mg
RO	NICOTINELL FRUIT, guma medicamentoasa masticabila 4 mg
SE	Nicotinell Fruit 4 mg.
SK	Nicotinell Fruit gum 4 mg
UK	NCH Fruit B 4mg Medicated Chewing Gum.

This leaflet was last approved in 03/2009.

Nicotinell Mint 2 mg medicated chewing-gum

Nicotine

Read all of this leaflet carefully because it contains important information for you.

This medicine is available without prescription. However, you still need to use Nicotinell Mint 2 mg medicated chewing-gum carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if you still need to use Nicotinell after 9 months.
- If any of the side effects gets serious, or if you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Nicotinell medicated chewing-gum is and what it is used for
2. Before you take Nicotinell medicated chewing-gum
3. How to take Nicotinell medicated chewing-gum
4. Possible side effects
5. How to store Nicotinell medicated chewing-gum
6. Further information

1. WHAT NICOTINELL MEDICATED CHEWING-GUM IS AND WHAT IT IS USED FOR

Nicotinell belongs to a group of medicines which are used to help you to stop smoking.

Nicotinell contains nicotine, which is one of the substances contained in tobacco.

When chewed, nicotine is released slowly and absorbed through the lining of the mouth.

This medicinal product is used to relieve the nicotine withdrawal symptoms in nicotine dependency, as an aid to smoking cessation.

Patient counselling and support normally improve the success rate.

2. BEFORE YOU TAKE NICOTINELL MEDICATED CHEWING-GUM

Do not take Nicotinell medicated chewing-gum

- If you are allergic (hypersensitive) to nicotine or any of the other ingredients of Nicotinell
- If you are a non-smoker.

Take special care with Nicotinell medicated chewing-gum

Please check with your doctor or pharmacist before taking Nicotinell if you have:

- heart disease, e.g. heart attack, heart failure, angina, Prinzmetal's angina or abnormalities in heart beat rhythm,
- had a "stroke" (cerebrovascular accident),
- high blood pressure (uncontrolled hypertension),
- problems with your circulation,
- diabetes (monitor your blood sugar levels more often when starting to use Nicotinell as you may find your insulin or medication requirements alter)
- overactive thyroid glands (hyperthyroidism),
- overactive adrenal glands (pheochromocytoma),
- kidney or liver disease,
- oesophagitis, inflammation in the mouth or throat, gastritis or peptic ulcer,
- fructose intolerance.

Even small quantities of nicotine are dangerous in children and may result in severe symptoms or death. It is therefore essential that you keep Nicotinell out of reach and sight of children at all times

People having problems with the joint of the jawbone and some denture wearers may experience difficulty in chewing the gum. If you do, it is recommended that you use a different pharmaceutical form of nicotine replacement therapy. Ask your doctor or pharmacist for advice.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. If you stop smoking and if you are using other medicines, your doctor may want to adjust the dose.

No information is available on interactions between Nicotinell and other medicines. However, apart from nicotine, other substances in cigarettes may have an effect on certain medicine.

Stopping smoking can affect the action of certain medicines e.g.:

- theophyllin (a medicine used for the treatment of bronchial asthma)
- tacrine (medicine used to treat Alzheimer's disease)
- olanzapine and clozapine (for the treatment of schizophrenia)

- Insulin dose (medicine used for the treatment of diabetes) may need to be adjusted

Taking Nicotinell medicated chewing-gum with food and drink

Coffee, acidic drinks (e.g. fruit juice) and soft drinks may decrease the absorption of nicotine and should be avoided for 15 minutes before chewing Nicotinell.

Pregnancy and breast-feeding

It is very important to stop smoking during pregnancy because it can result in poor growth of your baby. It can also lead to premature births and even stillbirths. Ideally you should try to give up smoking without the use of medicines. If you cannot manage this, Nicotinell may be recommended to help as the risk to the developing baby is less than that expected from continued smoking. Nicotine in any form may cause harm to your unborn baby. Nicotinell should only be used after consulting the healthcare professional who is managing your pregnancy, or a doctor that is specialised in helping people quit smoking.

Nicotinell like smoking itself should be avoided during breast-feeding as nicotine may be found in breast milk. If your doctor has recommended that you should take this medicinal product, the medicated chewing-gum should be taken just after breast-feeding and not during the two hours before breast-feeding.

Driving and using machines

There is no evidence of risk associated with driving or operating machinery if Nicotinell is taken according to the recommended dose but remember that smoking cessation can cause behavioural changes.

Important information about some of the ingredients of Nicotinell medicated chewing-gum

Because Nicotinell Mint contains sorbitol: if you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

The gum base contains butylhydroxytoluene (E321) which may cause local irritation to mucous membranes.

Each piece of Nicotinell Mint 2 mg contains sweeteners, including sorbitol (E420) 0.2 g, a source of 0.04 g fructose. Calorific value 1.0 kcal/piece.

Nicotinell Mint 2 mg contains 11.50 mg of sodium per piece. To be taken into consideration by patients on a controlled sodium diet.

3. HOW TO TAKE NICOTINELL MEDICATED CHEWING-GUM

Always take Nicotinell exactly as stated in this package leaflet. You should check with your doctor or pharmacist if you are not sure.

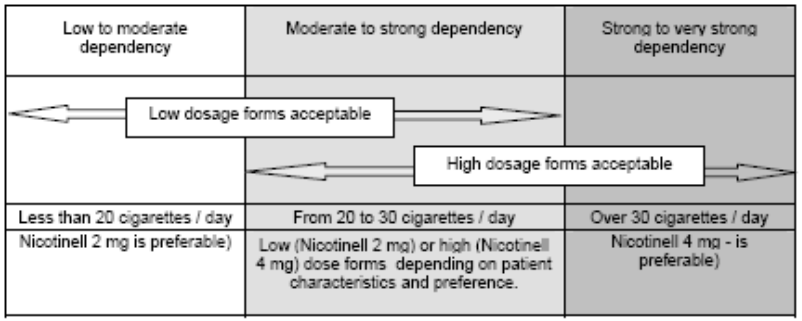
To improve your chances of giving up smoking you should stop smoking completely when you start to use Nicotinell and for the whole treatment duration.

Nicotinell is available in two strengths: 2 and 4 mg. The appropriate dose will depend on your previous smoking habits. You should use Nicotinell 4 mg if:

- you are a smoker with a strong or very strong nicotine dependency,
- you have previously failed to stop smoking with Nicotinell 2 mg,
- your withdrawal symptoms remain so strong as to threaten relapse.

Otherwise Nicotinell 2 mg should be used.

Select your optimal dosage from the following table:



If an adverse event occurs with the use of the high dose (Nicotinell 4 mg), use of the low dose (Nicotinell 2 mg) should be considered.

