NiQuitin 2 mg Lozenges
PL 00079/0606

NiQuitin 4 mg Lozenges
PL 00079/0607

UKPAR

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LAY SUMMARY

The MHRA granted Beecham Group PLC Marketing Authorisations (licences) for the medicinal products NiQuitin 2mg Lozenges and NiQuitin 4mg Lozenges on 29th March 2007. These products to be available on General sale list (GSL). NiQuitin Lozenges are a stop smoking aid. They can help you give up smoking straightaway or cut down smoking before stopping completely.

NiQuitin Lozenges contain a nicotine resin and when sucked, nicotine is released slowly from the resin and absorbed through the lining of the mouth. This nicotine relieves some of the unpleasant symptoms, such as feeling ill or irritable, that smokers often feel when they try to give up or when they are in situations where they cannot have a cigarette. The nicotine can also reduce your cravings for a cigarette and help you to resist the urge to smoke

These applications are duplicates of previously granted applications for NiQuitin CQ 2mg Lozenge and NiQuitin CQ 4mg Lozenge (PL 00079/0369-70), for which the marketing authorisation holder is Beecham Group plc and which was granted on 24th September 2001.

No new or unexpected safety concerns arose from these simple applications and it was, therefore, judged that the benefits of taking NiQuitin Lozenges outweigh the risks, hence Marketing Authorisations have been granted.

NiQuitin 2 mg Lozenges

PL 00079/0606

NiQuitin 4 mg Lozenges

PL 00079/0607

SCIENTIFIC DISCUSSION

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INTRODUCTION

The UK granted marketing authorisations for the medicinal products NiQuitin 2mg Lozenges and NiQuitin 4mg Lozenges (PL 00079/0606-7) to Beecham Group PLC on 29th March 2007. The products are available as General Sale List (GSL).

The applications were submitted as simple abridged applications according to Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC, cross-referring to NiQuitin CQ 2mg and 4mg Lozenges (PL 00079/0369-70).

NiQuitin Lozenges are indicated for the treatment of tobacco dependence by relief of nicotine withdrawal symptoms including cravings. Permanent cessation of tobacco use is the eventual objective. NiQuitin Lozenges can be used:

- for smoking cessation (abrupt and gradual).
- as an aid for smokers during temporary abstinence.

NiQuitin Lozenges should preferably be used in conjunction with a behavioral support programme.

NiQuitin Lozenges work by replacing some of the nicotine you are used to getting from cigarettes. It is the nicotine in cigarettes that can make you physically addicted to them. This type of treatment is called Nicotine Replacement Therapy (NRT).

No new data was submitted nor was it necessary for these simple applications, as the data are identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no PAR was generated for it.

PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 00079/0606-7
PROPRIETARY NAME: NiQuitin 2mg and 4mg Lozenge
ACTIVE(S): Nicotine Polacrilex
COMPANY NAME: Beecham Group PLC
E.C. ARTICLE: Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC
LEGAL STATUS: GSL

1. INTRODUCTION

This is a simple, piggy back application for NiQuitin 2mg and 4mg Lozenge submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is Beecham Group plc, 980 Great West ROAD, Brentford, Middlesex, TW8 9GS, UK.

The applications cross-refer to NiQuitin CQ 2mg and 4mg Lozenges (PL 00079/0369-70), approved on 24th September 2001 to the marketing authorisation holder Beecham Group PLC. The current applications are considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The proposed names of the products are NiQuitin 2 mg Lozenges and NiQuitin 4 mg Lozenges. The products have been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

The products contain 11.1 and 22.2 mg nicotine polacrilex, equivalent to 2 and 4 mg nicotine. It is to be stored in a Clear or opaque Polyvinyl Chloride, Polyethylene and Polyvinylidene Chloride blisters. The proposed shelf-life (3 years) and storage conditions (Do not store above 25 degrees and store in the original package) are consistent with the details registered for the cross-reference product.

2.3 Legal status

On approval, the products will be available as General Sale List (GSL).

2.4 Marketing authorisation holder/Contact Persons/Company

Beecham Group plc, 980 Great West Road, Brentford, Middlesex, TW8 9GS, United Kingdom

The QP responsible for pharmacovigilance is stated and his CV is included.

2.5 Manufacturers

The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of GMP compliance has been provided.

2.6 Qualitative and quantitative composition

The proposed composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

2.8 Finished product/shelf-life specification
The proposed finished product specifications are in line with the details registered for the cross-reference products.

2.9 Drug substance specification
The proposed drug substance specifications are consistent with the details registered for the cross-reference products.

2.10 TSE Compliance
No materials of animal or human origin are included in the products. This is consistent with the cross reference product.

3. EXPERT REPORTS
The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts' CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS
The proposed summary is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET/CARTON
PIL
The patient information leaflet has been prepared in-line with the details registered for the cross-reference product.

Carton and blister
The proposed artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements.

7. CONCLUSIONS
The data submitted with the applications are acceptable. Marketing Authorisations should be granted.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with these applications and none are required for an application of this type.

CLINICAL ASSESSMENT

No new clinical data have been supplied and none are required.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The data for these applications are consistent with that previously assessed for the cross-reference product and as such have been judged to be satisfactory.

PRECLINICAL
No new preclinical data were submitted and none are required for an application of this type.

EFFICACY
These applications are identical to previously granted applications for NiQuitin CG 2mg Lozenge and NiQuitin CG 4mg Lozenge (PL 00079/0369 and PL 00079/0370).

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with NiQuitin Lozenge is considered to have demonstrated the therapeutic value of the compound. The risk:benefit is, therefore, considered to be positive.

NiQuitin 2 mg Lozenges
PL 00079/0606

NiQuitin 4 mg Lozenges
PL 00079/0607

STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation applications on 02/05/2006.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 09/06/2006.
3	Following assessment of the application the MHRA requested further information on 26/09/2002 and 07/09/2006.
4	The applicant responded to the MHRA's requests, providing further information on 28/10/2006
5	The application was determined on 29/03/2007

NiQuitin 2 mg Lozenges
PL 00079/0606

NiQuitin 4 mg Lozenges
PL 00079/0607

STEPS TAKEN AFTER ASSESSMENT

Date submitted	Application type	Scope	Outcome
11/06/2007	Type II Medical	To update sections of SPC	17/09/2007 Approved
14/09/2007	Type II Medical	To reduce the frequency of the PSUR submission cycle to a 3 yearly submission cycle.	09/10/2007 Approved

NiQuitin 2 mg Lozenges
PL 00079/0606

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
NiQuitin 2 mg Lozenges

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each lozenge contains 2 mg nicotine (as 11.1 mg nicotine polacrilex). For excipients see Section 6.1.

3 PHARMACEUTICAL FORM
Lozenge

White, round lozenge with convex surfaces, debossed NL2 on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

NiQuitin Lozenges are indicated for the treatment of tobacco dependence by relief of nicotine withdrawal symptoms including cravings. Permanent cessation of tobacco use is the eventual objective. NiQuitin Lozenges can be used:

- for smoking cessation (abrupt and gradual).
- as an aid for smokers during temporary abstinence.

NiQuitin Lozenges should preferably be used in conjunction with a behavioral support programme.

4.2 Posology and method of administration

Directions for use:

NiQuitin 2 mg Lozenges are suitable for smokers who have their first cigarette of the day more than 30 minutes after waking up.

One lozenge should be placed in the mouth and allowed to dissolve. Periodically, the lozenge should be moved from one side of the mouth to the other, and repeated, until the lozenge is completely dissolved (approximately 20 – 30 minutes). The lozenge should not be chewed or swallowed whole.

