Summary of Product Characteristics

1. Name of the Medicinal Product
NOSMOK 2 mg
(Nicotine Lozenges 2 mg)

2. Qualitative and Quantitative Composition
Each lozenge contains:
Nicotine Polacrilex USP….10 mg
Equivalent to Nicotine……..2 mg
Sugar base…….q.s.

For a full list of excipients, see section 6.1

3. Pharmaceutical Form
Lozenge.

4. Clinical Particulars
4.1 Therapeutic indications
Stop smoking aid. As a temporary aid to those who want to stop smoking cigarettes or break the cigarette habit, when used as part of smoking cessation programme.
Reduces withdrawal symptoms, including nicotine craving, associated with quitting smoking.
The effectiveness of this product is directly related to your motivation to stop smoking.

4.2 Posology and method of administration
Smokers under 18 years of age, consult a doctor before use.
For NOSMOK (Nicotine Lozenges 2 mg):
Begin using the lozenge on quit day, if smoked first cigarette within 30 minutes of waking up, use 4 mg nicotine lozenge, if smoked first cigarette more than 30 minutes after waking up, use 2 mg nicotine lozenge according to the following 12-week schedule:

Weeks 1 to 6	Weeks 7 to 9	Weeks 10 to 12
1 lozenge every 1 to 2 hours	1 lozenge every 2 to 4 hours	1 lozenge every 4 to 8 hours

Nicotine lozenge is a medicine and must be used a certain way to get the best results. Place the lozenge in mouth and allow the lozenge to slowly dissolve (about 20 - 30 minutes). Minimize swallowing. Do not chew or swallow lozenge, may feel a warm or tingling sensation occasionally move the lozenge from one side of mouth to the other until completely dissolved (about 20-30 minutes), do not eat or drink 15 minutes before using or while the lozenge is in mouth to improve chances of quitting, use at least 9 lozenges per day for the first 6 weeks. Do not use more than one lozenge at a time or continuously use one lozenge after another, since this may cause hiccups, heartburn, nausea or other side effects. Do not use more than 5 lozenges in 6 hours. Do not use more than 20 lozenges per day. It is important to complete treatment. If former smoker feels need to use the lozenge for a longer period to keep from smoking, contact health care provider.

4.3 Contraindications

Hypersensitivity to any of components of the lozenge.

4.4 Special warnings and precautions for use

Any risks which may be associated with the use of NRT are substantially outweighed in virtually all circumstances by the well-established dangers of continued smoking.

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

Underlying cardiovascular disease: In stable cardiovascular disease this product presents a lesser hazard than continuing to smoke. However dependent smokers currently hospitalized as a result of myocardial infarction, unstable or worsening angina including Prinzmetal's angina, severe dysrhythmia or cerebrovascular accident and who are considered to be hemodynamically unstable and/or who have uncontrolled hypertension should be encouraged to stop smoking with non-pharmacological interventions. If this fails, this product 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 smoking is stopped and NRT is initiated as reductions in nicotine induced catecholamine release can affect carbohydrate metabolism.

Renal and hepatic impairment: Use 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.

Phaeochromocytoma and uncontrolled hyperthyroidism: Use with caution in patients with uncontrolled hyperthyroidism or phaeochromocytoma as nicotine causes release of catecholamines.

Gastrointestinal Disease: Nicotine may exacerbate symptoms in patients suffering from oesophagitis, gastric or peptic ulcers and NRT preparations should be used with caution in these conditions. Ulcerative stomatitis has been reported.

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.

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 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.

Choking hazard: Lozenges can represent a choking hazard, therefore keep out of the reach of children. Use with caution in individuals with aspiration and swallowing problems.

4.5 Interaction with other medicinal products and other forms of interaction

No clinically relevant interactions between nicotine replacement therapy and other drugs have 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.

4.6 Fertility, pregnancy and lactation

Fertility
In females tobacco smoking delays time to conception, decreases in-vitro fertilization success rates, and significantly increases the risk of infertility.
In males tobacco smoking reduces sperm production, increases oxidative stress, and DNA damage. Spermatozoa from smokers have reduced fertilizing capacity.
The specific contribution of nicotine to these effects in humans is unknown.

Pregnancy
Stopping smoking is the single most effective intervention for improving the health of both the pregnant smoker and her baby, and the earlier abstinence is achieved the better. Ideally smoking cessation during pregnancy should be achieved without NRT. Nicotine passes to the foetus and affects its breathing movements and circulation. The effect on the circulation is dose-dependent. However, if the mother cannot (or is considered unlikely to) quit without pharmacological support, NRT may be used as the risk to the foetus is lower than that expected with smoking tobacco. Stopping completely is by far the best option but if this is not achievable this product may be used in pregnancy as a safer alternative to smoking. Because of the potential for nicotine-free periods, intermittent dose forms are preferable, but patches may be necessary if there is significant nausea and/or vomiting. If patches are used they should, if possible, be removed at night when the foetus would not normally be exposed to nicotine.
Use of nicotine by the pregnant smoker should only be initiated after advice from a health care professional.

