SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Nicorette Novum 10 mg/16 hour transdermal patch
Nicorette Novum 15 mg/16 hour transdermal patch
Nicorette Novum 25 mg/16 hour transdermal patch

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 transdermal patch of 10 mg/16 hours contains 15.8 mg nicotine.
1 transdermal patch of 15 mg/16 hours contains 23.6 mg nicotine.
1 transdermal patch of 25 mg/16 hours contains 39.4 mg nicotine.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Transdermal patch.

Nicorette Novum transdermal patch is a semi-transparent patch. The patch is marked with Nicorette in light brown printing.

Patch sizes:
10 mg/16h: area 9 cm^2, size: 27,7 x 33,2 mm
15 mg/16h: area 13,5 cm^2, size: 33,2 x 41,3 mm
25mg/16h: area 22,5 cm^2, size: 43 x 53 mm

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For treatment of tobacco dependence by alleviating nicotine craving and withdrawal symptoms and thus assisting smoking cessation in smokers who are motivated to quit or to alleviate smoking reduction in smokers who are unable or unwilling to quit smoking**.**

Nicorette Novum transdermal patch should preferably be used in conjunction with a smoking cessation program.

4.2 Posology and method of administration

Nicorette Novum transdermal patch can be used as a single treatment or in combination with Nicorette 2 mg chewing gum/lozenge/sublingual tablet or Nicorette Inhalator 10 mg or Nicorette oromucosal spray 1 mg/spray.

Paediatric population
Nicorette Novum transdermal patch should not be used by adolescents (12-17 years) without recommendation from a healthcare professional. Nicorette Novum transdermal patches should not be used by children under the age of 12 years.

Adults and the elderly

Treatment with patches for single use
Nicorette Novum transdermal patch can be used both when you stop smoking abruptly, and to prolong smoke-free intervals with intention to reduce smoking as much as possible before an attempt to stop smoking is made.
Persons with **high** nicotine dependence (more than 20 cigarettes per day) are recommended to start with one 25 mg/16 hour transdermal patch daily. The period of treatment is individual. Normally treatment should continue for 2 months. The dose is then reduced gradually by using 15 mg/16 hour transdermal patches for 2 weeks followed by 10 mg/16 hour patches for an additional 2 weeks.

Persons with **low** nicotine dependence (maximum 20 cigarettes per day) are recommended to start with one 15 mg/16 hour transdermal patch daily. The period of treatment is individual. Normally treatment should continue for 2 months. The dose is then reduced gradually by using 10 mg/16 hour transdermal patches for the following 4 weeks.

Dosage given in tabular format:

Dosage at high nicotine dependence (more than 20 cigarettes/day)		**Dosage at low nicotine dependence (maximum 20 cigarettes/day)**	
Patch	*Duration*	*Patch*	*Duration*
25 mg/16 hours	Week 1-8		
15 mg/16 hours	Week 9-10	15 mg/16 hours	Week 1-8
10 mg/16 hours	Week 11-12	10 mg/16 hours	Week 9-12

Treatment for longer than 6 months is not recommended. Certain former smokers may however need treatment for longer in order not to return to smoking.

The patch is applied in the morning and taken off when going to bed.

The patch is applied on a clean, dry, hairless and uninjured area of skin on the trunk, arms or hips. To reduce the risk of local irritation the Nicorette Novum transdermal patches should be applied alternately at different sites.

The hands should be washed carefully after applying the transdermal patch to avoid irritation of the eyes with nicotine from the fingers.

Administration of nicotine should be temporarily discontinued if symptoms of nicotine overdose occur. Nicotine intake should be reduced by either reducing the dosing frequency or strength if symptoms of nicotine overdose persist (see section 4.9).

Treatment with Nicorette Novum transdermal patch in combination with either Nicorette chewing gum, lozenge, sublingual tablet, inhaler or oromucosal spray.
Highly dependent smokers, those who experience cravings despite use of nicotine medicine or those who have failed with single treatment with nicotine medicine, can use Nicorette Novum patch in combination with another nicotine medicine for fast relief of cravings.

