NEW ZEALAND DATA SHEET

1 PRODUCT NAME

NICORETTE® Cooldrops Lozenge
2 mg, 4mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

NICORETTE® Cooldrops Lozenge 2mg contains as active ingredient Nicotine-resin complex 20% 10 mg equivalent to nicotine 2 mg.

NICORETTE® Cooldrops Lozenge 4mg contains as active ingredient Nicotine-resin complex 20% 20 mg equivalent to nicotine 4 mg.

NICORETTE® Cooldrops Lozenge also contains sucralose and mannitol.

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

3 PHARMACEUTICAL FORM

NICORETTE® Cooldrops Lozenge is an oval, white to off-white film-coated lozenge with a size of about 14 x 9 x 7 mm, imprinted with "n" on one side and “2” on the other side of the 2mg lozenge, and “4” on the other side of the 4mg lozenge.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of tobacco dependence by relieving nicotine craving and withdrawal symptoms thus:

Facilitating smoking cessation in smokers motivated to quit.

Helping smokers to temporarily abstain from smoking.

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.

The initial dosage should be individualised on the basis of the patient’s nicotine dependence. NICORETTE® Cooldrops Lozenge should be used when the urge to smoke is felt.

NICORETTE® Cooldrops Lozenges 2 mg are suitable for smokers with a low nicotine dependency e.g those smoking their first cigarette of the day more than 30 minutes after waking up, or those who smoke fewer than 20 cigarettes per day.

NICORETTE® Cooldrops Lozenges 4 mg are suitable for smokers with a high nicotine dependency e.g those smoking their first cigarette of the day within 30 minutes after waking up, or those who smoke more than 20 cigarettes per day.

Children and Adolescents

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

NICORETTE® Cooldrops Lozenge may be administered to persons under 18 years of age only under the supervision of a health care professional. There is limited experience of treating this age group with NICORETTE® Cooldrops Lozenge.

Adults and Elderly

For single use
Use the lozenge whenever there is an urge to smoke. The initial dosage should be individualised on the basis of the patient's nicotine dependence. Most smokers require 8 to 12 lozenges per day. Not more than 15 lozenges should be used in one day.

Smoking cessation
Use the lozenge for at least 3 months. Gradual weaning from the lozenge should then be initiated. Treatment should be stopped when the dose is reduced to 1-2 lozenges per day.

Regular use of the lozenge beyond 9 months is generally not recommended. Smokers who use lozenges beyond 9 months are recommended to seek additional help and advice from a healthcare professional.

Smoking reduction
Use the lozenge between smoking episodes whenever there is an urge to smoke, 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.

Some ex-smokers may need longer treatment with the lozenge to avoid returning to smoking. Any spare lozenges should be retained, as craving may suddenly occur.

Advice and support normally improve the success rate.

Temporary abstinence
Use the lozenge during smoke-free periods, for example in smoke-free areas or in other situations when you wish to avoid smoking, and there is an urge to smoke.

In combination with nicotine patch
Persons who have failed with single treatment or want to reduce the daily intake of the lozenge because of local adverse events, can use NICORETTE® 16hr INVISIPATCH® patches in addition to the 2 mg lozenge.

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® Cooldrops 2 mg Lozenge should be used as required when cravings occur.

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

- using the 15mg/16hr patch for 2 weeks, followed by the 10mg/16hr patch for 2 weeks, while maintaining the number of 2mg lozenges that have been routinely used; then gradually reducing the number of lozenges once the patch is no longer used; or
- stopping use of the 25mg/16hr patch, and then gradually reducing the number of lozenges until you no longer need them.

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

- using the 10mg/16hr patch for 4 weeks, while maintaining the number of 2mg lozenges that have been routinely used; then gradually reducing the number of lozenges once the patch is no longer used; or
- stopping use of the 15mg/16hr patch, and then gradually reducing the number of lozegnes until you no longer need them.

Do not use NICORETTE® Cooldrops 4 mg lozenge in combination with NICORETTE® *INVISIPATCH® Patch.*

NICORETTE® Combination Therapy is more effective than using either product alone in people who have been unable to quit smoking using a single NRT product.

NICORETTE® Combination Therapy should not be used by adolescents.

4.3 Contraindications

NICORETTE® Cooldrops is contraindicated in non-tobacco users.

