Nicorette® Invisi Transdermal Patch

Nicotine (10mg/16hr, 15mg/16hr and 25mg/16hr)

WHAT IS NICORETTE® INVISI TRANSDERMAL PATCH FOR?

Nicorette® Invisi Transdermal Patch is used to relieve withdrawal symptoms and reduce the cravings for nicotine that you get when you try to stop smoking.

Advice and support normally improve the success rate.

How Nicorette® Invisi Transdermal Patch works

When you stop smoking, your body misses the nicotine that you have been absorbing. You may experience unpleasant feelings and a strong desire to smoke (craving). This indicates you were dependent on nicotine.

When you apply a Nicorette® Invisi Transdermal Patch to the skin, nicotine is released and passes into your body. The nicotine released from the patch is sufficient to relieve the unpleasant withdrawal symptoms. It will also help to stop the craving to smoke, but Nicorette® Invisi Transdermal Patch will not give you the "buzz" you get from smoking a cigarette.

The benefits of quitting smoking outweigh any risks associated with correctly administered nicotine replacement therapy (NRT).

Nicorette® Invisi Transdermal Patch is not to be administered to persons under 18 years of age without recommendation from health care professional. There is insufficient clinical data from controlled trials to recommend routine use in adolescents under the age of 18.

WHEN NOT TO USE NICORETTE® INVISI TRANSDERMAL PATCH

Do not use if you have an allergy to nicotine or any of the other ingredients.

WHAT SPECIAL PRECAUTIONS SHOULD YOU TAKE?

Before you start to use it

Talk to your doctor or pharmacist if you have the following conditions:

- Cardiovascular disease. Dependent smokers with a recent myocardial infarction, unstable or worsening angina including Prinzmetal's angina, severe cardiac arrhythmias, recent cerebrovascular accident, and/or who suffer from uncontrolled hypertension should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). If this fails, Nicorette® Invisi Transdermal Patch may be considered but as data on safety in this patient group are limited, initiation should only 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 NRT is initiated as reductions in nicotine-induced catecholamine release can affect carbohydrate metabolism.
- Renal and hepatic impairment. Use with caution in patients with moderate to severe 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.

- Gastrointestinal disease. Nicotine may exarcebate symptoms in patients suffering from oesophagitis, gastric or peptic ulcers. Nicotine Replacement Therapy (NRT) preparations should be used with caution in these conditions.
- Epilepsy and seizures. Caution should be exercised in patients with a history of epilepsy or seizures during introduction of nicotine replacement therapy. Tobacco smoke contains substances – including nicotine – which act on brain receptors, and the changes in intake of these when switching from smoked tobacco to nicotine replacement therapy during quitting may affect seizure threshold.

Nicorette® Invisi Transdermal Patch should be removed prior to undergoing any Magnetic Resonance Imaging (MRI) procedures to prevent the risk of burns.

Danger in children: Doses of nicotine tolerated by smokers can produce severe toxicity in children that may be fatal. Products containing nicotine should not be left where they may be handled or ingested by children.

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

Stopping smoking: Polycyclic aromatic hydrocarbons in tobacco smoke induce the metabolism of drugs metabolised by CYP1A2. When a smoker stops smoking, this may result in slower metabolism and a consequent rise in blood levels of such drugs. This is of potential clinical importance for products with a narrow therapeutic window, e.g. theophylline, tacrine, clozapine and ropinirole.

If you notice side effects, any other unwanted effects not listed in this leaflet, or have any other questions on the use of this product, stop use and consult your doctor or pharmacist.

Taking other medicines
No clinically relevant interactions between nicotine replacement therapy and other drugs 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.
Tell your doctor or pharmacist if you are taking or have recently taken other medicines, even those not prescribed. Stopping smoking may require the dose of these medicines to be adjusted.

Pregnancy and breast-feeding

- Women of childbearing potential/ Contraception in males and females
  In contrast to the well-known adverse effects of tobacco smoking on human conception and pregnancy, the effects of therapeutic nicotine treatment are unknown. Thus, whilst to date no specific advice regarding the need for female contraception has been found to be necessary, the most prudent state for women intending to become pregnant to be in is to be both non-smoking, and not using NRT.