Initial combination treatment
Nicorette Novum 25 mg/16 h patch should be applied to in the morning and removed at bedtime. Nicorette 2 mg chewing gum, lozenge or sublingual tablet can be used as required for fast relief of cravings (usually 5-6 chewing gums/tablets per day). Alternatively Nicorette Inhalator 10 mg (usually 4-5 cartridges per day) or Nicorette oromucosal spray 1 mg/spray (usually 13 sprays per day) can be used when cravings occur.

The dosing schedule for use of the oral pharmaceutical form in combination with the patch is flexible and the users are dosing based on their requirements.

The maximum recommended daily dose varies between dosage forms (2 mg chewing gums: 24 pieces, 2 mg lozenge: 15 pieces, sublingual tablet: 24 pieces, inhaler: 12 nicotine plugs, oromucosal spray: 32 sprays).

Smokers should stop completely during the course of the combination treatment. Normally, the treatment continues for 8 weeks.

Weaning from nicotine medicine:
After the initial 8 weeks, gradual weaning from nicotine medicine is started by either

- using a patch with a lower strength, i.e. 15 mg/16 hour during 2 weeks followed by 10 mg/16 hours for additional 2 weeks in combination with the initial dose of Nicorette chewing gum/lozenge/sublingual tablet/inhaler or oromucosal spray. Thereafter gradually reduce the number of chewing gums/lozenges/sublingual tablets/cartridges or sprays, up to 12 months.

  or

- stop using the patch and gradually reduce the number of chewing gums/lozenges/sublingual tablets, cartridges or sprays, up to 12 months.

Recommended dosage:

Initial treatment			
Time period	**Patch**	**Flexible dosage form (one of the following products can be used)**	**Dose per day in combination with patch**
Week 1-8	1 patch 25 mg/16 hours per day	2 mg chewing gum,	As needed. Usual dose is 5-6 chewing gums (max 24)
		2 mg lozenge	As needed. Usual dose is 5-6 lozenges (max 15)
		2 mg sublingual tablet	As needed. Usual dose is 5-6 sublingual tablets (max 24)
		inhaler	As needed. Usual dose is 4-5 cartridges (max 12)

		oromucosal spray	As needed. Usual dose is 13 sprays per day (max 32 sprays/day)

Weaning from nicotine medicine - alternative 1		
Time period	**Patch**	**Flexible dosage form**
Week 9-10	1 patch 15 mg/16 hours per day	Continue to use chewing gums/lozenges /sublingual tablets /inhaler/oromucosal spray as needed
Week 11-12	1 patch 10 mg/16 hours per day	Continue to use chewing gums/lozenges/ sublingual tablets/ inhaler/oromucosal spray as needed
Up to 12 months	---	Reduce the number of chewing gums/ lozenges/ sublingual tablets/ cartridges/sprays gradually
Weaning from nicotine medicine – alternative 2		
Up to 12 months	---	Continue to reduce the number of chewing gums/lozenges/sublingual tablets/cartridges/sprays gradually

4.3 Contraindications

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

4.4 Special warnings and special precautions for use

The benefits of quitting smoking outweigh any risks associated with correctly administered nicotine medicine.
A risk-benefit assessment should be made by an appropriate healthcare professional for patients with the following conditions:

- *Cardiovascular disease:* Dependent smokers with a recent myocardial infarction, unstable or worsening angina including Prinzmetal's angina, severe cardiac arrhythmias, recent cerebrovascular accident and/or who suffer with uncontrolled hypertension should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). If this fails, Nicorette Novum may be considered

but as data on safety in this patient group are limited, initiation should only be under close 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 nicotine medicine is initiated as reduction in nicotine induced catecholamine release can affect carbohydrate metabolism. They may need lower doses of insulin as a result of smoking cessation.

- *Renal and hepatic impairment:* Use 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.

- *Phaeochromocytoma and uncontrolled hyperthyroidism:* Nicotine, both from nicotine medicine and smoking, causes release of catecholamines from the adrenal medulla. Therefore Nicorette Novum transdermal patch should be used with caution by patients with uncontrolled hyperthyroidism or phaeochromocytoma.

