IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0030/021/010
Case No: 2067972

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Novartis Consumer Health UK Limited

Wimblehurst Road, **Horsham**, **West Sussex RH12 5AB**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

NCH 7 mg/24 hours Transdermal Patch

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **25/01/2010** until **31/05/2012**.

Signed on behalf of the Irish Medicines Board this

_____

A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

NCH 7 mg/24 hours Trandermal Patch

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each transdermal patch contains 17.5 mg of nicotine in a patch size of 10 cm^2, releasing a nominal 7 mg of nicotine per 24 hours.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Transdermal patch
Round, punched-out matrix patch with yellow-ochre backing foil.

7 mg/24h is code-marked CWC.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

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

Advice and support normally improve the success rate.

4.2 Posology and method of administration

Users should stop smoking completely during treatment with NCH.

Transdermal patches should also not be used simultaneously with another pharmaceutical form of nicotine replacement therapy such as gums or lozenges except under strict medical supervision.

Posology
NCH transdermal patch is available in three strengths: 7 mg/24h, 14 mg/24h, 21 mg/24h.

Adults
The degree of nicotine dependence is to be assessed by the number of cigarettes smoked daily, or by the Fagerström's Test for Nicotine Dependence (test available in package leaflet).

	Initial phase 3 to 4 weeks	**Treatment follow-up 3 to 4 weeks**	**Treatment withdrawal 3 to 4 weeks**
Score of 5 or more on Fagerström's test or smokers of 20 or more cigarettes / day	NCH 21 mg/24 h	NCH 14 mg/24 h or NCH 21 mg/24 h*	NCH 7 mg/24 h or NCH 14 mg/24 h then NCH 7 mg/24 h*
Score of less than 5 on Fagerström's test or smokers of less than 20 cigarettes / day	NCH 14 mg/24 h or increase to NCH 21 mg/24 h*	NCH 7 mg/24 h** or NCH 14 mg/24 h	Treatment discontinuation** or NCH 7 mg/24 h

*depending on the results on withdrawal symptoms
**in the event of satisfactory results

The strength of the transdermal patch is to be adapted to individual response: increase strength if abstinence from smoking is not complete or if withdrawal symptoms are observed, decrease in the event of suspected overdose.

The treatment duration is about 3 months but may vary as a function of individual response.

This medicinal product should not be used for more than 6 months unless otherwise directed by a physician.

Children and adolescents (< 18 years)
NCH should not be used by smokers under 18 years of age without recommendation from a healthcare professional. There is no clinical experience in treating adolescents under the age of 18 years with NCH.

Method of administration
After opening the sachet, the patch should be applied to an area of dry skin with no skin lesion and little hair (shoulder blade, hip, lateral surface of the arms, etc.).

A new patch is to be applied every 24 hours to a site different from the preceding site.

During handling, avoid contact with the eyes and nose and wash your hands after application.

4.3 Contraindications

- Non-smoker or occasional smoker.
- Hypersensitivity to nicotine or any of the excipients.

4.4 Special warnings and precautions for use

Dependent smokers with a recent myocardial infarction, unstable or worsening angina pectoris including Prinzmetal’s angina, severe cardiac arrhythmias, uncontrolled hypertension or recent cerebrovascular accident should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). If this fails, NCH may be considered but as data on safety in these patient groups are limited, initiation should only be under close medical supervision.

NCH should be used with caution in patients with:
- severe hypertension, stable angina pectoris, cerebrovascular disease, occlusive peripheral arterial disease, heart failure,
- diabetes mellitus, hyperthyroidism or pheochromocytoma,
- severe hepatic and/or renal impairment,
- active peptic ulcer.

Nicotine is a toxic substance. 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). Even used nicotine patches contain enough residual nicotine to be harmful to children. NCH must be kept out of the reach and sight of children.

NCH transdermal patch should be used with caution on diseased skin (please see section 4.2).

In the event of a severe or persistent skin reaction, discontinue treatment and use another pharmaceutical form.

4.5 Interaction with other medicinal products and other forms of interaction

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, ropinirole, clozapine and olanzapine.

Smoking may lead to reduced analgesic effects of opioids (e.g. dextropropoxyphene, pentazocine), reduced diuretic response to furosemide, reduced effect of beta-adrenergic blockers (e.g. propranolol) on blood pressure and heart rate decrease and reduced responder rates in ulcer healing with H_2-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 Pregnancy and lactation

Pregnancy

In pregnant women, complete cessation of tobacco consumption should always be recommended without nicotine substitution treatment.

Smoking in pregnant women can be the cause of delayed intra-uterine growth, in utero foetal death, premature birth and neonatal hypotrophy, which appear to be correlated with the extent of tobacco exposure during pregnancy as these effects are observed when tobacco exposure is continued during the third trimester.

Should smoking withdrawal not be achieved in heavily nicotine dependent pregnant smokers, a healthcare professional should be consulted before starting any nicotine substitution therapy. Quitting smoking, with or without nicotine replacement therapy, is not to be considered in isolation but in the context of overall management, taking into account the psychological and sociological context and any other associated substance dependencies. A specialized consultation on quitting smoking is therefore advisable.

The nicotine provided by substitution treatment is not without adverse reactions on the foetus, as evidenced by the hemodynamic impact observed in the third trimester (e.g. changes in heart rate), which may affect the foetus close to birth. However, the risk for the foetus is probably less than to be expected with continued smoking due to:

- Lower maximal plasma concentrations compared to inhaled nicotine, resulting in a nicotine exposure less or not more than associated with smoking.

- No exposure to polycyclic hydrocarbons and carbon monoxide.