Instructions for use:

1. Chew one piece of Nicotinell slowly until the taste becomes strong.
2. Allow Nicotinell to rest between your gum and cheek.
3. Chew again when taste has faded.
4. Repeat this routine for about 30 minutes, to get a gradual release of nicotine.

Do not swallow.

Dosage for adults over 18 years:

Chew one piece of Nicotinell when you feel the urge to smoke. In general one piece should be chewed every one or two hours. Normally 8-12 pieces per day are sufficient. If you still experience an urge to smoke, you can chew additional pieces of Nicotinell. Do not exceed 25 pieces a day of Nicotinell 2 mg.

The treatment duration is individual. Normally, treatment should continue for at least 3 months. After 3 months, you should gradually reduce the number of pieces of Nicotinell chewed each day. Treatment should be stopped when you have reduced your use of Nicotinell to 1-2 pieces per day. It is generally not recommended to use Nicotinell for longer than 6

months. However, some ex-smokers may need treatment with Nicotinell for longer to avoid returning to smoking.

If you are still using Nicotinell after 9 months, you should speak to your doctor or pharmacist.

Counselling may improve your chances of giving up smoking.

Children and adolescents(< 18 yrs)

Nicotinell should **not** be used by people under 18 years of age without recommendation from a doctor.

If you take more Nicotinell medicated chewing-gums than you should

Chewing too many Nicotinell pieces can result in the same symptoms as smoking too much. The general symptoms of nicotine overdose include weakness, sweating, increased production of saliva, dizziness, throat burn, nausea, vomiting, diarrhoea, pain in the abdomen, disturbance of hearing and vision, headache, fast or other disturbance in heart beat (tachycardia and cardiac arrhythmia), shortness of breath, prostration, circulatory problems, coma and terminal convulsions.

You should consult your doctor or pharmacist if you experience any problems.

If poisoning is suspected in a child, a doctor must be consulted immediately. Even small quantities of nicotine are dangerous in children and may result in severe symptoms or death.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Nicotinell can cause side effects, although not everybody gets them.

Some effects you may notice in the first few days are dizziness, headache and sleep disturbances. These may be withdrawal symptoms in connection with smoking cessation and may be caused by insufficient administration of nicotine.

Common side effects (occur in 1 to 10 users in 100)

- dizziness and headache.
- Hiccups, stomach trouble such as nausea, flatulence, vomiting, heartburn, increased saliva production, irritation of the mouth and throat and jaw muscle ache may also occur, especially as a result of intense chewing.
  Slower chewing will usually overcome these problems.

Uncommon side effects (occur in 1 to 10 users in 1,000)

- palpitations.
- red skin rash (erythema) and itching of raised bumps of the skin (urticaria). .

Rare side effects (occur in 1 to 10 users in 10,000)

- disturbances in heart beat rhythm and allergic reactions. These reactions may in very few cases be serious and include swelling of the skin, swelling of the face and mouth, low blood pressure and difficulty in breathing.

Mouth ulcers may be related to quitting smoking and not to your treatment.

Nicotinell can stick to and very rarely damage dentures or other dental work.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE NICOTINELL MEDICATED CHEWING-GUM

Keep out of the reach and sight of children.

Do not use Nicotinell after the expiry date which is stated on the label after "EXP". The expiry date refers to the last day of that month.

Do not store above 25°C.

Used Nicotinell should be disposed of with care.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Nicotinell medicated chewing-gum contains

The **active substance** is nicotine.

Each piece of Nicotinell medicated chewing-gum contains 2 mg of nicotine (as 10 mg nicotine-polacrilin)

The **other ingredients** are

- gum base (containing butylhydroxytoluene (E321)), calcium carbonate, sorbitol (E420), sodium carbonate anhydrous, sodium hydrogen carbonate, polacrilin, glycerol (E422), purified water, levomenthol, peppermint oil, eucalyptus oil, saccharin, sodium saccharin, acesulfame potassium, xylitol (E967), mannitol (E421), gelatin, titanium dioxide (E171), carnauba wax and talc.

What Nicotinell medicated chewing-gum looks like and contents of the pack

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

Nicotinell medicated chewing-gum is available in two strengths (2 and 4 mg) and four flavours (Fruit, Mint, Liquorice and Classic). This package leaflet deals with Nicotinell Mint 2 mg medicated chewing-gums.

The blisters are packed in boxes containing 2, 12, 24, 36, 48, 60, 72, 96 or 204 pieces of medicated chewing-gum. Not all pack sizes may be marketed.

Marketing Authorisation Holder

Novartis Consumer Health, Horsham, RH12 5AB.

Manufacturer

Novartis Consumer Health, Alfreton Trading Estate, Wimsey Way, Somercotes, Derbyshire DE55 4PT, United Kingdom.

FAMAR S.A., 48th km National Road Athens-Lamia, 19011, Avlonas, Attiki, Greece.

This medicinal product is authorised in the Member States of the EEA under the following names:

AT	Nicotinell Mint 2 mg - Kaugummi
BE	Nicotinell Mint, 2 mg, kauwgom
BG	NICOTINELL MINT 2 mg Medicated chewing-gum
CY	Nicotinell Mint 2mg medicated chewing-gum
CZ	Nicotinell Mint gum 2mg
DE	Nicotinell Kaugummi 2 mg Mint
DK	Nicotinell Mint
EE	Nicotinell Mint
EL	Nicotinell Mint
ES	Nicotinell mint 2 mg chicle medicamentoso
FI	Nicotinell Mint 2 mg lääkepurukumi
FR	NICOTINELL MENHTE 2 mg SANS SUCRE, gomme à mâcher médicamenteuse
HU	Nicotinell Mint 2 mg gyógyszeres rágógumi
IE	Nicotinell Mint 2mg Medicated Chewing Gum.
IS	Nicotinell Mint 2 mg lyfjatyggigúmmí
IT	Nicotinell Menta 2 mg gomma da masticare medicata
LT	Nicotinell Mint
LU	Nicotinell Mint, 2 mg, gomme à mâcher médicamenteuse
LV	Nicotinell Mint 2 mg medicated chewing gum
NL	Nicotinell Mint, 2 mg, kauwgom
NO	Nicotinell medisinsk tyggegummi med peppermyntesmak
PL	Nicotinell Mint
PT	Nicotinell Mint 2 mg
RO	NICOTINELL MINT, guma medicamentoasa masticabila 2 mg
SE	Nicotinell Mint 2 mg.
SK	Nicotinell Mint gum 2 mg
UK	Nicotinell Mint 2mg Medicated Chewing Gum.

This leaflet was last approved in 03/2009.

NCH Mint D 4 mg medicated chewing-gum

Nicotine

Read all of this leaflet carefully because it contains important information for you.

