NEW ZEALAND DATA SHEET

1 PRODUCT NAME

NICORETTE® Inhalator
15mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

NICORETTE® Inhalator contains nicotine 15mg

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

3 PHARMACEUTICAL FORM

NICORETTE® Inhalator consists of a white to slightly coloured porous plug in a sealed transparent plastic cartridge.

Prior to use the tube is inserted in a mouthpiece and the seals are broken. When air is drawn through the plug gaseous nicotine and menthol are released.

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,
- helping smokers to temporarily abstain from smoking or
- facilitating smoking reduction in smokers unable or unwilling to quit

4.2 Dose and method of administration

Could be used as a single treatment or in combination with nicotine patch.

Children and Adolescents

NICORETTE® Inhalator should not be administered to individuals under 18 years of age without recommendation from a physician. There is no experience of treating adolescents under the age of 18 with NICORETTE® Inhalator.

Adults and Elderly

For single use

NICORETTE® Inhalator should be used whenever there is an urge to smoke. The more the subject is able to use it, the easier it will be to stay smoke-free. NICORETTE® Inhalator can be used in the same way as a cigarette. The dose of nicotine from a puff of the inhalator is much less than that of a cigarette. Use

about 8-10 times as many puffs as when smoking a cigarette (if a cigarette is smoked in 8 puffs, 64-80 puffs on the inhalator substitutes one cigarette) to reach a suitable substitution degree. The subject needs to use the inhalator for longer periods than when smoking to control the cravings. Used like this each inhalator will last for approximately 40 minutes per session. For best results 3-6 cartridges should be used per day. Less than 3 cartridges per day may fail to help control the cravings.

One cartridge can replace 7 cigarettes (7 sessions with 80 puffs). The level of nicotine received from the inhalator depends on temperature. In colder temperatures the inhalator has to be used longer to achieve the same effect.

Smoking cessation

It is important that the treatment period is long enough. Normally the initial treatment period is 3 months. After that, the number of cartridges should be gradually reduced during 6-8 weeks to wean off.

Any spare cartridges should be retained, as craving may suddenly occur. Open cartridges should be used within 12 hours.

Smoking reduction

Use the inhalator between smoking episodes to prolong smoke-free intervals and with the intention to reduce your smoking as much as possible. If a reduction in number of cigarettes per day has not been achieved after 6 weeks it should be considered to seek professional advice.

A quit attempt should be made as soon as you feel ready but not later than 6 months after start of treatment. If it is not possible to make a serious quit attempt within 9 months after start of treatment then seek professional advice.

Regular use of the inhalator beyond 12 months is generally not recommended.

Advice and support normally improve the success rate.

Temporary abstinence

Use the inhalator during smoke-free periods, for example in smoke-free areas or in other situations when you wish to avoid smoking.

In combination with nicotine patch

Persons who have failed with single treatment or want to reduce the daily use of inhalator cartridges because of local adverse events, can use NICORETTE® 16 hr INVISIPATCH® in addition to the inhalator.

The NICORETTE® 16 hr INVISIPATCH® patch should be applied to an intact area of the skin upon waking and removed at bedtime. After applying the NICORETTE® 16 hr INVISIPATCH® patch, the NICORETTE® 15 mg Inhalator should be used as required when cravings occur (usual dose 2-3 inhalator cartridges per day; maximum 6 cartridges per day).

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 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.

4.3 Contraindications

NICORETTE® Inhalator should not be administered to non-tobacco users or patients with known hypersensitivity to nicotine or menthol.

4.4 Special warnings and precautions for use

NICORETTE® Inhalator should be used with caution in patients chronic throat diseases and bronchospastic disease.

Special warnings and precautions for the combination of nicotine patch with NICORETTE® Inhalator are the same as those for each treatment alone.

Underlying cardiovascular disease

NICORETTE® Inhalator should only be used after consulting a physician by particular cardiovascular patient groups: those who have experienced a serious cardiovascular event, or hospitalisation for a cardiovascular complaint, in the previous 4 weeks (e.g. stroke, myocardial infarction, unstable angina, cardiac arrhythmia, coronary artery bypass graft and angioplasty) or where they suffer with uncontrolled hypertension.

Use in hepatic impairment

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

Gastrointestinal Disease

NICORETTE® Inhalator should be used with caution in patients with active duodenal, oesophagitis, gastric or peptic ulcers.

Phaeochromocytoma and uncontrolled hyperthyroidism

Nicotine, both from Nicotine Replacement Therapy and smoking, causes the release of catecholamines from the adrenal medulla. Therefore NICORETTE® Inhalator should also be used with caution in patients with hypothyroidism or pheochromocytoma.

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.

Patients with diabetes mellitus may require lower doses of insulin as a result of smoking cessation.

Transferred dependence

Some users may continue to use NICORETTE® Inhalator after the recommended treatment period but the potential risk of longer-term use is far less than those associated with resuming to smoking.

Paediatric use

NICORETTE® Inhalator should not be administered to children under 12 years of age.

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.

If a child swallows, chews or sucks on the nicotine plug, (used as well as unused) there is a risk of poisoning the child.

