Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

NCH Mint 2 mg compressed lozenges.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each piece of lozenge contains:
Active substance: 2 mg nicotine (corresponding to 6.144 mg nicotine bitartrate dihydrate).
Excipient(s): aspartame (0.01 g), maltitol (0.9 g) and sodium (9.8 mg).
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Compressed lozenge
White, mint flavoured, round biconvex lozenge

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

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

The 2 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 NCH Mint lozenge.
NCH Mint 2 mg lozenge 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 (1 mg lozenge)	Low (1 mg lozenge) or high (2 mg lozenge) dose forms are acceptable depending on patient characteristics and preference.	High dose forms are preferable (2 mg lozenge)

If an adverse event occurs with the use of the high dose form (2 mg lozenge), use of the low dose form (1 mg lozenge) should be considered.

The initial dosage should be individualised on the basis of the patients nicotine dependence. One piece of lozenge to suck when the user feels the urge to smoke.
Initially, 1 lozenge should be taken every 1-2 hours. The usual dosage is 8-12 lozenges per day. The maximum daily dose is 15 lozenges.

Directions for use:

1. One lozenge to be sucked until the taste becomes strong.
2. The lozenge should then be lodged between the gum and cheek.
3. When the taste fades, sucking of the lozenge should commence again.
4. The sucking routine will be adapted individually and should be repeated until the lozenge dissolves completely (about 30 minutes).

The treatment duration is individual. Normally, treatment should continue for at least 3 months. After 3 months, the user should gradually reduce the number of lozenges or alternatively the user should switch to nicotine 1 mg lozenges and then gradually reduce the number of lozenges per day.

Treatment should be discontinued when the dose has been reduced to 1-2 lozenges per day. Use of nicotine medicinal products like NCH Mint 2 mg lozenge beyond 6 months is generally not recommended. Some ex-smokers may need treatment with the lozenge 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 sucking the lozenge.

Children and adolescents (< 18 years)

NCH Mint lozenge 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 with NCH Mint lozenge.

4.3 Contraindications

Hypersensitivity to nicotine or to any of the excipients.

NCH Mint lozenge 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, NCH Mint lozenges may be considered but as data on safety in this patient group are limited, initiation should only be under close medical supervision.

NCH Mint lozenges 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 and 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).*

Special warnings about excipients

NCH Mint lozenges contain sweeteners, including aspartame and maltitol.

Each NCH Mint 2 mg lozenge contains aspartame (E951), a source of phenylalanine equivalent to 5 mg/dose and may be harmful for people with phenylketonuria.

Because NCH Mint 2 mg lozenge contains maltitol (E965), a source of fructose:
- patients with rare hereditary conditions of fructose intolerance should not take this medicine,
- patients may experience a mild laxative effect.

Calorific value 2.3 kcal/g maltitol.

NCH Mint 2 mg lozenge contains 9.8 mg of sodium per piece

4.5 Interaction with other medicinal products and other forms of interaction

Drug Interactions: No information is available on interactions between NCH Mint lozenge 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 Fertility, 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 lozenge 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. The lozenge, like smoking itself, should therefore be avoided during breast-feeding. Should smoking withdrawal not be achieved, use of the lozenge by breast feeding smokers should only be initiated after advice from a physician. Where nicotine replacement therapy is used whilst breast-feeding, the lozenge 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 lozenge is used following the recommended dose. Nevertheless one should take into consideration that smoking cessation can cause behavioural changes.

4.8 Undesirable effects

NCH Mint lozenge 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: hypersensitivity, angioneurotic oedema and anaphylactic reactions.

Most of the adverse reactions which are reported by patients occur generally during the first 3-4 weeks after initiation of therapy.

Nicotine from lozenges may sometimes cause a slight irritation of the throat and increased 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 sucking will usually overcome this problem.

Excessive consumption of lozenges 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.

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: dizziness, headache

Gastrointestinal disorders:

Common: nausea, flatulence, hiccups, gastritis, dry mouth, stomatitis and oesophagitis.

Cardiac disorders:

Uncommon; palpitations

Rare: atrial arrhythmia

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 body weight, 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 NCH Mint 2 mg lozenge may only occur if many pieces are sucked simultaneously. Nicotine toxicity after ingestion will most likely be minimised as a result of early nausea and vomiting that occur following excessive nicotine exposure.

General symptoms of nicotine poisoning include: weakness, perspiration, salivation, throat burn, nausea, vomiting, diarrhoea, abdominal pain, hearing and visual disturbances, headache, tachycardia and cardiac arrhythmia, dyspnoea, prostration, circulatory collapse, coma and terminal convulsions.

Treatment of overdose:
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 lozenge 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

The absorbed amount of nicotine depends on the amount released into the mouth and absorbed through the buccal mucosa.

The main part of nicotine in NCH Mint 2 mg lozenge is absorbed through the buccal mucosa. A proportion, by the swallowing of nicotine containing saliva, reaches the stomach and intestine where it is inactivated. Due to the first-pass effect in the liver, the systemic bioavailability of nicotine is low. Consequently, in the treatment with NCH Mint 2 mg lozenge the high and quick systemic nicotine concentration, as seen when smoking, is rarely obtained.

Distribution volume after intravenous administration of nicotine is approximately 2-3 1/kg and the half-life is 2 hours. Nicotine is metabolised principally in the liver and the plasma clearance is approximately 1.2 l/min; nicotine also metabolises in the kidney and lungs. Nicotine crosses the blood-brain barrier.

More than 20 metabolites have been identified, all believed to be less active than nicotine. The main metabolite is cotinine which has a half-life of 15-20 hours and with approximately 10 times higher plasma concentration than nicotine. Nicotine's plasma-protein binding is less than 5%. Changes in nicotine binding from the use of concomitant medicinal products or due to altered disease state are not expected to have significant effect on nicotine kinetics. The main metabolite in urine is cotinine (15% of the dose) and trans-3-hydroxy cotinine (45% of the dose).

About 10% of the nicotine is excreted unchanged. Up to 30% may be excreted with urine in increased diuresis and the acidity under pH 5.

The peak value for the plasma concentration of NCH Mint 2 mg lozenge after a single dose is approximately 7.0 ng per ml and the maximal concentration at steady state (one 2 mg lozenge/hour for 12 hours) is approximately 22.5 ng per ml (average plasma concentration of nicotine after smoking one cigarette is 15-30 ng per ml). Peak plasma concentration is reached after about 48 minutes following sucking of a single lozenge and after about 30 minutes at steady state.

Studies have demonstrated that there is a linear dose-concentration proportionality between the 1 mg and 2 mg NCH Mint lozenges for both C_{max} and AUC. The T_{max} are similar for both strengths.

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

Maltitol (E965)
Sodium carbonate anhydrous
Sodium hydrogen carbonate
Polyacrylate dispersion 30 per cent
Xanthan gum
Colloidal anhydrous silica
Levomenthol
Peppermint oil
Aspartame (E951)
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

12, 36, 72, 96, 144 or 204 lozenges in opaque blisters consisting of aluminium foil and PVC/PE/PVDC/PE/PVC-film. Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

PA 30/52/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First date of authorisation: 04 Novmeber 2003

Last date of authorisation: 16 December 2008

10 DATE OF REVISION OF THE TEXT

August 2009