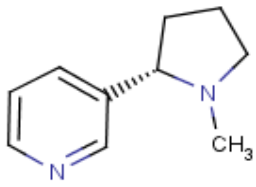
PRODUCT INFORMATION
QuitX® 7mg/24 hours, 14mg/24 hours & 21mg/24 hours TRANSDERMAL PATCH

NAME OF THE MEDICINE

QuitX nicotine 7 mg/24 hours, 9.7 cm^2 square patch with round corners
QuitX nicotine 14 mg/24 hours, 19.3 cm^2 square patch with round corners
QuitX nicotine 21 mg/24 hours, 29.0 cm^2 square patch with round corners.

DESCRIPTION

Chemical name: S-3-(1-methyl-2- pyrrolidinyl) pyridine.
Molecular formula: $C_{10}H_{14}N_2$.
MW: 162.26.
CAS Registry No. 54-11-5



Nicotine is the major pharmacologically active alkaloid of tobacco. The free alkaloid is absorbed rapidly through the skin and respiratory tract.

QuitX patches are square with rounded edges, adhesive transdermal patches containing the nicotine active ingredient dissolved within an adhesive layer.
Each patch is composed of the following excipients: polyethylene terephthalate, DOW CORNING (R) BIO-PSA SA7-4207 silicon adhesive (ID: 108330), No-Tox liquid ink FGN-3274 NT15 White (ID: 108309), Loparex Si-600-1A (ID: 108412 adhesive; Loparex Si-4400-1A adhesive (ID: 108351) and Duro-Tak 87-2194 acrylic adhesive (ID: 108551). Each unit is packaged in individually sealed pouches.

The patch is provided in three different sizes corresponding to the three dosage strengths, 9.7 cm^2 – 7 mg/24 hours, 19.3 cm^2 – 14 mg/24 hours, and 29.0 cm^2 – 21 mg/24 hours.

The following three systems are available as shown in **Table 1**.

QuitX Patch

	QuitX step 1	QuitX step 2	QuitX step 3
Content of nicotine (mg)	47.3	31.5	15.8
Drug release area (cm^2)	29.0	19.3	9.7
Nominal release rate (mg/24h)	21	14	7

To sustain the concentration gradients for diffusion, more nicotine is contained in the nicotine patch than is actually delivered over 24 hours. Nicotine patch releases approximately 0.72 mg/cm^2/24 hours of nicotine. Therefore, the average daily dose administered is determined largely by the size of the contact area of the system.

PHARMACOLOGY

Pharmacodynamics and mechanism of action

Nicotine acts primarily on cholinergic receptors of the nicotine type in the peripheral and in the central nervous system. Nicotine, the chief alkaloid in tobacco products, binds stereoselectively to acetylcholine receptors at the autonomic ganglia, in the adrenal medulla, at neuromuscular junctions and in the brain. Two types of central nervous system effects are believed to be the basis of nicotine's positively reinforcing properties. A stimulating effect, exerted mainly in the cortex via the locus ceruleus, produces increased alertness and cognitive performance. A "reward" effect via the "pleasure system" in the brain is exerted in the limbic system. At low doses the stimulant effects predominate while, at high doses, the reward effects predominate.

Intermittent administration of nicotine affects neurohormonal pathways, and results in the release of acetylcholine, noradrenaline, dopamine, serotonin, vasopressin, β-endorphin, growth hormone, cortisol and ACTH. These neuroregulators may be involved in the reported behavioural and subjective effects of smoking. Improved performance with some parameters such as finger tapping has been shown following nicotine administration in smokers who have been abstinent overnight.

The actions of nicotine in humans are complex, depending on dose, rate of delivery, prevalent autonomic tone, individual variation, and prior exposure (tolerance).

The cardiovascular effects of nicotine are due to stimulation of the central and the peripheral sympathetic nervous system. For example nicotine at the concentrations achieved during smoking causes increases in heart rate, increases of systolic and diastolic pressure, and also cutaneous vasoconstriction.

Partial or complete tolerance to some effects of nicotine develops rapidly: a second infusion after 60 or 120 minutes results in lesser heart rate acceleration and subjective effects than the initial infusion in spite of higher venous nicotine concentrations. When the second infusion is given after 210 minutes, the response is the same as that after the initial infusion.

