# Professional Information for NICORETTE® Transdermal Patch

## SCHEDULING STATUS

**S1**

## 1. NAME OF THE MEDICINE

NICORETTE® Transdermal Patch 10 mg

NICORETTE® Transdermal Patch 15 mg

NICORETTE® Transdermal Patch 25 mg

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each patch contains nicotine equivalent to 1,75 mg per 1,0 $cm^2$.

The following systems are available:

| | **NICORETTE® Transdermal Patch 10 mg** | **NICORETTE® Transdermal Patch 15 mg** | **NICORETTE® Transdermal Patch 25 mg** |
|---|---|---|---|
| Content of nicotine per patch | 15,75 mg | 23,62 mg | 39,37 mg |
| Average dose of nicotine delivered during 16 hours | 10 mg | 15 mg | 25 mg |
| Medicine releasing area | 9 $cm^2$ | 13,5 $cm^2$ | 22,5 $cm^2$ |

The amount of nicotine released from each $cm^2$ of the patch is constant and therefore the dose administered is determined by the size of contact area of the system.

For the full list of excipients, see section 6 .1.

## 3. PHARMACEUTICAL FORM

Transdermal patch.

Beige, semi-transparent patch consisting of pre-coated backing layer, nicotine source layer, and a skin contact adhesive layer on a pre-coated aluminised and siliconised release liner. Print on patch in light brown ink.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

NICORETTE® Transdermal Patch is indicated to be used as part of a smoking cessation programme as a temporary aid to the cigarette smoker seeking to give up the smoking habit.

### 4.2 Posology and method of administration

**Posology**

NICORETTE® Transdermal Patch can be used as monotherapy or in combination with 2 mg nicotine gum or a 1 mg/spray nicotine oromucosal spray.

***Monotherapy:***

***Adults and the elderly***

The patch should be applied to an intact area of the skin upon waking up in the morning and removed at bedtime. Patch treatment mimics the fluctuations of nicotine over the day in smokers, with no nicotine administration during sleep. Daytime nicotine patch treatment does not give the nicotine induced sleep disturbances seen with nicotine administration during sleep. Heavy smokers are recommended to start at Step 1 with the 25 mg/16 hours patch and use one patch daily for 8 weeks.

Gradual weaning from the patch should then be initiated. One 15 mg/16 hours patch should be used daily for 2 weeks followed by one 10 mg/16 hours patch daily for 2 weeks.
Light smokers are recommended to start at Step 2 (15 mg) for 8 weeks and decrease the dose to Step 3 (10 mg) for the final 4 weeks.

**Table 1**

| **Heavy smokers** | | | **Light Smokers** | | |
|---|---|---|---|---|---|
| **Dose regimen** | | **Duration** | **Dose regimen** | | **Duration** |
| Step 1 | Nicorette® Transdermal patch 25 mg | First 8 weeks | | | |
| Step 2 | Nicorette® Transdermal patch 15 mg | Next 2 weeks | Step 2 | Nicorette® Transdermal patch 15 mg | First 8 weeks |
| Step 3 | Nicorette® Transdermal patch 10 mg | Last 2 weeks | Step 3 | Nicorette® Transdermal patch 10 mg | Last 4 weeks |

Use of the patch beyond 6 months is generally not recommended.

***Children and adolescents***

NICORETTE® Transdermal patch should not be administered to persons under 18 years of age without recommendation from a health care provider. There is limited experience of treating this age group with NICORETTE® Transdermal Patch.

**Method of administration**

NICORETTE® Transdermal Patch should be applied to clean, dry intact areas of hairless skin, for example on the hip, upper arm, or chest. These areas should be varied each day and the same site should not be used on consecutive days.

1. Wash your hands before applying the patch.
2. Cut open the pouch with scissors along the side, as indicated. Select a clean, dry, hairless intact area of skin, such as the hip, upper arm or chest.
3. Peel one part of the silvery aluminium backing away as far as possible. Avoid touching the sticky surface of the patch with your fingers, as far as possible.
4. Apply the sticky part of the patch carefully onto the skin and peel off the remaining half of the silvery aluminium backing.
5. Press the patch firmly onto the skin with your palm or finger-tips.
6. Rub your fingers firmly round the edge to ensure that the patch sticks firmly.

