

DATA SHEET

NICOTROL® Patch

5mg/16h, 10mg/16h, 15mg/16h

Presentation

Nicotrol Patch is a transdermal delivery system for topical application, available in sizes of 30, 20 and 10 cm² each containing 0.83 mg/cm² of nicotine, releasing 15 mg, 10 mg and 5 mg respectively over 16 hours. Each patch is rectangular in shape and comprises 3 distinct layers; an outer beige matt finish backing layer, a patterned silvery middle layer and an inner clear release liner, which is removed prior to use. Each patch is packaged in a heat sealed multilaminate sachet.

Uses

Actions

Pharmacotherapeutic group: Drug for treatment of addiction.

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

General pharmacokinetic properties of nicotine

The volume of distribution following i.v. administration of nicotine is about 2 to 3 L/kg. Plasma protein binding of nicotine is <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 70 L/hour and the terminal half-life approximately 2 hours. The major eliminating organ is the liver, but the kidney and lung also metabolise 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 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 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 and based upon the patient's nicotine dependence. Progressive severity of renal impairment is associated with decreased clearance of nicotine. Raised nicotine levels have been seen in smoking patients undergoing hemodialysis. 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 clearance of nicotine has been demonstrated in healthy elderly patients, however not justifying adjustment of dosage.

Pharmacokinetic properties of Nicotrol Patch

Following application of the Nicotrol patch to the upper arm or hip, approximately 95% of the nicotine released from the system enters the systemic circulation. The remainder of the nicotine released from the system is lost via evaporation from the edge. All patches are labelled by the average amount of nicotine absorbed by the average patient over 16 hours.

Plasma levels of nicotine, obtained with patches, rise after application, and reach a maximum level after approximately 6-10 hours. The mean peak plasma level of nicotine achieved with the 15 mg/16 h patch is approximately 9-15 ng/mL. Nicotine kinetics is similar for application on the arm and hip.

After repeated applications, nicotine concentrations are not significantly higher than those after a single application. If the 15 mg/16 hour patch is left on for 24 hours, as opposed to 16 hours, plasma levels of nicotine decline from a mean of 7.2 to 5.6 ng/mL over the last 8 hours.

Plasma nicotine concentrations show a slight deviation from dose proportionality for the three patch doses (5, 10 and 15 mg); with increasing patch size the increase in concentration is somewhat less than expected.

Pharmacokinetic properties of the combination of Nicotrol® Patch and nicotine chewing gum and Nicotrol® Patch and nicotine inhaler, respectively.

The plasma levels of nicotine when combining one 15 mg/16 hour patch and 2 mg chewing gum and one 15 mg/16 hour patch and 10 mg inhaler, respectively will depend on the number of gums chewed or inhaler cartridges used and the dosing interval.

Combination of Nicotrol patch and nicotine chewing gum:

A simulation of plasma concentrations shows that if one 15 mg/16 hour patch is applied in the morning and five to six 2 mg gums are evenly distributed over the awake hours according to the recommended dosage, a maximum plasma level of about 19 - 20 ng/mL will be reached. The simulation is based on nicotine pharmacokinetics upon separate use of the 15 mg/16 hour patch and 2 mg gum, respectively.

Combination of Nicotrol patch and nicotine inhaler:

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

The treatment of nicotine dependence, and the relief of withdrawal symptoms associated with smoking cessation.

Dosage and Administration

Could be used as a single treatment or in combination with either nicotine chewing gum or nicotine inhaler.

Children and Adolescents

Nicotrol Patch should not be administered to individuals under 18 years of age without recommendation from a physician. There is limited experience of treating this age group.

Adults and Elderly

For single use

The recommended treatment programme for Nicotrol Patch should occupy 3 months. The daily dose is one patch delivering 15 mg, 10 mg or 5 mg nicotine as appropriate, with application limited to 16 hours in a 24 hour period in each case.