Application of nicotine patch (14mg/24hour patch) to smokers abstinent overnight resulted in small increases in mean heart rate (up to 6 beats per minute) and systolic blood pressure and a decrease in stroke volume. The changes in heart rate and stroke volume were still present at

day 10 after repeated application suggesting that development of complete tolerance to the effects of nicotine did not occur. The effects were smaller in magnitude than those produced by cigarette smoking, whereas no changes in skin temperature or blood flow were observed compared with placebo control.

During tobacco withdrawal, symptoms such as craving, irritability, frustration, anger, restlessness, nervous tension, anxiety, feeling of hunger, weight gain, difficulties of concentration, and sleep disturbances have been observed. During placebo controlled double blind clinical studies, nicotine replacement with nicotine patch in the first few weeks or months after stopping smoking increased the chances of successful abstinence with or without group support. There was also a strong trend towards reduction of withdrawal symptoms.

Pharmacokinetics

Nicotine is readily absorbed through the skin into the systemic circulation. The absorption profile after single application of nicotine patch to healthy abstinent smokers (patients undergoing a course of smoking cessation therapy with the patch) shows an initial one to two hours delay followed by a progressive rise in plasma concentrations, plateaus being attained at about eight to ten hours after application.

After the system is removed, plasma concentrations decline more slowly than would be predicted by the two hour elimination half-life for this agent after an intravenous infusion. About 10% of the total amount of nicotine that reaches the circulation is delivered from the skin after nicotine patch (21mg/24hour patch) is removed.

The area under the plasma concentration time curve (AUG 0-24h) varied in proportion to the dose delivered by nicotine patch, which in turn depends on the size of the patch.

In comparison with an IV infusion 76.8 ± 17.8% of the nicotine released from nicotine patch is systemically available. With repeated application of 14mg/24hour and 21mg/24 hour nicotine patches, mean minimum and maximum plasma concentrations at steady state were 7.1 and 12.0 nanogram/ml for the 14mg/24hour patches and 10.3 and 17.7 nanogram/ml for the 21mg/24hour patches.

These plasma concentrations were within the range observed during moderate cigarette smoking.

Analysis of residual nicotine content in systems worn for 24 hours indicates that total nicotine delivery into the circulation varies by a factor of two between individuals. However, within individual variability in the amount of nicotine delivered is small, indicating a high level of consistency in the performance of the system during once daily application of nicotine patch.

No data are available on the influence of gender on the pharmacokinetic parameters of nicotine following nicotine patch administration. AUG values do not seem to be related to bodyweight within the range 50 to 110 kg. No pharmacokinetic data exist for patients outside this weight range.

Nicotine is distributed widely in the body with a volume of distribution of approximately 180 L. It crosses the blood brain barrier, the placenta, and is also found in breast milk. Plasma

protein binding of nicotine is negligible, less than 5%. Therefore, changes in nicotine binding from use of concomitant drugs or alternations of plasma proteins by disease states would not be expected to have significant consequences.

Total plasma clearance of nicotine ranges from 0.92 to 2.43 L/minute. The major eliminating organ is the liver; the kidney and lung also metabolise nicotine. There is no significant skin metabolism of nicotine. One of the primary metabolites, cotinine, has a half-life of 15 to 20 hours and concentrations that exceed those of nicotine tenfold. Cotinine is metabolised further to a large extent. More than 20 metabolites of nicotine *have* been identified, all of which are believed to be less active than the parent compound.

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. As much as 30% may be extracted in the urine with high urine flow rates and urine acidification below pH 5. Renal excretion of unchanged nicotine is pH dependent, being negligible under alkaline conditions.

There is considerable individual variability in distribution, metabolism and bioavailability of nicotine from cigarettes, capsules and nicotine gum.

INDICATIONS

Treatment of nicotine dependence, as an aid to smoking cessation.

CONTRAINDICATIONS

Nicotine patches should not be used by non-smokers, children under 12 years, occasional smokers or those with diseases of the skin which may complicate patch therapy, or with hypersensitivity to nicotine or any of the excipients.

PRECAUTIONS

Nicotine is a toxic and addictive drug and milligram doses are potentially fatal if rapidly absorbed. For any smoker, with or without concomitant disease or pregnancy, the risk of nicotine replacement in a smoking cessation program should be weighed against the hazard of continued smoking while using nicotine patches and the likelihood of achieving cessation of smoking without nicotine replacement.