- *Gastrointestinal Disease:* Nicotine may exacerbate symptoms in patients suffering from esophagitis, gastric or peptic ulcers and nicotine medicine should be used with caution in these conditions.
- *Seizures*: Use with caution in subjects taking anti-convulsant therapy or with a history of epilepsy as cases of convulsions have been reported in association with nicotine (see section 4.8).

Nicorette Novum patch should be removed before examination with magnetic resonance imaging (MRI) to prevent burns.

Danger in children: Doses of nicotine tolerated by smokers can produce severe toxicity in children that may be fatal. Products containing nicotine should not be left where they may be handled or ingested by children, see section 4.9 Overdose.

Transferred dependence: Transferred dependence with Nicorette Novum is rare and both less harmful than tobacco and easier to break than smoking dependence.

Stopping smoking: Polycyclic aromatic hydrocarbons in tobacco smoke induce the metabolism of drugs metabolised 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, tacrine, clozapine and ropinirole.
The plasma concentration of other medicinal products metabolised in part by CYP 1A2 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 pentazocine may also be induced by smoking.

Special warnings and precautions for the combination of Nicorette Novum transdermal patch with Nicorette 2 mg chewing gum/lozenge/sublingual tablet/inhaler or oromucosal spray are the same as those for each treatment alone (see respectively Summary of Product Characteristics).

4.5 Interaction with other medicinal products and other forms of interaction

No clinically relevant interactions between nicotine medicines and other drugs have definitely been established. However nicotine may possibly enhance the haemodynamic effects of adenosine i.e. increase in blood pressure and heart rate and also increased pain response (angina-pectoris type chest pain) provoked by adenosine administration (see section 4.4, Stopping smoking).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/ contraception in males and females
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 to be in is to be both non-smoking, and not using nicotine medicine.
Whilst smoking may have adverse effects on male fertility, no evidence exists that particular contraceptive measures are required during nicotine medicine treatment by males.

Pregnancy
Smoking during pregnancy is associated with risks such as intra-uterine growth retardation, premature birth or stillbirth. Stopping smoking is the single most effective intervention for improving the health of both pregnant smoker and her baby. The earlier abstinence is achieved the better.
Nicotine passes over to the foetus and influences the foetal breathing pattern and circulation. The effect on the foetal circulation is dose-dependent. Pregnant smokers should therefore always be recommended to stop smoking completely without the use of nicotine medicine. The risk of continued smoking may however constitute a greater hazard to the foetus than use of nicotine medicine in a supervised smoking cessation programme. Nicorette Novum transdermal patches should only be used by pregnant patients with a high level of nicotine-dependence after advice from a healthcare professional.

Lactation
Nicotine passes over in breast milk in such quantities that may affect the child even at therapeutic doses. Nicorette Novum transdermal patch should therefore be avoided during breastfeeding. Should smoking cessation not be achieved, use of Nicorette Novum transdermal patch by breast feeding smokers should only be initiated after advice from a healthcare professional.

Fertility
Smoking increases the risk for infertility in women and men. *In vitro* studies have shown that nicotine can adversely affect human sperm quality. In rats, impaired sperm quality and reduced fertility has been shown.

4.7 Effects on ability to drive and use machines

Nicorette Novum transdermal patch has no or negligible effect on ability to drive cars or use machines.

4.8 Undesirable effects

Effects of smoking cessation
Regardless of the means used, a variety of symptoms are known to be associated with quitting habitual tobacco use. These include emotional or cognitive effects such as dysphoria or

depressed mood; insomnia; irritability, frustration or anger; anxiety; difficulty concentrating, and restlessness or impatience. There may also be physical effects such as decreased heart rate; increased appetite or weight gain, dizziness or presyncopal symptoms, cough, constipation, gingival bleeding or apthous ulceration, or nasopharyngitis. In addition, and of clinical significance, nicotine cravings may result in profound urges to smoke.