Users should not eat or drink while a lozenge is in the mouth.

Behavioural therapy, advice and support will normally improve the success rate.

Adults (18 years and over):

Abrupt cessation of smoking:

Users should make every effort to stop smoking completely during treatment with NiQuitin Lozenges.

Recommended treatment schedule:

Step 1 **Weeks 1 to 6**	**Step 2** **Weeks 7 to 9**	**Step 3 Weeks 10 to 12**
Initial treatment period	Step down treatment period	Step down treatment period
1 lozenge every 1 to 2 hours	1 lozenge every 2 to 4 hours	1 lozenge every 4 to 8 hours

During weeks 1 to 6 it is recommended that users take a minimum of 9 lozenges per day. Users should not exceed 15 lozenges per day.

To help stay smoke free beyond 12 weeks, users may take 1-2 lozenges per day only on occasions when they are strongly tempted to smoke

Those who use the lozenges beyond 9 months are recommended to seek additional help and advice from a healthcare professional.

Gradual cessation of smoking:

For smokers who are unwilling or unable to quit abruptly.
Use a lozenge whenever there is a strong urge to smoke in order to reduce the number of cigarettes smoked as far as possible and to refrain from smoking as long as possible.
The number of lozenges a day is variable and depends on the patients needs. Nonetheless it should not exceed 15 lozenges per day.
If a reduction in cigarette consumption has not been achieved after 6 weeks of treatment, a healthcare professional should be consulted.

Reduced tobacco consumption should lead to complete cessation of smoking. This should be attempted as soon as possible. When the number of cigarettes has been reduced to a level from which the user feels able to quit completely, then start on the schedule for “abrupt cessation” as given above.
If an attempt to stop smoking completely has not been started within 6 months after the beginning of treatment, it is recommended to consult a healthcare professional.

Temporary abstinence:

Use a lozenge every 1-2 hours to control troublesome withdrawal symptoms including cravings.
Users should not take more than 15 lozenges per day.

Users should be encouraged to stop smoking completely as soon as possible.
If users are still feeling the need to use lozenges on a regular basis 6 months after the start of treatment and have still been unable to undertake a permanent quit attempt, then it is recommended to seek additional help and advice from a healthcare professional.

Adolescents and children:

Adolescents (12-17 years) should follow the schedule of treatment for abrupt cessation of smoking as given above, but as data are limited, duration of NRT in this age group is restricted to 12 weeks. If longer treatment is required, or where adolescents are unwilling or unable to quit smoking abruptly, advice from a healthcare professional should be sought.

NiQuitin Lozenges are not recommended for use in children under 12 years of age.

4.3 Contraindications

NiQuitin Lozenges are contraindicated in:

- those with hypersensitivity to nicotine or any of the excipients;
- children under the age of 12 years and non-smokers.

4.4 Special warnings and precautions for use

The risks associated with the use of NRT are substantially outweighed in virtually all circumstances by the well established dangers of continued smoking.

Patients hospitalised for MI, severe dysrhythmia or CVA who are considered to be haemodynamically unstable should be encouraged to stop smoking with non-pharmacological interventions. If this fails, NiQuitin Lozenges may be considered, but as data on safety in this patient group are limited, initiation should only be under medical supervision. Once patients are discharged from hospital they can use NRT as normal.

Diabetes Mellitus: Patients with diabetes mellitus should be advised to monitor their blood sugar levels more closely than usual when NRT is initiated as catecholamines released by nicotine can affect carbohydrate metabolism.

Allergic reactions: Susceptibility to angioedema and urticaria

A risk-benefit assessment should be made by an appropriate healthcare professional for patients with the following conditions:

- *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:* Use with caution in patients with uncontrolled hyperthyroidism or phaeochromocytoma as nicotine causes release of catecholamines.
- *GI disease:* Swallowed nicotine may exacerbate symptoms in patients suffering from oesophagitis, gastric or peptic ulcers and oral NRT preparations should be used with caution in these conditions. Ulcerative stomatitis has been reported.

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

Stopping smoking: Polycyclic aromatic hydrocarbons in tobacco smoke induce the metabolism of drugs catalysed by CYP 1A2 (and possibly by CYP 1A1). When a smoker stops this may result in a slower metabolism and a consequent rise in blood levels of such drugs.

Transferred dependence: Transferred dependence is rare and is both less harmful and easier to break than smoking dependence.

Phenylketonuria: NiQuitin Lozenges are sugar free, but do contain aspartame which metabolises to phenylalanine, which is of relevance for those with phenylketonuria.

Sodium content: Each NiQuitin Lozenge contains 15 mg of sodium. People on a low sodium diet should take this into account.

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 haemodynamic effects of adenosine.

4.6 Pregnancy and lactation

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.

Ideally smoking cessation during pregnancy should be achieved without NRT. However for women unable to quit on their own, NRT may be recommended to assist a quit attempt. The risk of using NRT to the fetus is lower than that expected with tobacco smoking, due to lower maximal plasma nicotine concentration and no additional exposure to polycyclic hydrocarbons and carbon monoxide.

However, as nicotine passes to the fetus affecting breathing movements and has a dose dependent effect on placental/fetal circulation, the decision to use NRT should be made as early on in the pregnancy as possible. The aim should be to use NRT for only 2-3 months.

Intermittent dosing products may be preferable as these usually provide a lower daily dose of nicotine than patches. However patches may be preferred if the woman is suffering from nausea during pregnancy. If patches are used they should be removed before going to bed.

Lactation

Nicotine from smoking and NRT is found in breast milk. However the amount of nicotine the infant is exposed to from NRT is relatively small and less hazardous than the second-hand smoke they would otherwise be exposed to.

Using intermittent dose NRT preparations, compared with patches, may minimize the amount of nicotine in the breast milk as the time between administrations of NRT and feeding can be more easily prolonged.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

NRT can cause adverse reactions similar to those associated with nicotine administered in other ways including smoking. These may be attributed to the pharmacological effects of nicotine, some of which are dose dependent. At recommended doses NiQuitin Lozenges have not been found to

cause any serious adverse effects. Excessive consumption of NiQuitin Lozenges by those who have not been in the habit of inhaling tobacco smoke could possibly lead to nausea, faintness or headaches.

Certain symptoms which have been reported such as depression, irritability, anxiety and insomnia may be related to withdrawal symptoms associated with smoking cessation. Subjects quitting smoking by any means could expect to suffer from headache, dizziness, sleep disturbance, increased coughing or a cold.

Related adverse events with excess in active compared to placebo group in a controlled study.