  Whilst smoking may have adverse effects on male fertility, no evidence exists that particular contraceptive measures are required during NRT treatment by males.

- Fertility
  In females, tobacco smoking delays time to conception, decreases in-vitro fertilization 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 fertilizing capacity. The specific contribution of nicotine to these effects in humans is unknown.

- Pregnancy

Smoking during pregnancy is associated with risks such as intra-uterine growth retardation, premature birth or stillbirth. Stopping smoking is the single most effective intervention for improving the health of both the pregnant smoker and her baby. The earlier abstinence is achieved the better.

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 using nicotine replacement therapy. The risk of continued smoking may pose greater hazard to the foetus as compared with the use of nicotine replacement products in a supervised smoking cessation programme. Use of Nicorette® Invisi Transdermal Patch by the pregnant smoker should only be initiated after advice from a health care professional.

- Breastfeeding
  Nicotine passes freely into breast milk in quantities that may affect the child even with therapeutic doses. Nicotine should therefore be avoided during breast-feeding. Should smoking cessation not be achieved, use of the Nicorette® Invisi Transdermal Patch by breast feeding smokers should only be initiated after advice from a health care professional.

Effects on ability to drive or use machines
Nicorette® Invisi Transdermal Patch has no or negligible influence on the ability to drive and use machines.

HOW TO USE NICORETTE® INVISI TRANSDERMAL PATCH AND HOW MUCH

(A) Monotherapy

How much to use
- Use one new patch per day. Apply when you wake up (usually in the morning) and remove 16 hours later (usually at bedtime).
- Wash your hands before applying the patch.
- Each Nicorette® Invisi Transdermal Patch comes with a child-resistant sachet which can be opened by cutting along the edge with a pair of scissors.
- Remove the patch from its sachet and then peel one part of the silvery aluminum backing away. Avoid touching the sticky surface of the patch with your fingers. Carefully apply the sticky part of the patch to the chosen area of skin and then peel off the remaining half of the silvery backing foil.
- Press the patch firmly onto the skin with your palm or fingertips.
- Run your fingers around the edge to ensure it sticks firmly.
- If the patch comes off, replace with a new one. Use of skin oils or talc can prevent proper adhesion of the patch.

Administration of nicotine should be stopped temporarily if any symptoms of nicotine excess occur. Nicotine intake should be decreased by either lowering dosing frequency or strength if nicotine excess symptoms persist.

<u>How long to use it</u>
Heavy smokers (those smoking 15 or more cigarettes in a 24-hour period) are recommended to start at Step 1 with the 25mg/16 hours patch and use one patch daily for 8 weeks.

Gradual weaning from the patch should then be initiated. One 15mg/16 hours patch should be used daily for 2 weeks followed by one 10mg/16 hours patch daily for 2 weeks.

Light smokers (those smoking less than 15 cigarettes in a 24-hour period) are recommended to start at Step 2 (15mg/16 hours) for 8 weeks and decrease the dose to Step 3 (10mg/16 hours) for the final 4 weeks.

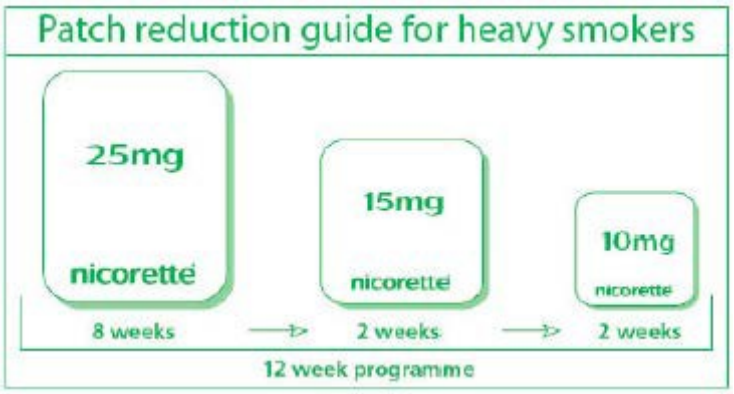

Table 1. Recommended dose regimen for heavy smokers

Dose regimen		**Duration**
Step 1	Nicorette® Invisi Transdermal Patch 25mg/16 hours	First 8 weeks
Step 2	Nicorette® Invisi Transdermal Patch 15mg/16 hours	Next 2 weeks
Step 3	Nicorette® Invisi Transdermal Patch 10mg/16 hours	Last 2 weeks

