Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Boots Nicotine Medicated Chewing Gum 2mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

For excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Medicated chewing gum
Each piece of uncoated chewing-gum is off-white in colour and rectangular in shape.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Boots Nicotine Chewing Gum treatment is indicated for the relief of nicotine withdrawal symptoms, in nicotine dependency as an aid to smoking cessation.

4.2 Posology and method of administration

Adults and Elderly: Users should stop smoking completely during treatment with Boots Nicotine Chewing Gum. One piece of Boots Nicotine Chewing Gum to be chewed when the user feels the urge to smoke.

Normally, 8-12 pieces per day, up to a maximum of 25 pieces per day.
The characteristics of 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 gum should be chewed until the taste becomes strong.
2. The 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.

After three months, the user should gradually cut down the number of pieces chewed each day until they have stopped using the product.

Boots Nicotine Medicated Chewing Gum is sugar-free.

Children and young adults:
Boots Nicotine Chewing Gum should not be used by people under 18 years of age without recommendation from a physician.

Concomitant use of acidic beverages such as coffee or soda may interfere with the buccal absorption of nicotine. Acidic beverages should be avoided for 15 minutes prior to chewing the gum.

4.3 Contraindications

Boots Nicotine Chewing Gum should not be used by non-smokers. Furthermore, people should not use the gum and smoke concomitantly.

Use is contra-indicated, in patients with acute myocardial infarction, unstable or worsening angina pectoris, severe cardiac arrhythmias and recent cerebrovascular accident.

4.4 Special warnings and precautions for use

Swallowed nicotine may exacerbate symptoms in subjects suffering from active oesophagitis, oral or pharyngeal inflammation**,** gastritis or peptic ulcer.

Use with caution in patients with hypertension, stable angina pectoris, cerebrovascular disease, occlusive peripheral arterial disease, heart failure, hyperthyroidism, diabetes mellitus, and renal or hepatic impairment.

Counselling may help smokers to quit.

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).

4.5 Interaction with other medicinal products and other forms of interaction

Drug Interactions:
No information is available on interactions between Boots Nicotine Chewing Gum and other drugs.

Smoking Cessation:
This is different in the case of smoking where interactions with other medications may occur due to a multitude of other substances contained in the smoke. Presumably due to the polycyclic aromatic hydrocarbons contained in the smoke, the metabolism of different medicinal products may be speeded up by enzyme induction: e.g. caffeine, theophylline, paracetamol, phenazone, phenylbutazone, pentazocine, lidocaine, benzodiazepines, imipramine, warfarin, oestrogen and vitamin B12.

Upon smoking cessation it may be expected that the hitherto increased metabolism of these medicinal products is slowed down or normalised. Unaltered dosage of the products may result in an increase in their blood concentration.

Therefore when prescribing Boots Nicotine Chewing Gum a possible dose adjustment should be considered in patients treated with the above mentioned medicinal products.

Other reported effects of smoking include a reduction of the analgesic effects of propoxyphene, reduced diuretic response to frusemide, change in the pharmacological effect of propranolol and altered responder rates in ulcer healing with H_2-antagonists.

Smoking and nicotine may raise the blood levels of cortisol and catecholamines. Dose adjustment of nifedipine, adrenergic agonists or adrenergic antagonists may be necessary.

Increased subcutaneous absorption of insulin which occurs under smoking cessation may necessitate a reduction in insulin dose.

4.6 Pregnancy and lactation

Patients should be advised to give up smoking without the use of nicotine replacement therapy. Should this fail, a medical assessment of the risk benefit of Boots Nicotine Chewing Gum should be made.

Reproductive toxicity studies with nicotine in several animal studies have demonstrated non-specific retardation of

foetal growth. Studies in rats produced evidence of decreased fertility, prolonged pregnancy, and behavioural disorders in the offspring. In mice the offspring of animals exposed to very high doses of nicotine showed skeletal defects in the peripheral parts of the limbs.

Overall, there are no clear cut grounds for believing that nicotine at the concentrations reached by treatment with nicotine gum has any teratogenic potential and/or inhibitory effects on fertility.

4.7 Effects on ability to drive and use machines

Smoking cessation can cause behavioural changes. There is no evidence of any risks associated with driving or operating machinery when the gum is used following the recommended dose.

4.8 Undesirable effects

In principle, Boots Nicotine Chewing Gum can cause adverse reactions similar to those associated with nicotine administered by smoking.

Nicotine from gum may sometimes cause a slight irritation of the throat and increase salivation at the start of treatment. Excessive swallowing of dissolved nicotine may, at first, cause hiccuping. Those with a tendency to indigestion may suffer initially from minor indigestion or heartburn. Slower chewing will usually overcome this problem. Excessive consumption of gum by subjects who have not been in the habit of inhaling tobacco smoke could possibly lead to nausea, faintness or headaches.

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 Boots Nicotine Chewing Gum may only occur if many pieces are chewed simultaneously. Risk of overdose is small as nausea or vomiting usually occurs at an early stage. Risk of poisoning by swallowing the gum is small. Since the release of nicotine from the 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, 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 overdosage:
In the event of overdosage, vomiting should be induced with syrup of ipecacuanha or gastric lavage carried out (wide bore tube). A suspension of activated charcoal should then be passed through the tube and left in the stomach. Artificial respiration with oxygen should be instituted if needed and continued for as long as necessary. Other therapy, including treatment of shock, is purely symptomatic.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Nicotine gum mimics the pharmacological effects of nicotine from smoking, and may therefore be used to help provide relief from nicotine withdrawal symptoms. In addition to effects on the central nervous system, nicotine produces haemodynamic effects such as increased heart rate and systolic blood pressure.

5.2 Pharmacokinetic properties

When the 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 peak plasma concentration of the 2 mg gum after a single dose is approximately 4.8 nanograms per ml and following steady state administration is approximately 14 nanograms per ml (average plasma concentration of nicotine when smoking a cigarette is 15-30 nanograms per ml).

For a chewing gum of 4 mg it has been calculated that a maximum plasma concentration of approximately 10nanog/ml is reached after approximately 30 minutes**.**

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

No animal studies have been undertaken on Boots Nicotine Chewing Gum.

The toxicity of nicotine as a constituent of tobacco has been well documented. Acute toxic effects include convulsions, cardiac insufficiency and paralysis of the respiratory system.

At high doses in cats and dogs, nicotine has been shown to potentiate histamine-induced peptic ulcer.

Nicotine has no genotoxic activity in most of the mutagenicity test systems. The well-known carcinogenicity of tobacco smoking is mainly caused by pyrolysis products. Application of nicotine chewing gum, however, avoids the high temperature required for the formation of these carcinogenic products**.**

All excipients used in Boots Nicotine Chewing Gum are of food grade.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gum base
Calcium carbonate
Sorbitol (E420)
Glycerol (E422)
Sodium carbonate anhydrous
Sodium hydrogen carbonate
Polacrilin
Purified water
Levomenthol
Peppermint oil
Eucalyptus oil
Butyhydroxytoluene (E321)
Acesulfame potassium
Saccharin
Sodium saccharin
Talc
Carnauba wax

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

2 years.

6.4 Special precautions for storage

Do not store above 25^{o}C.

6.5 Nature and contents of container

The chewing gum is packed in PVC/aluminium blister packs each containing 12 pieces of gum. The blisters are packed in boxes containing 12, 24, 36, 48, 60, 72 and 96 pieces of gum.

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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PA 30/40/1

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