AUSTRALIAN PRODUCT INFORMATION

NICORETTE® 16hr - INVISIPATCH® Patch 10mg/16hr, 15mg/16hr, 25mg/16hr (Nicotine)

1 NAME OF THE MEDICINE
Nicotine

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
NICORETTE® 16hr INVISIPATCH® patch is a transdermal delivery system for topical application, available in sizes of 22.5, 13.5 and 9 cm^2 each containing 1.75 mg/cm^2 of nicotine, releasing 25 mg, 15 mg and 10 mg respectively over 16 hours.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM
Transdermal patch. NICORETTE® 16hr INVISIPATCH® are semi-transparent, beige, imprinted, rectangular Transdermal Therapeutic System (TTS) with rounded corners, centrally located on a rectangular, aluminised and siliconised release liner.

4 CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
For the treatment of tobacco dependence by relieving nicotine craving and withdrawal symptoms, thereby facilitating smoking cessation in smokers motivated to quit. For smokers who are currently unable or not ready to stop smoking immediately, the Nicorette 25 mg/16 hour Invisipatch can also be used for two weeks by people who smoke 15 or more cigarettes per day in a preparation phase to reduce the need to smoke prior to stopping smoking immediately.

4.2 DOSE AND METHOD OF ADMINISTRATION
NICORETTE® 16hr INVISIPATCH® patch supports smoking cessation by relieving symptoms of smoking abstinence. A patient who is a candidate for NICORETTE® 16hr INVISIPATCH® patch must desire to stop smoking and should be instructed to ***stop smoking immediately*.**

At the initial visit, patients should be instructed on the application of a NICORETTE® 16hr INVISIPATCH® patch. NICORETTE® 16 hr INVISIPATCH® patch should be applied to an intact area of the skin upon waking up in the morning and removed at bedtime. The patch can be applied to any area of non-hairy, clean, dry skin, for example: the upper thigh, hip, under arm or chest. The site of application should be rotated each day.

Advice and support normally improve the success rate.

Children
NICORETTE® 16hr INVISIPATCH® patch should not be administered to children under 12 years of age.

Adults and elderly
For heavier smokers (15 or more cigarettes a day) prepared to quit immediately: use Nicorette 16 hr Invisipatches in a 3 step program over 12 weeks applying: one 25 mg/16 hour patch daily for the first 8 weeks followed by one 15 mg/16 hr patch daily for the next 2 weeks (weeks 9 and 10) and 10 mg/16 hr patch daily for a further 2 weeks (weeks 11 and 12).

	Dose	Duration	
Step 1	Nicorette 25 mg/16 hour Invisipatch	8 weeks	(weeks 1-8)
Step 2	Nicorette 15 mg/16 hour Invisipatch	2 weeks	(weeks 9-10)
Step 3	Nicorette 10 mg/16 hour Invisipatch	2 weeks	(weeks 11-12)

For heavier smokers (15 or more cigarettes a day) who want to begin their quit attempt without giving up immediately: Nicorette 16 hr Invisipatch 25 mg/16 hr can be used while still smoking *ad libitum* during a 2 week preparation period. At the end of the 2 week period, smokers will stop smoking completely and continue using Nicorette 16 hr Invisipatch 25 mg/16 hr as per the current dosing instructions (above).

When tobacco use ceases abruptly, the cravings can be intense and can be a cause of relapse to smoking. Use of the patch concurrently with smoking for 2 weeks prior to stopping helps prepare the body for quitting by gradually reducing the need to smoke. It provides a steady dose of nicotine which helps reduce conditioning and the reinforcing effects of smoking. The most intense cravings immediately after quitting are likely to be more manageable and the continued use of Nicorette 16 hr Invisipatch will manage cravings until it is no longer needed.

For lighter smokers (less than 15 cigarettes a day) prepared to quit immediately: use Nicorette 16 hr Invisipatches in a 2 step program over 12 weeks appyling: one 15 mg/16 hr patch/day for the forst 8 weeks followed by one 10 mg/16 hr patch/day for the next 4 weeks (weeks 9 to 12).

