Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nicorette Microtab 2 mg Sublingual tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains 17.4 mg of nicotine betadex equivalent to nicotine 2 mg.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Sublingual tablets.

A white to off-white flat round bevel-edged tablet, engraved 'NIC' on one side and '2' on the opposite side.

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.

4.2 Posology and method of administration

Adults and the Elderly

Smoking Cessation
The initial dose is based on the individual's nicotine dependence. The tablet is used sublingually with a recommended dose of one tablet per hour or, for heavy smokers (smoking more than 20 cigarettes per day), two tablets per hour. Increasing to two tablets per hour may be considered for patients who fail to stop smoking with the one tablet-per-hour regimen or for those whose nicotine withdrawal symptoms remain so strong as to threaten a relapse.
Most smokers require 8 to 12 or 16 to 24 tablets per day, not to exceed 40 tablets. The duration of treatment is individual. The nicotine dose should be gradually reduced by decreasing the total number of tablets used per day. The treatment should be stopped when the daily consumption is down to one or two tablets.

If not successful after 12 weeks the patient should be encouraged to make a fresh attempt to stop smoking. This may necessitate full or partial re-treatment with an NRT programme.

Adults and the Elderly – Temporary Abstinence
During periods of temporary abstinence, the patient should use one tablet per hour, or for heavy smokers, two tablets pe hour, to relieve nicotine cravings and withdrawal symptoms. Increasing to two tablets per hour may be considered for patients who find the one tablet per hour regimen is not relieving their cravings.

Children
The safety of Nicorette Microtab has not been established in individuals under eighteen years of age. The product shoul only be used in these subjects under medical supervision.

Concomitant Disease
Only severe renal impairment would be expected to affect the clearance of nicotine or its metabolites from the circulation. In patients smoking and undergoing renal 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.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

It is important that the treatment is supported with other activities in order to facilitate smoking cessation.

Nicorette 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 catecholamines from the adrenal medulla. Therefore, Nicorette should be used with caution in patients with hyperthyroidism or pheochromacytoma.

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 Microtab 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

Not applicable.

4.8 Undesirable effects

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

Common (>1/100)
CNS: Headache
Gastrointestinal: Nausea, gastrointestinal discomfort and/or pain, hiccups.
Respiratory: Coughing
Local: Sore mouth or throat, dry mouth, burning sensation in the mouth.

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

Rare (<1/1000)
Cardiovascular: Reversible atrial fibrillation
General: Allergic reactions

In clinical studies of Nicorette Microtab, the following adverse events were reported: heartburn, unpleasant taste and sensation of lump in the throat.

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

The pharmacological effects of nicotine are well documented. The response at any one time represents a summation of stimulant and depression actions from direct, reflex and chemical mediator influences on several organs. The principal pharmacological actions are central stimulation and/or depression; transient hyperpnoea; peripheral vasoconstriction (usually associated with a rise in systolic pressure); suppression of appetite and stimulation of peristalsis.

5.2 Pharmacokinetic properties

Most of the absorption of nicotine from Nicorette Microtab occurs directly through the buccal mucosa. The absolute

bioavailability, after sublingual administration of the tablet, is approximately 50%. The systemic bioavailability of orall administered nicotine is lower due to the amount removed initially by the liver (the first-pass effect). Hence, the high ar rapidly rising nicotine concentrations seen after smoking are rarely produced by treatment with Nicorette Microtab. Nicotine from smoking is rapidly absorbed from the lungs into arterial plasma whereas nicotine from sublingual tablets passes more slowly into the venous system.

Steady-state trough nicotine plasma concentrations, achieved after ten hourly doses of one tablet, are in the order of magnitude of 10 ng/mL, which is about 50% of normal smoking levels.

There is a slight deviation from dose-linearity of AUC_{inf} and C_{max} when single doses of one, two and three tablets are given. This deviation may be explained by a larger fraction of the higher doses being swallowed and subject to first-pas elimination.

The therapeutic blood concentrations of nicotine, i.e. the blood levels which relieve craving, are based on the individual nicotine dependence.

5.3 Preclinical safety data

No data are presented given the extensive published information that is available on nicotine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Betadex
Crospovidone
Magnesium stearate
Colloidal anhydrous silica

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

Package sizes:

30 sublingual tablets
105 sublingual tablets

The tablets are packed in press-through packages (blister packages) of 15 tablets/blister, in a cardboard box together with a dispenser and package insert.

The blister consists of PVC/PVDC film and a foil composed of polyester, aluminium and paper.

The dispenser is made of polypropylene.

Or

In Aluminium/heal seal lacquer press through blister strips, with 10 tablets per blister in a cardboard box.
Package sizes 20, 30, 90, 100 and 150.
Not all packs 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

Remove blister strip from the package and place it in the dispenser. Close the lid. Turn the blister in the direction of the arrow (clockwise) until you hear/feel it click. Ensure the mark in the blister is positioned towards the triangular mark in the dispenser and press out the sublingual tablet.

7 MARKETING AUTHORISATION HOLDER

McNeil Healthcare (Ireland) Ltd
Airton Road
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Dublin 24

8 MARKETING AUTHORISATION NUMBER

PA 0823/049/010

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 01 January 2007

10 DATE OF REVISION OF THE TEXT

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