This medicine is available without prescription. However, you still need to use NCH Mint D 4 mg medicated chewing-gum carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if you still need to use NCH after 9 months.
- If any of the side effects gets serious, or if you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What NCH medicated chewing-gum is and what it is used for
2. Before you take NCH medicated chewing-gum
3. How to take NCH medicated chewing-gum
4. Possible side effects
5. How to store NCH medicated chewing-gum
6. Further information

1. WHAT NCH MEDICATED CHEWING-GUM IS AND WHAT IT IS USED FOR

NCH belongs to a group of medicines which are used to help you to stop smoking.

NCH contains nicotine, which is one of the substances contained in tobacco.

When chewed, nicotine is released slowly and absorbed through the lining of the mouth.

This medicinal product is used to relieve the nicotine withdrawal symptoms in nicotine dependency, as an aid to smoking cessation.

Patient counselling and support normally improve the success rate.

2. BEFORE YOU TAKE NCH MEDICATED CHEWING-GUM

Do not take NCH medicated chewing-gum

- If you are allergic (hypersensitive) to nicotine or any of the other ingredients of NCH
- If you are a non-smoker.

Take special care with NCH medicated chewing-gum

Please check with your doctor or pharmacist before taking NCH if you have:

- heart disease, e.g. heart attack, heart failure, angina, Prinzmetal's angina or abnormalities in heart beat rhythm,
- had a "stroke" (cerebrovascular accident),
- high blood pressure (uncontrolled hypertension),
- problems with your circulation,
- diabetes (monitor your blood sugar levels more often when starting to use NCH as you may find your insulin or medication requirements alter)
- overactive thyroid glands (hyperthyroidism),
- overactive adrenal glands (pheochromocytoma),
- kidney or liver disease,
- oesophagitis, inflammation in the mouth or throat, gastritis or peptic ulcer,
- fructose intolerance.

Even small quantities of nicotine are dangerous in children and may result in severe symptoms or death. It is therefore essential that you keep NCH out of reach and sight of children at all times

People having problems with the joint of the jawbone and some denture wearers may experience difficulty in chewing the gum. If you do, it is recommended that you use a different pharmaceutical form of nicotine replacement therapy. Ask your doctor or pharmacist for advice.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. If you stop smoking and if you are using other medicines, your doctor may want to adjust the dose.

No information is available on interactions between NCH and other medicines. However, apart from nicotine, other substances in cigarettes may have an effect on certain medicine.

Stopping smoking can affect the action of certain medicines e.g.:

- theophyllin (a medicine used for the treatment of bronchial asthma)
- tacrine (medicine used to treat Alzheimer's disease)
- olanzapine and clozapine (for the treatment of schizophrenia)
- Insulin dose (medicine used for the treatment of diabetes) may need to be adjusted

Taking NCH medicated chewing-gum with food and drink

Coffee, acidic drinks (e.g. fruit juice) and soft drinks may decrease the absorption of nicotine and should be avoided for 15 minutes before chewing NCH.

Pregnancy and breast-feeding

It is very important to stop smoking during pregnancy because it can result in poor growth of your baby. It can also lead to premature births and even stillbirths. Ideally you should try to give up smoking without the use of medicines. If you cannot manage this, NCH may be recommended to help as the risk to the developing baby is less than that expected from continued smoking. Nicotine in any form may cause harm to your unborn baby. NCH should only be used after consulting the healthcare professional who is managing your pregnancy, or a doctor that is specialised in helping people quit smoking.

NCH like smoking itself should be avoided during breast-feeding as nicotine may be found in breast milk. If your doctor has recommended that you should take this medicinal product, the medicated chewing-gum should be taken just after breast-feeding and not during the two hours before breast-feeding.

Driving and using machines

There is no evidence of risk associated with driving or operating machinery if NCH is taken according to the recommended dose but remember that smoking cessation can cause behavioural changes.

Important information about some of the ingredients of NCH medicated chewing-gum

Because NCH Mint D contains sorbitol: if you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

The gum base contains butylhydroxytoluene (E321) which may cause local irritation to mucous membranes.

Each piece of NCH Mint D 4 mg contains sweeteners, including sorbitol (E420) 0.2 g, a source of 0.04 g fructose. Calorific value 0.9 kcal/piece.

NCH Mint D 4 mg contains 11.52 mg of sodium per piece. To be taken into consideration by patients on a controlled sodium diet.

3. HOW TO TAKE NCH MEDICATED CHEWING-GUM

Always take NCH exactly as stated in this package leaflet. You should check with your doctor or pharmacist if you are not sure.

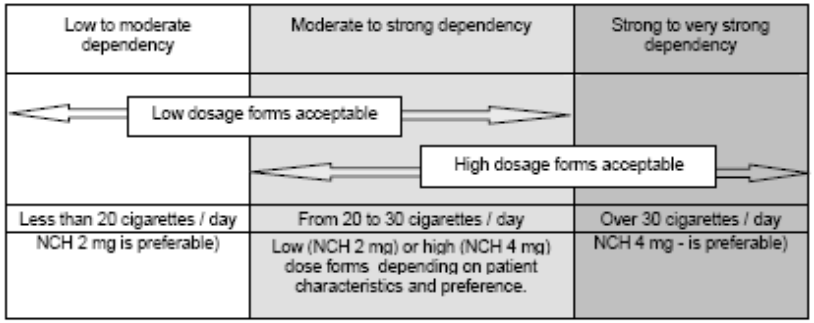
To improve your chances of giving up smoking you should stop smoking completely when you start to use NCH and for the whole treatment duration.

NCH is available in two strengths: 2 and 4 mg. The appropriate dose will depend on your previous smoking habits. You should use NCH 4 mg if:

- you are a smoker with a strong or very strong nicotine dependency,
- you have previously failed to stop smoking with NCH 2 mg,
- your withdrawal symptoms remain so strong as to threaten relapse.

Otherwise NCH 2 mg should be used.

Select your optimal dosage from the following table:



If an adverse event occurs with the use of the high dose (NCH 4 mg), use of the low dose (NCH 2 mg) should be considered.

Instructions for use:

1. Chew one piece of NCH slowly until the taste becomes strong.
2. Allow NCH to rest between your gum and cheek.
3. Chew again when taste has faded.
4. Repeat this routine for about 30 minutes, to get a gradual release of nicotine.

Do not swallow.

Dosage for adults over 18 years:

Chew one piece of NCH when you feel the urge to smoke. In general one piece should be chewed every one or two hours. Normally 8-12 pieces per day are sufficient. If you still experience an urge to smoke, you can chew additional pieces of NCH. Do not exceed 15 pieces per day of NCH 4mg.

The treatment duration is individual. Normally, treatment should continue for at least 3 months. After 3 months, you should gradually reduce the number of pieces of NCH chewed each day. Treatment should be stopped when you have reduced your use of NCH to 1-2 pieces per day. It is generally not recommended to use NCH for longer than 6 months. However, some ex-smokers may need treatment with NCH for longer to avoid returning to smoking.

If you are still using NCH after 9 months, you should speak to your doctor or pharmacist.