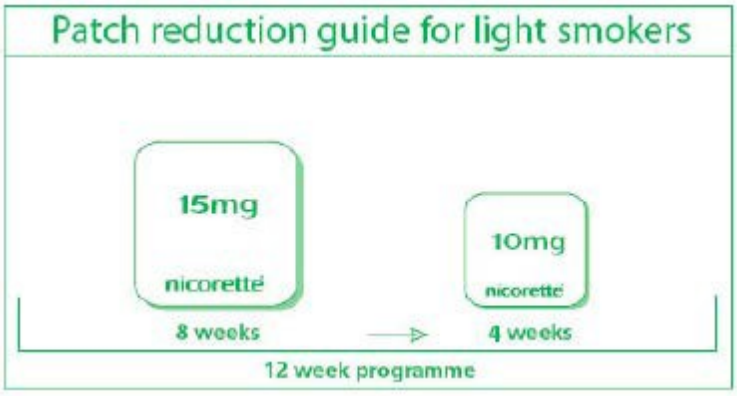

Table 2. Recommended dose regimen for light smokers

Dose regimen		**Duration**
Step 2	Nicorette® Invisi Transdermal Patch 15mg/16 hours	First 8 weeks
Step 3	Nicorette® Invisi Transdermal Patch 10mg/16 hours	Last 4 weeks

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

Nicorette® Invisi Transdermal Patch is usually not recommended for use over a period in excess of 6 months but some people may need longer treatment in order to avoid getting into a smoking habit again.

(B) Combination Therapy

Highly dependent smokers, smokers who experience ‘breakthrough’ cravings or those who have failed with single Nicotine Replacement Therapy (NRT) treatment, can use a flexible smoking cessation format, in combination with the patch for fast relief of cravings.

How to combine the use of Nicorette® Invisi Transdermal Patch with Nicorette® Icy Mint Gum 2mg:

- The treatment involves the addition of Nicorette® Icy Mint Gum 2mg to the patch.
- The Nicorette® Invisi Transdermal Patch should be applied daily to an intact area of the skin upon waking and removed at bedtime, and the 2mg Gum should be used as required when cravings occur.

For heavy smokers (more than 15 cigarettes in a 24-hour period):
Use one Nicorette® Invisi Transdermal Patch 25mg/16 hours per day for 12 weeks plus the Nicorette® Icy Mint Gum 2mg. For best results, try to use at least 4 2mg Gums every day. Most people will use 5 – 6 Gums. The maximum number of 2mg Gums that can be taken in conjunction with Nicorette® Invisi Transdermal Patch is 12.

The combination of Nicorette® Icy Mint Gum 2mg and Nicorette® Invisi Transdermal Patch should be used in this way for 12 weeks. After this, you should wean yourself off NRT by either:

1) Using the Nicorette® Invisi Transdermal Patch 15mg/16 hours for 2 weeks, followed by the Nicorette® Invisi Transdermal Patch 10mg/16 hours for 2 weeks, while using the same number of 2mg Gums a day that you have routinely used. Then, when a Patch is no longer needed, gradually reduce the number of 2mg Gums until you no longer need them. OR
2) Stop using the Nicorette® Invisi Transdermal Patch 25mg/16 hours, then gradually reduce the number of 2mg Gums that you use until you no longer need them.

For light smokers (less than 15 cigarettes in a 24-hour period):
Use one Nicorette® Invisi Transdermal Patch 15mg/16 hours per day for 12 weeks plus the Nicorette® Icy Mint Gum 2mg. For best results, try to use at least 4 2mg Gums every day. Most people will use 5 – 6 Gums. The maximum number of 2mg Gums that can be taken in conjunction with Nicorette® Invisi Transdermal Patch is 12.

