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NICOMILD - 2

Summary of Product Characteristics

1. Name of the medicinal product

NICOMILD - 2

2. Qualitative and quantitative composition

Each Chewing gum contains 2 mg nicotine.

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Chewing gum; Yellowish white, rectangular and plain on both sides

4. Clinical particulars

4.1 Therapeutic indications

NICOMILD - 2 relieves and/or prevents craving and nicotine withdrawal symptoms associated with tobacco dependence. It is indicated to aid smokers wishing to quit or reduce prior to quitting, to assist smokers who are unwilling or unable to smoke, and as a safer alternative to smoking for smokers and those around them.

4.2 Posology and method of administration

Adults and Children over 12 years of age

NICOMILD-2 should be chewed slowly according to the instructions.

The strength of gum to be used will depend on the smoking habits of the individual. In general, if the patient smokes 20 or less cigarettes a day, 2mg nicotine gum is indicated. If more than 20 cigarettes per day are smoked, 4mg nicotine gum will be needed to meet the withdrawal of the high serum nicotine levels from heavy smoking.

NICOMILD - 2 should be used whenever the urge to smoke is felt or to prevent cravings in situations where these are likely to occur.

Smokers willing or able to stop smoking immediately should initially replace all their cigarettes with the Gum and as soon as they are able, reduce the number of gums used until they have stopped completely.

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Smokers aiming to reduce cigarettes should use NICOMILD - 2, as needed, between smoking episodes to prolong smoke-free intervals and with the intention to reduce smoking as much as possible.

As soon as they are ready smokers should aim to quit smoking completely.

Maximum daily dose: 15 pieces per day.

When making a quit attempt behavioral therapy, advice and support will normally improve the success rate. Those who have quit smoking, but are having difficulty discontinuing NICOMILD - 2 are recommended to contact their pharmacist or doctor for advice.

For those using the 4mg gum, switching to the 2mg gum may be helpful when stopping treatment or reducing the number of gums used each day.

The chewing gums should be used whenever there is an urge to smoke according to the "chew and rest" technique described on the pack. After about 30 minutes of such use, the gum will be exhausted. Absorption of nicotine is through the buccal mucosa, any nicotine which is swallowed being destroyed by the liver.

4.3 Contraindications

Hypersensitivity to nicotine or any component of the chewing gum.
NICOMILD - 2 is contraindicated in children under the age of 12 years.

4.4 Special warnings and precautions for use

Any risks that may be associated with NRT are substantially outweighed 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 CVA and who are considered to be hemodynamically unstable and/or who suffer with 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.

GI disease: Nicotine may exacerbate symptoms in patients suffering from esophagitis, gastritis 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.

Renal or hepatic impairment: This product 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.

Danger in children: Doses of nicotine tolerated by adult and adolescent smokers can produce severe toxicity in children that may be fatal. Products containing nicotine should not be left where they may be misused, handled or ingested by children. Nicotine gum should be disposed of with care.

Phaeochromocytoma and uncontrolled hyperthyroidism: As nicotine causes release of catecholamines, this product should be used with caution in patients with uncontrolled hyperthyroidism or phaeochromocytoma.

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 metabolized 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.

Denture warning: Smokers who wear dentures may experience difficulty in chewing this product. The chewing gum may stick to, and may in rare cases damage dentures.

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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 hemodynamic 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

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 fetus 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 fetus 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 fetus 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 a health care professional. Women should take the product as soon as possible after breastfeeding.

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.

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, 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 abstinence from 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. Most of the undesirable effects reported by the patients occur during the first 3-4 weeks after start of treatment.

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. Excessive swallowing of dissolved nicotine may, at first, cause hiccupping.

Nicotine from the gum may sometimes cause a slight irritation of the throat at the start of treatment however most subjects adapt to this with ongoing use. This product may also cause increased salivation.

Allergic reactions (including symptoms of anaphylaxis) can occur during the use of the product.

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Those who are prone to indigestion may suffer initially from minor degrees of indigestion or heartburn if the 4mg nicotine gum is used; slower chewing and the use of the 2mg nicotine gum (if necessary, more frequently) will usually overcome this problem.

The chewing gum may stick to, and may in rare cases damage dentures.