Counselling may improve your chances of giving up smoking.

Children and adolescents(< 18 yrs)

NCH should **not** be used by people under 18 years of age without recommendation from a doctor.

If you take more NCH medicated chewing-gums than you should

Chewing too many NCH pieces can result in the same symptoms as smoking too much. The general symptoms of nicotine overdose include weakness, sweating, increased production of saliva, dizziness, throat burn, nausea, vomiting, diarrhoea, pain in the abdomen, disturbance of hearing and vision, headache, fast or other disturbance in heart beat (tachycardia and cardiac arrhythmia), shortness of breath, prostration, circulatory problems, coma and terminal convulsions.

You should consult your doctor or pharmacist if you experience any problems.

If poisoning is suspected in a child, a doctor must be consulted immediately. Even small quantities of nicotine are dangerous in children and may result in severe symptoms or death.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, NCH can cause side effects, although not everybody gets them.

Some effects you may notice in the first few days are dizziness, headache and sleep disturbances. These may be withdrawal symptoms in connection with smoking cessation and may be caused by insufficient administration of nicotine.

Common side effects (occur in 1 to 10 users in 100)

- dizziness and headache.
- Hiccups, stomach trouble such as nausea, flatulence, vomiting, heartburn, increased saliva production, irritation of the mouth and throat and jaw muscle ache may also occur, especially as a result of intense chewing.
  Slower chewing will usually overcome these problems.

Uncommon side effects (occur in 1 to 10 users in 1,000)

- palpitations.
- red skin rash (erythema) and itching of raised bumps of the skin (urticaria). .

Rare side effects (occur in 1 to 10 users in 10,000)

- disturbances in heart beat rhythm and allergic reactions. These reactions may in very few cases be serious and include swelling of the skin, swelling of the face and mouth, low blood pressure and difficulty in breathing.

Mouth ulcers may be related to quitting smoking and not to your treatment.

NCH can stick to and very rarely damage dentures or other dental work.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE NCH MEDICATED CHEWING-GUM

Keep out of the reach and sight of children.

Do not use NCH after the expiry date which is stated on the label after "EXP". The expiry date refers to the last day of that month.

Do not store above 25°C.

Used NCH should be disposed of with care.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What NCH medicated chewing-gum contains

The **active substance** is nicotine.

Each piece of NCH medicated chewing-gum contains 4 mg of nicotine (as 20 mg nicotine-polacrilin).

The **other ingredients** are

- gum base (containing butylhydroxytoluene (E321)), calcium carbonate, sorbitol (E420), sodium carbonate anhydrous, sodium hydrogen carbonate, polacrilin, glycerol (E422), purified water, levomenthol, peppermint oil, eucalyptus oil, saccharin, sodium saccharin, acesulfame potassium, xylitol (E967), mannitol (E421), gelatin, titanium dioxide (E171), carnauba wax and talc.

What NCH medicated chewing-gum looks like and contents of the pack

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

NCH medicated chewing-gum is available in two strengths (2 and 4 mg) and four flavours (Fruit, Mint, Liquorice and Classic). This package leaflet deals with NCH Mint D 4 mg medicated chewing-gums.

The blisters are packed in boxes containing 2, 12, 24, 36, 48, 60, 72, 96 or 204 pieces of medicated chewing-gum. Not all pack sizes may be marketed.

Marketing Authorisation Holder

Novartis Consumer Health, Horsham, RH12 5AB.

Manufacturer

Novartis Consumer Health, Alfreton Trading Estate, Wimsey Way, Somercotes, Derbyshire DE55 4PT, United Kingdom.

FAMAR S.A., 48th km National Road Athens-Lamia, 19011, Avlonas, Attiki, Greece.

This medicinal product is authorised in the Member States of the EEA under the following names:

AT	Nicotinell Mint 4 mg - Kaugummi
BE	Nicotinell Mint, 4 mg, kauwgom
CY	Nicotinell Mint 4mg medicated chewing-gum
CZ	Nicotinell Mint gum 4mg
DE	Nicotinell Kaugummi 4 mg Mint
DK	Nicotinell Mint
EE	Nicotinell Mint
EL	Nicotinell Mint
ES	Nicotinell mint 4 mg chicle medicamentoso
FI	Nicotinell Mint 4 mg lääkepurukumi
FR	NICOTINELL MENTHE 4 mg SANS SUCRE, gomme à mâcher médicamenteuse
IE	Nicotinell Mint 4mg Medicated Chewing Gum
IS	Nicotinell Mint 4 mg lyfjatyggigúmmí
IT	Nicotinell Menta 4 mg gomma da masticare medicata
LT	Nicotinell Mint
LU	Nicotinell Mint, 4 mg, gomme à mâcher médicamenteuse
LV	Nicotinell Mint 4 mg medicated chewing gum
NL	Nicotinell Mint, 4 mg, kauwgom
NO	Nicotinell medisinsk tyggegummi med peppermyntesmak
PL	Nicotinell Mint
PT	Nicotinell Mint 4 mg
RO	NICOTINELL MINT, guma medicamentoasa masticabila 4 mg
SE	Nicotinell Mint 4 mg.
SK	Nicotinell Mint gum 4 mg
UK	NCH Mint D 4mg Medicated Chewing Gum.

This leaflet was last approved in 03/2009.

Module 4
Labelling

Please note that the labelling submitted are the text versions submitted to the UK only and may differ from those submitted to other member states. The marketing authorisation holder has committed to submitting mock-ups to the regulatory authorities for approval before marketing any products.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

1. NAME OF THE MEDICINAL PRODUCT

Nicotinell Fruit 2 mg medicated chewing-gum

Nicotine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each piece of Nicotinell medicated chewing-gum contains 2 mg of nicotine (as 10 mg nicotine-polacrilin (1:4)).

3. LIST OF EXCIPIENTS

Contains sorbitol (E420), gum base (containing butylhydroxytoluene (E321)), calcium carbonate, 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 and talc.

Read the leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

2, 12, 24, 36, 48, 60, 72, 96, 204 pieces of medicated chewing-gum

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oromucosal use

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Not applicable

8. EXPIRY DATE

EXP {MM/YYYY}

9. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

To dispose of used gum, wrap in paper before putting into a waste bin.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Consumer Health, Horsham, RH12 5AB.

12. MARKETING AUTHORISATION NUMBER(S)

PL 00030/0162

13. BATCH NUMBER

Batch {number}

14. GENERAL CLASSIFICATION FOR SUPPLY

GSL

15. INSTRUCTIONS ON USE

Indication: Relief of nicotine withdrawal symptoms, in nicotine dependency as an aid to smoking cessation

Patient counselling and support normally improve the success rate.