Adverse Drug Reactions
Nicorette Novum transdermal patches may cause side effects resembling those that occur when nicotine is administered by a different route. Most of the side effects reported by users occur early in treatment and they are largely dose-dependent. During the first weeks of treatment approx. 20% of treated patients experience undesirable effects, usually in the form of local mild skin reactions.

Allergic reactions (including symptoms of anaphylaxis) rarely occur with the use of Nicorette Novum patches.

The adverse reactions observed in patients treated with nicotine patch formulations during clinical trials and post-marketing experience are listed below by system organ class. The frequency categories have been estimated from clinical trials for the adverse reactions identified during post-marketing experience.Very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1 000, <1/100); rare (≥1/10 0000, <1/1 000); very rare (<1/10 000), not known frequency (cannot be estimated from the available data).

System Organ Class	Reported adverse event
Immune System Disorders	
Uncommon	Hypersensitivity
Rare	Anaphylactic reaction
Nervous system disorders	
Common	Headache
Uncommon	Paraesthesia
Not known	Seizure*
Cardiac disorders	
Uncommon	Palpitations, Tachycardia
Rare	Atrial fibrillation
Vascular Disorders	
Uncommon	Flushing, Hypertension
Respiratory, Thoracic and Mediastinal Disorders	
Uncommon	Dyspnoea
Skin and subcutaneous tissue disorders	
Very common	Pruritus
Common	Rash, Urticaria
Uncommon	Hyperhidrosis
Rare	Angioedema, Erythema
Gastrointestinal disorders	
Common	Nausea, Vomiting
Rare	Gastrointestinal discomfort
Musculoskeletal and connective tissue disorders	
Uncommon	Myalgia
Rare	Pain in extremity
General disorders and administration site conditions	
Uncommon	Reactions at the administration site, Asthenia, Chest discomfort and pain, Malaise, Fatigue

*Cases of seizures have been reported in subjects taking anti-convulsant therapy or with a history of epilepsy.

Adverse events that may occur during the use of combination treatment (patch and chewing gum, lozenge, sublingual tablet, inhaler or oromucosal spray) only differ from those of each treatment alone in terms of local adverse events related to the pharmaceutical forms. The frequency of these adverse events is comparable to that listed in the Summary of Product Characteristics of each product.

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 to (see details below).

Medical Products Agency
Box 26
751 03 Uppsala
Website: www.lakemedelsverket.se

4.9 Overdose

Symptoms of overdosage with nicotine may occur if the patient has low nicotine consumption before treatment or uses other concomitant sources of nicotine.

The symptoms of overdosage are the same as the symptoms of acute nicotine poisoning, such as nausea, vomiting, increased salivation, abdominal pain, diarrhoea, sweating, headache, dizziness, disturbed hearing and a profound feeling of weakness. At high doses these symptoms may be accompanied by low blood pressure, weak and irregular pulse, breathing difficulties, exhaustion, circulatory collapse and general convulsions.

Nicotine doses that are tolerated by adult smokers during treatment may cause serious symptoms of poisoning in children that may have a fatal outcome.
Suspected nicotine poisoning in a child should be considered a medical emergency and treated immediately.

Management of overdose: Administration of nicotine must be stopped immediately and the patient should be treated symptomatically. Remove the patch and rinse application site with water. If excessive amount of nicotine is swallowed, activated charcoal reduces the gastrointestinal absorption of nicotine.

The acute minimum lethal oral dose of nicotine in man is believed to be 40 to 60 mg.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Agent for nicotine dependence.
ATC code: N07BA01

Abruptly interrupted use of tobacco products after a long period of daily use may give characteristic withdrawal symptoms comprising four or more of the following: dysphoria or depressed mood, insomnia, irritability, frustration or aggression, anxiety, difficulty in concentrating, restlessness or impatience, reduced heart rate, increased appetite or increase in weight. Urge to smoke, recognized as a clinically relevant symptom, is an important part of the withdrawal symptoms when giving up smoking.

Clinical studies have shown that nicotine medications may help smokers to refrain from smoking.

Comparative studies of effects between different forms of preparation of Nicorette have not been carried out.

