

Data Sheet

NICORETTE® Inhaler

Nicotine 10 mg

Presentation

Nicotine for inhalation.

Excipients: Levomenthol and porous plug.

Uses

Actions

Pharmacotherapeutic group: 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 smoking.

Pharmacokinetics

Pharmacokinetic properties of NICORETTE® Inhaler

The major fraction of the nicotine in NICORETTE® Inhaler is deposited in the oral cavity. Continuous, rapid inhalations over 20 minutes release up to about 4mg of the nicotine from each cartridge and about 50% of the released nicotine is systemically available, i.e about 2mg. Absorption of nicotine through the buccal mucosa is slow and does not produce the high and rapid nicotine plasma concentrations seen with cigarette smoking. Self-administration (ad lib. at clinical use) typically produces nicotine plasma levels of 6-8ng/ml, which are only about 1/3 of those achieved with cigarette smoking. The plasma levels following clinical use correspond to once hourly chewing of NICORETTE® chewing gum 2mg and once hourly use of NICORETTE® Nasal Spray. Maximal plasma concentrations are reached within 15 minutes after the end of inhalation.

Steady state plasma levels of approximately 20ng/ml are achieved with continuous, rapid inhalations during 20 minutes per hour, 1 fresh cartridge

each hour, for 11 hours at ambient room temperature in a laboratory setting. The release of nicotine from the NICORETTE[®] Inhaler is temperature dependent resulting in an increase of the biologically available dose at increasing temperatures as compared to that at 25°C. Corresponding plasma levels at 30°C and 40°C will be 25 and 30 ng/ml, respectively.

General pharmacokinetic properties of NICORETTE[®] Inhaler

The volume of distribution following i.v. administration of nicotine is approximately 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 significant effects on nicotine kinetics.

The average plasma clearance following intravenous administration of nicotine is about 70L/hour and the terminal half-life approximately 2 hours. The major eliminating organ is the liver, but the kidney and lung also metabolize nicotine. There is no significant skin metabolism of 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 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-hydroxycotinine (45% of the dose). About 10% of nicotine is excreted unchanged in the urine, but as much as 30% may be excreted unchanged in the urine with high flow rates and acidification of the urine below pH 5.

The therapeutic blood concentrations of nicotine i.e. the levels that relieve craving are individual based upon the patient's nicotine dependence. Progressive severity of renal impairment is associated with decreased total clearance of nicotine. Raised nicotine levels have been seen in smoking patients undergoing haemodialysis. The pharmacokinetics of nicotine is unaffected in cirrhotic patients with mild liver impairment (Child score 5) but a slightly decreased clearance of nicotine has been observed in cirrhotic patients with moderate liver impairment (Child score 7). A minor reduction in total clearance of nicotine has been demonstrated in healthy elderly patients, however not justifying adjustment of dosage.

Pharmacokinetic properties of the combination of NICORETTE[®] patch and NICORETTE[®] Inhaler

The plasma levels of nicotine when combining one 15 mg/16 hour patch and 10 mg inhaler, will depend on the number of inhaler cartridges used and the dosing interval.

A simulation of plasma concentrations shows that if one 15 mg/ 16 hour patch is applied in the morning and four to five 10 mg inhaler cartridges are evenly distributed over the awake hours according to the recommended dosage, a maximum plasma level of about 17 - 19 ng/mL will be reached. The simulation is based on nicotine pharmacokinetics upon separate use of the 15 mg/16 hour patch and 10 mg inhaler, respectively.

Indications

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

- facilitating smoking cessation in smokers motivated to quit,
 - helping smokers to temporarily abstain from smoking or
 - facilitating smoking reduction in smokers unable or unwilling to quit
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Dosage and Administration

Could be used as a single treatment or in combination with nicotine patch.

Children and Adolescents

NICORETTE[®] Inhaler should not be administered to individuals under 18 years of age without recommendation from a physician. There is no experience of treating adolescents under the age of 18 with NICORETTE[®] Inhaler.

Adults and Elderly

For single use

NICORETTE[®] Inhaler should be used whenever there is an urge to smoke. The more the subject is able to use it, the easier it will be to stay smoke-free. NICORETTE[®] Inhaler can be used in the same way as a cigarette. The dose of nicotine from a puff of the inhaler is much less than that of a cigarette. Therefore, the subject needs to use the inhaler for longer periods than when smoking to control the cravings. Each cartridge should be used for approximately 20 minutes per session and with twice as many puffs as on a cigarette. Used like this each inhaler will last for approximately 4 sessions. For best results 6-12 cartridges should be used per day. Less than 6 cartridges per day may fail to help control the cravings.

Recommended dosage:

Number of cigarettes smoked per day	Recommended number of cartridges per day
1 - 24	6
25 - 32	8
33 - 40	10
More than 40	12

One cartridge can replace 4 cigarettes. The level of nicotine received from the inhaler depends on temperature. In colder temperatures the inhaler has to be used longer to achieve the same effect.

Smoking cessation

It is important that the treatment period is long enough. Normally the initial treatment period is 3 months. After that, the number of cartridges should be gradually reduced during 6-8 weeks to wean off.