	Dose	Duration	
Step 1	Nicorette 15 mg/16 hour Invisipatch	8 weeks	(weeks 1-8)
Step 2	Nicorette 10 mg/16 hour Invisipatch	4 weeks	(weeks 9-12)

Regular use of NRT beyond 9 months is not recommended. Some ex-smokers may need longer treatment with NRT to avoid returning to smoking.

Adolescents (12 to 18 years)
When deciding whether to recommend NRT an assessment should be made on the individual's nicotine dependance, motivation to quit and willingness to accept counselling. Counselling is considered to be vitally important in the effective treatment of tobacco dependence in this age group.

The dose and method of use are as for adults however as data are limited in this age group, the recommended duration of treatment is 12 weeks. If longer treatment is required, advice should be sought from a healthcare professional.

Before a recommendation to extend treatment beyond 12 weeks is made the patient should be reassessed for commitment to quitting, expected benefit of continued treatment and maturity. Treatment should not be extended by more than a further 4 weeks.

Combination treatment
Combination therapy may be beneficial for some patients who have relapsed in the past or if they experience cravings using single therapy.

If patients have repeatedly relapsed using single therapy they should seek professional advice from their doctor or pharmacist.

NICORETTE® 16hr INVISIPATCH® patch in combination with NICORETTE® 2mg Gum, NICORETTE® 2mg Lozenge, NICORETTE® 15mg Inhalator or NICORETTE® QuickMist Mouth Spray can be used if breakthrough craving is experienced or there is difficulty in controlling cravings

for cigarettes. In people who have been unable to quit smoking using single NRT product, the combination is more effective than either product alone, increasing the patient's chances of successfully quitting.

The treatment involves the addition of NICORETTE® 2mg gum, NICORETTE® 2mg Lozenge, NICORETTE® 15mg Inhalator or NICORETTE® QuickMist Mouth Spray to the patch. The NICORETTE® 16hr INVISIPATCH® patch should be applied daily to an intact area of the skin upon waking and removed at bedtime, and the NICORETTE® 2mg Gum, NICORETTE® 2mg Lozenge, NICORETTE® 15mg Inhalator or NICORETTE® QuickMist Mouth Spray should be used as required when cravings occur.

NICORETTE® 2mg Gum or NICORETTE® 2 mg Lozenge in combination with NICORETTE® 16hr INVISIPATCH® Patch

For heavier smokers (more than 15 cigarettes a day): use one NICORETTE® 25 mg/16 hr INVISIPATCH® patch per day for 12 weeks plus the 2 mg gum or 2 mg lozenge (at least 4 gums or lozenges; usual dose 5-6 gums or lozenges; maximum 12 gums or lozenges per day). After the initial 12 weeks treatment period, weaning may be done by either:

1. Using the NICORETTE® 15 mg/16 hr INVISIPATCH® patch for 2 weeks, followed by the NICORETTE® 10 mg/16 hr INVISIPATCH® patch for 2 weeks, while maintaining the number of 2 mg gums or 2 mg lozenges that have been routinely used; then gradually reducing the number of 2 mg gums or 2 mg lozenges once the patch is no longer used; OR

2. Stopping use of the NICORETTE® 25 mg/16 hr INVISIPATCH® patch, and then gradually reducing the number of 2 mg gums or 2 mg lozenges.

For lighter smokers (less than 15 cigarettes a day): use one NICORETTE® 15 mg/16 hr INVISIPATCH® patch per day for 12 weeks plus the 2 mg gum or 2 mg lozenge (at least 4 gums or lozenges; usual dose 5-6 gums or lozenges; maximum 12 gums or lozenges per day). After the initial 12 weeks treatment period, weaning may be done by either:

1. Using the NICORETTE® 10 mg/16 hr INVISIPATCH® patch for 4 weeks, while maintaining the number of 2 mg gums or 2 mg lozenges that have been routinely used; then gradually reducing the number of 2 mg gums or 2 mg lozenges once the patch is no longer used; OR

2. Stopping use of the NICORETTE® 15mg/16 hr INVISIPATCH® patch, and then gradually reducing the number of 2 mg gums or 2 mg lozenges.

The NICORETTE® 16hr INVISIPATCH® patch should not be used with NICORETTE® 4mg gums or 4mg lozenges.

