Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Boots Nicotine Transdermal Patch 14 mg/24 hour

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each patch contains 35mg S (-) nicotine, average absorption rate 14mg in 24 hours.
Drug releasing surface area – 20cm^2.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Transdermal Patch
Transdermal therapeutic system, consisting of a round, flat, matrix-type self-adhesive yellowish-ochre coloured patch printed 'CG FEF' on the patch surface.
It is protected by a rectangular metallic release liner backing to be discarded before application.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

The treatment of nicotine dependence, as an aid to smoking cessation.

4.2 Posology and method of administration

Adults

Users should stop smoking completely during treatment with the Boots Nicotine Patch 14 mg/24 Hour.

For individuals smoking 20 cigarettes or more a day, it is recommended that treatment be started with Boots Nicotine Patches 21mg/24 Hour (step 1) daily, applied to a dry non-hairy area of the skin on the trunk or upper arm. Those smoking less than this are recommended to start with Boots Nicotine Patches 14mg/24 Hour (step 2). Sizes of 30cm^2, 20cm^2 and 10cm^2 are available to permit gradual withdrawal of nicotine replacement, using treatment periods of 3-4 weeks for each size. The size of patch may be adjusted according to individual response, maintaining or increasing the dose if abstinence is not achieved or if withdrawal symptoms are experienced. Total treatment periods of more than 3 months and daily doses above 30cm^2 have not been evaluated. The treatment is designed to be used continuously for 3 months but not beyond.

However, if abstinence is not achieved at the end of the 3 month treatment period, further treatments may be recommended following a re-evaluation of the patient's motivation.

The dosage must not be adjusted by cutting a patch.

The Boots Nicotine Patch 14mg/24 Hour should be used as soon as it has been removed from the child-resistant pouch. Following removal of the metallic backing, the Boots Nicotine Patch 14mg/24 Hour should be applied to the skin and held in position for 10-20 seconds with the palm of the hand. Each patch should be removed after 24 hours and disposed of safely (see "Warnings"). A different site of application should be chosen each day and several days should be allowed to elapse before a new patch is applied to the same area of skin.

Children

The Boots Nicotine Patch 14mg/24 Hour should not be administered to persons under 18 years of age without recommendation

from a physician. There is no experience in treating adolescents under the age of 18 with the Boots Nicotine Patch 14mg/24 Hour.

Elderly

Experience in the use of the Boots Nicotine Patch 14mg/24 Hour in smokers over the age of 65 years is limited. The Boots Nicotine Patch 14mg/24 Hour does not appear to pose safety problems in this age group.

Potential for abuse and dependence

Transdermal nicotine is likely to have a very low abuse potential because of its slow onset of action, low fluctuations in blood concentrations, inability to produce high blood concentrations of nicotine, and the infrequent (once daily) use. Moreover, gradual weaning from Boots Nicotine Patches 14mg/24 Hour is instituted within the treatment schedule, and the risk of dependence after therapy is minimal. The effects of abrupt withdrawal from Boots Nicotine Patches 14mg/24 Hour are likely to be similar to those observed with tobacco withdrawal from comparable nicotine concentrations.

4.3 Contraindications

The Boots Nicotine Patches 14mg/24 Hour should not be administered to non-smokers ***or*** occasional smokers. The system is also contra-indicated in acute myocardial infarction, unstable or worsening angina pectoris, severe cardiac arrhythmias, recent cerebrovascular accident, diseases of the skin which may complicate patch therapy, and known hypersensitivity to nicotine or any of the components of the patch.

4.4 Special warnings and precautions for use

Warnings: Nicotine is a toxic drug and milligram doses are potentially fatal if rapidly absorbed. Treatment with ***Boots Nicotine Patches 14mg/24 Hour*** should be discontinued if symptoms of nicotine overdosage appear. Mild intoxication produces nausea, vomiting, abdominal pain, diarrhoea, headache, sweating and pallor (see 'Overdosage').