Treatment with nicotine patches should be discontinued if symptoms of nicotine *overdosage* appear. Mild intoxication produces nausea, vomiting, abdominal pain, diarrhoea, headache, sweating and pallor (see *Overdosage).*

Nicotine is a toxic substance. Doses of nicotine that are tolerated by adult smokers during treatment can produce severe symptoms of poisoning in small children and may prove fatal. Both before and after use, nicotine patch contains a significant amount of nicotine. Patients must be cautioned that the patches are not to be handled casually or left where they might be

inadvertently misused or consumed by children. Care must be exercised in the handling and disposal of both the fresh and the used patches so that they do not fall into the hands of children under any circumstances.
As soon as a patch is removed from the skin, it should be folded firmly in half, with the sticky sides together, and disposed of with utmost care. Similarly, the patches should not be stored or disposed of where they might be consumed by pets.

Occasional smokers are not expected to benefit from the use of nicotine patches.

Dependent smokers with a recent myocardial infarction, unstable or worsening angina pectoris including Prinzmetal angina, severe cardiac arrhythmias, uncontrolled hypertension or recent cerebrovascular accident should be encouraged to stop smoking with non-pharmacological interventions (such as counselling). If this fails, nicotine patches may be considered but as data on safety in these patient groups are limited, initiation should only be under close medical supervision.

Nicotine patches should be used with caution in patients with: severe hypertension, stable angina pectoris, cerebrovascular disease, occlusive peripheral arterial disease, heart failure; hyperthyroidism or pheochromocytoma; moderate to severe hepatic and/or severe renal impairment.

Smokers with diabetes mellitus should be advised to monitor their blood sugar levels more closely than usual when NRT is initiated because catecholamine release can affect carbohydrate metabolism and vasoconstriction may delay or reduce insulin absorption.

Nicotine patches should be used with caution in patients who are susceptible to angioedema and/or urticaria. Patients with generalised dermatological disorders such as psoriasis or chronic dermatitis should not use the patch (see Contraindications).

In the event of a severe or persistent skin reaction, discontinue treatment and use another pharmaceutical form.

Carcinogenesis, mutagenesis, impairment of fertility.

Carcinogenicity. As an ingredient of tobacco smoke, which contains potent carcinogens, nicotine is generally implicated as a co-carcinogen. Nicotine *per* se does not appear to be a potential carcinogen in laboratory animals.

Mutagenicity. In an *Escherichia coli* test system, nicotine induced DNA damage. In bacterial test systems as a whole and in cytogenetic assays with mammalian cell cultures, nicotine did not display any potentially genotoxic action.

Reproduction toxicity. Teratogenicity studies with nicotine in *several* animal species *have* demonstrated nonspecific retardation of fetal growth. In the mouse, the unborn offspring of dams treated with nicotine 25 mg/kg subcutaneously (SC), corresponding to approximately 120 times the human transdermal dose, showed some skeletal defects in the peripheral parts of the limbs. Chronic SC administration of 1.5 or 3 mg/kg in pregnant rats caused some behavioural disorders in the offspring. In rats and rabbits, implantation of the blastocyst in the uterine epithelium may be inhibited or delayed to a certain extent by a reduction in DNA

synthesis which appears to be caused by nicotine. *Overall,* there are no clear cut grounds for believing that nicotine has any teratogenic potential and/or inhibitory effects on fertility at concentrations reached by the use of nicotine patches.

Use in pregnancy (Category D)
In pregnant women, complete cessation of tobacco consumption should always be recommended without nicotine replacement therapy (NRT). However, for women unable to quit on their own, NRT may be recommended to assist a quit attempt.

Nicotine is harmful to the foetus. However, the risk for the foetus is probably less than to be expected with continued smoking due to: lower maximal plasma concentrations compared to inhaled nicotine, resulting in a nicotine exposure less or not more than associated with smoking; no exposure to polycyclic hydrocarbons and carbon monoxide.

As nicotine does pass to the foetus, the decision to use NRT should be made as early on in pregnancy as possible with the aim of discontinuing after use for two to three months.

If NRT is used during pregnancy, intermittent dosing products (nicotine chewing gum) should preferably be used while pregnant as the gums usually provide a lower daily dose of nicotine than patches. However, if the woman suffers from nausea and/or vomiting, the patch may be preferred but should be removed before going to bed.