NICORETTE® 15 mg Inhalator in combination with NICORETTE® 16hr INVISIPATCH® Patch

For heavier smokers (more than 15 cigarettes a day): use one NICORETTE® 25 mg/16 hr INVISIPATCH® patch per day for 12 weeks plus the NICORETTE® 15 mg Inhalator (usual dose 2-3 inhalator cartridges per day; maximum 6 cartridges per day). After the initial 12 weeks treatment period, weaning may be done by either:

1. Using the NICORETTE® 15 mg/16 hr INVISIPATCH® patch for 2 weeks, followed by the NICORETTE® 10 mg/16 hr INVISIPATCH® patch for 2 weeks, while maintaining the number of inhalator cartirdges that have been routinely used; then gradually reducing the number of inhalator cartridges once the patch is no longer used; OR

2. Stopping use of the NICORETTE® 25 mg/16 hr INVISIPATCH® patch, and then gradually reducing the number of inhalator cartridges.

For lighter smokers (less than 15 cigarettes a day): use one NICORETTE® 15 mg/16 hr INVISIPATCH® patch per day for 12 weeks plus the NICORETTE® 15 mg Inhalator (usual dose 2-3 inhalator cartridges per day; maximum 6 cartridges per day). After the initial 12 weeks treatment period, weaning may be done by either:

1. Using the NICORETTE® 10 mg/16 hr INVISIPATCH® patch for 4 weeks, while maintaining the number of inhalator cartridges that have been routinely used; then gradually reducing the number of inhalator cartridges once the patch is no longer used; OR

2. Stopping use of the NICORETTE® 15 mg/16 hr INVISIPATCH® patch, and then gradually reducing the number of inhalator cartridges.

NICORETTE® QuickMist in combination with NICORETTE® 16 hr INVISIPATCH®Patch

For heavier smokers (more than 15 cigarettes a day): One NICORETTE® 25 mg/16 hr INVISIPATCH® Patch should be applied daily for 12 weeks. The NICORETTE® QuickMist mouth spray should be used as required when breakthrough cravings occur, at a dose of 1 or 2 sprays every 30 – 60 minutes. The maximum number of doses of mouth spray used in conjunction with the NICORETTE® 25 mg/16 hr INVISIPATCH® is 32 sprays per day (two sprays per hour for 16 hours).

After the initial 12 weeks treatment period, weaning may be done by either:

1. Using the NICORETTE® 15 mg/16 hr INVISIPATCH® patch for 2 weeks, followed by the NICORETTE® 10 mg/16 hr INVISIPATCH® patch for 2 weeks, while maintaining the number of sprays of mouth spray that have been routinely used; then gradually reducing the number of sprays once the patch is no longer used;

OR

2. Stopping use of the NICORETTE® 25 mg/16 hr INVISIPATCH® patch, and then gradually reducing the sprays from the mouth spray.

For lighter smokers (less than 15 cigarettes a day): One NICORETTE® 15 mg/16 hr INVISIPATCH® patch should be applied daily for 12 weeks. The NICORETTE® QuickMist mouth spray should be used as required when breakthrough cravings occur, at a dose of 1 or 2 sprays every 30 – 60 minutes. The maximum number of doses of mouth spray used in conjunction with the NICORETTE® 15 mg/16 hr INVISIPATCH® is 32 sprays per day (two sprays per hour for 16 hours).

After the initial 12 weeks treatment period, weaning may be done by either:

1. Using the NICORETTE® 10 mg/16 hr INVISIPATCH® patch for 4 weeks, while maintaining the number of sprays of mouth spray that have been routinely used; then gradually reducing the number of sprays once the patch is no longer used;

OR

2. Stopping use of the NICORETTE® 15 mg/16 hour INVISIPATCH Patch and then gradually reducing the number of doses of NICORETTE® QuickMist that are being used.

4.3 CONTRAINDICATIONS

NICORETTE® 16hr INVISIPATCH® patch is contraindicated in patients with generalised chronic dermatological disorders, such as psoriasis, chronic dermatitis or urticaria.

NICORETTE® 16hr INVISIPATCH® patch is contraindicated in non-tobacco users and in patients with known hypersensitivity to nicotine or any component of the patch.

NICORETTE® 16hr INVISIPATCH® patch is contraindicated in patients with hypersensitivity to nicotine or to any of the ingredients in this product.