After removal, used patches should be disposed of carefully.

Advice and support improve the success rate.

**Combination therapy**

Highly dependent smokers, smokers who experience breakthrough cravings or those who have failed with single nicotine replacement therapy (NRT), can use NICORETTE® Transdermal Patch in combination with an oromucosal NRT product for fast relief of cravings.

The oromucosal format to consider in combination with the NICORETTE® Transdermal Patch are 2 mg nicotine gum or 1 mg/spray nicotine oromucosal spray.

Smokers should use the same dosing recommendations for the patch and for the chosen oromucosal format as in monotherapy.

For the dosing recommendations for the oromucosal format chosen,

the user needs to refer to the product information of the specific product.

NICORETTE® Transdermal Patch 25 mg should be applied in the morning and removed at bedtime.

The dosing schedule for use of the oral pharmaceutical form in combination with the patch is flexible and the users are dosing based on their requirements.

For combination therapy, patients are advised to only use one oromucusal format over a 24 h period.

Smokers should stop smoking completely during the course of treatment with NICORETTE® Transdermal Patch.

### 4.3 Contraindications

NICORETTE® Transdermal Patch is contraindicated in the following circumstances:

- Known hypersensitivity of the skin or allergy to nicotine or any of the excipients of NICORETTE® Transdermal Patch (see section 6.1), and generalised skin disorders.
- Hypersensitivity to any component of the patch (see section 6.1).
- In persons during the immediate post-myocardial infarction period (within 3 months).
- In persons with severe, life-threatening cardiac dysrhythmias
- In persons with severe or worsening angina pectoris.
- In persons with Prinzmetal's variant angina.
- In persons with stroke in the acute phase.
- Pregnancy and lactation.
- Women who are planning to fall pregnant.

## 4.4 Special warnings and precautions for use

Persons diagnosed with the following conditions, should be carefully screened and evaluated, by a health care provider before NICORETTE® Transdermal Patch is prescribed:

- Cardiovascular disease: Serious cardiovascular event, or hospitalisation due to cardiovascular complaint, in the previous 4 weeks (e.g. stroke, myocardial infarction, unstable angina, cardiac dysrhythmia, coronary artery bypass graft and angioplasty) or those who suffer from uncontrolled hypertension (see section 4.3). Patients should be encouraged to stop smoking and non-pharmacological interventions (such as counselling) should be considered. If this fails, the initiation of pharmacological intervention should be under close medical supervision.
- Diabetes mellitus: Patients with diabetes mellitus should be advised to monitor their blood sugar levels more closely than usual when smoking is stopped, and NICORETTE® Transdermal Patch is initiated as reductions in nicotine-induced catecholamine release can affect carbohydrate metabolism. Patients with diabetes mellitus may require lower doses of insulin as a result of smoking cessation.
- Vasospastic diseases (Buerger's disease).
- Renal and hepatic impairment: Use with caution in patients with severe to moderate hepatic impairment and/or severe renal impairment as the clearance of nicotine or its metabolites may be decreased with the potential for increased adverse effects.
- Phaeochromocytoma and uncontrolled hyperthyroidism: Use with caution in patients with uncontrolled hyperthyroidism or phaeochromocytoma as nicotine causes release of catecholamines from the adrenal medulla.

- Gastrointestinal disease: Nicotine may exacerbate symptoms in patients suffering from oesophagitis; active duodenal and gastric ulcers. NICORETTE® Transdermal Patch should be used with caution in these conditions.
- Occlusive peripheral arterial diseases.
- Heart failure.

In case of severe or persistent skin reaction, treatment should be discontinued.

Cigarette smoking is thought to play a perpetuating role in hypertension and peptic ulcer disease, therefore, NICORETTE® Transdermal Patch should not be used in patients with systemic hypertension or history of peptic ulcer.

NICORETTE® Transdermal Patch should not be administered to persons under the age of 18 years of age without recommendation from a health care provider. There is limited experience of treating this age group with NICORETTE® Transdermal Patch.

NICORETTE® Transdermal Patch must be kept out of reach of children at all times i.e. before and after use.