Use in lactation
Nicotine is excreted in breast milk in quantities that may affect the child even in therapeutic doses. Like smoking, nicotine replacement therapy should be avoided during breastfeeding. Nicotine patch should not be used while breastfeeding.

Intermittent NRT products such as nicotine chewing gum may be used. Women should breastfeed just before they use the product to allow time between NRT use and feeding to be as long as possible.

Paediatric Use
Use in children and adolescents. Data on the use of NRT in treating adolescents under the age of 18 years are limited.

NRT should only be used in adolescents 12 to 17 years after consultation with a health care professional and use should be restricted to 12 weeks. If treatment is required for longer than 12 weeks, this should be discussed with a healthcare professional.

Do not use in children under 12 years.

Effect on ability to drive or operate machinery
When nicotine patch is used as recommended there are minimal risks for driving vehicles or operating machinery.

INTERACTIONS WITH OTHER MEDICINES

No clinically relevant interactions between NRT and other drugs have definitely been established. However, nicotine may enhance the haemodynamic effects of adenosine.

Smoking but not nicotine is associated with increased CYP1A2, and possibly CYP1A1, activity. After cessation of smoking there may be reduced clearance of substrates for these enzymes and increased plasma levels of some medicinal products. This is of potential clinical importance in products with a narrow therapeutic window, e.g. theophylline, ropinirole, clozapine and olanzapine.

Cessation of smoking, with or without NRT, may alter the individual's response to concomitant medication and may require adjustment of dose. In particular, anticonvulsants may require special monitoring and/or dosage adjustment.

Dose reduction may be required for: caffeine, oestrogens, imipramine, lignocaine, oxazepam, pentazocine, theophylline, warfarin, possibly due to reversal of hepatic enzyme induction on smoking cessation; insulin, possibly due to increase in subcutaneous absorption on smoking cessation; adrenergic antagonists (e.g. prazosin, labetalol), possibly due to reduction in circulating catecholamines on smoking cessation.

Dose increase may be required for: adrenergic agonists (e.g. isoprenaline, phenylephrine), possibly due to reduction in circulating catecholamines on smoking cessation.

Smoking may lead to reduced analgesic effects of opioids (e.g. dextropropoxyphene, pentazocine), reduced diuretic response to furosemide, reduced effect of β-adrenergic blockers (e.g. propranolol) on blood pressure and heart rate decrease and reduced responder rates in ulcer healing with H 2-antagonists.

Both smoking and nicotine may raise the blood levels of cortisol and catecholamines. Dosages of nifedipine, adrenergic antagonists and adrenergic agonists may need to be adjusted.

ADVERSE EFFECTS

In principle, nicotine patches can cause adverse reactions similar to those associated with nicotine administered by smoking. Since the maximum plasma concentrations of nicotine that are produced by nicotine patches are lower than those produced by smoking and fluctuate less, nicotine-related adverse reactions occurring during treatment with nicotine patches can be expected to be less marked than during smoking.

Some of the symptoms listed below are hard to differentiate from recognised tobacco withdrawal symptoms when comparison with placebo is made. The placebo used contained about 13% of the nicotine of matching nicotine patches, to match colour and odour exactly for blinding purposes.

The most common adverse event associated with topical nicotine is a short lived erythema, pruritus or burning at the application site, which was seen at least once in 35% of clinical trial subjects. Local erythema after patch removal was noted at least once in 17% of patients and local oedema in 3%. Erythema generally resolved within 24 hours. Cutaneous hypersensitivity (contact sensitisation) occurred in 1.5% of patients on nicotine patches (see Precautions).

Skin reactions led to premature discontinuation of nicotine patches in about 6% of clinical trial participants. Oedema, burning sensation, blisters, rash, or pinching at the application site were noted. The majority of these reactions were mild. Most of the skin reactions resolved within 48 hours, but in more severe cases the erythema and infiltration lasted from one to three weeks. The onset of important skin reactions occurred between three and eight weeks from the start of therapy. In isolated cases the skin reactions extended beyond the application sites. Isolated cases of urticaria, angioneurotic oedema and dyspnoea were reported.

Table 2 shows the adverse events/withdrawal symptoms most commonly reported in three double blind clinical trials irrespective of causal association with study drug.