Use in children
NICORETTE® 16hr INVISIPATCH® patch, as with other nicotine containing transdermal patches, should not be administered to children under 12 years of age.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Any risks that may be associated with NRT are substantially outweighed by the well established dangers of continued smoking.

Danger in small children
Doses of nicotine tolerated by adult and adolescent smokers can produce severe toxicity in small children that may be fatal. Products containing nicotine should not be left where they may be misused, handled or ingested by children. After removal, the patch should be folded in half, adhesive side innermost, and placed inside the opened sachet., or in a piece of aluminium foil. The used patch should then be disposed of carefully, away from the reach of children or animals. Suspected nicotine poisoning in a child should be considered a medical emergency and treated immediately.

Underlying cardiovascular disease
In stable cardiovascular disease NICORETTE® 16hr INVISIPATCH® patch presents a lesser hazard than continuing to smoke. However dependent smokers currently hospitalised as a result of myocardial infarction, severe dysrhythmia or cerebrovascular accident (CVA) and who are considered to be haemodynamically unstable should be encouraged to stop smoking with non-pharmacological interventions. If this fails, NICORETTE® 16hr INVISIPATCH® ptach may be considered, but as data on safety in this patient group are limited, initiation should only be under medical supervision.

Diabetes mellitus
Patients with diabetes mellitus should be advised to monitor their blood sugar levels more closely than usual when NRT is initiated as catecholamines released by nicotine can affect carbohydrate metabolism.

Phaeochromocytoma and uncontrolled hyperthyroidism
Nicotine, from both NRT and smoking, causes the release of catecholamines from the adrenal medulla. Therefore, NICORETTE® 16hr INVISIPATCH® patch should be used with caution in patients with uncontrolled hyperthyroidism or phaeochromocytoma.

Epilepsy and seizures
NICORETTE® 16hr INVISIPATCH® patch should be used with caution 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.

Transferred dependence
Transferred dependence is rare and is both less harmful and easier to break than smoking dependence.

Generalised dermatological disorders
Patients with chronic generalised dermatological disorders such as psoriasis, chronic dermatitis or urticaria should not use NICORETTE® 16hr INVISIPATCH® patch

Erythema may occur. If it is severe or persistent, treatment should be discontinued.

Continued smoking while using NRT
Patients must be made aware that should they continue to smoke whilst using NICORETTE® 16hr INVISIPATCH® patch they may experience increased adverse effects due to the increased levels of nicotine beyond those normally experienced with smoking alone. Such adverse effects include cardiovascular effects (eg. angina, rapid or irregular heart beats).

Smoking while using intermittent forms of NICORETTE® products such as gum, lozenge, mouth spray and inhalator has not been shown to lead to an increase in adverse effects related to nicotine.

Use in hepatic impairment
NICORETTE® 16hr INVISIPATCH® patch should be used with caution in patients with moderate to severe hepatic impairment as the clearance of nicotine or its metabolites may be decreased with the potential for increased adverse effects.

Use in renal impairment
NICORETTE® 16hr INVISIPATCH® patch should be used with caution in patients with severe renal impairment as the clearance of nicotine or its metabolites may be decreased with the potential for increased adverse effects.

Use in the elderly
A minor reduction in total clearance of nicotine has been demonstrated in healthy elderly patients, however, not justifying an adjustment of dosage.

Paediatric use
NICORETTE® 16hr INVISIPATCH® patch should not be administered to children under 12 years of age.

Effects on laboratory tests
No data available.

4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS
No clinically relevant interactions between nicotine replacement therapy and other drugs has definitely been established. However nicotine may possibly enhance the haemodynamic effects of adenosine i.e. increase in blood pressure and heart rate and also increase pain response (angina-pectoris type chest pain) provoked by adenosine administration.

Use in Magnetic Resonance Imaging
NICORETTE® 16hr INVISIPATCH® patch should be removed prior to undergoing any Magnetic Resonance Imaging (MRI) procedures.

Stopping smoking
Polycyclic aromatic hydrocarbons in tobacco smoke induce the metabolism of drugs metabolised by CYP 1A2 (and possibly by CYP 1A1). 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, clozapine and ropinirole.

The plasma concentration of other drugs metabolised in part by CYP1A2, for example imipramine, olanzapine, clomipramine, fluvoxamine and caffeine may also increase on cessation of smoking, although data to support this are lacking and the possible clinical significance of this effect is unknown.