Platelet bleeding and clotting disorders

Uncommon >1/1000; <1/100: gingival bleeding; nosebleed

Psychiatric disorders

Common >1/100; <1/10: insomnia; anxiety; irritability; increased appetite

Uncommon >1/1000; <1/100: anger; aggravated anxiety; abnormal dreaming; abnormal hunger; mood swings; wakefulness

Central and peripheral nervous system disorders

Common >1/100; <1/10: headache

Uncommon >1/1000; <1/100: lightheaded feeling; localised numbness

Heart rate and rhythm disorders

Uncommon >1/1000; <1/100: aggravated palpitations; palpitations; tachycardia

Vascular (extracardiac) disorders

Uncommon >1/1000; <1/100: vascular disorder; flushing; skin flushed

Respiratory system disorders

Common >1/100; <1/10: pharyngitis

Uncommon >1/1000; <1/100: laryngismus; aggravated asthma; lower respiratory tract infection; coughing; nasal irritation; throat irritation; nasal congestion

Gastrointestinal system disorders

Very common >1/10: nausea

Common >1/100; <1/10: vomiting; dyspepsia, heartburn, indigestion; hiccup; mouth irritation, mouth ulceration; tongue ulceration; diarrhoea; belching; flatulence

Uncommon >1/1000; <1/100: peptic ucler; dysphagia; aggravated dyspepsia; gastroesophageal reflux; hiatus hernia; oesophagitis; eructation; buccal mucosa ulceration; borborygmus; dry lips; dry throat; tongue disorder; tooth ache

Special senses other, disorders

Uncommon >1/1000; <1/100: parageusia, metallic taste; taste perversion

Skin and appendages disorders

Uncommon >1/1000; <1/100: erythema; itching; rash; skin reaction localised; increased

sweating

Musculoskeletal system disorders

Uncommon >1/1000; <1/100: jaw pain

Urinary system disorders

Uncommon >1/1000; <1/100: nocturia

Body as a whole - general disorders

Uncommon >1/1000; <1/100: overdose effect; pain; leg pain; oedema legs

4.9 Overdose

Symptoms: 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, 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 with oxygen should be instituted if necessary. Activated charcoal reduces the gastro-intestinal absorption of nicotine.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: N07B A01

Nicotine is an agonist at nicotine receptors in the peripheral and central nervous system and has pronounced CNS and cardiovascular effects. When consumed in tobacco products, it has been shown to be addictive and abstinence is linked to craving and withdrawal symptoms. These craving and withdrawal symptoms include urge to smoke, depressed mood, insomnia, irritability, frustration or anger, anxiety, difficulty in concentrating, restlessness and increased appetite or weight gain. The lozenges replace some of the nicotine provided by tobacco and help reduce the severity of these nicotine craving and withdrawal symptoms.

5.2 Pharmacokinetic properties

NiQuitin Lozenges completely dissolve in the oral cavity, and the entire amount of nicotine contained in the lozenge becomes available for buccal absorption or ingestion (swallowing). The complete dissolution of NiQuitin Lozenge is typically achieved in 20-30 minutes. The peak plasma concentrations of nicotine achieved after a single dose are approximately 4.4 ng/ml. When dosed every 1.5 hours, the steady state peak and trough concentrations are 12.7 and 9.4 ng/ml respectively. Ingestion of NiQuitin Lozenges not following dosing instructions (chewed, retained in the mouth, and swallowed; chewed and immediately swallowed) does not result in faster or higher absorption, but a substantial amount of nicotine (80-93%) is still absorbed.

As the plasma protein binding of nicotine is low (4.9% - 20%), the volume of distribution of nicotine is large (2.5 l/kg). The distribution of nicotine to tissue is pH dependent, with the highest concentrations of nicotine found in the brain, stomach, kidney and liver.

Nicotine is extensively metabolized to a number of metabolites, all of which are less active than the parent compound. The metabolism of nicotine primarily occurs in the liver, but also in the lung and kidney. Nicotine is metabolized primarily to cotinine but is also metabolized to nicotine N′-oxide. Cotinine has a half-life of 15-20 hours and its blood levels are 10 times higher than nicotine. Cotinine is further oxidized to *trans*-3′-hydroxycotinine, which is the most abundant metabolite of nicotine in the urine. Both nicotine and cotinine undergo glucuronidation.

The elimination half-life of nicotine is approximately 2 hours (range 1 - 4 hours). Total clearance for nicotine ranges from approximately 62 to 89 l/hr. Non-renal clearance for nicotine is estimated to be about 75% of total clearance. Nicotine and its metabolites are excreted almost exclusively in the urine. The renal excretion of unchanged nicotine is highly dependent on urinary pH, with greater excretion occurring at acidic pH.

5.3 Preclinical safety data

The general toxicity of nicotine is well known and taken into account in the recommended posology. Nicotine was not mutagenic in appropriate assays. The results of carcinogenicity assays did not provide any clear evidence of a tumorigenic effect of nicotine. In studies in pregnant animals, nicotine showed maternal toxicity, and consequential mild fetal toxicity. Additional effects included pre- and postnatal growth retardation and delays and changes in postnatal CNS development.

Effects were only noted following exposure to nicotine at levels in excess of those which will result from recommended use of NiQuitin Lozenges. Effects on fertility have not been established.

Comparison of the systemic exposure necessary to elicit these adverse responses from preclinical test systems with that associated with the recommended use of NiQuitin Lozenges indicate that the potential risk is low and outweighed by the demonstrable benefit of nicotine therapy in smoking cessation. However, NiQuitin Lozenges should only be used by pregnant women on medical advice if other forms of treatment have failed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol

Sodium alginate

Xanthan gum

Potassium bicarbonate

Calcium polycarbophil

Sodium carbonate anhydrous

Aspartame

Magnesium stearate

Menthol mint flavour

6.2 Incompatibilities

None known.

6.3 Shelf life

Three years

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

Clear or opaque Polyvinyl Chloride/Polyethylene/Polyvinylidene Chloride blisters in packs of 12, 36, 72, 96, 108 and 144.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Beecham Group plc

980 Great West Road

Brentford

Middlesex

TW8 9GS

United Kingdom

T/A GlaxoSmithKline Consumer Healthcare
Brentford TW8 9GS, UK.

8 MARKETING AUTHORISATION NUMBER(S)

PL 00079/0606

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29/03/2007

10 DATE OF REVISION OF THE TEXT

17/09/2007

NiQuitin 4 mg Lozenges
PL 00079/0607

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
NiQuitin 4 mg Lozenges

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each lozenge contains 4 mg nicotine (as 22.2 mg nicotine polacrilex). For excipients see Section 6.1.

3 PHARMACEUTICAL FORM
Lozenge

White, round lozenge with convex surfaces, debossed NL4 on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

NiQuitin Lozenges are indicated for the treatment of tobacco dependence by relief of nicotine withdrawal symptoms including cravings. Permanent cessation of tobacco use is the eventual objective. NiQuitin Lozenges can be used:

- for smoking cessation (abrupt and gradual).
- as an aid for smokers during temporary abstinence.

NiQuitin Lozenges should preferably be used in conjunction with a behavioral support programme.

4.2 Posology and method of administration

Directions for use:

NiQuitin 4 mg Lozenges are suitable for smokers who have their first cigarette of the day within 30 minutes of waking up.

One lozenge should be placed in the mouth and allowed to dissolve. Periodically, the lozenge should be moved from one side of the mouth to the other, and repeated, until the lozenge is completely dissolved (approximately 20 – 30 minutes). The lozenge should not be chewed or swallowed whole.

Users should not eat or drink while a lozenge is in the mouth.

Behavioural therapy, advice & support will normally improve the success rate.

Adults (18 years and over):

Abrupt cessation of smoking:

Users should make every effort to stop smoking completely during treatment with NiQuitin Lozenges.

Recommended treatment schedule:

Step 1 **Weeks 1 to 6**	**Step 2** **Weeks 7 to 9**	**Step 3 Weeks 10 to 12**
Initial treatment period	Step down treatment period	Step down treatment period
1 lozenge every 1 to 2 hours	1 lozenge every 2 to 4 hours	1 lozenge every 4 to 8 hours

During weeks 1 to 6 it is recommended that users take a minimum of 9 lozenges per day. Users should not exceed 15 lozenges per day.

To help stay smoke free beyond 12 weeks, users may take 1-2 lozenges per day only on occasions when they are strongly tempted to smoke

Those who use the lozenges beyond 9 months are recommended to seek additional help and advice from a healthcare professional.