Therefore, after the sixth month of pregnancy, the patch 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. Nicotine replacement therapy products, like smoking itself, should therefore be avoided during breast-feeding. Should smoking withdrawal not be achieved, use of oral forms should be preferred compared with patches. The use of the patch by breast-feeding smokers should only be initiated after advice from a doctor.

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 patch is used following the recommended dose. Nevertheless one should take into consideration that smoking cessation can cause behavioural changes.

4.8 Undesirable effects

In principle, NCH transdermal patch can cause adverse reactions similar to those associated with nicotine administered by smoking.

SYSTEM ORGAN CLASS (MedDRA classification)	VERY COMMON (≥1/10)	COMMON (≥1/100 to <1/10)	UNCOMMON (≥1/1,000 to <1/100)	RARE (≥1/10,000 to <1/1000)
Immune system disorders	-	-	-	hypersensitivity, angioneurotic and anaphylactic reactions
Psychiatric disorders	-	insomnia	abnormal dreams	-
Nervous system disorders	-	dizziness, headache	-	-
Cardiac disorders	-	-	palpitations	cardiac arrhythmias (e.g. atrial fibrillation)
Gastrointestinal disorders	-	nausea	vomiting	-
General disorders and administration site conditions	application site reactions such as erythema and pruritus	application site reactions such as oedema and burning	-	-

The vast majority of these effects are moderate and regress spontaneously and rapidly after removal of the patch.

In the event of severe or persistent skin reaction, treatment should be discontinued and another form of nicotine replacement product used.

Some symptoms such as dizziness, headache and insomnia may be related to smoking cessation.

An increased occurrence of oral aphthae may occur after quitting smoking. No causal relationship has been clearly demonstrated.

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 NCH transdermal patch may occur when many pieces are applied simultaneously on the skin.

General symptoms of nicotine poisoning may include: weakness, perspiration, salivation, 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:

Following overdose, symptoms may develop rapidly particularly in children.
Immediately discontinue nicotine administration and institute symptomatic treatment. Monitor vital signs.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group : DRUGS USED IN NICOTINE DEPENDENCE
ATC code : N07BA01

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. On consumption of tobacco products, nicotine has proven to be addictive.

Quitting smoking abruptly after prolonged, daily consumption induces a withdrawal syndrome consisting of at least four of the following symptoms: dysphoria or depressive mood, insomnia, irritability, feelings of frustration or anger, anxiety, difficulty concentrating, agitation or impatience, slowed cardiac rhythm, increased appetite and weight gain. The craving for nicotine is considered as a recognised clinical symptom of the withdrawal syndrome.

Clinical trials have shown that nicotine replacement products may help smokers refrain from smoking or reduce their smoking habits by decreasing the withdrawal symptoms.

5.2 Pharmacokinetic properties

Nicotine is directly absorbed through the skin and enters the systemic circulation.

A single application of NCH 7 mg/24 hours transdermal patch by a healthy smoker having quit smoking shows that absorption occurs progressively and that the first detectable nicotine levels are found 1 to 2 hours post-application. Plasma concentrations then gradually rise to a plateau reached about 8 to 10 hours post-application.

Following withdrawal of the patch, plasma nicotine levels fall more slowly than would be expected given the plasma elimination half-life of nicotine (after intravenous administration: 2 hours).

The probable existence of a cutaneous deposit explains why about 10% of the nicotine reaching the blood derives from the skin after patch withdrawal. The absolute bioavailability of the patch, compared to intravenous nicotine perfusion, is about 77%.

The area under the plasma concentration curve (0-24 h) increases in proportion to the dose of nicotine delivered by the patches: *NCH 7 mg, 14 mg and 21 mg per 24 h.* After repeated application of the patches *14 mg/24 h and 21 mg/24 h*, the mean plasma concentrations at the steady state ranges from 7.1 to 12.0 ng/ml and from 7.1 to 12.0 ng/ ml and from 10.3 to 17.7 ng/ ml, respectively.

The distribution volume of nicotine is high, between 1 and 3 l/kg.

Nicotine crosses the blood-brain barrier and placenta and is excreted in breast-milk. The plasma protein binding of nicotine is negligible (< 5%). Elimination is mainly by the hepatic route and the main metabolites are cotinine and nicotine 1'-N-oxide. The renal elimination of unchanged nicotine is pH-dependent and minimal in the event of an alkaline urinary pH.

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 fetuses.

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

Drug solution:
Basic butylated methacrylate copolymer (Eudragit E 100)

External layer:
Aluminium coated polyester foil

Matrix layer:
Acrylate-vinylacetate copolymer (Duro-Tak 387-2516)
Triglycerides, medium-chain (Miglyol 812)
Basic butylated methacrylate copolyer (Eudragit E 100)

Non-woven backing:
Paper 26g/m^2

Adhesive layer:
Acrylate-vinylacetate copolymer (Duro-Tak 387-2516)
Triglycerides, medium-chain (Miglyol 812)

Detachable protective film:
Siliconised aluminised polyester film

Printing ink:
Brown ink

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

One transdermal patch per sachet (Paper/Aluminium/Polyamide/Polyacrylonitrile).

Box of 7, 14, 21 and 28.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

The transdermal patch should be folded in half sticky side inwards before being discarded.

7 MARKETING AUTHORISATION HOLDER

Novartis Consumer Health (UK) Limited
Wimblehurst Road
Horsham
West Sussex RH12 5AB
UK

8 MARKETING AUTHORISATION NUMBER

PA 30/21/10

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st June 2007.

10 DATE OF REVISION OF THE TEXT

October 2008