

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Zonnic Mint 2 mg oromucosal pouch.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One pouch contains 2 mg nicotine.

Excipient with known effect: aspartame (E 951)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oromucosal pouch

Rectangular, powder filled pouch.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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 smoking.

4.2 Posology and method of administration

Posology

The patient should not eat or drink while using the pouch. 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 pouch.

One pouch is placed under the upper lip for 30 minutes. In order to increase the release of nicotine the pouch can occasionally be moved around with the tongue.

Adults and elderly

Initially one pouch can be taken every 1-2 hours. The usual dosage is 8-12 pouches a day. The maximum daily dose is 24 pouches.

Paediatric population

Zonnic Mint oromucosal pouch should not be administered to adolescents below 18 years of age without recommendations from a physician.

There is no experience in treating adolescents below 18 years of age with Zonnic Mint oromucosal pouch.

Smoking cessation

The duration of treatment is individual. Normally, the treatment should continue for at least 3 months.

Gradually weaning from the pouches should then be initiated. Treatment should be discontinued when the dose is reduced to 1-2 pouches per day. Regular use of Zonnic Mint oromucosal pouch for more than one year is generally not recommended. In some cases a longer treatment period might be necessary in order to avoid relapse. Any spare pouches should be retained, as craving may suddenly occur.

Counselling may help smokers to quit.

Smoking reduction

Zonnic Mint oromucosal pouch is used between periods of smoking in order to extend the smoking – free intervals and with regard 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 oromucosal pouch for more than 1 year is generally not recommended. Some ex- smokers may need treatment with the pouch for a longer period in order to avoid relapse. Any spare pouches should be retained, as craving may suddenly occur.

Renal and hepatic impairment

See section 4.4

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Recent myocardial infarction (within 3 months).

Unstable and progressive angina pectoris.

Prinzmetal's variant angina.

Severe cardiac arrhythmia.

Stroke in acute phase.

4.4 Special warnings and precautions for use

Zonnic Mint should be used with caution in patients with 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.

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.

Contains a source of phenylalanine. May be harmful for people with phenylketonuria.

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

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 highly dependent smoker should only be initiated after advice from a physician.

Breastfeeding

Nicotine passes freely into breast milk in quantities that may affect the child even with therapeutic doses. Zonnic Mint should therefore be avoided during breast-feeding.

Should smoking withdrawal not be achieved, use of Zonnic Mint by breast feeding smokers should only be initiated after advice from a physician. Where nicotine replacement therapy is used whilst breast-feeding, Zonnic Mint should be taken just after breastfeeding and not during the two hours before breastfeeding.

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.

Very common ($\geq 1/10$); common ($\geq 1/100$, $< 1/10$); uncommon ($\geq 1/1\ 000$, $< 1/100$); rare ($\geq 1/10\ 000$, $< 1/1\ 000$); 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 sleeplessness 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.

5.2 Pharmacokinetic properties

Absorption

The amount of released nicotine being absorbed from a nicotine pouch depends on the amount of nicotine released in the oral cavity and the amount thereof that is swallowed. The main part of nicotine released is absorbed through the buccal mucosa. The systemic bioavailability of swallowed nicotine is lower due to first- passage elimination. The high and rapidly rising nicotine concentrations observed after smoking are rarely produced by treatment with the pouch.

In normal case approximately 1.5 mg of nicotine is released from a 2 mg pouch. Maximal blood concentration is achieved after 30 minutes of use and is then comparable to the concentration, appearing 20-30 minutes after smoking a cigarette (medium strength).

Distribution

The volume of distribution following i.v. administration of nicotine is about (2-) 3 l/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-hydroxycotinine (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

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

Cellulose, microcrystalline
Mint flavour
Ascorbyl palmitate (E 304)
Trisodium phosphate
Acesulfame potassium (E 950)
Aspartame (E 951)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

20 pouches in a child resistant plastic jar with screw cap (polypropylene) in an outer aluminium bag.
20 pouches in a child resistant plastic jar with screw cap (polypropylene).

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)

To be completed nationally.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 2012-04-18
Date of latest renewal: 2017-04-18

10. DATE OF REVISION OF THE TEXT

2022-03-04