How to take Nicotinell medicated chewing-gum

If you smoke:

- Less than 20 cigarettes per day: use Nicotinell 2 mg medicated chewing-gum
- 20 to 30 cigarettes per day: you can use either Nicotinell 2 mg or Nicotinell 4 mg medicated chewing-gum
- More than 30 cigarettes per day: use Nicotinell 4 mg medicated chewing-gum

For adults over 18 years of age.

Contraindications: If you are allergic (hypersensitive) to nicotine or any of the other ingredients of Nicotinell chewing-gum. If you are a non-smoker.

Warnings: Read carefully the package leaflet before use.

If you need advice before starting to use nicotine medicated chewing-gums, talk to a healthcare professional.

16. INFORMATION IN BRAILLE

To be submitted prior to marketing.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

1. NAME OF THE MEDICINAL PRODUCT

Nicotinell Fruit 2 mg medicated chewing-gum

Nicotine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Novartis Consumer Health

3. EXPIRY DATE

EXP {MM/YYYY}

4. BATCH NUMBER

Batch {number}

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

1. NAME OF THE MEDICINAL PRODUCT

NCH Fruit B 4 mg medicated chewing-gum

Nicotine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each piece of NCH medicated chewing-gum contains 4 mg of nicotine (as 20 mg nicotine-polacrilin (1:4)).

3. LIST OF EXCIPIENTS

Contains sorbitol (E420), gum base (containing butylhydroxytoluene (E321)), calcium carbonate, 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 and talc.

Read the leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

2, 12, 24, 36, 48, 60, 72, 96, 204 pieces of medicated chewing-gum

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oromucosal use

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Not applicable

8. EXPIRY DATE

EXP {MM/YYYY}

9. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

To dispose of used gum, wrap in paper before putting into a waste bin.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Consumer Health, Horsham, RH12 5AB.

12. MARKETING AUTHORISATION NUMBER(S)

PL 00030/0171

13. BATCH NUMBER

Batch {number}

14. GENERAL CLASSIFICATION FOR SUPPLY

GSL

15. INSTRUCTIONS ON USE

Indication: Relief of nicotine withdrawal symptoms, in nicotine dependency as an aid to smoking cessation

Patient counselling and support normally improve the success rate.

How to take NCH medicated chewing-gum

If you smoke:

- Less than 20 cigarettes per day: use NCH 2 mg medicated chewing-gum
- 20 to 30 cigarettes per day: you can use either NCH 2 mg or NCH 4 mg medicated chewing-gum
- More than 30 cigarettes per day: use NCH 4 mg medicated chewing-gum

For adults over 18 years of age.

Contraindications: If you are allergic (hypersensitive) to nicotine or any of the other ingredients of NCH chewing-gum. If you are a non-smoker.

Warnings: Read carefully the package leaflet before use.

If you need advice before starting to use nicotine medicated chewing-gums, talk to a healthcare professional.

16. INFORMATION IN BRAILLE

To be submitted prior to marketing.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

1. NAME OF THE MEDICINAL PRODUCT

NCH Fruit B 4 mg medicated chewing-gum

Nicotine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Novartis Consumer Health

3. EXPIRY DATE

EXP {MM/YYYY}

4. BATCH NUMBER

Batch {number}

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

1. NAME OF THE MEDICINAL PRODUCT

Nicotinell Mint 2 mg medicated chewing-gum

Nicotine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each piece of Nicotinell medicated chewing-gum contains 2 mg of nicotine (as 10 mg nicotine-polacrilin (1:4)).

3. LIST OF EXCIPIENTS

Contains sorbitol (E420), gum base (containing butylhydroxytoluene (E321)), calcium carbonate, sodium carbonate anhydrous, sodium hydrogen carbonate, polacrilin, glycerol (E422), purified water, levomenthol, peppermint oil, eucalyptus oil, saccharin, sodium saccharin, acesulfame potassium, xylitol (E967), mannitol (E421), gelatin, titanium dioxide (E171), carnauba wax and talc.

Read the leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

2, 12, 24, 36, 48, 60, 72, 96, 204 pieces of medicated chewing-gum

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oromucosal use

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Not applicable

8. EXPIRY DATE

EXP {MM/YYYY}

9. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

To dispose of used gum, wrap in paper before putting into a waste bin.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Consumer Health

Horsham

RH12 5AB

12. MARKETING AUTHORISATION NUMBER(S)

PL 00030/0164

13. BATCH NUMBER

Batch {number}

14. GENERAL CLASSIFICATION FOR SUPPLY

GSL

15. INSTRUCTIONS ON USE

Indication: Relief of nicotine withdrawal symptoms, in nicotine dependency as an aid to smoking cessation

Patient counselling and support normally improve the success rate.

How to take Nicotinell medicated chewing-gum

If you smoke:

- Less than 20 cigarettes per day: use Nicotinell 2 mg medicated chewing-gum
- 20 to 30 cigarettes per day: you can use either Nicotinell 2 mg or Nicotinell 4 mg medicated chewing-gum
- More than 30 cigarettes per day: use Nicotinell 4 mg medicated chewing-gum

For adults over 18 years of age.

Contraindications: If you are allergic (hypersensitive) to nicotine or any of the other ingredients of Nicotinell chewing-gum. If you are a non-smoker.

Warnings: Read carefully the package leaflet before use.

If you need advice before starting to use nicotine medicated chewing-gums, talk to a healthcare professional.

16. INFORMATION IN BRAILLE

To be added prior to marketing.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

1. NAME OF THE MEDICINAL PRODUCT

Nicotinell Mint 2 mg medicated chewing-gum

Nicotine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

PL 00030/0164

3. EXPIRY DATE

EXP {MM/YYYY}

4. BATCH NUMBER

Batch {number}

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

1. NAME OF THE MEDICINAL PRODUCT

NCH Mint D 4 mg medicated chewing-gum

Nicotine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each piece of NCH medicated chewing-gum contains 4 mg of nicotine (as 20 mg nicotine-polacrilin (1:4)).

3. LIST OF EXCIPIENTS

Contains sorbitol (E420), gum base (containing butylhydroxytoluene (E321)), calcium carbonate, sodium carbonate anhydrous, sodium hydrogen carbonate, polacrilin, glycerol (E422), purified water, levomenthol, peppermint oil, eucalyptus oil, saccharin, sodium saccharin, acesulfame potassium, xylitol (E967), mannitol (E421), gelatin, titanium dioxide (E171), carnauba wax and talc.

Read the leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

2, 12, 24, 36, 48, 60, 72, 96, 204 pieces of medicated chewing-gum

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oromucosal use

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Not applicable

8. EXPIRY DATE

EXP {MM/YYYY}

9. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

To dispose of used gum, wrap in paper before putting into a waste bin.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Consumer Health

Horsham

RH12 5AB

12. MARKETING AUTHORISATION NUMBER(S)

PL 00030/0173

13. BATCH NUMBER

Batch {number}

14. GENERAL CLASSIFICATION FOR SUPPLY

GSL

15. INSTRUCTIONS ON USE

Indication: Relief of nicotine withdrawal symptoms, in nicotine dependency as an aid to smoking cessation

Patient counselling and support normally improve the success rate.