Lactation
Nicotine should be avoided during breast-feeding. The relatively small amounts of nicotine found in breast milk during NRT use are less hazardous to the infant than second-hand smoke. Intermittent dose forms would minimize the amount of nicotine in breast milk and permit feeding when levels were at their lowest.
Use of the nicotine by breast feeding smokers should only be initiated after advice from health care professional. Women should take the product as soon as possible after breastfeeding.

4.7 Effects on ability to drive and use machines
This product has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects
Effects of Smoking Cessation
Some symptoms may be related to nicotine withdrawal associated with stopping smoking. These can include: irritability/aggression, frustration/anger, dysphoria/depressed mood, anxiety, restlessness, poor concentration, increased appetite/weight gain, urges to smoke (cravings), night-time awakenings/sleep disturbance, decreased heart rate, dizziness, presyncopal symptoms, cough, constipation, gingival bleeding or nasopharyngitis.
Increased frequency of aphthous ulcer may occur after stopping smoking. The causality is unclear.
Adverse Drug Reactions
This product may cause adverse reactions similar to those associated with nicotine given by other means, including smoking, and these are mainly dose-dependent. At recommended doses this product has not been found to cause any serious adverse effects. Excessive consumption of this

product by those who have not been in the habit of inhaling tobacco smoke could possibly lead to nausea, faintness or headaches.
Most of the undesirable effects reported by the patient occur during the first 3-4 weeks after start of treatment. During the first few days of treatment irritation in the mouth and throat may be experienced. Most patients will get used to this sensation after the first few days.
Allergic reactions (including symptoms of anaphylaxis) can occur during the use of the product.
The adverse reactions observed in patients treated with oral nicotine formulations during clinical trials and post-marketing experience are listed below by system organ class (SOC). Frequencies are defined in accordance with current guidance as: Very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1 000, <1/100); rare (≥1/10 000, <1/1 000); very rare (<1/10 000); not known (cannot be estimated from the available data).

Body System	**Incidence**	**Reported adverse event (Preferred Term)**
Immune system disorders	Common	Hypersensitivity [a]
	Not known	Anaphylactic reaction [a]
Psychiatric disorders	Uncommon	Abnormal dreams*
Nervous system disorders	Very common	Headache[#]
	Common	Burning sensation [c]
	Common	Dizziness
	Common	Dysgeusia
	Common	Paraesthesia [a]
	Not known	Seizures
Eye disorders	Not known	Blurred vision
	Not known	Lacrimation increased
Cardiac disorders	Uncommon	Palpitations [a]
	Uncommon	Tachycardia [a]
	Very rare	Reversible atrial fibrillation
Vascular disorders	Uncommon	Flushing [a]
	Uncommon	Hypertension [a]
Respiratory, thoracic and mediastinal disorders	Common	Cough[**]
	Very common	Sore mouth or throat
	Very common	Throat irritation[**]
	Uncommon	Bronchospasm
	Uncommon	Dysphonia
	Uncommon	Dyspnoea [a]
	Uncommon	Nasal congestion
	Uncommon	Sneezing
	Uncommon	Throat tightness

Gastrointestinal disorders	Very Common	Hiccups****
	Very common	Nausea [a]
	Common	Abdominal pain
	Common	Diarrhoea***
	Common	Dry mouth
	Common	Dyspepsia
	Common	Flatulence
	Common	Salivary hypersecretion
	Common	Stomatitis
	Common	Vomiting [a]
	Uncommon	Eructation
	Uncommon	Glossitis
	Uncommon	Oral mucosal blistering and exfoliation
	Uncommon	Paraesthesia oral***
	Rare	Dysphagia
	Rare	Hypoaesthesia oral***
	Rare	Retching
	Not known	Dry throat
	Not known	Gastrointestinal discomfort [a]
	Not known	Lip pain
Musculoskeletal and connective tissue disorders	Uncommon	Pain in Jaw [b]
	Not known	Muscle tightness [b]
Skin and Subcutaneous Tissue Disorders	Uncommon	Hyperhidrosis [a]
	Uncommon	Pruritus [a]
	Uncommon	Rash [a]
	Uncommon	Urticaria [a]
	Not known	Erythema [a]
General disorders and administration site conditions	Common	Fatigue [a]
	Uncommon	Asthenia [a]
	Uncommon	Chest discomfort and pain [a]
	Uncommon	Malaise [a]
	Rare	Allergic reactions including angioedema

[a] Systemic effects; [b] Tightness of jaw and pain in jaw with nicotine gum formulation
[c] At the application site
*Identified only for formulations applied during the night
**Higher frequency observed in clinical studies with inhaler formulation.

