SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Zonnic Mint 2 mg lozenges
Zonnic Mint 4 mg lozenges

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2 mg: Each lozenge contains nicotine ditartrate dihydrate equivalent to 2 mg nicotine.
4 mg: Each lozenge contains nicotine ditartrate dihydrate equivalent to 4 mg nicotine.

Excipients with known effect:
2 mg: isomalt 1913 mg, maltitol 368 mg
4 mg: isomalt 1904 mg, maltitol 368 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Lozenge

Blue, round with an arc shaped imprint, approx.19x7 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Zonnic Mint is indicated for the treatment of tobacco dependence by relieving nicotine craving and withdrawal symptoms, thereby facilitating smoking cessation in smokers motivated to quit or to facilitate smoking reduction in smokers who are not able or willing to quit.
If possible, when stopping smoking, Zonnic Mint should be used in conjunction with a behavioural support program.

4.2 Posology and method of administration

Posology
Adults and elderly
The initial dosage should be individualised on the basis of the nicotine dependence. Smokers with lower dependence for example those smoking their first cigarette in the day more than 30 min after awakening should use the 2 mg lozenge. Higher dependent smokers or those who have still experienced an urge to smoke using the 2 mg lozenge, should use the 4 mg strength.

Initially one lozenge can be taken every 1-2 hours. The usual dosage is 8-12 lozenges a day. The maximum daily dose is 15 lozenges for 4 mg strength and 24 lozenges for 2 mg strength.

Smoking cessation
The duration of treatment is individual. Normally, the treatment should continue for at least 3 months. Gradually weaning from the lozenges should then be initiated. Treatment should be discontinued when the dose is reduced to 1-2 lozenges per day. Regular use of Zonnic Mint for more than six months is generally not recommended. In some cases a longer treatment period might be necessary in order to avoid relapse. Any spare lozenges should be retained, as craving may suddenly occur.

Smoking reduction
Zonnic Mint is used between periods of smoking in order to extend the smoke-free intervals and to reduce smoking as much as possible. Professional help should be consulted if a decrease in number of cigarettes has not been achieved after 6 weeks of treatment.

An attempt to quit smoking should be made as soon as the smoker is motivated, however no later than 6 months after treatment start. Professional help should be consulted if there is no possibility to perform a serious attempt to quit smoking within 9 months. Regular use of Zonnic Mint for more than 1 year is generally not recommended. Some ex-smokers may need treatment with the lozenge for a longer period in order to avoid relapse. Any spare lozenges should be retained, as craving may suddenly occur.

Paediatric population
Zonnic Mint is contraindicated for use in children below 12 years of age due to lack of data on safety and efficacy.
Zonnic Mint Lozenges should only be used in adolescents (12-17 years) with advice from a physician.

Method of administration
Place the lozenge in the mouth and let it dissolve. Occasionally move the lozenge from one side to the other until it completely dissolves (approx. 10-15 minutes). The lozenges should not be chewed or swallowed. Users should not eat or drink while using lozenges. Drinks, which lower the pH in the mouth, e.g. coffee, fruit juice or sodas, may reduce the buccal absorption of nicotine. To achieve the maximum absorption of nicotine, these drinks should be avoided up to 15 minutes prior to using the lozenge.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Children below 12 years
Non-smokers

4.4 Special warnings and precautions for use

Zonnic Mint should be used with caution in patients with recent myocardial infarction (within 3 months), unstable and progressive angina pectoris, Prinzmetal's variant angina, severe cardiac arrhythmia, stroke in acute phase., severe cardiovascular diseases (e.g. occlusive peripheral arterial disease, cerebrovascular disease, stable angina pectoris and uncompensated heart failure), vasospasm, uncontrolled hypertension, severe/moderate hepatic impairment, severe renal impairment, active duodenal- and gastric ulcers. The risk with continuing smoking is always a greater danger than the usage of Zonnic Mint.

If the lozenge is swallowed the symptoms may get worse for patients suffering from active easofagit, oral or pharyngeal inflammation or gastritis.

Nicotine both from nicotine replacement therapy and smoking, cause release of catecholamines from adrenal medulla. Therefore Zonnic Mint should also be used with caution in patients with hyperthyroidism or phaeochromocytoma.

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

Contains isomalt and maltitol. Patients with rare hereditary of fructose intolerance should not take this medicine. May generally also have a mild laxative effect.

Continued nicotine dependence may occur but to a lower extent. The use of nicotine itself is however less harmful than smoking/use of tobacco.

4.5 Interaction with other medicinal products and other forms of interaction

Smoking, (but not nicotine), is associated with increased activity of CYP1A2. After smoking cessation, reduced clearance of substrates for this enzyme may occur. This may lead to an increase in plasma levels for some medicinal products. The increase may have a 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. Data to support this are although 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

Pregnancy
Smoking during pregnancy is associated with risks such as intra-uterine growth retardation, premature birth or stillbirth, which seem to be correlated with the quantity of cigarettes smoked and the period of pregnancy, since such effects are observed when smoking is continued in the third trimester. Stopping smoking is the single most effective intervention for improving the health of both pregnant smoker and her baby and most important is to achieve stopping smoking before the first trimester of pregnancy. 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. Use of Zonnic Mint by the pregnant smoker should only be initiated after advice from ahealthcare professional.