Doses of nicotine that are tolerated by adult smokers during treatment can produce severe symptoms of poisoning in small children and may prove fatal. Both before and after use, the ***Boots Nicotine Patch 14mg/24 Hour*** contains a significant amount of nicotine. Subjects must be cautioned that the patches must not be handled casually or left where they might be inadvertently misused or consumed by children. Used patches must be disposed of with care by folding them in half with the adhesive sides inwards, and ensuring that they do not fall into the hands of children under any circumstances.

Precautions: Users should stop smoking completely during therapy with ***Boots Nicotine Patches 14mg/24 Hour***. They should be informed that if they continue to smoke while using ***Boots Nicotine Patches 14mg/24 Hour***, they may experience increased adverse effects due to the hazards of smoking, including cardiovascular effects.

In subjects with the conditions listed below, ***Boots Nicotine Patches 14mg/24 Hour*** should only be used following a careful risk-benefit assessment, and only in cases where subjects have found it impossible to stop smoking without use of ***Boots Nicotine Patches 14mg/24 Hour***: hypertension, stable angina pectoris, cerebrovascular disease, occlusive peripheral arterial disease, heart failure, hyperthyroidism, diabetes mellitus, renal or hepatic impairment and peptic ulcer.

Discontinuation of treatment may be advisable in cases of severe or persistent skin reactions.

Contact sensitisation was reported in a few patients using transdermal nicotine in clinical trials. Patients who develop contact sensitisation to nicotine should be cautioned that a severe reaction could occur from smoking or exposure to other nicotine containing products.

When the ***Boots Nicotine Patch 14mg/24 Hour*** is used as recommended, there are minimal risks for driving vehicles or operating machinery.

4.5 Interaction with other medicinal products and other forms of interaction

No information is available on interactions between ***Boots Nicotine Patches 14mg/24 Hour*** and other drugs.

Cessation of smoking, with or without nicotine replacement, may alter the individual's response to concomitant medication and may require adjustment of dose. Smoking is thought to increase the metabolism through enzyme induction and thus to lower the blood concentrations of drugs such as antipyrine, caffeine, oestrogens, desmethyldiazepam, imipramine, lignocaine, oxazepam, pentazocine, phenacetin, theophylline, and warfarin. Cessation of smoking may result in increased concentrations of these drugs.

Other reported effects of smoking include reduced analgesic efficacy of propoxyphene, reduced diuretic response to frusemide and reduced pharmacological response to propranolol, as well as reduced rates of ulcer healing with H_2-antagonists.

Both smoking and nicotine can increase levels of circulating cortisol and catecholamines. Dosages of nifedipine, adrenergic agonists, or adrenergic blocking agents may need to be adjusted.

4.6 Pregnancy and lactation

Patients should be advised to give up smoking without use of nicotine replacement therapy. Should this fail, a medical assessment of the risk benefit of the Boots Nicotine Patch 14mg/24 Hour should be made.

Teratogenicity studies with nicotine in several animal species have demonstrated non-specific retardation of foetal growth. Studies in pregnant rats have indicated the presence of behavioural disorders in the offspring, and in the mouse the unborn offspring of animals treated with approximately 120 times the human transdermal dose showed skeletal defects in the peripheral parts of the limbs. Embryo implantation in rats and rabbits may be inhibited or delayed by nicotine. Overall, there are no clear cut grounds for believing that nicotine at the concentrations reached by treatment with the Boots Nicotine Patch 14mg/24 Hour has any teratogenic potential and/or inhibitory effects on fertility.

4.7 Effects on ability to drive and use machines

When the ***Boots Nicotine Patch 14mg/24 Hour*** is used as recommended, there are minimal risks for driving vehicles or operating machinery.