4.5 Interaction with other medicines and other forms of interaction

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 (anginapectoris type chest pain) provoked by adenosine administration.

Smoking (but not nicotine) is associated with increase in CYP1A2 activity. After cessation of smoking, reduced clearance of substrates for this enzyme may

occur. This may lead to an increase in plasma levels for some medicinal products of potential clinical importance for products with a narrow therapeutic window, e.g. theophylline, tacrine clozapine and ropinirole.

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

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

4.6 Fertility, pregnancy and lactation

Nicotine passes to the foetus and affects its breathing movements and circulation. The effect on the circulation is dose dependent. Smoking can seriously harm the foetus or infant and should be stopped. Pregnant or breast-feeding smokers should only use NICORETTE® Inhalator after consulting a health care professional. The risks for the foetus from NICORETTE® Inhalator are not fully known. The benefits of nicotine replacement therapy in pregnant women who cannot abstain without such therapy substantially outweigh the risk of continued smoking.

Nicotine passes into breast milk in small quantities that may affect the infant, even at therapeutic doses. To reduce the exposure to the child the NICORETTE® Inhalator should be used just after breast-feeding.

4.7 Effects on ability to drive and use machines

NICORETTE® Inhalator has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Nicorette Inhalator may cause adverse reactions similar to those associated with nicotine administered by other means and are dose-dependent.

Most of the undesirable effects reported by the patients occur during the first 3-4 weeks after start of treatment.

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

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 oromucosal 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 Oromucosal Formulations

System Organ Class Preferred Term	Active N = 3914(%)	Placebo N = 2819 (%)
Gastrointestinal Disorders		
Abdominal Pain	1.8	1.2
Dry Mouth	3.2	2.7
Dyspepsia	6.1	3.3
Flatulence	1.8	1.4
Nausea[a]	10.4	5.8
Salivary hypersecretion	2.6	1.0
Stomatitis	2.6	2.0
Vomiting[a]	2.7	1.2
General Disorders and Administration Site Conditions		
Fatigue[a]	1.0	0.6
*Burning sensation**	1.0	0.5
Immune System Disorders		
Hypersensitivity[a]	1.4	1.22
Nervous System Disorders		
Headache[a#]	11.5	13.0
Paraesthesia[a]*	1.3	0.8
Dysgeusia	3.2	2.8
Respiratory, Thoracic and Mediastinal Disorders		
*Cough***	9.3	10.7
*Hiccups****	16.4	2.3
*Throat irritation***	11.8	4.4

a:Systemic effects
*At the application site
** Higher frequency observed in clinical studies with inhaler formulation
*** Higher frequency observed in clinical studies with mouth spray formulation
# 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 Oromucosal Formulations with Frequency Category Estimated from Clinical Trials

System Organ Class Frequency category	**Preferred Term**
Cardiac Disorders	
Uncommon	*Palpitations***
Uncommon	*Tachycardia***
Eye Disorders	
Not known	*Blurred vision*
Not known	*Lacrimation increased*
Gastrointestinal Disorders	
Common	*Diarrhoea*[#]
Not known	*Dry Throat*
Rare	*Dysphagia*
Uncommon	*Eructation*
Not known	*Gastrointestinal discomfort***
Uncommon	*Glossitis*
Rare	*Hypoaesthesia oral*[#]
Uncommon	*Oral mucosal blistering and exfoliation*
Not known	*Lip pain*
Uncommon	*Paraesthesia oral*[#]
Rare	*Retching*
General Disorders and Administration site Conditions	
Uncommon	*Asthenia***
Uncommon	*Chest discomfort and pain***
Uncommon	*Malaise***
Immune System Disorders	
Not known	*Anaphylactic reaction***
Musculoskeletal and Connective Tissue Disorders	
Not known	*Muscle tightness**
Unknown	*Pain in jaw**
Psychiatric Disorders	
Uncommon	*Abnormal dream**,***
Respiratory, Thoracic and Mediastinal Disorders	
Uncommon	*Dyspnoea***
Uncommon	*Bronchospasm*
Uncommon	*Dysphonia*
Uncommon	*Nasal congestion*
Uncommon	*Oropharyngeal pain*
Uncommon	*Sneezing*
Uncommon	*Throat tightness*

Skin and Subcutaneous Tissue Disorders	
Not known	*Angioedema***
Not known	*Erythema***
Uncommon	*Hyperhidrosis***
Uncommon	*Pruritus***
Uncommon	*Rash***
Uncommon	*Urticaria***
Vascular Disorders	
Uncommon	*Flushing***
Uncommon	*Hypertension***

*Tightness of jaw and pain in jaw with nicotine gum formulation
**systemic effects
***systemic effect, identified only for formulations administered during night
reported the same or less frequently than placebo

Adverse reactions that may occur when using the combination treatment (patch and inhalator) only differ from each treatment alone in terms of local adverse events associated with the formulations. The frequencies of these adverse events are comparable to those reported for each product respectively.

Reporting Suspected Adverse Events

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

Excessive use of nicotine from either Nicotine Replacement Therapy and/or smoking might cause symptoms of an overdose.