NICORETTE® Cooldrops is contraindicated in patients with Hypersensitivity to nicotine or to any of the ingredients in this product.

NICORETTE® Cooldrops patch, as with other nicotine containing products should not be administered to children under 12 years of age.

4.4 Special warnings and precautions for use

The risk of using nicotine replacement therapy should be weighed against the risk of continued smoking.

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

Underlying cardiovascular disease
NICORETTE® Cooldrops Lozenge 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® Cooldrops Lozenge 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® Cooldrops Lozenge 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® Cooldrops Lozenge should be used with caution in patients with active duodenal, oesophagitis, gastric or peptic ulcers.

Phaeochromocytoma and uncontrolled hyperthyroidism
Nicotine, both from nicotine replacement products and smoking, causes the release of catecholamines from the adrenal medulla. Therefore NICORETTE® Cooldrops Lozenge should also be used with caution in patients with uncontrolled hyperthyroidism or pheochromocytoma.

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. 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® Cooldrops Lozenge after the recommended period, but the potential risk of longer term use is far less than those associated with resuming to smoking.

Paediatric use

NICORETTE® Cooldrops Lozenge 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.

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.

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.

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® Cooldrops Lozenge after consulting a health care professional. The risks for the foetus from NICORETTE® Cooldrops Lozenge 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® Cooldrops Lozenge should be used just after breast-feeding.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

NICORETTE® Cooldrops Lozenge may cause adverse reactions similar to those associated with nicotine administered by other means and are mainly 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 lozenge) 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. The risk of poisoning as a result of swallowing the lozenge is very small, as absorption in the absence of sucking is slow and incomplete.

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.

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

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

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 or reduce their smoking.

5.2 Pharmacokinetic properties

NICORETTE® Cooldrops Lozenge completely dissolves in the oral cavity, and the entire amount of nicotine contained in the lozenge becomes available for buccal absorption or ingestion (swallowing). Complete dissolution of NICORETTE® Cooldrops Lozenge is typically achieved in 16-19 minutes.

Concurrent consumption of liquids which lower pH in the mouth, such as coffee, juice and carbonated drinks, can drastically reduce the absorption of nicotine. The peak plasma concentration of nicotine achieved after a single dose is approximately 5 ng/ml for NICORETTE® Cooldrops Lozenge 2 mg and approximately 8 ng/ml for NICORETTE® Cooldrops Lozenge 4 mg. Ingestion of NICORETTE® Cooldrops Lozenge not following dosing instructions (chewed, retained in the mouth and swallowed; chewed and immediately swallowed) gives a slower and a somewhat reduced absorption of nicotine.

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

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.

Progressive severity of renal impairment is associated with decreased total clearance of nicotine. Raised nicotine levels have been seen in smoking patients undergoing hemodialysis. 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-pugh score 7). Raised nicotine levels have been seen in smoking patients undergoing haemodialysis.

5.3 Preclinical safety data

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

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 NICORETTE® Cooldrops Lozenge.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

NICORETTE® Cooldrops Lozenge 2 mg
mannitol
xanthan gum
anhydrous sodium carbonate
sucralose
acesulfame potassium
magnesium stearate
hypromellose
titanium dioxide
winterfresh flavour
polysorbate 80
sepifilm gloss

NICORETTE® Cooldrops Lozenge 4 mg
mannitol
xanthan gum
anhydrous sodium carbonate
sucralose
acesulfame potassium
magnesium stearate
hypromellose
titanium dioxide
winterfresh flavour
polysorbate 80
sepifilm gloss

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

NICORETTE® Cooldrops Lozenge 2 mg: polypropylene flip-pack dispenser containing 20 lozenges, in single packs (20 lozenges), packs of 4 dispensers (80 lozenges), packs of 6 dispensers (120 lozenges) and packs of 8 dispensers (160 lozenges).

NICORETTE® Cooldrops Lozenge 4 mg: polypropylene flip-pack dispenser containing 20 lozenges, in single packs (20 lozenges) and packs of 4 dispensers (80 lozenges).

6.6 Special precautions for disposal

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

7 MEDICINE SCHEDULE

General Sales Medicine

8 SPONSOR

Johnson & Johnson (New Zealand) Ltd
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P.O. Box 62-185, Sylvia Park
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9 DATE OF FIRST APPROVAL

06 December 2012

10 DATE OF REVISION OF THE TEXT

03 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