***Reported the same or less frequently than placebo
****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.

4.9 Overdose

Symptoms: Symptoms of overdose with nicotine from this product may occur in smokers who have previously had a low nicotine intake from cigarettes or if other sources of nicotine are used concomitantly with this product.

Acute or chronic toxicity of nicotine in man is highly dependent on mode and route of administration. Adaptation to nicotine (e.g. in smokers) is known to significantly increase tolerability compared with non-smokers. The minimum lethal dose of nicotine in a non-tolerant man has been estimated to be 40 to 60 mg. Symptoms of acute nicotine poisoning include nausea, vomiting, increased salivation, abdominal pain, diarrhoea, sweating, headache, dizziness, disturbed hearing and marked weakness. In extreme cases, these symptoms may be followed by hypotension, rapid or weak or irregular pulse, breathing difficulties, prostration, circulatory collapse and terminal convulsions.

Management of an overdose: All nicotine intake should stop immediately and the patient should be treated symptomatically. Artificial respiration should be instituted if necessary. Activated charcoal reduces the gastro-intestinal absorption of nicotine.

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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drug used in nicotine dependence.

ATC code: N07B A01

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 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 is an important element in the withdrawal syndrome after smoking cessation.

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

Increased appetite is a recognized symptom of nicotine withdrawal and post-cessation weight gain is common. Clinical trials have demonstrated that Nicotine Replacement Therapy can help control weight following a quit attempt.

A bioequivalence study for NOSMOK (Nicotine Lozenges 2mg and 4mg) measured relief in urges to smoke (i.e. craving relief) at specified intervals after the start of study drug administration.

5.2 Pharmacokinetic properties

Absorption
A Nicotine 2 mg Lozenge dissolves completely, typically in 10-20 minutes. Assuming complete dissolution in the mouth, most of its nicotine is absorbed through the oral mucosa. This fraction is almost entirely delivered to the systemic circulation. The remaining nicotine released in the mouth is swallowed and undergoes considerable first-pass metabolism in the intestine and liver. As a consequence, only a small part of the total nicotine given with a lozenge reaches the circulation via the intestine.
A maximum nicotine plasma concentration of about 5 ng/mL is achieved after a single-dose of the NOSMOK (2mg Nicotine Lozenges), and about 8 ng/mL after a single-dose of the NOSMOK (2mg Nicotine Lozenges). Area under the time vs. plasma concentration curve extrapolated to infinity (AUC_{∞}) after a single-dose of a NOSMOK (2mg Nicotine Lozenges) is about 16 h*ng/mL, and about 31 h*ng/mL after a single-dose of a NOSMOK (2mg Nicotine Lozenges).

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 drugs or alterations of plasma proteins by disease states would not be expected to have any significant effects on the nicotine pharmacokinetics.

Biotransformation
The major 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 terminal half-life of 15 to 20 hours and concentrations that exceed nicotine by 10-fold.

Elimination
The average plasma clearance is about 70 l/h and the elimination half-life is approximately 2-3 hours.
The primary urinary metabolites are cotinine (12% of the dose) and trans-3-hydroxy-nicotinine (37% of the dose). About 10% of nicotine is excreted unchanged in the urine, but as much as 30% of nicotine may be excreted unchanged with high flow rates and acidification of the urine below pH 5.

Characteristics in specific groups of subjects
Renal Impairment
Progressive severity of renal impairment is associated with decreased total clearance of nicotine. Nicotine clearance was decreased by on average 50% in subjects with severe renal impairment. Raised nicotine levels have been seen in smoking subjects undergoing hemodialysis.

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

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

5.3 Preclinical safety data
Preclinical data indicate that nicotine is neither mutagenic nor genotoxic.
There are no other findings derived from preclinical testing of relevance to the prescriber in determining the safety of the product which have not been considered in other relevant sections of this Summary of Product Characteristics.

6. Pharmaceutical particulars

6.1 List of excipients
Citric Acid Monohydrate BP
Liquid Glucose BP
Sucrose BP
Colour BQ supra
Flavour Mentha Piperita
Purified Water BP

6.2 Incompatibilities
Not Applicable.

6.3 Shelf life
2 years

6.4 Special precautions for storage
Store below 30°C in a dry place. Keep out of reach of children.

6.5 Nature and contents of container
ALU-PVC blister of 12 lozenges.

6.6 Special precautions for disposal and other handling
Not Applicable

7. Marketing Authorization Holder
UNIQUE PHARMACEUTICAL LABORATORIES
(A Div. of J. B. Chemicals and Pharmaceuticals Ltd.)
Neelam Centre, B wing, 4th Floor, Hind Cycle Road, Worli Mumbai - 400 030

8. Marketing Authorization Number
05125/3926/NMR/2017

9. Date of First Authorization/Renewal of the Authorization
Date of First Authorization: 20/04/2020
10. Date of revision of the text
27/07/2023