Transferred dependence: Transferred dependence can occur but is unusual and is both less harmful and easier to break than smoking

dependence.

Non-smokers should not use NICORETTE® Transdermal Patch as they may experience adverse reactions similar to those associated with nicotine administration.

Patients should not smoke whilst using NICORETTE® Transdermal Patch. If the NICORETTE® Transdermal Patch is being used to supplement a behavioural tobacco withdrawal programme, the dosage should be adapted accordingly, in order to avoid intoxication and presentation of the side effects of nicotine.

NICORETTE® Transdermal Patch should be removed prior to undergoing any magnetic resonance imaging (MRI) procedures to prevent the risk of burns.
If symptoms persist or get worse, or if new symptoms occur, patients should stop use and consult a physician.

Special warnings and precautions for the combination of NICORETTE® Transdermal Patch with nicotine 2 mg chewing gum/ or oromucosal spray 1 mg/spray are the same as those for each treatment alone (refer to the Professional Information of each
product respectively).

### 4.5 Interaction with other medicines and other forms of interaction

Smoking cessation, with or without nicotine substitutes, may alter response to concomitant medication in ex-smokers.
Smoking (but not nicotine) is associated with an increase in CYP1A2 enzyme activity, and therefore, considered to increase the metabolism and thus lower blood levels of medicines with a narrow therapeutic window, such as caffeine, theophylline, imipramine, tacrine, clozapine and ropinirole, through enzyme induction. Limited data indicate that the metabolism of flecainide and pentazocine may also be induced by smoking.
After cessation of smoking, reduced clearance of the substrates for the CYP1A2 enzyme may occur and result in increased plasma levels of other medicines (including olanzapine, clomipramine and fluvoxamine); however data in support of this is lacking and the possible clinical significance of this effect for these medicines is unknown.
Absorption of glutethimide may be decreased and the “first pass” metabolism of propoxyphene decreased by smoking cessation.

Other reported effects of smoking, which do not involve enzyme induction, include reduced diuretic effects of furosemide and decreased cardiac output, and increased blood pressure with propranolol, which may also relate to the hormonal effects of nicotine. Smoking cessation may reverse these actions.

Both smoking and nicotine can increase circulating cortisol and catecholamines. Therapy with adrenergic agonists or with adrenergic blockers may need to be adjusted according to changes in nicotine therapy or smoking status.

No clinically relevant interactions between NICORETTE® Transdermal Patch and other medicines have definitely been established. However, nicotine may possibly enhance the haemodynamic effects of adenosine i.e. increase in blood pressure and heart rate and also increased pain response (angina pectoris type chest pain) provoked by adenosine administration.

### 4.6 Fertility, pregnancy and lactation

**Pregnancy:**

The nicotine in NICORETTE® Transdermal Patch may cause foetal harm when administered to pregnant women and is therefore contraindicated in women who are or who may become pregnant. Nicotine passes 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 use of nicotine replacement therapy.

The risks to the foetus from NICORETTE® Transdermal Patch are not known. Maternal smoking in pregnancy is associated with low birth weight infants and increased risk of abortion, still birth and neonatal death.

**Lactation:**

Nicotine passes freely into breast milk in quantities that even at therapeutic doses may affect the infant, therefore the NICORETTE® Transdermal Patch is contraindicated during lactation or breastfeeding.

**Fertility**

In females, tobacco smoking delays time to conception, decreases *in-vitro* fertilisation success rates, and significantly increases the risk of infertility. In males, tobacco smoking reduces sperm production, increases oxidative stress, and DNA damage. Spermatozoa from smokers have reduced fertilising capacity. The specific contribution of nicotine to these effects in humans is unknown.

Female patients should be advised to take adequate precautions to avoid becoming pregnant. The doctor may wish to consider a pregnancy test before instituting therapy with NICORETTE® Transdermal Patch.

## 4.7 Effects on ability to drive and use machines

NICORETTE® Transdermal Patch can cause side effects, such as dizziness. Caution is advised before driving a vehicle or operating machinery until the effects of NICORETTE® Transdermal Patch are known.