Gradual cessation of smoking:

For smokers who are unwilling or unable to quit abruptly.
Use a lozenge whenever there is a strong urge to smoke in order to reduce the number of cigarettes smoked as far as possible and to refrain from smoking as long as possible.
The number of lozenges a day is variable and depends on the patients needs. Nonetheless it should not exceed 15 lozenges per day.
If a reduction in cigarette consumption has not been achieved after 6 weeks of treatment, a healthcare professional should be consulted.

Reduced tobacco consumption should lead to complete cessation of smoking. This should be attempted as soon as possible. When the number of cigarettes has been reduced to a level from which the user feels able to quit completely, then start on the schedule for “abrupt cessation” as given above.
If an attempt to stop smoking completely has not been started within 6 months after the beginning of treatment, it is recommended to consult a healthcare professional.

Temporary abstinence:

Use a lozenge every 1-2 hours to control troublesome withdrawal symptoms including cravings.
Users should not take more than 15 lozenges per day.
Users should be encouraged to stop smoking completely as soon as possible.

If users are still feeling the need to use lozenges on a regular basis 6 months after the start of treatment and have still been unable to undertake a permanent quit attempt, then it is recommended to seek additional help and advice from a healthcare professional.

Adolescents and children:

Adolescents (12-17 years) should follow the schedule of treatment for abrupt cessation of smoking as given above but, as data are limited, duration of NRT in this age group is restricted to 12 weeks. If longer treatment is required, or where adolescents are unwilling or unable to quit smoking abruptly, advice from a healthcare professional should be sought.

NiQuitin Lozenges are not recommended for use in children under 12 years of age.

4.3 Contraindications

NiQuitin Lozenges are contraindicated in:

- those with hypersensitivity to nicotine or any of the excipients;
- children under the age of 12 years and non-smokers.

4.4 Special warnings and precautions for use

The risks associated with the use of NRT are substantially outweighed in virtually all circumstances by the well established dangers of continued smoking.

Patients hospitalised for MI, severe dysrhythmia or CVA who are considered to be haemodynamically unstable should be encouraged to stop smoking with non-pharmacological interventions. If this fails, NiQuitin Lozenges may be considered, but as data on safety in this patient group are limited, initiation should only be under medical supervision. Once patients are discharged from hospital they can use NRT as normal.

Diabetes Mellitus: Patients with diabetes mellitus should be advised to monitor their blood sugar levels more closely than usual when NRT is initiated as catecholamines released by nicotine can affect carbohydrate metabolism.

Allergic reactions: Susceptibility to angioedema and urticaria

A risk-benefit assessment should be made by an appropriate healthcare professional for patients with the following conditions:

- *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:* Use with caution in patients with uncontrolled hyperthyroidism or phaeochromocytoma as nicotine causes release of catecholamines.
- *GI disease*: Swallowed nicotine may exacerbate symptoms in patients suffering from oesophagitis, gastric or peptic ulcers and oral NRT preparations should be used with caution in these conditions. Ulcerative stomatitis has been reported.

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

Stopping smoking: Polycyclic aromatic hydrocarbons in tobacco smoke induce the metabolism of drugs catalysed by CYP 1A2 (and possibly by CYP 1A1). When a smoker stops this may result in a slower metabolism and a consequent rise in blood levels of such drugs.

Transferred dependence: Transferred dependence is rare and is both less harmful and easier to break than smoking dependence.

Phenylketonuria: NiQuitin Lozenges are sugar free, but do contain aspartame which metabolises to phenylalanine, which is of relevance for those with phenylketonuria.

Sodium content: Each NiQuitin Lozenge contains 15 mg of sodium. People on a low sodium diet should take this into account.

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 haemodynamic effects of adenosine.

4.6 Pregnancy and lactation

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.

Ideally smoking cessation during pregnancy should be achieved without NRT. However for women unable to quit on their own, NRT may be recommended to assist a quit attempt. The risk of using NRT to the fetus is lower than that expected with tobacco smoking, due to lower maximal plasma nicotine concentration and no additional exposure to polycyclic hydrocarbons and carbon monoxide.

However, as nicotine passes to the fetus affecting breathing movements and has a dose dependent effect on placental/fetal circulation, the decision to use NRT should be made as early on in the pregnancy as possible. The aim should be to use NRT for only 2-3 months.

Intermittent dosing products may be preferable as these usually provide a lower daily dose of nicotine than patches. However patches may be preferred if the woman is suffering from nausea during pregnancy. If patches are used they should be removed before going to bed.

Lactation

Nicotine from smoking and NRT is found in breast milk. However the amount of nicotine the infant is exposed to from NRT is relatively small and less hazardous than the second-hand smoke they would otherwise be exposed to.

Using intermittent dose NRT preparations, compared with patches, may minimize the amount of nicotine in the breast milk as the time between administrations of NRT and feeding can be more easily prolonged.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

NRT can cause adverse reactions similar to those associated with nicotine administered in other ways, including smoking. These may be attributed to the pharmacological effects of nicotine, some of which are dose dependent. At recommended doses NiQuitin Lozenges have not been found to cause any serious adverse effects. Excessive consumption of NiQuitin Lozenges by those who have not been in the habit of inhaling tobacco smoke could possible lead to nausea, faintness or headaches.

Certain symptoms which have been reported such as depression, irritability, anxiety and insomnia may be related to withdrawal symptoms associated with smoking cessation. Subjects quitting

smoking by any means could expect to suffer from headache, dizziness, sleep disturbance, increased coughing or a cold.

Related adverse events with excess in active compared to placebo group in a controlled study.

Platelet, bleeding and clotting disorders

Uncommon >1/1000; <1/100: gingival bleeding

Metabolic and nutritional disorders

Uncommon >1/1000; <1/100: thirst; excessive thirst

Psychiatric disorders

Common >1/100; <1/10: insomnia

Uncommon >1/1000; <1/100: anxiety; anxiety attack; anxiety reaction; nightmares; marked restlessness; decreased appetite; lost appetite; lethargy

Central and peripheral nervous system disorders

Common >1/100; <1/10: dizziness; headache

Uncommon >1/1000; <1/100; migraine*;* mucosal burning; burning sensation; paraesthesia mouth; sensory disturbance; hyperalertness

Respiratory system disorders

Common >1/100; <1/10: coughing; pharyngitis; sore throat

Uncommon >1/1000; <1/100: dyspnoea; shortness of breath; aggravated cough; lower respiratory tract infection; respiratory disorder; excessive sneezing

Gastrointestinal system disorders

Very common >1/10: nausea; hiccup, flatulence

Common >1/100; <1/10: vomiting; constipation, diarrheoa; dysphagia; dyspepsia; heartburn; indigestion; belching; mouth irritation, mouth ulceration; tongue ulceration; dry mouth; bloating

Uncommon >1/1000; <1/100: gastroesophageal reflux; oesophageal reflux aggravated; retching; eructation; gagging; catarrh; increased saliva; lip ulceration; GI disorder; abdominal griping; sore lips; dry throat

Special senses other, disorders:

Uncommon >1/1000; <1/100: taste perversion

Skin and appendages disorders:

Uncommon >1/1000; <1/100: itching; rash

Body as a whole: general disorders:

Uncommon >1/1000; <1/100: throat swelling; chest pain; tightness of chest; overdose effect; withdrawal syndrome; malaise; hot flushes; halitosis

4.9 Overdose

Symptoms: 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, 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 with oxygen should be instituted if necessary. Activated charcoal reduces the gastro-intestinal absorption of nicotine.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: N07B A01

Nicotine is an agonist at nicotine receptors in the peripheral and central nervous system and has pronounced CNS and cardiovascular effects. When consumed in tobacco products, it has been shown to be addictive and abstinence is linked to craving and withdrawal symptoms. These craving and withdrawal symptoms include urge to smoke, depressed mood, insomnia, irritability, frustration or anger, anxiety, difficulty in concentrating, restlessness and increased appetite or weight gain. The lozenges replace some of the nicotine provided by tobacco and help reduce the severity of these nicotine craving and withdrawal symptoms.