Limited data indicate that the metabolism of flecainide and pentazocine may also be induced by smoking.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

Studies have shown a decrease of litter size in rats treated with nicotine during the time of fertilisation.

Use in Pregnancy: Category D

Nicotine is harmful to the foetus. The harmful effects of cigarette smoking on maternal and foetal health are clearly established. Short-term exposure during the first trimester is unlikely to cause a hazard to the fetus.

NRT is not contraindicated in pregnancy. The decision to use NRT should be made on a risk-benefit assessment as early on in the pregnancy as possible with the aim of discontinuing use as soon as possible.

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 pregnant smoker and her baby. The earlier abstinence is achieved the better.

Ideally smoking cessation during pregnancy should be achieved without NRT. However for women unable to quit on their own, NRT may be recommended to assist a quit attempt.

Nicotine passes to the fetus affecting breathing movements and has a dose-dependent effect on placental/fetal circulation. However the risk of using NRT to the fetus is lower than that expected with tobacco smoking, due to lower maximal plasma nicotine concentration and no additional exposure to polycyclic hydrocarbons and carbon monoxide.

Intermittent dosing products such as NICORETTE® gums, lozenges, mouth spray or inhalator may be preferable as these usually provide a lower daily dose of nicotine than patches. However, patches may be preferred if the woman is suffering from nausea during pregnancy. If patches are used they should be removed before going to bed.

Use in Lactation

NRT is not contraindicated in lactation. Nicotine from smoking and NRT is found in breast milk. However the amount of nicotine the infant is exposed to is relatively small and less hazardous than the second-hand smoke they would otherwise be exposed to.

NICORETTE® 16hr INVISIPATCH® patch should not be used while breastfeeding. Using intermittent dose NRT preparations such as NICORETTE® gums, lozenges, mouth spray or inhalator may minimize the amount of nicotine in the breast milk as the time between administrations of NRT and feeding can be more easily prolonged.

Women should breastfeed just before using the intermittent NRT product.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

NICORETTE® 16hr INVISIPATCH® patch may cause adverse reactions similar to those associated with nicotine administered by other means, such as gum and inhaler, and are mainly dose dependent.

About 20% of users experience mild local skin reactions, during the first few weeks of treatment.

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 PT occurred at a frequency ≥1% in other formulations 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 PT was identified as a systemic ADR was greater in the active group than the placebo group.

Post Marketing Data

ADRs first identified during post-marketing experience with nicotine are presented in Table 2. Frequencies are provided 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)

Table 2. ADRs Identified During Post-Marketing Experience with Nicotine Patch Formulations with Frequency Category Estimated from Clinical Trials

System Organ Class Frequency category	**Preferred Term**
Cardiac Disorders	
Uncommon	*Palpitations***
Uncommon	*Tachycardia***
Gastrointestinal Disorders	
Not known	*Gastrointestinal discomfort**

General Disorders and Administration site Conditions	
Uncommon	*Application site reactions*
Uncommon	*Asthenia***
Uncommon	*Chest discomfort and pain***
Uncommon	*Malaise***
Not known	*Anaphylactic reaction***
Musculoskeletal and Connective Tissue Disorders	
Uncommon	*Myalgia**
Not known	*Pain in extremity*
Nervous System Disorder	
Not known	*Seizure***
Psychiatric Disorders	
Uncommon	*Abnormal dream**,***
Respiratory, Thoracic and Mediastinal Disorders	
Uncommon	*Dyspnoea***
Skin and Subcutaneous Tissue Disorders	
Not known	*Angioedema***
Not known	*Erythema***
Uncommon	*Hyperhidrosis***
Common	*Rash***
Common	*Urticaria***
Vascular Disorders	
Uncommon	*Flushing***
Uncommon	*Hypertension***

*In vicinity/region of patch
**Systemic effects
***Systemic effect, identified only for formulations administered during night
Reported the same or less frequently than placebo

Some symptoms, such as dizziness, headache, and sleep disturbances, reported in association with the use of NICORETTE® 16hr INVISIPATCH® patch, may be described as withdrawal symptoms associated with smoking cessation. Increased frequency of aphthous ulcers may occur after abstinence from smoking. The causality is unclear.