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

In the event of overdose or poisoning activated charcoal should be given as soon as possible. Contact the Poisons Information Centre (0800 764 766) for advice on treatment.

Administration of nicotine must be stopped immediately and the patient should be treated symptomatically. Activated charcoal reduces gastrointestinal absorption of nicotine.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drug for treatment of nicotine dependence.

ATC code: N07B A01.

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; irritability; 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.

5.2 Pharmacokinetic properties

Pharmacokinetic properties of NICORETTE® Inhalator

The major fraction of the nicotine in NICORETTE® Inhalator is deposited in the oral cavity. Continuous, rapid inhalations over 40 minutes release up to about 7mg of the nicotine from each cartridge and about 50% of the released nicotine is systemically available, i.e about 4mg. Absorption of nicotine through the buccal mucosa is slow and does not produce the high and rapid nicotine plasma concentrations seen with cigarette smoking. Self-administration (ad lib. at clinical use) typically produces nicotine plasma levels of 6-8ng/ml, which are only about 1/3 of those achieved with cigarette smoking. The plasma levels following clinical use correspond to once hourly chewing of NICORETTE® chewing gum 2mg and once hourly use of NICORETTE® Nasal Spray.

Steady state plasma levels of approximately 20ng/ml are achieved with continuous, rapid inhalations during 20 minutes per hour, 1 fresh cartridge each hour, for 12 hours at ambient room temperature in a laboratory setting. The release of nicotine from the NICORETTE® Inhalator is temperature dependent resulting in an increase of the biologically available dose at increasing temperatures as compared to that at 25°C. Corresponding plasma levels at 30°C and 40°C will be 25 and 30 ng/ml, respectively.

General pharmacokinetic properties of NICORETTE® Inhalator

The volume of distribution following i.v. administration of nicotine is approximately 2 to 3 L/kg. 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.

The average plasma clearance following intravenous administration of nicotine is about 70L/hour and the terminal half-life approximately 2 hours. The major eliminating organ is the liver, but the kidney and lung also metabolize nicotine. There is no significant skin metabolism of 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. The primary urinary metabolites are cotinine (15% of the dose) and trans-3-hydroxycotinine (45% of the dose). About 10% of nicotine is excreted unchanged in the urine, but as much as 30% may be excreted unchanged in the urine with high flow rates and acidification of the urine below pH 5.

The therapeutic blood concentrations of nicotine i.e. the levels that relieve craving are individual based upon the patient's nicotine dependence. Progressive severity of renal impairment is associated with decreased total clearance of nicotine. Raised nicotine levels have been seen in smoking patients undergoing haemodialysis. The pharmacokinetics of nicotine is unaffected in cirrhotic patients with mild liver impairment (Child score 5) but a slightly decreased clearance of nicotine has been observed in cirrhotic patients with moderate liver impairment (Child score 7). A minor reduction in total clearance of nicotine has been demonstrated in healthy elderly patients, however not justifying adjustment of dosage.

Pharmacokinetic properties of the combination of NICORETTE® patch and NICORETTE® Inhalator

The plasma levels of nicotine when combining one 15 mg/16 hour patch or one 25 mg/16 hour Invisipatch® patch and 15 mg inhalator, will depend on the number of inhalator cartridges used and the dosing interval.

5.3 Preclinical safety data

There are no pre-clinical data on the safety of NICORETTE® Inhalator.

The toxicity of nicotine as a component of tobacco is, however, well documented. Typical symptoms of acute poisoning are weak and irregular pulse, breathing difficulties, and general convulsions.

There are no clear evidence of nicotine being genotoxic or mutagenic. The well established carcinogenicity of tobacco smoke is mainly related to substances formed by the pyrolysis of tobacco. None of these occur in nicotine inhalator.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Levomenthol and porous plug.

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 from the date of manufacture.

6.4 Special precautions for storage

Store at or below 25°C.

6.5 Nature and contents of container

4 cartridges in a blister tray with a mouthpiece
20 cartridges in a blister tray with 2 mouthpieces

6.6 Special precautions for disposal

After removing the mouthpiece and the sealed tray from the box the mouthpiece is separated into two parts and the seal is removed from the tray.

One sealed unit (tube containing a nicotine plug) is removed from the tray and inserted into the mouthpiece. The tray with remaining units is returned to the box.

When the mouthpiece is re-assembled the seal on both ends of the unit are broken.

After use the unit is removed from the mouthpiece and disposed of in a safe way out of reach of children and pets. The mouthpiece should be stored in the box for further use.

7 MEDICINE SCHEDULE

General Sale Medicine.

8 SPONSOR

Johnson & Johnson (New Zealand) Ltd
507 Mt. Wellington Highway
Mt. Wellington, Auckland 1060

P.O. Box 62-185, Sylvia Park
Auckland 1644

9 DATE OF FIRST APPROVAL

11 August 2009.

10 DATE OF REVISION OF THE TEXT

04 October 2019

Summary table of changes

Section changed	Summary of new information
All	Update to new Datasheet format. Addition of new packaging material. Addition of more restrictive safety and related statements. Updates to Adverse event data.