5.2 Pharmacokinetic properties

NiQuitin Lozenges dissolve completely in the oral cavity, and the entire amount of nicotine contained in the lozenge becomes available for buccal absorption or ingestion (swallowing). The complete dissolution of NiQuitin Lozenges is typically achieved in 20-30 minutes. The peak plasma concentrations of nicotine achieved after single dose are approximately 10.8 ng/ml. When dosed every 1.5 hours, the steady state peak and trough concentrations are 26.0 and 19.7 ng/ml respectively. Ingestion of NiQuitin Lozenges not following dosing instruction (chewed, retained in the mouth, and swallowed; chewed and immediately swallowed) does not result in faster or higher absorption, but a substantial amount of nicotine (80-93%) is still absorbed.

As the plasma protein binding of nicotine is low (4.9% - 20%), the volume of distribution of nicotine is large (2.5 l/kg). The distribution of nicotine to tissue is pH dependent, with the highest concentrations of nicotine found in the brain, stomach, kidney and liver.

Nicotine is extensively metabolized to a number of metabolites, all of which are less active than the parent compound. The metabolism of nicotine primarily occurs in the liver, but also in the lung and kidney. Nicotine is metabolized primarily to cotinine but is also metabolized to nicotine N′-oxide. Cotinine has a half-life of 15-20 hours and its blood levels are 10 times higher than nicotine. Cotinine is further oxidized to *trans*-3′-hydroxycotinine, which is the most abundant metabolite of nicotine in the urine. Both nicotine and cotinine undergo glucuronidation.

The elimination half-life of nicotine is approximately 2 hours (range 1 - 4 hours). Total clearance for nicotine ranges from approximately 62 to 89 l/hr. Non-renal clearance for nicotine is estimated to be about 75% of total clearance. Nicotine and its metabolites are excreted almost exclusively in the urine. The renal excretion of unchanged nicotine is highly dependent on urinary pH, with greater excretion occurring at acidic pH.

5.3 Preclinical safety data

The general toxicity of nicotine is well known and taken into account in the recommended posology. Nicotine was not mutagenic in appropriate assays. The results of carcinogenicity assays did not provide any clear evidence of a tumorigenic effect of nicotine. In studies in pregnant animals,

nicotine showed maternal toxicity, and consequential mild fetal toxicity. Additional effects included pre- and postnatal growth retardation and delays and changes in postnatal CNS development.

Effects were only noted following exposure to nicotine at levels in excess of those which will result from recommended use of NiQuitin Lozenges. Effects on fertility have not been established.

Comparison of the systemic exposure necessary to elicit these adverse responses from preclinical test systems with that associated with the recommended use of NiQuitin Lozenges indicate that the potential risk is low and outweighed by the demonstrable benefit of nicotine therapy in smoking cessation. However, NiQuitin Lozenges should only be used by pregnant women on medical advice if other forms of treatment have failed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol

Sodium alginate

Xanthan gum

Potassium bicarbonate

Calcium polycarbophil

Sodium carbonate anhydrous

Aspartame

Magnesium stearate

Menthol mint flavour

6.2 Incompatibilities

None known.

6.3 Shelf life

Three years

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

Clear or opaque Polyvinyl Chloride/Polyethylene/Polyvinylidene Chloride blisters in packs of 12, 36, 72, 96, 108 and 144.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Beecham Group plc

980 Great West Road

Brentford

Middlesex

TW8 9GS

United Kingdom

T/A GlaxoSmithKline Consumer Healthcare
Brentford, TW8 9GS, UK

8 MARKETING AUTHORISATION NUMBER(S)
PL 00079/0607

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
29/03/2007

10 DATE OF REVISION OF THE TEXT
17/09/2007

PATIENT INFORMATION LEAFLET

NiQuitin® 2 mg LOZENGE

Nicotine

11mm

DUMMY

8mm

Please read this leaflet before you start to use your lozenges and keep it until you have used all of them as you may want to read it again. If you are unsure about anything ask a healthcare professional e.g. doctor, nurse, smoking cessation advisor or pharmacist.

What are NiQuitin Lozenges and what are they used for?

What is in NiQuitin 2 mg Lozenges?

Each lozenge contains 2 mg nicotine in the form of a resin complex (nicotine polacrilex 11.1mg). Other ingredients are mannitol (E 421), sodium alginate, xanthan gum, potassium bicarbonate, calcium polycarbophil, sodium carbonate, aspartame (E 951), magnesium stearate and mint flavour.
NiQuitin 2 mg Lozenges are available in packs of 36 and 72 lozenges.

Who makes NiQuitin Lozenges?

The Marketing Authorisation Holder is GlaxoSmithKline Consumer Healthcare, Brentford TW8 9GS, U.K. and all enquiries should be sent to this address.
The manufacturer of **NiQuitin Lozenges** is Cardinal Health, Sedge Close, Headway, Great Oakley, Corby, Northamptonshire NN18 8HS.

What are NiQuitin Lozenges for?

NiQuitin Lozenges are a stop smoking aid. They can help you give up smoking straightaway or cut down smoking before stopping completely. See "How should you use NiQuitin Lozenges" for further details.

NiQuitin Lozenges work by replacing some of the nicotine you are used to getting from cigarettes. It is the nicotine in cigarettes that can make you physically addicted to them. This type of treatment is called Nicotine Replacement Therapy (NRT). **NiQuitin Lozenges** contain a nicotine resin and when sucked, nicotine is released slowly from the resin and absorbed through the lining of the mouth. This nicotine relieves some of the unpleasant symptoms, such as feeling ill or irritable, that smokers often feel when they try to give up or when they are in situations where they cannot have a cigarette. The nicotine can also reduce your cravings for a cigarette and help you to resist the urge to smoke.

Because NiQuitin Lozenges do not contain the tar, carbon monoxide or other toxins in cigarette smoke, they do not have the health dangers of tobacco.

NiQuitin Lozenges come in two strengths, each strength comes in its own pack. This pack contains **NiQuitin 2 mg Lozenges** which are for smokers who have their first cigarette of the day more than 30 minutes after waking up. **NiQuitin 4 mg Lozenges** are available for people who usually have their first cigarette within 30 minutes of waking up.
If possible, NiQuitin Lozenges should be used with a stop smoking behavioural support programme – see the insert in this pack for more details. Behavioural therapy, advice and support will normally improve your success rate.

Can you use NiQuitin Lozenges?

IMPORTANT

Do not use NiQuitin Lozenges if:

- you are allergic to nicotine or any of the other ingredients in the product
- you are a non-smoker or under the age of 12 years.

There are no health benefits to smoking. It is always better to give up smoking and using NRT can help. In general any possible side effects associated with NRT are far outweighed by the well established dangers of continuing to smoke.

If you are in hospital because of a heart attack, severe heart rhythm disturbances or a stroke you should try to quit smoking without using NRT unless your doctor tells you to use it. Once you are discharged from hospital, you can use NRT as normal.