NICORETTE® 16hr INVISIPATCH® patch differs from other nicotine containing transdermal patches in that it is intended to be worn for 16 hours. Therefore during the 8 hour "sleep" period the body has a respite from exposure to nicotine. In clinical trials fewer nocturnal and local adverse events have been described in comparison to the continuous exposure of 24 hour nicotine containing transdermal patches.

Reporting Suspected Adverse Events
Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product.

Healthcare professionals are asked to report any suspected adverse reactions at: https://www.tga.gov.au/reporting-problems.

4.9 OVERDOSE
Excessive use of nicotine from either NRT and/or smoking might cause symptoms of an overdose.

Symptoms of overdosage are those of acute nicotine poisoning and include nausea, salivation, vomiting, 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.

Overdosage with nicotine can occur if the patient has a very low pre-treatment nicotine intake and uses other forms of nicotine. The acute minimum lethal oral dose of nicotine in non-smokers is believed to be 40-60 mg.

Doses of nicotine that are tolerated by adult smokers during treatment may produce severe symptoms of poisoning in small children and may prove fatal. The lethal dose of nicotine in a small child is approximately 10-15 mg. Suspected nicotine poisoning in a child should be considered a medical emergency and treated immediately.

Management of overdosage
In view of the lack of actual experience in the treatment of NICORETTE® 16hr INVISIPATCH® patch overdose, the procedures recommended are those that have been suggested for the treatment of acute nicotine poisoning.

Overdose from Topical Exposure
In case of intoxication, immediately remove all nicotine patches. The skin may be flushed with water and dried. Soap should not be used since it may increase nicotine absorption. The patient may deteriorate during the following hours, due to the slow distribution of nicotine from the patch area. The patient should therefore be carefully supervised for a prolonged period.

Overdose from Ingestion of the Patch
If a patch is ingested, activated charcoal should be given as soon as possible. Contact the Poisons Information Centre (13 11 26) for advice on treatment. The administration of nicotine from any other source must be stopped immediately and the patient should be treated symptomatically. Activated charcoal reduces gatrointestinal absorption of nicotine. Repeated doses of activated charcoal should be administered as long as the patch remains in the gastrointestinal tract as it will continue to release nicotine for many hours.

For information on the management of overdose, contact the Poison Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action
Nicotine is a natural alkaloid which has ganglion stimulating properties and produces a wide range of pharmacological actions.

The use of nicotine is widespread in the form of tobacco products, chronic use of which is causally linked to a variety of serious diseases. Many smokers develop a dependence due to an interaction of pharmacological, social and psychological factors.

Clinical trials
NICORETTE® 16hr INVISIPATCH® patch is a treatment aid in smoking cessation. Clinical studies have shown that nicotine replacement from nicotine containing products can help people give up smokiong by relief of abstinence symptoms associated with smoking cessation.

Abrupt cessation of the use of tobacco containing products following a prolonged period of daily use results in a characteristic withdrawal syndrome that includes four or more of the following: dysphoria or depressed mood; insomnia; irratability; frustration or anger; anxiety; difficulty concentrating; restlessness or impatience; decreased heart rate; and increased appetite or weight gain. Nicotine craving, which is recognised as a clinically relevant symptom, is also an important element in nicotine withdrawal.

Clinical studies have shown that nicotine replacement products can help smokers abstain from smoking by relieving these withdrawal symptoms.

In placebo-controlled double blind clinical studies, nicotine replacement with NICORETTE® 16hr INVISIPATCH® patch for periods up to 3 months increased the chances of successful abstinence without group support.

The post marketing, double blind, Collaborative European Anti-Smoking Evaluation (CEASE) study (n=3575 adult smokers smoking > 15 cigarettes per day) comparing an 8-week treatment period (plus 4 weeks taper with lower strength patches) with a 22 week treatment period (plus 4 weeks taper with lower strength patches) found no evidence of benefit from the longer treatment period. The primary outcome measure for this study was continuous self reported abstinence at 12 months (verified by CO monitoring).

5.2 PHARMACOKINETIC PROPERTIES

There are no differences in nicotine kinetics between men and women.

Absorption

NICORETTE® 16hr INVISIPATCH® patch contains 1.75mg/cm^2 nicotine.
Delivery of nicotine is controlled by the patch to assure reproducible plasma nicotine levels.