Daily treatment commences with one 15 mg (30 cm²) patch, applied on waking (usually in the morning) and removed 16 hours later (usually at bedtime). Treatment should continue at this dose for an initial period of 8 weeks. Patients who have successfully abstained from smoking during this 8 week period should be supported through a further 4 week weaning period, using the lower strength patches. Downward titration of dose is achieved by applying one 10 mg (20 cm²) patch daily for 2 weeks followed by one 5 mg (10 cm²) patch daily for a further 2 weeks. Patients should be reviewed at 3 months. Following this review, if abstinence has not been achieved, further courses of treatment may be recommended if it is considered that the patient would benefit.

Nicotrol Patch should be applied to clean, dry intact areas of hairless skin, for example on the hip, upper arm, or chest. These areas should be varied each day and the same site should not be used on consecutive days.

There is no clinically significant difference in bioavailability of nicotine when the patch is applied to the hip, upper arm or chest.

After removal, used patches should be disposed of carefully.

Experience with treatment of nicotine dependence shows that success rates are improved if patients also receive supportive therapy and counselling.

In combination with nicotine chewing gum or nicotine inhaler

Persons who experience 'breakthrough' cravings or have failed with single treatment, can use a faster acting smoking cessation preparation such as nicotine 2mg chewing gum or nicotine 10 mg inhaler, in addition to the patch for fast relief.

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 either the 2mg gum or 10mg inhaler. Use a minimum of 4 x 2 mg gums per day; usually 5 - 6 gums will be adequate for effect. Do not use more than 24 gums per day. Usually 4 - 5 inhaler cartridges will be adequate for effect. Do not use more than 12 inhaler 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 gum 2mg/inhaler 10mg as the initial treatment period, and then gradually reduce the amount of gum/inhaler up to 12 months. Alternatively stop using the patch and gradually reduce the number of gums/inhaler cartridges up to 12 months.

Recommended dosage:

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

Contraindications

Hypersensitivity to nicotine or any component of the patch.

Warnings and Precautions

Nicorette patch 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 patch should be used with caution in patients with severe or moderate hepatic impairment, severe renal impairment, active duodenal and gastric ulcers.

Nicotine, both from nicotine replacement products and smoking, causes the release of catecholamines from the adrenal medulla. Therefore Nicotrol patch should also be used with caution in patients with hyperthyroidism or pheochromocytoma.

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

Special warnings and precautions for the combination of nicotine patch with either nicotine 2mg gum or nicotine 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 patch after consulting a health care professional. The risks for the foetus from Nicorette patch 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.

Effects on ability to drive and use machines

Nicotine patch has no or negligible influence on the ability to drive and use machines.

Adverse Effects

Nicotine patch may cause adverse reactions similar to those associated with nicotine administered by other means and are mainly dose-dependent.

About 20% of users experienced mild local skin reactions during the first weeks of 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:	Common:	Dizziness, headache
Cardiac disorders:	Uncommon:	Palpitations
	Very rare:	Reversible atrial fibrillation
Gastrointestinal disorders:	Common:	Gastro-intestinal discomfort, nausea, vomiting
Skin and subcutaneous tissue disorders:	Uncommon:	Urticaria

General disorders and administration site disorders:	Very common:	Itching
	Common:	Erythema

Adverse reactions that may occur when using the combination treatment (patch and gum or 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 used alone.

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 flecanide and pentazocine may also be induced by smoking.

Overdosage

Excessive use of nicotine from either nicotine replacement products 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 overdosage

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

Pharmaceutical Precautions

Store below 25°C.

Medicine Classification

General Sales Medicine.

Package Quantities

5mg/16h: 7 patches.

10mg/16h: 7 patches.

15mg/16h: 7 patches.

Further Information

Preclinical safety data

There are no pre-clinical data on the safety of Nicotrol transdermal patch.

The toxicity of nicotine as a component of tobacco is, however, well documented. Typical symptoms of acute poisoning are weak and irregular pulse, breathing difficulties, and general convulsions.

There are no clear evidence of nicotine being genotoxic or mutagenic. The well established carcinogenicity of tobacco smoke is mainly related to substances formed by the pyrolysis of tobacco. None of these occur in nicotine patch.

Excipients

Skin coloured backing film (pigmented layer, aluminium and polyester), polyisobutylenes, polybutene, polyester and release liner (siliconised polyester).

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