If you have diabetes you should monitor your blood sugar levels more often than usual when starting **NiQuitin Lozenges** as you may find your insulin/medication requirements alter.

If you have had allergic reactions that involve swelling of the lips, face and throat (angioedema) or itchy skin rash (urticaria), using NRT can sometimes trigger this type of reaction.
There are some circumstances (listed below) where you should get help and advice from a healthcare professional.

Get help and advice from a healthcare professional if you have:

- **Serious liver or kidney disease** because you may be more prone to side effects.
- **Uncontrolled, overactive thyroid gland or phaeochromocytoma** (a tumour of the adrenal gland that can affect blood pressure) – your doctor will have told you this – because nicotine may make your symptoms worse.
- **Stomach/duodenal ulcers or inflammation of the oesophagus** (the passage between the mouth and stomach) because swallowing nicotine can make your symptoms worse. Some people have reported getting mouth ulcers. If your symptoms do get worse you should talk to your doctor and you might want to use a non-oral format of NRT instead e.g. patches.

If you are pregnant or breast feeding it is best if you can give up smoking without the use of NRT. However, it is better to stop smoking using NRT than to continue smoking. See below for more information.

If you are pregnant
Smoking during pregnancy has risks such as poor growth of your baby before birth, premature birth or stillbirth. Stopping smoking is the best way to improve both your health and that of your baby and the earlier you stop smoking the better.

Ideally, if you are pregnant you should stop smoking without using NRT. However, if you have tried and this hasn't worked, NRT may be recommended to help you stop smoking. This is because it is better for your developing baby than if you carry on smoking. The decision to use NRT should be made as early on in your pregnancy as possible and you should aim to use it for only 2-3 months. Remember, the most important thing is to stop smoking.

Products that are taken intermittently, such as lozenges, may be preferable to nicotine patches. However, patches may be preferred if you have nausea or sickness.

If you are breast feeding
Tobacco smoke causes breathing difficulties and other problems in babies and children. If you need to use NRT to help you quit, the amount of nicotine your baby may receive is much smaller and less harmful than breathing in second hand smoke. It is best to use NRT products that are taken intermittently (e.g. gum or lozenge, rather than patches) and to breast feed just before you take the product. This helps your baby to get the smallest amount of nicotine possible.

Other things you may need to know about **NiQuitin Lozenges:**

Sodium
Each lozenge contains about 15 mg sodium and the maximum daily dose of **NiQuitin Lozenges** (15 lozenges) contains 225 mg sodium. The maximum daily dose may be harmful if you are on a low sodium diet.

Phenylketonuria
NiQuitin Lozenges are sugar free, but do contain aspartame, a source of phenylalanine which may be harmful to you if you suffer from phenylketonuria.

Children (under 12 years)
Doses of nicotine that may be used by smoking adults are not suitable for small children who are more susceptible to its effects. Severe toxicity can be fatal. Make sure you keep nicotine containing products out of the reach and sight of children at all times.

Giving up smoking & other medicines
Stopping smoking may alter the effect of other medicines you may be taking. If you have any questions or concerns about this, talk to a healthcare professional.

Transferred dependence
Some people worry that they will quit smoking but become dependent on the nicotine lozenges. This is very rare, and if it did happen, it is less harmful to you than continuing to smoke, and an easier habit to break.

How should you use NiQuitin Lozenges?

NiQuitin 2mg Lozenges are suitable for smokers who have their first cigarette of the day more than 30 minutes after waking up.

They can be used for:
- **Stopping smoking straightaway**
- **Cutting down before stopping**

Please see sections below for further details.

continued overleaf

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If you think you can stop smoking straight away then you should. However, if you feel this is too big a step, then you may wish to try cutting down the amount of cigarettes you smoke as a first step before stopping completely.

How to use your lozenges

Put one lozenge in your mouth and periodically move it from one side of your mouth to the other, until it has completely dissolved. This should take 20 to 30 minutes.
- Do not chew the lozenge or swallow it whole.
- You should not eat or drink while a lozenge is in your mouth as this may reduce the absorption of the nicotine.
- Do not use more than 15 lozenges a day.

If you feel you need to use the lozenges for longer than 9 months (3 months for 12-17 years olds), you should talk to a healthcare professional.

Adults (18 years and over)

Stopping smoking straightaway

It is important that you make every effort to stop smoking completely if you are trying to give up straightaway. However, if you do smoke a cigarette while you are using NRT, you should continue your quit attempt but talking to a healthcare professional may help.

For the first 6 weeks use at least 9 lozenges a day (maximum 15) and take one lozenge every 1-2 hours when you have an urge to smoke. You should then gradually reduce the number of lozenges you use by taking one lozenge every 2-4 hours during weeks 7-9 and one lozenge every 4-8 hours during weeks 10-12. To help you stay smoke free you can then take 1-2 lozenges a day but only when you have a very strong urge to smoke.

Once you are using only 1-2 lozenges a day, try to stop using them altogether. However, you may occasionally feel a sudden craving to smoke, even a long time after you've given up, and you can take a lozenge if this happens.

Cutting down before stopping smoking

If stopping smoking straightaway is too big a step for you, you can try cutting down the number of cigarettes you smoke first.

When you feel an urge to smoke, use a lozenge instead of a cigarette. Cut down the number of cigarettes you smoke each day by as many as possible. If you have not been able to cut down the number of cigarettes you smoke each day after 6 weeks, talk to a healthcare professional.

As soon as you feel able, you should give up cigarettes completely. Follow the instructions for stopping smoking straightaway given above. Do this as soon as possible. If you have not been able to make a quit attempt within 6 months of starting to use the lozenges, speak to a healthcare professional.

Young people aged 12 to 17 years old

You should follow the instructions above for stopping smoking straightaway, but you should not use the lozenges for longer than 12 weeks. Use at least 9 lozenges a day (maximum 15) for the first 6 weeks then gradually reduce the number of lozenges you use before stopping completely. If you think you may need to use the lozenges for longer than 12 weeks, or if you are not ready to stop smoking straightaway, get advice from a healthcare professional.

Do not exceed the stated dose.

Children under 12 years old should not use **NiQuitin Lozenges.**

If you are worried that you may start smoking again, or are finding it difficult to stop using NRT completely, talk to a healthcare professional. If you do start to smoke again, they can advise you on how to get the best results from further courses of NRT.

What should you do if you take too many lozenges?

If you take too many **NiQuitin Lozenges** you may start to feel sick, dizzy and unwell. Stop using the lozenges and get immediate medical advice from a doctor or hospital casualty department. If possible, show them the packet or this leaflet.

The lozenges are not suitable for children under 12 or non-smokers. They may develop signs of nicotine overdose including headache, sickness, stomach pains and diarrhoea. If a child has used or eaten any of the lozenges, contact your doctor or nearest hospital casualty department immediately. If possible show them the packet or this leaflet.

Are there any side effects?

At the recommended doses **NiQuitin Lozenges** have not been found to cause any serious side effects.
Stopping smoking itself can cause some symptoms such as dizziness, headache, sleep disturbance, cough and cold-like symptoms. Symptoms such as depression, irritability, anxiety and insomnia may also be related to withdrawal symptoms associated with giving up smoking.
Side effects of the nicotine in all NRT products are similar to those you might get from the nicotine in cigarettes, and are more likely the more nicotine you take. They include feeling/being sick, hiccups, burping, wind, feeling bloated, diarrhoea, constipation, difficulty swallowing, dry mouth/throat/lips, sore throat, mouth irritation, ulcers in/around mouth, indigestion, heartburn.