Plasma levels of nicotine obtained with the patch slowly rise during the first hours after application. The maximum level is attained after approximately 9 hours. The peak plasma level nicotine achieved with the 25mg/hr (22.5cm^2) patch is approximately 26.5ng/mL.

The 25mg/16hr patch (22.5cm^2) delivers approximately 25mg nicotine during the 16 hour application period. This indicates a residual nicotine content of approximately 15mg following 16 hours of skin contact. The absolute bioavailability of nicotine from the patch is high (>90%).

After repeated application nicotine concentrations are not significantly higher than those after a single application. Plasma nicotine concentrations show dose proportionality for different patches with different surfaces areas. Nicotine kinetics are similar following application on the arm and hip.

Distribution

Plasma protein binding of nicotine is less than 5%. Therefore, changes in nicotine binding from use of concomitant drugs or alterations of plasma proteins by disease states would not be expected to have significant effects on nicotine kinetics.

Metabolism

The volume of distribution following IV administration of nicotine is about 2 to 3L/kg and the half-life approximately 2 hours. The major eliminating organ is the liver, and average plasma clearance is about 70L/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. 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.

Excretion

Following removal of the patch, nicotine is eliminated from the blood with a half-life of approximately 4 hours.

The primary urinary metabolites are cotinine (15% of the dose) and trans-3-hydroxy-cotinine (45% of the dose). About 10% of nicotine is excreted unchanged in the urine. As much as 30% of nicotine may be excreted unchanged in the urine with high flow rates and acidification of the urine below pH 5.

Progressive severity of renal impairment is associated with decreased total clearance of nicotine. The pharmacokinetics of nicotine is unaffected in cirrhotic patients with mild liver impairment (Child score 5) and decreased in cirrhotic patients with moderate liver impairment (Child score 7). Raised nicotine levels have been seen in smoking patients undergoing hemodialysis.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

Neither nicotine nor cotinine was mutagenic in the Ames *Salmonella* test.

Carcinogenicity

Literature reports indicate that nicotine is neither an initiator nor a tumour-promoter in mice. There is inconclusive evidence to suggest that cotinine, an oxidised metabolite of nicotine, may be carcinogenic in rats.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Medium chain triglycerides
Eudragit E100 (PI no. 1753)
Durotak 387-2051 (PI no. 4753)
Potassium hydroxide,
Croscarmellose sodium,
Aluminium (from aluminium acetylacetonate)
Printing ink XD2K25 (beige/brown).

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

36 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C.

6.5 NATURE AND CONTENTS OF CONTAINER

Each patch is packaged in a heat sealed multilaminate sachet.

Pack sizes:
10mg/16hr: 7, 14’s, 28’s
15mg/16hr: 7, 14’s, 28’s
25mg/16hr: 7, 14’s, 28’s

Not all pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

After application of a patch, as after removal, the hands should be thoroughly washed with water and dried after handling to avoid possible contact with sensitive areas such as the eyes.

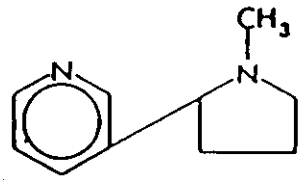
NICORETTE® 16hr INVISIPATCH® patches are intended to be worn for 16 hours.

After removal, a used patch should be folded over and placed in its original pouch. It should then be disposed of immediately to prevent access by children or animals. As used patches contain some residual nicotine, both new and used patches must be kept out of the reach of children at all times.

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSIOCHEMICAL PROPERTIES

Chemical Structure



CAS number
54-11-5

7 MEDICINE SCHEDULE (POISONS STANDARD)

Unscheduled

8 SPONSOR

Johnson & Johnson Pacific
45 Jones Street
Ultimo NSW 2007

® Registered trademark

9 DATE OF FIRST APPROVAL

Date of first inclusion in the ARTG: 26 November 2012

10 DATE OF REVISION

Date of revision: 28 April 2023

Summary table of changes

Section changed	Summary of new information
All	Update to new PI format. Addition of more restrictive safety-related information to section 4.3, 4.4 and 4.8.
3	Updated visual ID
4.4, 4.8	Addition of safety-related information on epilepsy and seizures