The combination of Nicorette® Icy Mint Gum 2mg and Nicorette® Invisi Transdermal Patch should be used in this way for 12 weeks. After this, you should wean yourself off NRT by either:

1) Using the Nicorette® Invisi Transdermal Patch 10mg/16 hours for 4 weeks, while using the same number of 2mg Gums a day that you have routinely used. Then, when a Patch is no longer needed, gradually reduce the number of 2mg Gums until you no longer need them. OR
2) Stop using the Nicorette® Invisi Transdermal Patch 15mg/16 hours, then gradually reduce the number of 2mg Gums that you use until you no longer need them.

The Nicorette® Invisi Transdermal Patch should **NOT** be used with Nicorette® Icy Mint Gum 4mg.

Smokers should stop smoking completely during the course of treatment with Nicorette® Icy Mint Gum and Nicorette® Invisi Transdermal Patch.

While you are using it

Things you must do
Before applying Nicorette® Invisi Transdermal Patch, choose a completely clean, dry area of hairless skin on the front or side of the chest, upper arm or hip.

Things you must not do
Do not use more than one patch at a time. If you lose a patch while swimming, bathing or showering, you can replace it with another patch.
Do not apply oil, lotion or talcum powder to the skin before putting on the patch as this may prevent it from sticking properly.

The patch should not be kept on at night while sleeping as it may cause nicotine-induced sleep disturbance. If you forget to remove the patch the night before, continue treatment the following morning by removing the old patch and applying the new one.

Things to be careful of
Avoid placing the patch onto any area of skin that is red, cut or irritated.
Do not use the same area for two consecutive days to help avoid skin irritation.

UNDESIRED EFFECTS

Like all medicines, Nicorette® Invisi Transdermal Patch can cause side-effects.

As many of the effects are due to nicotine, they can also occur when nicotine is obtained by smoking.

Effects of smoking cessation

Regardless of the means used, a variety of symptoms are known to be associated with quitting habitual tobacco use. These include emotional or cognitive effects such as dysphoria or depressed mood; insomnia; irritability, frustration or anger; anxiety; difficulty concentrating, and restlessness or impatience. There may also be physical effects such as decreased heart rate; increased appetite or weight gain, dizziness or presyncopal symptoms, cough, constipation, gingival bleeding or aphthous ulceration, or nasopharyngitis. In addition, and of clinical significance, nicotine cravings may result in profound urges to smoke.

Adverse Drug Reactions

Most of the undesirable effects reported by the subjects occur during the early phase of treatment and are mainly dose dependent.

Allergic reactions (including symptoms of anaphylaxis) occur rarely during use of nicotine products.

About 20% of users experienced mild local skin reactions during the first weeks of treatment.

As would be expected, the types of adverse reactions seen for nicotine in clinical trials are similar to those associated with nicotine administered by other means.

Clinical Trial Data

The safety of nicotine from clinical trial data is based on data on a meta-analysis of randomized clinical trials (RCTs) for the treatment of smoking cessation.

Adverse Drug Reactions (ADRs) with patch formulations identified from clinical trials are presented below in Table 1.

Table 1. ADRs Reported with a Frequency ≥1% Identified from Meta-analysis of Clinical Trial Data with Nicotine Patch Formulations

System Organ Class Preferred Term	Active N = 3917 (%)	Placebo N = 1366 (%)
Gastrointestinal Disorders		
Nausea[a#]	4.7	6.1
Vomiting[a]	1.5	0.1
General Disorders and Administration Site Conditions		

Fatigue[a*#]	0.4	1.0
Immune System Disorders		
Hypersensitivity[a*]	0.4	0.2
Nervous System Disorders		
Headache[a#]	5.2	6.1
Paraesthesia[a]	0.4	0.3
Skin and Subcutaneous Tissue Disorders		
Pruritus	18.0	10.7

[a]: Systemic effects
*Although the frequency is <1% the Preferred Term (PT) occurred at a frequency ≥1% in any other formulation in which the PT was identified as a systemic ADR.
#Although the frequency in the active group is less than that of the placebo group, the frequency in the specific formulation in which the Preferred Term (PT) was identified as a systemic ADR was greater in the active group than the placebo group.