How to take NCH medicated chewing-gum

If you smoke:

- Less than 20 cigarettes per day: use NCH 2 mg medicated chewing-gum
- 20 to 30 cigarettes per day: you can use either NCH 2 mg or NCH 4 mg medicated chewing-gum
- More than 30 cigarettes per day: use NCH 4 mg medicated chewing-gum

For adults over 18 years of age.

Contraindications: If you are allergic (hypersensitive) to nicotine or any of the other ingredients of NCH chewing-gum. If you are a non-smoker.

Warnings: Read carefully the package leaflet before use.

If you need advice before starting to use nicotine medicated chewing-gums, talk to a healthcare professional.

16. INFORMATION IN BRAILLE

To be submitted prior to marketing.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

1. NAME OF THE MEDICINAL PRODUCT

NCH Mint D 4 mg medicated chewing-gum

Nicotine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Novartis Consumer Health

3. EXPIRY DATE

EXP {MM/YYYY}

4. BATCH NUMBER

Batch {number}

5. OTHER

Module 5
Scientific discussion during initial procedure

I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, Cyprus, Czech Republic, Estonia, Greece, Hungary, Italy, Lithuania, Latvia, Poland and Slovak Republic considered that the applications for Nicotinell Fruit 2mg and 4mg Chewing Gum (UK/H/0407/001-2/E02) and Nicotinell Mint 2mg and 4mg Chewing Gum (UK/H/0408/001-2/E02) could be approved. These products have been granted licences by the mutual recognition procedure (MRP), with the UK as reference member state (RMS). The licences had previously been granted in the UK on 22nd August 2000, and successfully completed two mutual recognition procedures in Ireland and The Netherlands on 20th February 2001 (UK/H/0407-8/001-2/MR) and in Austria, Belgium, France, Luxembourg, Portugal and Spain on 9th July 2003 (UK/H/0407-8/001-2/E01).

These are applications made under Article 10.1 of 2001/83 EC, as amended, claiming to be generic medicinal products of Nicorette 2 and 4mg Chewing Gum (Pharmacia Limited), which were the reference product for these applications. The active substance nicotine resinate belongs to the pharmacotherapeutic group “drugs used in nicotine dependence” (N07B A01).

The products are available on General Sales Licences (GSL) for the relief of nicotine withdrawal symptoms, in nicotine dependency as an aid to smoking cessation. Permanent cessation of tobacco use is the eventual objective. Nicotinell Fruit/Mint 2mg and 4mg Chewing Gum should preferably be used in conjunction with a behavioural support programme.

Nicotine is a liquid alkaloid obtained from the dried leaves of the tobacco plant, *Nicotiana tabacum* and related species (*Solanaceae*). Tobacco leaves contain 0.5 to 8% of nicotine combined as malate or citrate. Nicotine is readily absorbed through mucous membranes and the skin; bioavailability of oral nicotine is low due to extensive first pass metabolism. Nicotine is widely distributed; it crosses the blood brain barrier and the placenta and is found in breast milk. The elimination half life is about 1 to 2 hours. Nicotine is metabolised mainly in the liver via the cytochrome P450 isoenzyme CYP2A6 to cotine and nicotine-N-oxide. Nicotine and its metabolites are excreted in the urine.

No new preclinical studies were conducted, which is acceptable given that the applications were based on claims to be generic medicinal products to a product that has been licensed for over 10 years.

No clinical studies were conducted, which is acceptable given that the applications were based on claims to be generic medicinal products to a product that has been licensed for over 10 years. The bioequivalence study was carried out in accordance with Good Clinical Practice (GCP).

The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of this product prior to granting its national authorisation. The RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

II. ABOUT THE PRODUCT

Name of the product in the Reference Member State	Nicotinell Fruit 2mg Chewing Gum Nicotinell Fruit 4mg Chewing Gum Nicotinell Mint 2mg Chewing Gum Nicotinell Mint 4mg Chewing Gum
Name(s) of the active substance(s) (INN)	Nicotine (as nicotine resinate)
Pharmacotherapeutic classification (ATC code)	Drugs used in nicotine dependence" (N07B A01)
Pharmaceutical form and strength(s)	Medicated chewing gum 2 and 4mg
Reference numbers for the Decentralised Procedure	UK/H/0407-8/001-2/E02
Reference Member State	United Kingdom
Member States concerned	Cyprus, Czech Republic, Estonia, Greece, Hungary, Italy, Lithuania, Latvia, Poland, Slovak Republic
Marketing Authorisation Number(s)	PL 00030/0162-5
Name and address of the authorisation holder	Novartis Consumer Health UK Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB

III SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 QUALITY ASPECTS

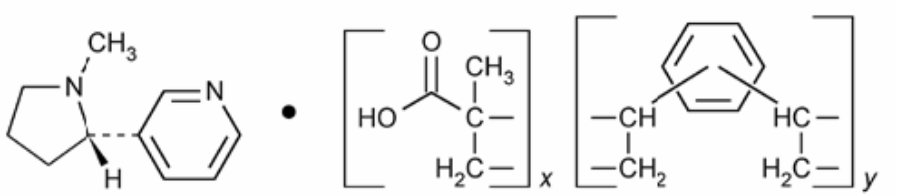
S. Active Substance

INN/Ph.Eur name: Nicotine (as nicotine resinate)

Chemical name: 2-propenoic acid, 2-methyl, polymer with diethenylbenzene, complex with 1-methyl-2-(3-pyridyl)pyrrolidine.

Methacrylic acid polymer with divinylbenzene, complex with nicotine-S-3-(1-methyl-2-pyrrolidinyl)pyridine.

Structural formula:



Molecular formula: $C_{10}H_{14}N_2$ $(C_4H_6O_2)x$ $(C_{10}H_{10})y$

Appearance: White to faintly yellow powder, practically insoluble in water and insoluble to slightly soluble in most solvents

Molecular weight: 162 + 86(x) + 130(y)

Chirality: The only chiral centre is at the pyrrole carbon attached to the pyridine.

Nicotine is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and quality control of the active substance nicotine resinate is covered by an EDQM certificate of suitability.

Specifications for all packaging used to store the active substance have been provided. The primary packaging has been shown to comply with current legislation concerning materials in contact with food.

Appropriate stability data have been generated showing the active substance to be a physically and chemically stable drug, and supporting the proposed retest period of 1 year.

P. Medicinal Product

Other Ingredients

Other ingredients consist of pharmaceutical excipients gum base (containing butylhydroxytoluene), calcium carbonate, sorbitol (E420), sodium carbonate anhydrous, sodium hydrogen carbonate, polacrilin, glycerol, purified water, levomenthol, saccharin, sodium saccharin, acesulfame potassium, xylitol, mannitol (E421), gelatin, titanium dioxide (E171), carnauba wax and talc. In addition, Nicotinell Fruit 2 and 4mg Chewing Gum contain tutti flavouring, and Nicotinell Mint 2 and 4mg contain peppermint oil and eucalyptus oil.