Less common side effects are bad dreams, restlessness, lethargy, alertness, migraine, bad breath, increase in saliva, shortness of breath, tight chest, chest pain, stomach pains, changes in appetite, taste changes, rash, itchy skin, hot flushes and feeling unwell.

None of the above side effects are usually serious, and often wear off after a few days' treatment. If they are troublesome and do not improve, or if you experience any other unwanted effects, stop using the lozenges and tell a healthcare professional.

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Further Information

Where should I keep NiQuitin Lozenges?

Keep all lozenges in the carton, in their blister pack, until you are ready to use one. Do not store above 25°C. Do not use the lozenges after the 'EXP' date shown on the pack
Remember: Keep all medicines out of the reach and sight of children.
Date of leaflet revision: February 2007.
If you have any questions or comments about **NiQuitin Lozenge**
please FREEPHONE our Information Line on 0500 100 222.

GlaxoSmithKline

GlaxoSmithKline Consumer Healthcare, Brentford, TW8 9GS, U.K.
NiQuitin is a registered trademark of the GlaxoSmithKline group of companies.

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NiQuitin® 4 mg LOZENGE

Nicotine

11mm

DUMMY

8mm

Please read this leaflet before you start to use your lozenges and keep it until you have used all of them as you may want to read it again. If you are unsure about anything ask a healthcare professional e.g. doctor, nurse, smoking cessation advisor or pharmacist.

What are NiQuitin Lozenges and what are they used for?

What is in NiQuitin 4 mg Lozenges?

Each lozenge contains 4 mg nicotine in the form of a resin complex (nicotine polacrilex 22.2 mg). Other ingredients are mannitol (E 421), sodium alginate, xanthan gum, potassium bicarbonate, calcium polycarbophil, sodium carbonate, aspartame (E 951), magnesium stearate and mint flavour.
NiQuitin 4 mg Lozenges are available in packs of 36 and 72 lozenges.

Who makes NiQuitin Lozenges?

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What are NiQuitin Lozenges for?

NiQuitin Lozenges are a stop smoking aid. They can help you give up smoking straightaway or cut down smoking before stopping completely. See "How should you use NiQuitin Lozenges" for further details.

NiQuitin Lozenges work by replacing some of the nicotine you are used to getting from cigarettes. It is the nicotine in cigarettes that can make you physically addicted to them. This type of treatment is called Nicotine Replacement Therapy (NRT). **NiQuitin Lozenges** contain a nicotine resin and when sucked, nicotine is released slowly from the resin and absorbed through the lining of the mouth. This nicotine relieves some of the unpleasant symptoms, such as feeling ill or irritable, that smokers often feel when they try to give up or when they are in situations where they cannot have a cigarette. The nicotine can also reduce your cravings for a cigarette and help you to resist the urge to smoke.

Because NiQuitin Lozenges do not contain the tar, carbon monoxide or other toxins in cigarette smoke, they do not have the health dangers of tobacco.

NiQuitin Lozenges come in two strengths, each strength comes in its own pack. This pack contains **NiQuitin 4 mg Lozenges** which are for smokers who have their first cigarette of the day within 30 minutes of waking up. **NiQuitin 2 mg Lozenges** are available for people who usually have their first cigarette more than 30 minutes after waking up.
If possible, NiQuitin Lozenges should be used with a stop smoking behavioural support programme – see the insert in this pack for more details. Behavioural therapy, advice and support will normally improve your success rate.

Can you use NiQuitin Lozenges?

IMPORTANT

Do not use NiQuitin Lozenges if:

- you are allergic to nicotine or any of the other ingredients in the product
- you are a non-smoker or under the age of 12 years.

There are no health benefits to smoking. It is always better to give up smoking and using NRT can help. In general any possible side effects associated with NRT are far outweighed by the well established dangers of continuing to smoke.

If you are in hospital because of a heart attack, severe heart rhythm disturbances or a stroke you should try to quit smoking without using NRT unless your doctor tells you to use it. Once you are discharged from hospital, you can use NRT as normal.

If you have diabetes you should monitor your blood sugar levels more often than usual when starting **NiQuitin Lozenges** as you may find your insulin/medication requirements alter.

If you have had allergic reactions that involve swelling of the lips, face and throat (angioedema) or itchy skin rash (urticaria), using NRT can sometimes trigger this type of reaction.
There are some circumstances (listed below) where you should get help and advice from a healthcare professional.

Get help and advice from a healthcare professional if you have:

- **Serious liver or kidney disease because you may be more prone to side effects.**
- **Uncontrolled, overactive thyroid gland or phaeochromocytoma (a tumour of the adrenal gland that can affect blood pressure) – your doctor will have told you this – because nicotine may make your symptoms worse.**
- **Stomach/duodenal ulcers or inflammation of the oesophagus (the passage between the mouth and stomach) because swallowing nicotine can make your symptoms worse. Some people have reported getting mouth ulcers. If your symptoms do get worse you should talk to your doctor and you might want to use a non-oral format of NRT instead e.g. patches.**

If you are pregnant or breast feeding it is best if you can give up smoking without the use of NRT. However, it is better to stop smoking using NRT than to continue smoking. See below for more information.

If you are pregnant
Smoking during pregnancy has risks such as poor growth of your baby before birth, premature birth or stillbirth. Stopping smoking is the best way to improve both your health and that of your baby and the earlier you stop smoking the better.

Ideally, if you are pregnant you should stop smoking without using NRT. However, if you have tried and this hasn't worked, NRT may be recommended to help you stop smoking. This is because it is better for your developing baby than if you carry on smoking. The decision to use NRT should be made as early on in your pregnancy as possible and you should aim to use it for only 2-3 months. Remember, the most important thing is to stop smoking.

Products that are taken intermittently, such as lozenges, may be preferable to nicotine patches. However, patches may be preferred if you have nausea or sickness.

If you are breast feeding
Tobacco smoke causes breathing difficulties and other problems in babies and children. If you need to use NRT to help you quit, the amount of nicotine your baby may receive is much smaller and less harmful than breathing in second hand smoke. It is best to use NRT products that are taken intermittently (e.g. gum or lozenge, rather than patches) and to breast feed just before you take the product. This helps your baby to get the smallest amount of nicotine possible.

Other things you may need to know about **NiQuitin Lozenges:**

Sodium
Each lozenge contains about 15 mg sodium and the maximum daily dose of **NiQuitin Lozenges** (15 lozenges) contains 225 mg sodium. The maximum daily dose may be harmful if you are on a low sodium diet.

Phenylketonuria
NiQuitin Lozenges are sugar free but do contain aspartame which may be harmful to you if you suffer from phenylketonuria.

Children (under 12 years)
Doses of nicotine that may be used by smoking adults are not suitable for small children who are more susceptible to its effects. Severe toxicity can be fatal. Make sure you keep nicotine containing products out of the reach and sight of children at all times.

Giving up smoking & other medicines
Stopping smoking may alter the effect of other medicines you may be taking. If you have any questions or concerns about this, talk to a healthcare professional.

Transferred dependence
Some people worry that they will quit smoking but become dependent on the nicotine lozenges. This is very rare, and if it did happen, it is less harmful to you than continuing to smoke, and an easier habit to break.

How should you use NiQuitin Lozenges?

NiQuitin 4 mg Lozenges are suitable for smokers who have their first cigarette of the day within 30 minutes of waking up.

They can be used for:

- **Stopping smoking straightaway**
- **Cutting down before stopping**

Please see sections below for further details.

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If you think you can stop smoking straight away then you should. However, if you feel this is too big a step, then you may wish to try cutting down the amount of cigarettes you smoke as a first step before stopping completely.