4.8 Undesirable effects

In principle, ***Boots Nicotine Patches 14mg/24 Hour*** can cause adverse reactions similar to those associated with nicotine administered by smoking. Since the maximum plasma concentrations of nicotine that are produced by the ***Boots Nicotine Patch 14mg/24 Hour*** are lower than those produced by smoking and fluctuate less, nicotine-related adverse reactions occurring during treatment with the ***Boots Nicotine Patch 14mg/24 Hour*** can be expected to be less marked than during smoking.

Some of the symptoms listed below are hard to differentiate from recognised tobacco withdrawal symptoms when comparison with placebo is made. The placebo used contained about 13% of the nicotine of a matching ***Boots Nicotine Patch 14mg/24 Hour*** (to match colour and odour for blinding purposes).

The main unwanted effect of ***Boots Nicotine Patches 14mg/24 Hour*** is application site reaction. This led to premature discontinuation of ***Boots Nicotine Patches 14mg/24 Hour*** in about 6% of clinical trial participants. Skin reactions consisted of erythema or pruritus at the patch site. Oedema, burning sensation, blisters, rash, or pinching sensation at the application site was also noted. The majority of these reactions were mild. Most of the skin reactions resolved within 48 hours, but in more severe cases the erythema and infiltration lasted from 1 to 3 weeks. The time of onset of important skin reactions was between 3 and 8 weeks from the start of therapy. In isolated cases the skin reactions extended beyond the application sites. Isolated cases of urticaria, angioneurotic oedema and dyspnoea were reported.

The following are the adverse events/withdrawal symptoms most commonly reported in three double-blind clinical trials irrespective of causal association to study drug.

	Boots Nicotine Patch 14mg/24 Hour (N=401)	Placebo (N=391)
Application site reaction	34.9%	17.6%
Headache	29.7%	29.2%
Cold and flu-like symptoms	12.0%	8.4%
Dysmenorrhoea (% of female subjects)	6.6%	8.8%
Insomnia	6.5%	5.4%
Nausea	6.2%	4.6%
Myalgia	6.0%	4.1%
Dizziness	6.0%	5.9%

Other unwanted experiences reported (irrespective of causal association with ***Boots Nicotine Patches 14mg/24 Hour***) with an incidence of 1% - 5.9% and more frequently than placebo, included: abdominal pain, vomiting, dyspepsia, allergy, motor dysfunction, chest pain, vivid dreams, blood pressure changes, generalised rash, somnolence, impaired concentration and fatigue.

4.9 Overdose

The toxicity of nicotine cannot be directly compared with that of smoking, because tobacco smoke contains additional toxic substances (eg carbon monoxide, and tar).
Chronic smokers can tolerate doses of nicotine that, in a non-smoker, would be more toxic, because of the development of tolerance.

Application of several ***Boots Nicotine Patches 14mg/24 Hour*** could result in serious overdosage. Slower absorption after cutaneous exposure to nicotine favours the development of tolerance to toxic effects.

Rapid systemic delivery of nicotine from ***Boots Nicotine Patches 14mg/24 Hour*** would not be expected on chewing and swallowing, owing to the slow release of nicotine from the patch and first-pass metabolism.

Acute toxic effects:

Signs and symptoms of overdosage would be the same as those of acute nicotine poisoning. In non-smoking children and adults, these include pallor, sweating, nausea, salivation, vomiting, abdominal cramps, diarrhoea, headache, dizziness, hearing and vision disturbances, tremor, mental confusion, muscle weakness, convulsions, prostration, absence of neurological reaction, and respiratory failure. Lethal doses may produce convulsions, and death follows as a result of peripheral or central respiratory paralysis, or, less frequently, cardiac failure.

The acute lethal oral dose of nicotine in non-smoking adults is approximately 60mg.

Management:

If the patient shows signs of overdosage, the ***Boots Nicotine Patch 14mg/24 Hour*** should be removed immediately. The skin surface may be washed with water and dried (no soap should be used). The skin will continue to deliver nicotine into the blood stream for several hours after removal of the system, possibly because of a depot of nicotine in the skin.

Other treatment measures for acute nicotine poisoning include artificial respiration in the case of respiratory paralysis, maintaining normal body temperature, and treatment of hypotension and cardiovascular collapse.