Breast-feeding
Nicotine passes freely into breast milk in quantities that may affect the child even with therapeutic doses. Zonnic Mint should therefore be avoided during breastfeeding.
Should smoking withdrawal not be achieved, use of Zonnic Mint by breast-feeding smokers should only be initiated after advice from ahealthcare professional. Where nicotine replacement therapy is used whilst breastfeeding, Zonnic Mint should be taken just after breastfeeding and not during the two hours before breastfeeding.

Fertility
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.

4.7 Effects on ability to drive and use machines

Zonnic Mint has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Zonnic Mint may cause adverse reactions similar to those associated with nicotine administered by other means and are dose dependent. Most of undesirable effects reported by the patient usually occur during the first 3-4 weeks after treatment start. Effects of nicotine lozenges are mainly due to incorrect usage technique or due to the pharmacological effects of nicotine, which are dose dependent.

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	**Undesirable effects**
Nervous system disorders	
Common	Dizziness, headache
Cardiac disorders	
Uncommon	Palpitations
Rare	Atrial fibrillation
Skin and subcutaneous tissue disorders	
Uncommon	Erythema, hives
Gastrointestinal disorders	
Common	Gastrointestinal discomfort, hiccups, nausea, vomiting.
General disorders and administration site conditions	
Common	Irritated mouth or throat
Rare	Allergic reaction such as e.g. angio-oedema

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

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in
[To be completed nationally]

4.9 Overdose

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in nicotine dependence

ATC code: N07BA01

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 by relieving these withdrawal symptoms.
Six week smoking cessation rates for Nicotine Lozenge 2 mg were 46.0% and 29.7% in active and placebo groups respectively. Rates at six months were 24.2% and 14.4 % in active and placebo groups respectively. Odds ratios, adjusted for centre effects, at six weeks and six months were calculated as 2.10 and 1.96 respectively.
Six week smoking cessation rates for Nicotine Mint Lozenge 4 mg were 48.7% and 20.8% in active and placebo groups respectively. Rates at six months were 23.6% and 10.2 % in active and placebo groups respectively. Odds ratios, adjusted for centre effects, at six weeks and six months were calculated as 3.69 and 2.76 respectively.

5.2 Pharmacokinetic properties

Absorption
Zonnic Mint Lozenges dissolve completely 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 Zonnic Mint Lozenges is typically achieved in 10-15 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 of nicotine 4 mg lozenges is approximately 10.8 ng/ml. When dosed every 1.5 hours, the steady state peak and trough concentrations are 26.0 and 19.7 ng/ml respectively. Ingestion of Zonnic Mint Lozenges not following dosing instruction (chewed, retained in the mouth and swallowed; chewed and immediately swallowed) gives a slower and a somewhat reduced absorption of nicotine.

Distribution
The volume of distribution following i.v. administration of nicotine is about (2-) 3l/kg and its half-life is about 2 hours. Other diseases or concomitant use of other drugs which influence levels of plasma proteins are not expected to have any significant effect on kinetics of nicotine.

Biotransformation
Nicotine is metabolized mainly in the liver and plasma clearance is in average about 70 l/ hour. Nicotine is metabolized also in kidneys and lungs. More than 20 metabolites are identified whereof all are believed to be less active than nicotine. The primary metabolite of nicotine is cotinine which has a half-life of 15-20 hours and which give plasma concentrations that exceed nicotine by 10-fold. Plasma protein binding is less than 5 %.

Elimination
The major metabolites in urine are cotinine (15 % of the dose) and trans-3-hydroxycotinin (45% of the dose). About 10% of nicotine is excreted unchanged in the urine. As much as 30% of nicotine may be excreted in the urine at increased diuresis and acidification of the urine below pH 5.

Special populations
Heavily impaired kidney function is assumed to exert influence on total clearance of nicotine.

The pharmacokinetics of nicotine is unaffected in cirrhotic patients with mild liver impairment (Child score 5) and decreased in liver cirrhosis patients with moderately liver impairment (Child score 7). Increased nicotine levels have been observed in smoking haemodialysis patients.

Minor reduction of total clearance of nicotine has been demonstrated in healthy, elderly users, however, adjusting of the dose is not necessary.

No differences in nicotine kinetics have been observed between males and females.

5.3 Preclinical safety data

The general toxicity of nicotine is well known and has been considered in the dosing recommendation.
Nicotine was positive in some *in vitro* genotoxicity tests but there are also negative results with the same test systems. Nicotine was negative in *in vivo* tests.
Animal experiments have shown that nicotine induces post-implantation loss and reduces the growth of foetuses.
The results of carcinogenicity assays did not provide any clear evidence of a tumorigenic effect of nicotine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

2 mg and 4 mg:
Isomalt (E 953)
Maltitol liquid (E965)
Sodium carbonate anhydrous
Mint flavour
Brilliant Blue FCF (E133)
Acesulfame potassium (E950)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store in the original package. Sensitive to light.

This medicinal product does not require any special temperature storage conditions.

6.5 Nature and contents of container

Blister of aluminium/PVC/PVdC in cardboard boxes containing 12, 24, 72 or 144 lozenges.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Niconovum AB
Box 31008
SE-200 49 Malmö
Sweden

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

2021-06-04