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, <1/1000); very rare (<1/10 000), Not known - cannot be estimated from the available data.

System Organ Class	Reported Adverse Event	Incidence
Immune System Disorders	Hypersensitivity[a]	Common
	Anaphylactic reaction[a]	Not known
Psychiatric disorders	Abnormal dreams*	Uncommon
Nervous System Disorders	Headache[a#]	Very Common
	Burning sensation[c]	Common
	Dizziness	Common
	Dysgeusia	Common
	Paraesthesia[a]	Common
	Seizures	Not known
Eye Disorders	Blurred Vision	Not known
	Lacrimation increased	Not known
Cardiac Disorders	Palpitations[a]	Uncommon
	Tachycardia[a]	Uncommon
	Reversible atrial fibrillation	Very Rare
Vascular Disorders	Flushing[a]	Uncommon
	Hypertension[a]	Uncommon
Respiratory, Thoracic and Mediastinal Disorders	Cough**	Common
	Throat irritation**	Very common
	Bronchospasm	Uncommon
	Dysphonia	Uncommon
	Dyspnoea[a]	Uncommon
	Nasal Congestion	Uncommon

	Sneezing	Uncommon
	Throat tightness	Uncommon
Gastrointestinal Disorders	Nausea[a]	Very Common
	Hiccups****	Very Common
	Abdominal pain	Common
	Diarrhea***	Common
	Dry mouth	Common
	Flatulence	Common
	Salivary hypersecretion	Common
	Stomatitis	Common
	Vomiting[a]	Common
	Dyspepsia	Common
	Eructation	Uncommon
	Glossitis	Uncommon
	Oral mucosal blistering and exfoliation	Uncommon
	Paresthesia oral***	Uncommon
	Dysphagia	Rare
	Hypoesthesia oral***	Rare
	Retching	Rare
	Dry throat	Not known
	Gastrointestinal discomfort[a]	Not known
	Lip pain	Not known
Skin and Subcutaneous Tissue Disorders	Urticaria[a]	Uncommon
	Hyperhidrosis[a]	Uncommon
	Pruritus[a]	Uncommon
	Rash[a]	Uncommon
	Erythema[a]	Not known
Musculoskeletal and Connective Tissue Disorders	Pain in jaw[b]	Uncommon
	Muscle tightness[b]	Not known
General Disorders and Administration Site Conditions	Fatigue[a]	Common
	Asthenia[a]	Uncommon
	Chest discomfort and pain[a]	Uncommon

	Malaise[a]	Uncommon
	Allergic reactions including angioedema	Rare

[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 60mg. 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.

The risk of poisoning as a result of swallowing the gum is very small, as absorption in the absence of chewing is slow and incomplete.

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: Drugs used in nicotine dependence

ATC code: N07B A01

The pharmacological effects of nicotine are well documented. Those resulting from chewing NICOMILD - 2 are comparatively small. The response at any one time represents a summation of stimulant and depressant actions from direct, reflex and chemical mediator influences on several organs. The main pharmacological actions are central stimulation and/or depression; transient hyperpnoea; peripheral vasoconstriction (usually associated with a rise in systolic pressure); suppression of appetite and stimulation of peristalsis.

Increased appetite is a recognised 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.

5.2 Pharmacokinetic properties

Nicotine administered in chewing gums is readily absorbed from the buccal mucous membranes. Demonstrable blood levels are obtained within 5 – 7 minutes and reach a maximum about 30 minutes after the start of chewing. Blood levels are roughly proportional to the amount of nicotine chewed and have been shown never to exceed those obtained from smoking cigarettes.

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

Gum Base
Sucrose
Liquid Glucose
Hydrogenated Vegetable Oil
Menthol
Peppermint Oil
Sodium Carbonate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Tentative 2 years

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

Blister pack of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 and 15 pieces packed/unpack in small paper box of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 24, 25, 30, 40, 50 packs and packed in large paper box of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 24, 25, 27, 28, 30, 40, 50, 100 packs/small paper boxes.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Dispose of NICOMILD - 2 sensibly.

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

7. Marketing authorization holder

Millimed Co., Ltd.
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8. Marketing authorization number(s)

1A 427/49

9. Date of first authorization/renewal of the authorization

28th December 2006

10. Date of revision of the text

18th June 2024