Any spare cartridges should be retained, as craving may suddenly occur. Open cartridges should be used within 12 hours.

Smoking reduction

Use the inhaler between smoking episodes 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.

Regular use of the inhaler beyond 12 months is generally not recommended.

Advice and support normally improve the success rate.

Temporary abstinence

Use the inhaler during smoke-free periods, for example in smoke-free areas or in other situations when you wish to avoid smoking.

In combination with nicotine patch

Persons who have failed with single treatment or want to reduce the daily use of inhaler cartridges because of local adverse events, can use nicotine patches in addition to the inhaler.

Initial treatment:

The treatment should begin with one 15 mg/16 hour patch daily, applied to an intact area of the skin upon waking up in the morning and removed at bedtime, combined with the 10mg inhaler. Usually 4 - 5 inhaler cartridges per day will be adequate for effect. Do not use more than 12 cartridges per day. This full dose should be used for 6 - 12 weeks whereafter gradual weaning from the products should be initiated.

Weaning from combination:

This can be done in two ways, either by using lower strength patches i.e. 3 - 6 weeks on 10 mg/16 hour patches and then 3 - 6 weeks on 5 mg/16 hour patches, using the same amount of the inhaler cartridges as the initial treatment period, and then gradually reducing the inhaler use up to 12 months. Alternatively stop using the patch and gradually reduce the number of inhaler cartridges used up to 12 months.

Recommended dosage:

Initial treatment		
Time period	Patch	Inhaler 10 mg
First 6 - 12 weeks	1 patch 15 mg/16 hour per day	Ad libitum Recommended 4 - 5 cartridges per day
Weaning - alternative 1		
Next 3 - 6 weeks	1 patch 10 mg/16 hour per day	Continue to use cartridges as needed
Following 3 - 6 weeks	1 patch 5 mg/16 hour per day	Continue to use cartridges as needed.
Up to 12 months		Gradually wean from inhaler use
Weaning - alternative 2		
Up to 12 months	-----	Continue to gradually wean from inhaler use

Contraindications

Hypersensitivity to nicotine or any other component of the inhaler.

Warnings and Precautions

NICORETTE® Inhaler 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.

NICORETTE® Inhaler should be used with caution in patients with severe or moderate hepatic impairment, severe renal impairment, active duodenal and gastric ulcers, chronic throat diseases and bronchospastic disease.

Nicotine, both from Nicotine Replacement Therapy and smoking, causes the release of catecholamines from the adrenal medulla. Therefore NICORETTE® Inhaler should also be used with caution in patients with hypothyroidism or pheochromocytoma.

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

Some users may continue to use NICORETTE® Inhaler after the recommended treatment period but the potential risk of longer-term use is far less than those associated with resuming to smoking.

If a child swallows, chews or sucks on the nicotine plug, (used as well as unused) there is a risk of poisoning the child.

Special warnings and precautions for the combination of nicotine patch with NICORETTE[®] Inhaler are the same as those for each treatment alone.

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

Effects on ability to drive and use machines

NICORETTE[®] Inhaler has no or negligible influence on the ability to drive and use machines.

Adverse Effects

NICORETTE[®] Inhaler may cause adverse reactions similar to those associated with nicotine administered by other means and are dose-dependent.

About 40% of the users experienced mild local reactions such as cough and irritation in the mouth and throat. Most of the undesirable effects reported by the patient occur during the first weeks after start of the treatment.

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.

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), including isolated reports.

Nervous system disorders:	Very common:	Headache
	Common:	Dizziness
Cardiac disorders:	Uncommon:	Palpitations
	Very rare:	Reversible atrial fibrillation
Respiratory, thoracic and mediastinal disorders:	Very common:	Coughing
Gastrointestinal disorders:	Common:	Gastrointestinal discomfort, hiccups, nausea, vomiting
General disorders and administration site disorders:	Very common:	Irritation in mouth and throat
	Common:	Nasal congestion

Adverse reactions that may occur when using the combination treatment (patch and inhaler) 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.

Interactions

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 pentazocaine may also be induced by smoking.

Overdosage

Excessive use of nicotine from either Nicotine Replacement Therapy and/or smoking might cause symptoms of an overdose.

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.

Management of overdose

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

Pharmaceutical Precautions

Instructions for Use/Handling

After removing the mouthpiece and the sealed tray from the box the mouthpiece is separated into two parts and the seal is removed from the tray.

One sealed unit (tube containing a nicotine plug) is removed from the tray and inserted into the mouthpiece. The tray with remaining units is returned to the box.

When the mouthpiece is re-assembled the seal on both ends of the unit are broken.

As air is inhaled the nicotine is vaporised and absorbed in the mouth.

After use the unit is removed from the mouthpiece and disposed of in a safe way out of reach of children and pets. The mouthpiece should be stored in the box for further use.

Shelf Life

36 months from the date of manufacture.

Special Precautions for Storage

Store at or below 25°C.

Medicine Classification

General Sale Medicine.

Package Quantities

The pack contains 18 cartridges and a mouthpiece.

Further Information

Nil

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