Post Marketing Data

Adverse drug reactions (ADRs) first identified during post-marketing experience with nicotine are presented below. Frequencies are given according to the following convention:

- Very common ≥1/10
- Common ≥1/100 and <1/10
- Uncommon ≥1/1,000 and <1/100
- Rare ≥1/10,000, <1/1,000
- Very rare <1/10,000
- Not known (cannot be estimated from the available data)

Frequency categories are estimated from clinical trials.

- *Frequency category: Common*

Undesirable Effects: Rash**, Urticaria** (hives).

- *Frequency category: Uncommon*

Undesirable Effects: Palpitations**, Tachycardia**, Application site reactions, Asthenia** (abnormal body weakness), Chest discomfort and pain**, Malaise**, Myalgia* (muscle pain), Abnormal dream**,***, Dyspnoea** (shortness of breath), Hyperhidrosis** (increased sweating), Flushing**, Hypertension** (high blood pressure).

- *Frequency category: Not known*

Undesirable Effects: Gastrointestinal discomfort*, Anaphylactic reaction**, Pain in extremity, Angioedema**, Erythema**, Seizure**

Notes:
*In vicinity/region of patch
**systemic effects
***systemic effect, identified only for formulations administered during night

OVERDOSE

Symptoms of overdose with nicotine from Nicorette® Invisi Transdermal Patch may occur in smokers who have previously had a low nicotine intake from cigarettes or if other sources of nicotine are used concomitantly with Nicorette® Invisi Transdermal Patch.

Acute or chronic toxicity of nicotine in man is highly dependent on mode and route of administration. Adaptation to nicotine (e.g. in smokers) is known to significantly increase tolerability compared with non-smokers. The acute minimum lethal oral dose of nicotine is believed to be 40 to 60 mg in children (oral intake of tobacco from cigarettes) or 0.8 to 1.0 mg/kg in adult non-smokers.

Symptoms of overdose are those of acute nicotine poisoning and include nausea, vomiting, increased 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 children and may prove fatal. Suspected nicotine poisoning in a child should be considered a medical emergency and treated immediately.

Management of overdose: Administration of nicotine must be stopped immediately and the patient should be treated symptomatically.

Remove patch and rinse application site with water.

Keep out of reach of children. In the event of overdose, get medical help right away.

HOW TO STORE NICORETTE® INVISI TRANSDERMAL PATCH

Storage
Keep out of the reach and sight of children.
Store below 30ºC.
Do not use Nicorette® Invisi Transdermal Patch after the expiry date which is stated on the pouch and on the carton. The expiry date refers to the last day of that month.

Disposal
After removal, fold the patch into half with sticky side inwards and place inside the opened sachet or a piece of aluminium foil. Dispose the used patch carefully in the household rubbish, away from reach of children and animals.
Ask your pharmacist how to dispose of medicines no longer required.

WHAT IS IN NICORETTE® INVISI TRANSDERMAL PATCH

What it looks like
Semi-transparent, beige, imprinted, rectangular transdermal patch, with rounded corners. It consists of pre-coated backing layer, nicotine source layer, and a skin contact adhesive layer on a pre-coated aluminized and siliconized release liner.

Each strength of the patch has a different size:
10mg: 9.0cm^2
15mg: 13.5cm^2
25mg: 22.5cm^2

Ingredients:
Active: Nicotine
Inactive Ingredients: Medium chain triglycerides, basic butylated methacrylate copolymer, polyethylenterephthalate film (PET), acrylic adhesive solution, potassium hydroxide, croscarmellose sodium, aluminium acetylacetonate, siliconized PET release liner with aluminized single side, printing inks.

SIN Numbers:
10mg/16 hours: SIN14294P
15mg/16 hours: SIN14295P
25mg/16 hours: SIN14296P

Manufacturer

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Product Registrant

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Singapore Consumer Hotline: 800-601-1460

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