All excipients comply with their European Pharmacopoeia monograph, with the exception of gum base, tutti flavouring and polacrilin (which are controlled to suitable in-house specifications).

With the exception of gelatin, none of the excipients contain materials of animal or human origin. Current TSE Certificates of Suitability have been provided for all suppliers of gelatin. No genetically modified organisms (GMO) have been used in the preparation of these products.

Pharmaceutical Development
The objective of the development programme was to formulate stable, acceptable formulations of Nicotinell Mint 2 and 4 mg Chewing Gum, and Nicotinell Fruit 2 and 4mg Chewing Gum, comparable to Nicorette 2 and 4mg Chewing Gum (Pharmacia Limited), which were the reference products for these applications.

The rationale for the type of pharmaceutical form developed and formulation variables evaluated during development have been stated and are satisfactory.

The rationale and function of each excipient added is discussed. Levels of each ingredient are typical for a product of this nature and have been optimised on the basis of results from development studies.

In vivo chew tests have shown that the rate of nicotine release from both strengths is comparable with their respective reference products.

Manufacturing Process
Satisfactory batch formulae have been provided for the manufacture of both strengths of the mint- and fruit-flavoured products, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished Product Specification
The finished product specifications proposed for both strengths of the mint- and fruit-flavoured products are acceptable. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specifications. Certificates of analysis have been provided for any working standards used.

Container-Closure System
Both strengths of tablets are packaged in polyvinylchloride/polyvinylidene chloride/aluminium blisters, each containing either 2 or 12 pieces of gum. These are packed into boxes of 2, 12, 24, 36, 48, 60, 72, 96 and 204 pieces of gum.

Satisfactory specifications and certificates of analysis have been provided for all packaging components. All primary packaging complies with the relevant regulations concerning use of materials in contact with food.

Stability of the Product
Stability studies were performed on batches of all strengths of finished product in the packaging proposed for marketing and in accordance with current guidelines. These data support a shelf-life of 2 years with the storage conditions “Do not store above 25°C”.

Summary of Product Characteristics (SPC), Patient Information Leaflet (PIL), Labels
The SPC, PIL and labelling are pharmaceutically acceptable.

The marketing authorisation holder has stated that they do not wish to market the product in the UK at the current time, but have committed to submitting mock-ups of the PIL and packaging, and user testing of the PIL, before marketing any of the products.

MAA Forms
The MAA forms are pharmaceutically satisfactory.

Expert report
The pharmaceutical expert report has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical dossier.

Conclusion
The grant of marketing authorisations is recommended.

III.2 PRE-CLINICAL ASPECTS

INTRODUCTION
The product is indicated for the relief of nicotine withdrawal symptoms, in nicotine dependency as an aid to smoking cessation. The applications claim to be generic medicinal products of Nicorette in terms of its composition and clinical indication, and the absence of data on pharmaco-toxicology specific to this application was considered acceptable.

The inclusion of a gum that is different from that used in the reference products is noted, but it is accepted that no further animal testing is required because the gum in question is an accepted material for its purpose. The justification for the absence of local tolerance studies in animals is also noted and accepted.

IMPURITIES/DEGRADATION PRODUCTS
The preclinical expert report included a discussion of the impurities and degradation products. The limits for nicotine N-oxide and nicotinic acid are acceptable.

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)
The SPC is satisfactory from a preclinical viewpoint.

EXPERT REPORT
The expert report is written by an appropriately qualified person and provides a review of published literature on the pharmacology and toxicology of nicotine, and discussed relevant information on the formulation.

CONCLUSIONS
The absence of new preclinical studies is justified for this type of application. The expert has adequately discussed the published literature on nicotine. It is considered that there is sufficient information available to conclude that the benefit/risk ratio is favourable and there are no preclinical objections to the grant of marketing authorisations for Nicotinell Fruit/Mint 2mg and 4mg Chewing Gums for the relief of nicotine withdrawal symptoms, in nicotine dependency as an aid to smoking cessation.

III.3 CLINICAL ASPECTS

Clinical Pharmacology

The clinical pharmacology of the alkaloid nicotine is also well-known and is described in a very extensive literature. There was no evidence in the dossier submitted by the applicant to suggest that the formulation of these products had significantly altered the pharmacology of the active substance. At the time when the original four applications for these products were made, there were no data provided on human exposure. The applicant was requested to provide evidence of bioavailability and bioequivalence and was asked that when conducting an appropriate human experiment to obtain the necessary kinetic information to consider the possibility of an interaction between the menthol/peppermint oil flavouring and nicotine in the new formulations. The latter information was requested on the basis of the known clinical pharmacological effects of the compounds in question.

Bioavailability

A three-way, multiple-dose, randomised, crossover, comparative bioavailability study was conducted. The 2mg formulation then proposed for marketing for each flavour was compared to the 2mg cross-reference product. The design and conduct of the study were found to be satisfactory and compliant with the principles of Good Clinical Practice.

A comprehensive report of the study has been provided. The results of the analyses of whole blood samples taken from these persons were used in the derivation of the reported pharmacokinetic parameters.

This was a small but well designed and conducted study, which would appear to have satisfactorily met its objective. It provided a limited, but usable, pharmacokinetic profile of plasma nicotine absorbed from the two flavours of nicotine chewing gum. The results from this study were accepted as being directly supportive of the approval of the 2mg gums and as forming a scientific basis for the approval by extrapolation to the 4mg gums.

Bioequivalence

The results from the above study were considered as showing that bioequivalence had been demonstrated between the Nicotinell Mint/Fruit 2mg Chewing Gum and their respective comparator products. The limits reported were found to be within those considered appropriate and in compliance with those described in current European guidelines.

As these products meet all the criteria as specified in the Note for Guidance on the investigation of bioavailability and bioequivalence (CPMP/EWP/QWP/1401/98), the results and conclusions of the bioequivalence study on the 2mg strength can be extrapolated to the 4mg strength gum.

Special Groups

No new clinical information on exposure to or use in special high risk groups were provided in the dossier. This was not considered to be a significant deficiency given the nature of the products and the intended user population. However, it was considered essential to ensure that due attention was paid to possible adverse effects for all major at risk groups in the warnings and precautions texts in the summary of product characteristics for each of the four products.

These four products are contraindicated for use in children, pregnancy and non-smokers.

Additional Studies

In the dossier prepared by the applicant, for submission to the Concerned Member States for this mutual recognition procedure, reports from an addition human experiment are provided. This new experiment is described as a clinical trial on nicotine chewing gum 4 mg versus Nicorette® 4 mg - a comparison of release from two different flavours. A review of the documents provided appears to indicate that this experiment was designed and conducted in a manner compliant with the principles of Good Clinical Practice.