## 4.8 Undesirable effects

NICORETTE® Transdermal Patch can cause adverse reactions similar to those associated with nicotine administered by other means and are mainly dose-dependent. About 20 % of users

experienced mild local skin reactions during the first weeks of treatment. The best way to avoid this is to regularly alternate the position where the patch is applied.

Some symptoms, such as dizziness, headache and sleeplessness may be related to withdrawal symptoms associated with abstinence from smoking. Increased frequency of aphthous ulcer may occur after abstinence from smoking is achieved. The causality is unclear.

If the user continues to smoke whilst applying the NICORETTE® Transdermal Patch, the central nervous system (CNS) adverse effects may become more frequent and more pronounced, and become indistinguishable from the tobacco withdrawal symptoms. The most commonly reported adverse or withdrawal symptoms include systemic and local effects.

**Immune system disorders:**

*Less frequent:* hypersensitivity

**Nervous system disorders:**

*Frequent:* dizziness, headache

*Less frequent:* sleep disorders, vivid dreams, irritability, paraesthesia

**Cardiac disorders:**

*Less frequent:* palpitations, reversible atrial fibrillation

**Gastrointestinal disorders:**

*Frequent:* gastrointestinal discomfort, nausea, vomiting, constipation

**Skin and subcutaneous tissue disorders:**

*Frequent:* itching, erythema

*Less frequent:* urticaria

**General disorders and administration site conditions:**

*Less frequent:* fatigue

***Post-marketing experience:***

**Immune system disorders:**

*Frequency unknown:* anaphylactic reaction**, angioedema**

**Psychiatric disorders:**

*Less frequent:* abnormal dream**, ***

**Cardiac disorders:**

*Less frequent:* tachycardia**

**Vascular disorders:**

*Less frequent:* flushing**, hypertension**

**Respiratory, thoracic and mediastinal disorders:**

*Less frequent:* dyspnoea**

**Skin and subcutaneous tissue disorders:**

*Frequent:* rash**, urticaria**

*Less frequent:* hyperhidrosis**

**Musculoskeletal and connective tissue disorders:**

*Less frequent:* myalgia*

*Frequency unknown:* pain in extremity

**General disorders and administration site conditions:**

*Less frequent:* application site reaction, asthenia**, chest discomfort and pain**, malaise**

* In vicinity/region of patch

** systemic effects

*** systemic effect, identified only for formulations administered during night

Adverse events that may occur during the use of combination treatment (patch and chewing gum, oromucosal spray) only differ from those of each treatment alone in terms of local adverse events related to the pharmaceutical forms. The frequency of these adverse events is comparable to that listed in the Professional Information of each product.

**Reporting of suspected adverse reactions:**

Reporting suspected adverse reactions after authorisation of NICORETTE® Transdermal Patch is important. It allows continued monitoring of the benefit/risk balance of NICORETTE® Transdermal Patch. Healthcare providers are asked to report any suspected adverse reactions

to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

For further information, please contact the Johnson & Johnson call centre on 0860 410032 (landline).

### 4.9 Overdose

Excessive use of nicotine from either nicotine replacement products and / or smoking might cause symptoms of an overdose.

Overdosage of NICORETTE® Transdermal Patch can only occur if more than one patch is applied simultaneously, or if the user has very low nicotine dependence or uses other forms of nicotine concomitantly including smoking. The fatal oral dose of nicotine in man is about 60 mg.

Symptoms of overdosage are those associated with nicotine poisoning and include nausea, salivation, abdominal pain, vomiting, diarrhoea, cold sweat, headache, tremor, dizziness, faintness, disturbed hearing and vision, mental confusion 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. Death may result within a few minutes from respiratory failure caused by paralysis of the muscles of respiration.

Doses of nicotine that are tolerated by adult smokers during treatment may produce severe symptoms of poisoning in small children and may prove fatal.

Nicotine is excreted four times more rapidly in acid than alkaline urine.

