Professional information for NICORETTE® QUICKMIST

SCHEDULING STATUS: S1

1 NAME OF THE MEDICINE

NICORETTE® QUICKMIST 1 mg/spray oromucosal spray, solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0,07 mL spray contains 1 mg nicotine.

Sugar free.

Contains sweeteners (0,1 mg sucralose and 0,1 mg acesulfame potassium/spray).

Excipients with known effect:

Propylene glycol 11 mg/spray

Butylated hydroxytoluene 363 ng/spray

Alcohol (7,1 mg ethanol/spray).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oromucosal spray, solution.

A clear to weakly opalescent, colourless to light yellow solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

NICORETTE® QUICKMIST is to be used for the treatment of tobacco dependence in adults by relief of nicotine withdrawal symptoms, including cravings, during a quit attempt.

Permanent cessation of tobacco use is the eventual objective. NICORETTE® QUICKMIST should preferably be used in conjunction with a behavioural support program.

4.2 Posology and method of administration

Posology

Patients should stop smoking completely during the course of treatment with NICORETTE® QUICKMIST.

Adults and elderly

The following chart lists the recommended usage schedule for NICORETTE® QUICKMIST during full treatment (Step I) and during tapering (Step II and Step III). Up to 4 sprays per hour may be used. Do not exceed 2 sprays per dosing episode and do not exceed 64 sprays (4 sprays per hour, over 16 hours) in any 24-hour period.

Step I: Weeks 1 – 6

Use 1 or 2 sprays when cigarettes normally would have been smoked or if cravings emerge. If after a single spray, cravings are not controlled within a few minutes, a second spray should be used. If 2 sprays are required, future doses may be delivered as 2 consecutive sprays. Most smokers will require 1 – 2 sprays every 30 minutes to 1 hour.

Step II: Weeks 7 – 9

Start reducing the number of sprays per day. By the end of week 9 patients should be using HALF the average number of sprays per day that was used in Step I.

Step III: Weeks 10 – 12

Continue reducing the number of sprays per day so that patients are not using more than 4 sprays per day during week 12. When patients have reduced to 2 – 4 sprays per day, oromucosal spray use should be discontinued.

Example: If an average of 15 cigarettes per day are usually smoked, 1 – 2 sprays should be used at least 15 times during the day.

To help stay smoke free after Step III, patients may continue to use NICORETTE® QUICKMIST in situations when they are strongly tempted to smoke. One spray may be used in situations where there is an urge to smoke, with a second spray if one spray does not help within a few minutes. No more than four sprays per day should be used during this period. Regular use of NICORETTE® QUICKMIST beyond 6 months is generally not recommended. Some ex-smokers may need treatment with NICORETTE® QUICKMIST longer to avoid returning to smoking. Any remaining NICORETTE® QUICKMIST should be retained to be used in the event of sudden cravings.

Paediatric population

Do not administer NICORETTE® QUICKMIST to persons under 18 years of age. There is no experience of treating adolescents under the age of 18 with NICORETTE® QUICKMIST.

Method of administration

After priming, point the spray nozzle as close to the open mouth as possible. Press firmly the top of the dispenser and release one spray into the mouth, avoiding the lips. Subjects should not inhale while spraying to avoid getting spray into the respiratory tract. For best results, do not swallow for a few seconds after spraying.

Patients should not eat or drink when administering NICORETTE® QUICKMIST.

Behavioural therapy advice and support will normally improve the success rate.

4.3 Contraindications

- Hypersensitivity to nicotine, or any of the excipients of NICORETTE® QUICKMIST listed in sections 2 and 6.1.
- Children under the age of 18 years.
- Those who have never smoked.

4.4 Special warnings and precautions for use

NICORETTE® QUICKMIST should not be used by non-smokers.

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

A risk-benefit assessment should be made by an appropriate healthcare professional for patients with the following conditions:

Cardiovascular disease: Dependent smokers with a recent myocardial infarction, unstable or worsening angina including Prinzmetal's angina, severe cardiac dysrhythmias, recent cerebrovascular accident and/or who suffer with uncontrolled hypertension should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). If this fails, NICORETTE® QUICKMIST 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 reduction in nicotine-induced catecholamine release can affect carbohydrate metabolism.

Allergic reactions: Susceptibility to angioedema and urticaria.

Renal and hepatic impairment: NICORETTE® QUICKMIST should be used 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.

Pheochromocytoma and uncontrolled hyperthyroidism: As nicotine causes release of catecholamines, NICORETTE® QUICKMIST should be used with caution in patients with uncontrolled hyperthyroidism or pheochromocytoma.

Gastrointestinal (GI) disease: Swallowed nicotine may exacerbate symptoms in patients suffering from oesophagitis, gastritis or peptic ulcers and oral NRT preparations should be used with caution in these conditions.