The gums were chewed for various defined periods of time under 'controlled conditions'. The chewed gums were then harvested and analysed for residual nicotine and the amount of nicotine released calculated. A difference in release rates between test and reference products was recorded. The release rates from the test products were statistically significantly less than from the reference product. It was concluded by the applicant that such observations had no clinical significance for products that were going to be self-titrated by the users, a view not disputed by this assessor.

It should be noted that this study did not form part of the original evidence supporting the UK approval of these four nicotine chewing gums. The UK marketing approval was granted in May 1995, some months before the experiment was done.

Efficacy

The clinical efficacy of chewing gum and other nicotine delivery systems in relieving the withdrawal symptoms associated with cessation of tobacco smoking is well-documented. No new data arising from applicant-sponsored clinical trials were provided in respect of these particular products. Therefore, on the basis of the published reports concerning the clinical use of nicotine-containing medicinal products referred to by the applicant in the dossiers and in view of the fact that these were abridged applications, the clinical efficacy of these products was considered to have been sufficiently supported for approval when considered in conjunction with the bioavailability data also presented.

Safety

The clinical hazards associated with the use of medicinal products containing nicotine when inhaled, ingested, absorbed transdermally or otherwise administered to human beings have been documented. The hazards to humans of nicotine administration under experimental conditions has been extensively documented, as has the 'adverse' effects in animals.

No new clinical safety information was provided by the applicant save that arising from the bioavailability study. The profile of adverse effects reported was consistent with the known effects of nicotine. It was interesting to note the observations made during the bioavailability study, that the incidence of buccal and upper gastrointestinal side effects was significantly less with the two test gums containing menthol/peppermint oil when compared to the reference product. While this phenomenon was not unexpected given the known uses and effects of menthol/peppermint oil, it was accepted as showing better tolerance of the new products. No further information was requested concerning this nicotine with menthol/peppermint oil interaction, as the latter compounds were listed as flavourings generally regarded as safe and not active substances. There did not appear to be a significant safety or public health issue to be investigated or resolved.

This particular phenomenon was also recorded in the reports of the *in-vivo* release experiment done after the original approval. It would appear that the presence of the flavouring menthol/peppermint oil has an advantageous effect on product tolerance.

There was no evidence or reason to suggest that these nicotine gum products would be more or less hazardous in normal use than similar currently approved products. It was, therefore, considered that once adequate warnings and precautions were given in the summary of product characteristics for each product (based on the known adverse reaction profile of nicotine) this would suffice and that no additional safety data would be necessary prior to approval. No special mention of the effects of the menthol/peppermint oil were considered necessary for inclusion in the approved summary of product characteristics for any of the products.

Prior to approval, appropriate contraindications, safety warnings and precautions were included in the summary of product characteristics for each product.

A brief comment, in the current dossier, by the applicant on the post marketing experience since the launch in the UK reports that no adverse reaction were reported to the company.

Expert Reports
The preclinical expert report was a brief review of the hazards of nicotine and essentially similar to that for similar products.

The clinical expert report in the current dossiers has a brief review of the role of nicotine substitution in smokers. The report also comments in a factual manner on the two studies in human volunteers with the four formulations, but makes no significant comments on the safety profile of the active or the products proposed for marketing.

The comments of the expert in respect of the effects of menthol concern enhancement of absorption, but not the altered adverse event profile clearly recorded in two independent experiments. A more detailed and critical commentary on the safety and efficacy of the products proposed for marketing in the concerned member states would have been more helpful.

Summary of Product Characteristics (SPC)
The SPC is medically satisfactory and is consistent with those for the reference products.

Patient Information Leaflet (PIL)
The PIL is medically satisfactory and is consistent with those for the reference products.

Labelling
The labelling provided is medically satisfactory.

Discussion
The dossiers in these mutual recognition applications have been revised since the original UK applications were made and approval granted. There are data provided on the effects of exposure of humans to these new formulations under controlled conditions. Prior to approval the reports of the bioavailability study were assessed and found to be supportive of the final approval. New data in the current dossiers arise from a more recent human experiment to determine *in vivo* release rate. The first study was done using the 2mg gums and the second the 4mg gums; it should be remembered that both strengths were approved at the same time.

It would appear that the basis of these products and their potential clinical use is essentially sound. The applicant has satisfactorily revised all appropriate texts and the expanded the expert comments on the safety and efficacy of the products now proposed for marketing in the Concerned Member States. The evidence now available supports the applicants claims of

essential similarity, the evidence from human exposure is limited but sufficient to show a pharmacokinetic profile and to demonstrate that plasma levels of the active nicotine can be achieved which can reasonably be expected to relieve nicotine withdrawal symptoms in nicotine dependent persons who have stopped smoking. There is no evidence to suggest that the safety profile for these products is or will be any different from other similar products already approved and in the market place.

Conclusions
The grant of marketing authorisations is recommended.

IV OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The important quality characteristics of Nicotinell Fruit/Mint 2mg and 4mg Chewing Gum are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL
No new preclinical data were submitted and none are required for applications of this type.

EFFICACY
A bioequivalence study comparing the proposed test 2mg chewing gum versus Nicorette 2mg Chewing Gum showed that these products can be considered bioequivalent. As these products meet all the criteria as specified in the Note for Guidance on the investigation of bioavailability and bioequivalence (CPMP/EWP/QWP/1401/98), the results and conclusions of the bioequivalence study on the 2mg gum can be extrapolated to the 4mg gum.

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for other similar products.

RISK-BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with nicotine is considered to have demonstrated the therapeutic value of the compound. The risk benefit is, therefore, considered to be positive.

Module 5

STEPS TAKEN AFTER INITIAL PROCEDURE - SUMMARY

Date submitted	Application type	Scope	Outcome
25/06/2008	Type II	To introduce the changes for harmonisation with the agreed SPC text during the repeat use MRP of Nicotinell Fruit/Mint gums (UK/H/407-408/01-02/E02) and Nicotinell Liquorice gums (UK/H/409/1-2/E01), and the Type II SPC variations for Nicotinell Classic gums (UK/H/591/1-2/II/014) and Nicotinell Mint/Duo 2 mg lozenges (SE/H/178/02/II/020, SE/H/299/01/II/003). The SPC is also revised according to the latest QRD template (version 7.2, 10/2006). Harmonised labelling and PIL, reflecting the proposed changes to the SPC and the results of the PIL user testing conducted in 2007 (Report dated August 2007) on Nicotinell Liquorice 4mg medicated chewing-gum, are also submitted.	Approved 09/03/2009
31/10/2008	Type IB	To add a pack size of 204 gums to the product licence-section 6.5 (Nature and content of container) of the SPC and labelling are updated.	Approved 25/02/2009