

# DATA SHEET

## NICORETTE® Nasal Spray

*10mg/ml*

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### Presentation

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NICORETTE Nasal Spray containing 10mg/ml nicotine is a clear to weakly opalescent, colourless to light yellow solution filled in a brown glass container with a spray pump delivering 50 microL per spray.

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### Uses

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#### ***Actions***

NICORETTE Nasal Spray is a treatment aid to smoking cessation. Clinical studies have shown that the nicotine replacement from nicotine containing products can help people give up smoking.

Nicotine is an agonist of nicotinic receptors in the peripheral and central nervous systems. In man as in animals nicotine had been shown to produce both behavioural stimulation and depression.

The administration of NICORETTE Nasal Spray eliminates the other ingredients contained in tobacco smoke such as tar, carbon monoxide and irritating gases.

#### ***Pharmacokinetics***

Following administration of one dose NICORETTE Nasal Spray approximately 56% of the nicotine enters the systemic circulation.

The volume of distribution following iv administration of nicotine is approximately (2 to) 3 L/kg and the half life ranges from 1-2 hours. The major eliminating organ is the liver, and average plasma clearance is about 1.2 L/min; 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 nicotine. The primary metabolite of nicotine in plasma, cotinine, has a half life of 15-20 hours and concentrations exceed nicotine by 10-fold.

Plasma protein binding of nicotine is <5%. Therefore changes in nicotine binding from the use of concomitant medicines or alterations of plasma proteins by disease states would not be expected to have a significant effect on nicotine kinetics.

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

Plasma levels of nicotine obtained with NICORETTE Nasal Spray rise rapidly, reaching a maximum plasma level of nicotine - after steady state is achieved - given 1 dose/hour, 2 doses/hour and 3 doses/hour are approximately 10, 19 and 28ng/ml respectively.

After repeated administration of NICORETTE Nasal Spray the AUC was significantly higher during the last dosing interval as compared to the first given an accumulation ratio of 3.1. No dose-dependency has been shown for doses of 0.5mg and 1mg nicotine.

The therapeutic blood concentrations of nicotine (i.e. the blood levels) which relieve craving are individually based on the patient's nicotine dependence.

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

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## Indications

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NICORETTE Nasal Spray is indicated as a treatment aid in smoking cessation for the relief of tobacco withdrawal symptoms.

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## Dosage and Administration

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### Adults (including elderly)

The nasal spray can be used on patients who for different reasons do not find nicotine chewing gum or patch acceptable. The recommended dose is normally 1-2 doses per hour up to a maximum of 3 doses per hour. Each dose consisting of one spray into each nostril.

The recommended treatment period is 3 months. After this initial period patients should be weaned off by reduction of the daily dose over the following 6-8 weeks. Use of NICORETTE Nasal Spray should not be continued beyond 6 months.

Advice and support normally improve the success rate.

## **Children**

NICORETTE Nasal Spray 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 Nasal Spray.

## **Concomitant disease**

Only severe renal impairment would be expected to affect the clearance of nicotine or its metabolites from the circulation. In patients smoking and undergoing haemodialysis elevated nicotine levels have been seen.

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## **Contraindications**

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Hypersensitivity to nicotine or any component of the nasal spray.

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## **Warnings and Precautions**

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A few cases of exacerbation of bronchospasm in patients with asthma bronchiale has been reported. Use of the spray in patients with hyperreactive airways is not recommended.

NICORETTE Nasal Spray should only be used after consulting a physician by particular 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.

NICORETTE Nasal Spray should be used with caution in patients with severe/moderate hepatic impairment, severe renal impairment, active duodenal and gastric ulcers.

Nicotine, both from nicotine replacement therapy and smoking, causes the release of catecholamines from the adrenal medulla. Therefore, NICORETTE Nasal Spray should be used in caution in patients with uncontrolled hyperthyroidism or pheochromocytoma.

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

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

## ***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 Nasal Spray after consulting a health care professional. The risks for the foetus from NICORETTE Nasal Spray 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 exposition to the child the NICORETTE Nasal Spray should be used just after breast-feeding.

## ***Effects on ability to drive and use machines***

No effects.

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## **Adverse Effects**

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NICORETTE Nasal Spray may cause adverse reactions similar to those produced by nicotine administered by other means and are dose-dependent.

During the first 2 days of treatment, nasal irritation as sneezing, running nose, watering eyes, cough was reported by nearly all (94%) of the patients. Both the frequency and severity declined with continued use.

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.

Very common (>1/10); common (>1/100, <1/10); uncommon (>1/1000, <1/100); rare (>1/10000, <1/1000); very rare (<1/10000), including isolated reports

<b>Nervous system disorders:</b>	Common:	Dizziness, headache
<b>Cardiac disorders:</b>	Uncommon:	Palpitations
	Very rare:	Reversible atrial fibrillation
<b>Respiratory, thoracic and Mediastinal disorders:</b>	Common:	Coughing
<b>Gastro-intestinal disorders:</b>	Common:	Gastrointestinal discomfort, nausea, vomiting
<b>General disorders and administration site conditions:</b>	Very common	Epistaxis, running nose, sneezing, watering eyes

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## Interactions

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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 pentazocine may also be induced by smoking.

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## Overdosage

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

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.

### Management of overdosage

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

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## Pharmaceutical Precautions

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Store below 25° C protected from light.

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## **Medicine Classification**

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Prescription Medicine.

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## **Package Quantities**

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10ml in brown glass bottle.

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## **Further Information**

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## **Name and Address**

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Johnson & Johnson Pacific (NZ) Ltd  
Ground Floor, Ericsson House  
105 Carlton Gore Road  
Newmarket  
Auckland

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## **Date of Preparation**

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13 September 2004

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