Each ***Boots Nicotine Patch 14mg/24 Hour*** is sealed in a child-resistant sachet and the product must be kept out of the reach of children at all times (see "Warnings"). Even doses of nicotine which are tolerated by adults during treatment with ***Boots Nicotine Patches 14mg/24 Hour*** could produce severe symptoms of poisoning in small children following accidental application, and may prove fatal.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mode of action: S(-)-nicotine is the most pharmacologically active form of nicotine, the major alkaloid of tobacco. S(-)-nicotine acts primarily on cholinergic receptors of the nicotinic type in the peripheral and central nervous system. For many effects, low doses of S(-)-nicotine have a stimulant action, and high doses a depressant effect. Intermittent administration of S(-)-nicotine affects neurohormonal pathways, and results in the release of acetylcholine, noradrenaline, dopamine, serotinin, vasopressin, beta-endorphin, growth hormone, cortisol and ACTH. These neuroregulators may be involved in the reported behavioural and subjective effects of smoking.

Nicotine replacement is an established therapy as an aid to smoking cessation. The ***Boots Nicotine Patch 14mg/24 Hour*** provides for a convenient once daily administration by exploiting the fact that S(-)-nicotine is readily absorbed through the skin into the systemic circulation. Placebo-controlled, double-blind studies have shown that nicotine replacement with the ***Boots Nicotine Patch 14mg/24 Hour*** produces smoking abstinence rates statistically significantly better than placebo, with or without group support. There was also a strong trend towards reduction of withdrawal symptoms.

Application of the ***Boots Nicotine Patch 14mg/24 Hour*** to smokers abstinent overnight resulted in small increases in mean heart

rate and systolic blood pressure and a decrease in stroke volume. The effects were smaller in magnitude than those produced by cigarette smoking.

5.2 Pharmacokinetic properties

Following single application of the Boots Nicotine Patch 14mg/24 Hour to the skin of healthy abstinent smokers there is an initial 1-2 hours delay followed by a progressive rise in nicotine plasma concentrations, with a plateau attained at about 8-10 hours after application.

In the majority of subjects the area under the plasma concentration curve (AUC 0-24 hours) varies approximately in proportion to the drug releasing area of the patch. The ***Boots Nicotine Patch 14mg/24 Hour*** is designed to deliver approximately 0.7mg/cm^2/24 hours. In comparison with an i.v. infusion, 76.8% of the nicotine released from the ***Boots Nicotine Patch 14mg/24 Hour*** is systemically available. Steady state plasma concentrations after repeated daily administration are within the range observed during moderate cigarette smoking.

Absorption of nicotine over 24 hours varies by a factor of two between different individuals; however within-individual variability is small indicating consistent performance of the transdermal system.

S(-)-nicotine is distributed widely in the body with a volume of distribution of approximately 180 litres. It crosses the blood-brain barrier, placenta and is detectable in breast milk. Plasma protein binding is only 5%. Total plasma clearance of nicotine ranges from 0.92 to 2.43 litres/min. It is eliminated mainly via hepatic metabolism. Only small amounts of nicotine are eliminated in unchanged form via the kidneys, a process which is pH dependent, being negligible under alkaline conditions.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acrylate esters vinylacetate co-polymers
Fractionated coconut oil
Methacrylic acid esters co-polymers
Aluminised polyester backing film
Aluminised and siliconised polyester film release liner

6.2 Incompatibilities

None known.

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

Each ***Boots Nicotine Patch 14mg/24 Hour*** is sealed in a child resistant sachet composed of heat-sealed paper/aluminium/polyamide/polyacrylnitrile.

The sachets are packed in a cardboard carton:

Boots Nicotine Patches 14mg/24 Hour: Packs of 2, 3, 7 and 21 patches

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

Novartis Consumer Health UK Ltd.

Trading as:

Novartis Consumer Health
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PA 30/40/5

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