	Nicotine Patch (N=401)	**Placebo (N=391)**
Application site reaction	34.9%	17.6%
Headache	29.7%	29.2%
Cold and flu-like symptoms	12.0%	8.4%
Dysmenorrhoea	6.6% **	8.8% **
Insomnia	6.5%	5.4%
Nausea	6.2%	4.6%
Myalgia	6.0%	4.1%
Dizziness	6.0%	5.9%
** % of female subjects		

The following unwanted experiences were also reported, irrespective of causal association with nicotine patches, at incidences of < 6%.

Incidence ≥ 2% *and greater than placebo (by* at *least 0.5%).* Abdominal pain, dyspepsia, allergy, motor dysfunction, coughing, abnormal dreaming, arthritis.

Incidence ≥ 2% *and similar* to *or less than placebo.* Anxiety, emotional lability, irritability, constipation, diarrhoea, toothache, arthralgia, back pain, pharyngitis, rhinitis, sinusitis, upper respiratory symptoms.

Incidence between 1 *and* 2%. Somnolence, impaired concentration, vomiting, chest pain, fatigue, pain, blood pressure changes, bronchitis, rash, herpetic rash, earache.

Incidence ≤ 1%*. Hot flushes, local oedema, weight increase, extrasystoles, hypertension, palpitation, gastric ulcer, dry mouth, flatulence, gingivitis, dysphagia, abnormal stool, thyroid disorders, lymph gland tenderness, taste perversion, abnormal vision, dyspnoea, cystitis, paraesthesia, memory impairment, twitching, confusion, agitation, increased appetite, leg cramps, migraine, pruritus, increased sweating, urticaria, acne.

*Only events considered by the investigator to be possibly related to Nicotine patch are included in this list, but the overall incidence was ≤ 1 % irrespective of relationship to study drug.

A similar profile has also been observed in previous clinical trials.

Other adverse reactions reported during postmarketing surveillance (incidence unknown).
Vasculitis, tachycardia, hypotension, euphoria, vertigo, tremor, hyperactivity, light-headedness, bone pain, pain in the extremities, hyperventilation, hoarseness.

DOSAGE AND ADMINISTRATION

The patient should be advised to stop smoking completely when starting treatment with QUITX patches.

For individuals smoking 20 cigarettes or more a day, it is recommended that treatment be started with nicotine 21mg/24 hours patch (Step 1) once daily. Those smoking less than 20 cigarettes are recommended starting with nicotine 14mg/24 hours patch (Step 2).

Patients starting on Nicotine patch Step 1 should use this strength for 4 weeks, before moving onto Step 2 for 4 weeks and finally Step 3 for 4 weeks.

Patients starting on Nicotine patch Step 2 may switch to Step 3 after 4 weeks followed by 8 weeks of Step 3.
How quickly the patient moves through the program will vary depending on individual response, and maintaining or increasing the dose may be necessary if abstinence is not achieved or if withdrawal symptoms are experienced.

The treatment duration is about 3 months but may vary as a function of individual response. Intermittent dosing products (such as Nicotine Chewing Gum) may be used beyond 3 months if necessary, but those using NRT for more than 9 months should seek advice from a healthcare professional.

Use in children under 18 years:

When deciding whether to recommend NRT an assessment should be made on the individual's nicotine dependence, motivation to quit and willingness to accept counselling. Counselling is considered to be vitally important in the effective treatment of tobacco dependence in this age group.

Children aged 12 to 17 years should only use QuitX patch under the advice of a health care professional. Treatment should not exceed 12 weeks without consultation with a healthcare professional, who can reassess the patient for their commitment to quit and the benefits of continued treatment. If treatment is continued, it should not be extended for more than another four weeks.

Do not use in children under 12 years.

Use in the Elderly:

Experience in the use of these patches in smokers over the age of 65 years is limited. Nicotine patch does not appear to pose safety problems in this age group.

Instruction for use

Nicotine patches should be applied as soon as it has been removed from the child resistant pouch. The sachet has a pre-cut edge to facilitate removal of the contents. Following removal of the backing, the nicotine patch should be immediately applied to a clean non hairy, dry area of intact skin on the trunk or upper arm. The patch should be held in position for 10 to 20 seconds with the palm of the hand. A different site of application should be chosen each day. One should allow several days to elapse before using the same area again.

Combination therapy

If smokers have previously relapsed with use of one form of nicotine replacement therapy (NRT), combination therapy could be beneficial. Smokers who experience breakthrough cravings or have difficulty controlling cravings using one form of NRT alone could combine the use of nicotine patch Step 1 with another form of NRT such as nicotine chewing gum 2 mg. Nicotine chewing gum 4 mg should not be used with nicotine patches.