Seizures: Potential risks and benefits of nicotine should be carefully evaluated before use in subjects with a history of epilepsy as cases of convulsions have been reported in association with nicotine.

Paediatric population

Danger in 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 (see section 4.9 Overdose).

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

Stopping smoking: Polycyclic aromatic hydrocarbons in tobacco smoke induce the metabolism of medicines 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 medicines. This is of potential clinical importance for products with a narrow therapeutic window, e.g. theophylline, clozapine and ropinirole.

The plasma concentration of other medicines 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 medicines is unknown. Limited data indicate that the metabolism of flecainide and pentazocine may also be induced by smoking.

Excipients: NICORETTE® QUICKMIST contains small amounts of ethanol (alcohol), less than 100 mg per dose (1 or 2 sprays). NICORETTE® QUICKMIST contains 11 mg propylene glycol in each spray which is equivalent to 150 mg/mL. Due to the presence of butylated hydroxytoluene (BHT), NICORETTE® QUICKMIST may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes.

Care should be taken not to spray the eyes whilst administering the spray.

4.5 Interaction with other medicines and other forms of interaction

No clinically relevant interactions between nicotine replacement therapy and other medicines 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 (see section 4.4, Stopping smoking).

4.6 Fertility, pregnancy and lactation

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 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.

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 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 use of 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. The use of NICORETTE® QUICKMIST by the pregnant smoker should only be initiated after advice from a health care provider.

Lactation

Nicotine passes freely into breast milk in quantities that may affect the child even with therapeutic doses. NICORETTE® QUICKMIST should therefore be avoided during breastfeeding. Should smoking cessation not be achieved, use of NICORETTE® QUICKMIST by breastfeeding smokers should only be initiated after advice from a healthcare professional. Women should take the product just after having breastfed and leave as long a time as is possible (2 hours is suggested) between taking the mouth spray and the next feed.

Fertility

Smoking increases the risk for infertility in women and men. *In vitro* studies have shown that nicotine can adversely affect human sperm quality. In rats, impaired sperm quality and reduced fertility has been shown.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

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.

NICORETTE® QUICKMIST may cause adverse reactions similar to those associated with nicotine given by other means and these are mainly dose dependent. Allergic reactions such as angioedema, urticaria or anaphylaxis may occur in susceptible individuals.

Local adverse effects of administration are similar to those seen with other orally delivered forms. During the first few days of treatment irritation in the mouth and throat may be experienced, and hiccups are particularly common. Tolerance is normal with continued use.

Daily collection of data from trial subjects demonstrated that very commonly occurring adverse events were reported with onset in the first 2 – 3 weeks of use of NICORETTE® QUICKMIST and declined thereafter.

Adverse reactions identified from clinical trials and during post- marketing experience are as follows:

Immune system disorders:

Frequent:	hypersensitivity
Frequency unknown:	allergic reactions including angioedema and anaphylaxis

Psychiatric disorders:

Less frequent:	abnormal dreams

Nervous system disorders:

Frequent:	headache, dysgeusia, paraesthesia
Frequency unknown:	seizure

Eye disorders:

Frequency unknown:	blurred vision, increased lacrimation

Cardiac disorders:

Less frequent:	palpitations, tachycardia
Frequency unknown:	atrial fibrillation

Vascular disorders:

Less frequent:	flushing, hypertension

Respiratory, thoracic and mediastinal disorders:

Frequent:	hiccups, throat irritation
Less frequent:	bronchospasm, rhinorrhoea, dysphonia, dyspnoea, nasal congestion, oropharyngeal pain, sneezing, throat tightness

Gastrointestinal disorders:

Frequent:	nausea, abdominal pain, diarrhoea, dry mouth, dyspepsia, flatulence, salivary hypersecretion, stomatitis, vomiting
Less frequent:	eructation, gingivitis, glossitis, oral mucosal blistering and exfoliation, oral paraesthesia, dysphagia, oral hypoesthesia, retching
Frequency unknown:	dry throat, gastrointestinal discomfort, lip pain

Skin and subcutaneous tissue disorders:

Less frequent: hyperhidrosis, pruritus, rash, urticaria

Frequency unknown: erythema

General disorders and administration site conditions:

Frequent: burning sensation, fatigue

Less frequent: asthenia, chest discomfort and pain, malaise

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of NICORETTE® QUICKMIST is important. It allows continued monitoring of the benefit/risk balance of NICORETTE® QUICKMIST. Healthcare professionals are asked to report any suspected adverse reactions via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: http://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

When used as directed, symptoms of overdose with nicotine may occur in patients with low pre-treatment nicotine intake or if other sources of nicotine are used concomitantly.

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.

