Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nicorette Inhaler 10mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Nicotine 10mg per cartridge

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Inhalation cartridge for oromucosal use
White to slightly coloured porous plugs in sealed, transparent plastic cartridges.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

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

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

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

4.2 Posology and method of administration

Adults (including the elderly)

Dosage

Smoking Cessation

The frequency of use should depend on the previous smoking habit of the individual. Nicorette Inhaler should be used whenever the urge to smoke is felt, up to a maximum usage of 12 cartridges per day.

In the treatment of nicotine dependence, a course not exceeding three months is suggested, the patient stopping smoking completely at the start of the course.

a) For up to 8 weeks the patient uses not less than six and not more that 12 cartridges each day to relieve craving.

b) Over the following two weeks the aim is to reduce the number of cartridges used by half, over the next two weeks to reduce the number to zero by the last day.

c) If abstinence has not been achieved, further courses of treatment may be recommended, if it is considered that the patient would benefit.

d) Counselling and support from family, friends and health professionals can improve the chances of abstinence.

Temporary Abstinence

During periods of temporary abstinence, the patient should use the Inhaler when required to relieve nicotine cravings and withdrawal symptoms. No more than 12 cartridges should be used in a 24 hour period.

Gradual cessation

For smokers who are unwilling or unable to quit abruptly.
Use the inhaler whenever there is a strong urge to smoke in order to reduce the number of cigarettes smoked as far as possible and to refrain from smoking as long as possible.

The number of cartridges is variable and depends on the patients needs. Not more than 12 cartridges should be used per day.

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

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

Method of administration
The cartridge is inserted into the mouthpiece according to the instructions. The patient draws air into the mouth through the mouthpiece: there is a greater effort needed than with a cigarette. The patient may find deep drawing or short sucks on the mouthpiece most effective – patients soon find a favoured technique. Nicotine vapour passing through the mouth is absorbed by the buccal mucosa: little reaches the lungs. After about 20 minutes of intense use the maximal dose is achieved and it is then that the nicotine amounts released from the cartridge begin to fall away, such that the user rejects the cartridge. The actual time that the cartridge is active depends on the intensity of use.

Concomitant disease
Only severe renal impairment would be expected to affect the clearance of nicotine or its metabolites from circulation. In patients smoking and undergoing haemodialysis elevated nicotine levels have been seen.

A minor reduction in total clearance of nicotine has been demonstrated in healthy elderly patients, however, not justifying adjustment of dosage.
Patients with obstructive lung disease may find use of the Inhaler difficult. Nicotine gum, patch, microtab or nasal spray may be preferred in such cases.

4.3 Contraindications

- Use in non-smokers
- Use in persons hypersensitive to nicotine or any ingredient in Nicorette Inhaler.

4.4 Special warnings and precautions for use

Nicorette Inhaler should be used with caution in patients with cardiovascular disease, severe/moderate hepatic impairment, severe renal impairment, active and duodenal ulcers.

Nicotine, both from NRT and smoking, causes the release of catecholames from the adrenal medulla. Therefore, Nicorette should be used with caution in patients with hyperthyroidism or pheochromocytoma.

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

Nicotine in any dose form is capable of inducing a dependence syndrome after chronic use and is highly toxic after

acute use. However, dependence with Nicorette Inhaler is a rare side effect and is both less harmful and easier to break than smoking dependence.

4.5 Interaction with other medicinal products and other forms of interaction

Smoking (but not nicotine) is associated with an increase in CYP1A2 activity. After cessation of smoking, reduced clearance of substrates for this enzyme may occur. This may lead to an increase in plasma levels for some medicinal products of potential clinical importance and for products with a narrow therapeutic window, e.g. theophylline, tacrine and clozapine.
The plasma concentration of other drugs metabolised in part by CYP1A2 e.g. imipramine, olanzapin, clonipramine and fluvoxamine may also increase on cessation of smoking, although data to support this are lacking and the possible clinical significance of this effect is unknown.
Limited data indicate the metabolism of flecainide and pentazocine may also be induced by smoking.

4.6 Fertility, pregnancy and lactation

Pregnancy:
Nicotine passes freely to the foetus and affects its breathing movements and circulation. The effect on the circulation is dose-dependent.
Therefore, the pregnant smoker should always be advised to stop smoking completely without the use of nicotine replacement therapy. The risk of continued smoking may pose a greater hazard to the foetus as compared with the use of nicotine replacement therapy products in a supervised cessation programme.

Use of Nicorette should only be initiated after advice from a physician.

Lactation:
Nicotine passes freely into breast milk in quantities that may affect the child even in therapeutic dose. Nicorette should therefore not be used during breast-feeding.