When using nicotine patch Step 1 in addition of nicotine chewing gum 2 mg, it is recommended that 4 to 12 pieces are used each day. Most people will use 5 to 6 pieces. Do not exceed 12 pieces a day.

Combination therapy should be used for 12 weeks, after which one of the two following programs should be followed.

1. Stop use of nicotine patch and gradually reduce the number of gums used until they are no longer needed.
2. Continue with nicotine patch Step 2 for 3 to 4 weeks, then nicotine patch Step 3 for a further 3 to 4 weeks while maintaining the number of nicotine chewing gum 2 mg that is used each day. After use of patches is ceased, gradually reduce the number of gums used until they are no longer needed.

Potential for abuse and dependence:

Nicotine patches are used as an aid to smoking cessation, providing replacement for tobacco based nicotine. Transdermal nicotine is likely to have a very low abuse potential because of its slow onset of action, low fluctuations in blood concentrations, inability to produce high blood concentrations of nicotine, and infrequent use (i.e. once daily). Moreover, gradual weaning from nicotine patches is instituted within the treatment schedule, and the risk of dependence after therapy is minimal. The effects of abrupt withdrawal from nicotine patches are likely to be similar to those observed with tobacco withdrawal from comparable nicotine concentrations. Patients should be encouraged to wean themselves gradually over the treatment period.

OVERDOSAGE

Contact the Poisons Information Centre on 13 11 26 for advice on management of overdose.

The effects of applying several QuitX patches simultaneously or swallowing QuitX patches are unknown (see Precautions).

The oral minimum acute lethal dose for nicotine in human adults is reported to be 40 to 60 mg (< 1 mg/kg).

The minimum lethal dose of nicotine in a non-tolerant man has been estimated to be 40 to 60 mg. Symptoms of acute nicotine poisoning include nausea, 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.

Overdose from topical exposure

QuitX patches should be removed immediately if the patient shows signs of overdosage, and the patient should seek immediate medical care. The skin surface may be flushed with water and dried. No soap should be used, since it may increase nicotine absorption. Nicotine will continue to be delivered into the bloodstream for several hours (see Pharmacokinetics) after removal of the patch because of a depot of nicotine in the skin.

Overdose from ingestion

People ingesting QuitX patches should be referred to a health care facility for management. Due to the possibility of nicotine induced seizures, activated charcoal should be administered. In unconscious patients with a secure airway, instil activated charcoal via a nasogastric tube. A saline cathartic or sorbitol added to the first dose of activated charcoal may speed gastrointestinal passage of the patch. Repeated doses of activated charcoal should be administered as long as the patch remains in the gastrointestinal tract since it will continue to release nicotine for many hours.

Management of nicotine poisoning

All nicotine intake should stop immediately and the patient should be treated symptomatically. Artificial respiration with oxygen should be instituted if necessary. Activated charcoal reduces the gastrointestinal absorption of nicotine.

Other supportive measures include diazepam for seizures, atropine for excessive bronchial secretions or diarrhoea, respiratory support for respiratory failure, and vigorous fluid support for hypotension and cardiovascular collapse.

PRESENTATION AND STORAGE CONDITIONS

Each dosage unit is composed of an impermeable, translucent backing, a nicotine infused silicone adhesive layer, an acrylic adhesive layer, and a removable polyester release liner.

QuitX nicotine 7 mg/24 hours, 9.7 cm^2 square with round corners
QuitX nicotine 14 mg/24 hours, 19.3 cm^2 square with round corners
QuitX nicotine 21 mg/24 hours, 29.0 cm^2 square with round corners.

Available in packs of 7, 14* and 28* sachets.

Store below 25°C

* currently not marketed in Australia

NAME AND ADDRESS OF THE SPONSOR

Medis Pharma Pty Ltd
Level 3, 5 Essex St
The Rocks, Sydney
NSW 2000
Australia

NAME AND ADDRESS OF THE DISTRIBUTOR

Alphapharm Pty Limited
Level 1, 30 The Bond
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ABN 93 002 359 739
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POISON SCHEDULE OF THE MEDICINE

Not Scheduled

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (the ARTG)

5 October 2012

DATE OF MOST RECENT AMENDMENT

10 February 2014