5.2 Pharmacokinetic properties

Nicotine is released slowly from Nicorette Novum transdermal patches and absorbed continuously through the skin. Nicorette Novum transdermal patches are intended for use during waking hours, i.e. approx. 16 hours, in order to resemble the period of supply of nicotine when smoking. Sleeping disturbances induced by nicotine administration during

sleep is then avoided. Absolute bioavailability is more than 90% and is independent of site of application.

A linear relationship exists between released amount nicotine and plasma levels of nicotine over the therapeutic dose range 10-25 mg/16 hours.

The maximum level of plasma concentration (t_{max}) after administration is reached after approximately 9 hours (7-11 hours).The plasma peak is thus in the afternoon/evening when the risk of relapse is highest.
The measured maximum plasma level for the 25 mg patch is 26,5 ng/mL, 15.5 ng/mL for the 15 mg patch and 10 ng/mL for the 10 mg patch.

The volume of distribution after intravenous administration of nicotine is around 2-3 l/kg and the half-life is approx. 2 hours. Nicotine is metabolized largely in the liver and plasma clearance is on average around 70 l/hour. Nicotine is also metabolized in kidneys and lungs. More than 20 metabolites have been identified, of which all are believed to be less active than nicotine. The main metabolite is cotinine, which has a half-life of 15-20 hours and which gives approx. 10 times as high a plasma concentration as nicotine.

The plasma protein binding of nicotine is less than 5%. Other diseases or concomitant use of other medicinal products that affect the level of plasma proteins are not expected to have a significant effect on the nicotine kinetics.

The main metabolites in urine are cotinine (12% of the dose) and trans-3-hydroxy cotinine (37% of the dose). Approx. 10% of the nicotine is excreted unchanged with the urine. Up to 30% may be excreted with the urine via increased diuresis and acidification below pH 5.

Greatly impaired renal function is assumed to affect total clearance of nicotine and its metabolites. The pharmacokinetics of nicotine is unaffected in liver cirrhosis patients with mild impairment of liver function (Child score 5) and reduced in liver cirrhosis patients with moderate impairment of liver function (Child score 7). Elevated nicotine levels have been seen in smoking haemodialysis patients.

A smaller reduction in total clearance of nicotine has been shown in healthy elderly users, but adjustment of the dose is not necessary.

No differences in nicotine kinetics have been observed between men and women.

5.3 Preclinical safety data

There is no preclinical safety data for Nicorette Novum.

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

There is no evidence that nicotine would be genotoxic. The well-known carcinogenic properties of tobacco smoke are formed mainly during pyrolysis of tobacco. This does not occur with Nicorette Novum transdermal patches.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Triglycerides, medium-chain
Basic butylated methacrylate copolymer
Polyethylene terephthalate (PET) film

Acrylate Matrix
Acrylic adhesive solution
Potassium hydroxide
Croscarmellose sodium
Aluminium acetylacetonate

Release Liner
Polyethylene terephthalate (PET) film single side aluminised, both sides siliconised

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25 ºC.

6.5 Nature and contents of container

Pack sizes:

10 mg/16 hour: 7, 14 patches
15 mg/16 hour: 7, 14, 21, 28 patches
25 mg/16 hour: 7,14, 21, 28 patches

Each patch is packed in a sealed laminate pouch consisting of paper, PET-film and aluminium acrylnitrilcopolymer or cyclo olefin copolymer coextrudate.

All pack sizes may not be marketed.

6.6 Special precautions for disposal

The patch should be folded after use with the sticky side inwards and disposed of where children cannot reach it.

7 MARKETING AUTHORISATION HOLDER

McNeil Sweden AB
Box 4007
169 04 Solna

8 MARKETING AUTHORISATION NUMBER

10 mg/16 hours: 23996
15 mg/16 hours: 23997
25 mg/16 hours: 23998

9 DATE OF FIRST AUTHORISATION /RENEWAL OF THE AUTHORISATION

2009-09-11/2013-08-31

10 DATE OF REVISION OF THE TEXT

2023-08-23