4.7 Effects on ability to drive and use machines

None

4.8 Undesirable effects

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

<u>Common (>1/100)</u>
CNS: Headache
Gastrointestinal: Nausea, gastrointestinal discomfort and/or pain, hiccups, vomiting
Respiratory: Coughing
Local: Irritation of mouth and throat, nasal congestion

<u>Less common (1/100-1/1000)</u>
Circulation: Palpitations

<u>Rare (<1/1000)</u>
Cardiovascular: Reversible atrial fibrillation

Symptoms such as dizziness, headache and sleeplessness may be related to withdrawal symptoms associated with smoking cessation. Increased incidence of aphthous ulcer may occur after smoking cessation. The causality is unclear

4.9 Overdose

Excessive use of nicotine from either NRT and/or smoking might cause symptoms of an overdose. Symptoms of an overdose are those of acute nicotine poisoning and include nausea, salivation, abdominal pain, diarrhoea, sweating, headache, dizziness, disturbed hearing and marked weakness. At high doses, these symptoms may be followed by hypotension, weak and irregular pulse, breathing difficulties, prostration, circulatory collapse and general convulsions. Doses of nicotine that are tolerated by adult smokers during treatment may produce severe symptoms of poisoning in small children and may prove fatal.

Management of overdose:
The administration of nicotine must be stopped immediately and the patient should be treated symptomatically. Tachycardia causing circulatory impairment may require treatment with a ß-blocker. Excitation and convulsions may be treated with diazepam. Mechanically assisted ventilation should be instituted if necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Nicorette Inhaler facilitates uptake of nicotine through the buccal mucosa into the venous circulation. The amount taken up alleviates the craving symptoms caused by the absence of nicotine from smoking.

5.2 Pharmacokinetic properties

Nicotine given iv has a volume of distribution of 2 to 3L/kg with half-life of 1-2 hours. Average plasma clearance is about 1-2L/min mainly in the liver. More than 20 metabolites are known, all less active than nicotine: cotinine, with a half life of 15-20 hours and concentrations ten times that of nicotine is the main one.

Plasma binding of nicotine below 5% means significant displacement of drugs or nicotine is unlikely. Nicotine is excreted in the urine principally as cotinine (15%), 3-hydroxycotinine (45%), nicotine (10%).

Most inhaled nicotine is absorbed via the buccal mucosa. Forced rapid inhalation over 20 minutes will remove 40% of the nicotine from the cartridge. Uptake is slow and free of peaks resultant from cigarette smoking – about one-third that from smoking and equivalent to an hourly 2mg nicotine chewing gum.

Peak plasma levels occur within 15 minutes after the end of inhalation. Forced rapid inhalation for 20 minutes per hour for 12 hours achieved steady state levels of 20-25 ng/ml.

Ambient temperatures affects volatilisation of nicotine, the biologically available dose rising by 35% for each 10°C above 20°C. Use below 15°C is not recommended.

Because the pattern of use is decided by the patient up to a limit of 12 cartridges per day to relieve craving, therapeutic levels of nicotine are individual, dictated by the level of dependence.

5.3 Preclinical safety data

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

6 PHARMACEUTICAL PARTICULARS

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Aluminum foil sealed plastic cartridge
Pack sizes: Packs containing 18 or 42 cartridges and a plastic mouthpiece.
Packs containing 2 plastic mouthpieces only.

Not all pack sizes will 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

1. Remove the Aluminium foil sealed tray and the mouthpiece from the carton box.
2. Peel back the foil from the tray. Pull the mouthpiece apart.
3. Insert a cartridge into the mouthpiece, whereby the seal of the inserted end of the cartridge is perforated.
4. Push the other part of the mouthpiece back into place over the cartridge. The product is now ready to use.

Grip the mouthpiece in the lips as air is inhaled, the nicotine is vaporised and absorbed in the mouth.

<u>Disposal Instructions</u>
Because of residual nicotine, used cartridges may be a hazard to children, animals and fish and so should never be thrown away or left lying around. They should be kept in the case and disposed of in with household rubbish.

<u>Cleaning the mouthpiece</u>
The empty mouthpiece should be rinsed in water several times a week.

Nicorette Inhaler should be used when the patient has the urge for a cigarette or feels the onset of other withdrawal symptoms, up to a maximum of twelve cartridges per day.

The number, frequency, puffing/inhalation time and technique vary individually. Studies show that different inhalation techniques give similar effects: deep inhalation (the cigarette smoker's way) or shallow puffing (the pipe smoker's way). The amount of nicotine from a puff is less than that from a cigarette.

To compensate for less nicotine delivery from a puff, it is necessary to inhale more often than when smoking a cigarette, i.e. use the Nicorette Inhaler for longer periods at a time. After using a few cartridges the patient will have found a method that suits him/her and gives the best effect.

This product works best at room temperature. In cold conditions the nicotine evaporates less readily and it will be necessary to inhale more frequently, whilst in warm conditions nicotine will evaporate more readily and inhalation should be less frequent to avoid overdose.

7 MARKETING AUTHORISATION HOLDER

McNeil Healthcare (Ireland) Ltd
Airton Road
Tallaght
Dublin 24

8 MARKETING AUTHORISATION NUMBER

PA 0823/049/009

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 June 1998

Date of last renewal: 01 January 2007

10 DATE OF REVISION OF THE TEXT

December 2012