Paediatric population

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 an overdose

All nicotine intake should stop immediately, and the patient should be treated symptomatically. If excessive amount of nicotine is swallowed, activated charcoal reduces the gastrointestinal absorption of nicotine.

The acute minimum lethal oral dose of nicotine in man is believed to be 40 to 60 mg.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 32.16 Other.

Pharmacotherapeutic group: Drugs used in nicotine dependence.

ATC code: N07BA01.

Nicotine is an agonist at nicotine receptors in the peripheral and central nervous system and has pronounced CNS and cardiovascular effects.

Abrupt cessation of the established, regular use of tobacco-containing products results in the characteristic syndrome, with withdrawal symptoms including cravings (urges to smoke).

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

5.2 Pharmacokinetic properties

Variations in delivery format have been found to have significant effects on the rate and extent of absorption.

The pharmacokinetic properties of the oromucosal spray has been studied in 4 studies. The studies included 141 subjects.

Absorption

A maximum concentration of 5,3 ng/mL is reached within 13 minutes after administration of a 2 mg dose. Comparing the AUC over the first 10 minutes after administration the estimates of the oromucosal spray at a dose of 1 and 2 mg exceeds those of nicotine gum as well as nicotine lozenge at doses of 4 mg (0,48 and 0,64 h*ng/mL vs. 0,33 and 0,33 h*ng/mL).

AUC_{∞} estimates show the bioavailability of nicotine administered by oromucosal spray is similar to that of nicotine gum or lozenge. The AUC_{∞} of the oromucosal spray 2 mg measured 14,0 h*ng/mL in comparison with 23,0 h*ng/mL and 26,7 h*ng/mL for nicotine gum 4 mg and nicotine lozenge 4 mg, respectively.

Steady-state average nicotine plasma concentrations achieved after administration of the maximum dose (i.e. 2 sprays of the oromucosal spray 1 mg every 30 minutes) are in the order of magnitude approximately 28,8 ng/mL as compared with 23,3 ng/mL for nicotine gum 4 mg (1 gum, hourly) and 25,5 ng/mL for nicotine lozenge 4 mg (1 lozenge, hourly).

Distribution

The volume of distribution following intravenous administration of nicotine is about 2 to 3 L/kg.

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 any significant effects on the nicotine pharmacokinetics.

Biotransformation

The major nicotine-eliminating organ is the liver, although 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.

Elimination

The average plasma clearance of nicotine is 70 L/hour and the half-life is 2 – 3 hours.
The primary urinary metabolites are cotinine (12 % of the dose) and trans-3-hydroxy-cotinine (37 % 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.

Linearity/non-linearity

There is only a small deviation from dose-linearity of AUC_{∞} and C_{max} as shown when single doses of 1, 2, 3 and 4 sprays of the 1 mg oromucosal spray are given.

Renal impairment

Progressive severity of renal impairment is associated with decreased total clearance of nicotine. Nicotine clearance was on average decreased by 50 % in subjects with severe renal impairment. Raised nicotine levels have been seen in smokers undergoing haemodialysis.

Hepatic impairment

The pharmacokinetics of nicotine are unaffected in patients with mild liver impairment (Child-Pugh score 5) and decreased by 40 – 50 % in patients with moderate liver impairment (Child-Pugh score 7). There is no information available in subjects with a Child-Pugh score > 7.

Elderly

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

5.3 Preclinical safety data

In vitro genotoxicity testing of nicotine has yielded predominantly negative results. There are some equivocal results when testing at high nicotine concentrations.

In vivo tests of genotoxicity have been negative.

Animal experiments have shown that nicotine exposure results in decreased birthweight, decreased litter size and decreased survival of offspring.

Results of carcinogenicity assays do not provide any clear evidence of a tumorigenic effect of nicotine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol (E1520)

Anhydrous ethanol

Trometamol

Poloxamer 407

Glycerol (E422)

Sodium hydrogen carbonate

Levomenthol

Mint flavour

Cooling flavour

Sucralose

Acesulfame potassium

Butylated hydroxytoluene (E321)

Hydrochloric acid (for pH adjustment)

Purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store at or below 30 °C.

6.5 Nature and contents of container

Transparent polyethylene terephthalate (PET) bottle with 13,2 mL solution. One bottle contains 150 sprays of 1 mg. The bottle is placed in a dispenser with a mechanical spray pump with an actuator. The dispenser has a child resistant feature.

Pack sizes:

1 x 1 dispenser, 2 x 1 dispensers.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Johnson & Johnson (Pty) Ltd.

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8 REGISTRATION NUMBER

50/32.16/0547

9 DATE OF FIRST AUTHORISATION

24 July 2020.

10 DATE OF REVISION OF THE TEXT

22 January 2024.