**Management of overdosage:**

Prompt treatment is essential. If patient shows signs of overdosage, the patch or administration of nicotine must be removed or stopped immediately and the patient should be treated symptomatically. Activated charcoal reduces gastrointestinal absorption of nicotine.
Other therapy, including treatment of shock, is purely symptomatic.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Category and class: A 32.16 Others

Pharmacotherapeutic group: Drug used in nicotine dependence

ATC code: N07B A01

Nicotine has both stimulant and depressant phases of action, effected by binding to and acting on a variety of neuro-effector and
chemo-sensitive sites, i.e. peripheral nervous system, central nervous system, cardiovascular system, gastrointestinal tract and exocrine glands.

### 5.2 Pharmacokinetic properties

Nicotine is readily absorbed from the respiratory tract, buccal membranes and skin.
Tolerance develops to some of the effects of nicotine.
A significant (29 %) increased exposure to nicotine has been demonstrated in healthy elderly patients.
All patches are labelled by the average amount of nicotine absorbed by the average patient over 16 hours.

A linear relationship exists between released amount of nicotine (dose) and plasma levels of nicotine over the therapeutic dose range, 10 – 25 mg/16 hours. The mean peak plasma levels of nicotine ($C_{max}$) achieved are calculated to be:

| Dose nicotine (mg/16 hours) | $C_{max}$ (ng/mL) |
|---|---|
| 10 | 10 |
| 15 | 15,5 |
| 25 | 26,5 |

The calculated peak plasma levels are in the same range as true measured peak plasma concentrations: 11 ng/mL for the 10 mg patch and 25 ng/mL for the 25 mg patch.
Interpolation yields a peak plasma concentration of 16 ng/mL for the 15 mg patch.
The maximum level of plasma concentration after administration is reached after approximately 9 hours ($t_{max}$). The plasma peak is in the afternoon/ evening when the risk of relapse is highest.
The volume of distribution of nicotine is about 2 to 3 L/kg and the half-life approximately 3 hours. The major eliminating organ is the liver, and average plasma clearance is about 70 L/hour. The kidney and lung also metabolise nicotine. More than 20 metabolites of nicotine have been identified, all of which are believed to be less active than the parent compound.
Plasma protein binding of nicotine is less than 5 %. Therefore, changes in nicotine binding from use of concomitant medicines or alterations of plasma proteins by disease states would not be expected to have significant effects on nicotine kinetics.
The primary metabolite of nicotine in plasma, cotinine, has a half-life of 15 to 20 hours and concentrations that exceed nicotine by 10-fold.

## 5.3 Preclinical safety data

*In vitro* and *in vivo* genotoxicity testing of nicotine has yielded predominantly non-genotoxic results. Some positive findings from *in vitro* and *in vivo* genotoxicity tests have been reported but investigations using regulatory accepted assays and protocols have shown no evidence of genotoxic activity at therapeutic doses.

Analysis of the results from long-term carcinogenicity assays data with nicotine or cotinine, major nicotine metabolite, predominately indicate nicotine does not have any significant or relevant carcinogenic activity.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Triglycerides, medium-chain

Basic butylated methacrylated copolymer

Polyethyleneterephtalate-film (PET)

**Acrylate matrix**

Acrylic adhesive solution

Potassium hydroxide

Croscarmellose sodium

Aluminium acetylacetonate

**Release liner**

Polyethylenterephthalate (PET) film single-side aluminised, both sides siliconised.

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

3 years.

### 6.4 Special precautions for storage

Store at or below 25 °C.

KEEP OUT OF REACH OF CHILDREN BOTH BEFORE AND AFTER USE.

### 6.5 Nature and contents of container

Cartons containing 7, 14 and 28 sealed, childproof pouches of NICORETTE® Transdermal 10 mg, 15 mg and 25 mg patches.

### 6.6 Special precautions for disposal and other handling

No special precautions.

## 7. HOLDER OF CERTIFICATE OF REGISTRATION

Johnson & Johnson (Pty) Ltd.

241 Main Road

Retreat

7945

South Africa

## 8. REGISTRATION NUMBERS

Nicorette Transdermal Patch 10 mg: 45/32.16/0952

Nicorette Transdermal Patch 15 mg: 45/32.16/0953

Nicorette Transdermal Patch 25 mg: 45/32.16/0954

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

31 May 2016

## 10. DATE OF REVISION OF THE TEXT

22 February 2025.