How to use your lozenges

Put one lozenge in your mouth and periodically move it from one side of your mouth to the other, until it has completely dissolved. This should take 20 to 30 minutes.
- Do not chew the lozenge or swallow it whole.
- You should not eat or drink while a lozenge is in your mouth as this may reduce the absorption of the nicotine.
- Do not use more than 15 lozenges a day.

If you feel you need to use the lozenges for longer than 9 months (3 months for 12-17 years olds), you should talk to a healthcare professional.

Adults (18 years and over)

Stopping smoking straightaway

It is important that you make every effort to stop smoking completely if you are trying to give up straightaway. However, if you do smoke a cigarette while you are using NRT, you should continue your quit attempt but talking to a healthcare professional may help.

For the first 6 weeks use at least 9 lozenges a day (maximum 15) and take one lozenge every 1-2 hours when you have an urge to smoke. You should then gradually reduce the number of lozenges you use by taking one lozenge every 2-4 hours during weeks 7-9 and one lozenge every 4-8 hours during weeks 10-12. To help you stay smoke free you can then take 1-2 lozenges a day but only when you have a very strong urge to smoke.

Once you are using only 1-2 lozenges a day, try to stop using them altogether. However, you may occasionally feel a sudden craving to smoke, even a long time after you've given up, and you can take a lozenge if this happens.

Cutting down before stopping smoking

If stopping smoking straightaway is too big a step for you, you can try cutting down the number of cigarettes you smoke first.

When you feel an urge to smoke, use a lozenge instead of a cigarette. Cut down the number of cigarettes you smoke each day by as many as possible. If you have not been able to cut down the number of cigarettes you smoke each day after 6 weeks, talk to a healthcare professional.

As soon as you feel able, you should give up cigarettes completely. Follow the instructions for stopping smoking straightaway given above. Do this as soon as possible. If you have not been able to make a quit attempt within 6 months of starting to use the lozenges, speak to a healthcare professional.

Young people aged 12 to 17 years old

You should follow the instructions above for stopping smoking straightaway, but you should not use the lozenges for longer than 12 weeks. Use at least 9 lozenges a day (maximum 15) for the first 6 weeks then gradually reduce the number of lozenges you use before stopping completely. If you think you may need to use the lozenges for longer than 12 weeks, or if you are not ready to stop smoking straightaway, get advice from a healthcare professional.

Do not exceed the stated dose.

Children under 12 years old should not use **NiQuitin Lozenges.**

If you are worried that you may start smoking again, or are finding it difficult to stop using NRT completely, talk to a healthcare professional. If you do start to smoke again, they can advise you on how to get the best results from further courses of NRT.

What should you do if you take too many lozenges?

If you take too many **NiQuitin Lozenges** you may start to feel sick, dizzy and unwell. Stop using the lozenges and get immediate medical advice from a doctor or hospital casualty department. If possible, show them the packet or this leaflet.

The lozenges are not suitable for children under 12 or non-smokers. They may develop signs of nicotine overdose including headache, sickness, stomach pains and diarrhoea. If a child has used or eaten any of the lozenges, contact your doctor or nearest hospital casualty department immediately. If possible show them the packet or this leaflet.

Are there any side effects?

At the recommended doses **NiQuitin Lozenges** have not been found to cause any serious side effects.
Stopping smoking itself can cause some symptoms such as dizziness, headache, sleep disturbance, cough and cold-like symptoms. Symptoms such as depression, irritability, anxiety and insomnia may also be related to withdrawal symptoms associated with giving up smoking.
Side effects of the nicotine in all NRT products are similar to those you might get from the nicotine in cigarettes, and are more likely the more nicotine you take. They include feeling/being sick, hiccups, burping, wind, feeling bloated, diarrhoea, constipation, difficulty swallowing, dry mouth/throat/lips, sore throat, mouth irritation, ulcers in/around mouth, indigestion, heartburn.

Less common side effects are bad dreams, restlessness, lethargy, alertness, migraine, bad breath, increase in saliva, shortness of breath, tight chest, chest pain, stomach pains, changes in appetite, taste changes, rash, itchy skin, hot flushes and feeling unwell.

None of the above side effects are usually serious, and often wear off after a few days' treatment. If they are troublesome and do not improve, or if you experience any other unwanted effects, stop using the lozenges and tell a healthcare professional.

11mm

Further Information

Where should I keep NiQuitin Lozenges?

Keep all lozenges in the carton, in their blister pack, until you are ready to use one. Do not store above 25°C. Do not use the lozenges after the 'EXP' date shown on the pack
Remember: Keep all medicines out of the reach and sight of children.
Date of leaflet revision: February 2007.
If you have any questions or comments about **NiQuitin Lozenge**
please FREEPHONE our Information Line on 0500 100 222.

GlaxoSmithKline

GlaxoSmithKline Consumer Healthcare, Brentford, TW8 9GS, U.K.
NiQuitin is a registered trademark of the GlaxoSmithKline group of companies.

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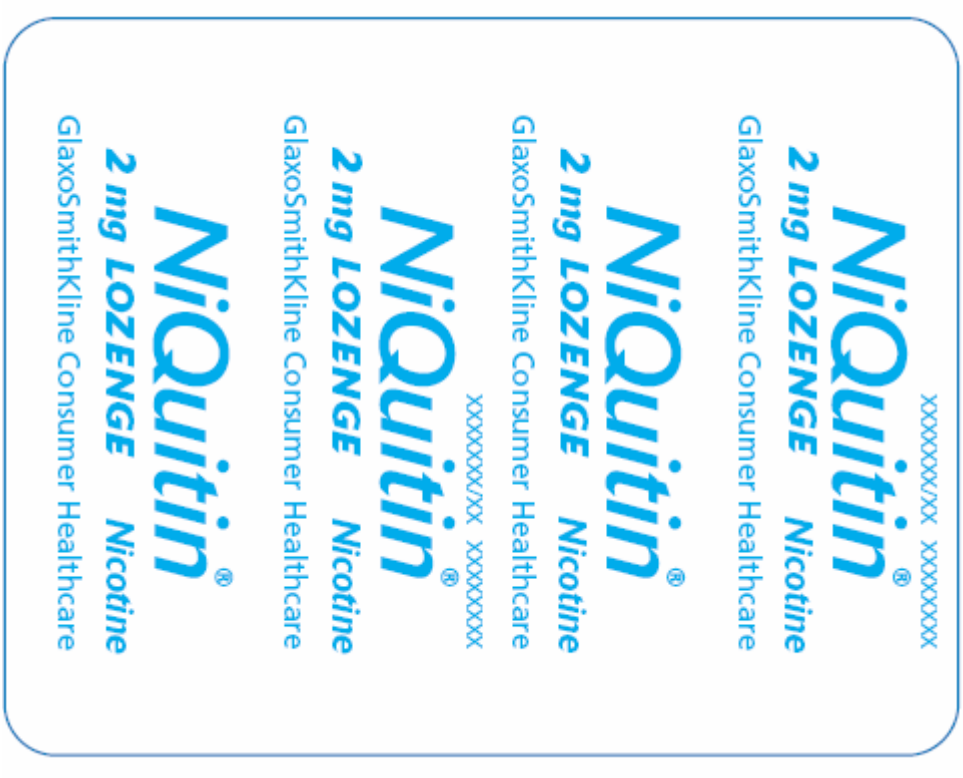
LABELLING


NiQuitin®
2 mg LOZENGE Nicotine
GlaxoSmithKline Consumer Healthcare
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NiQuitin®
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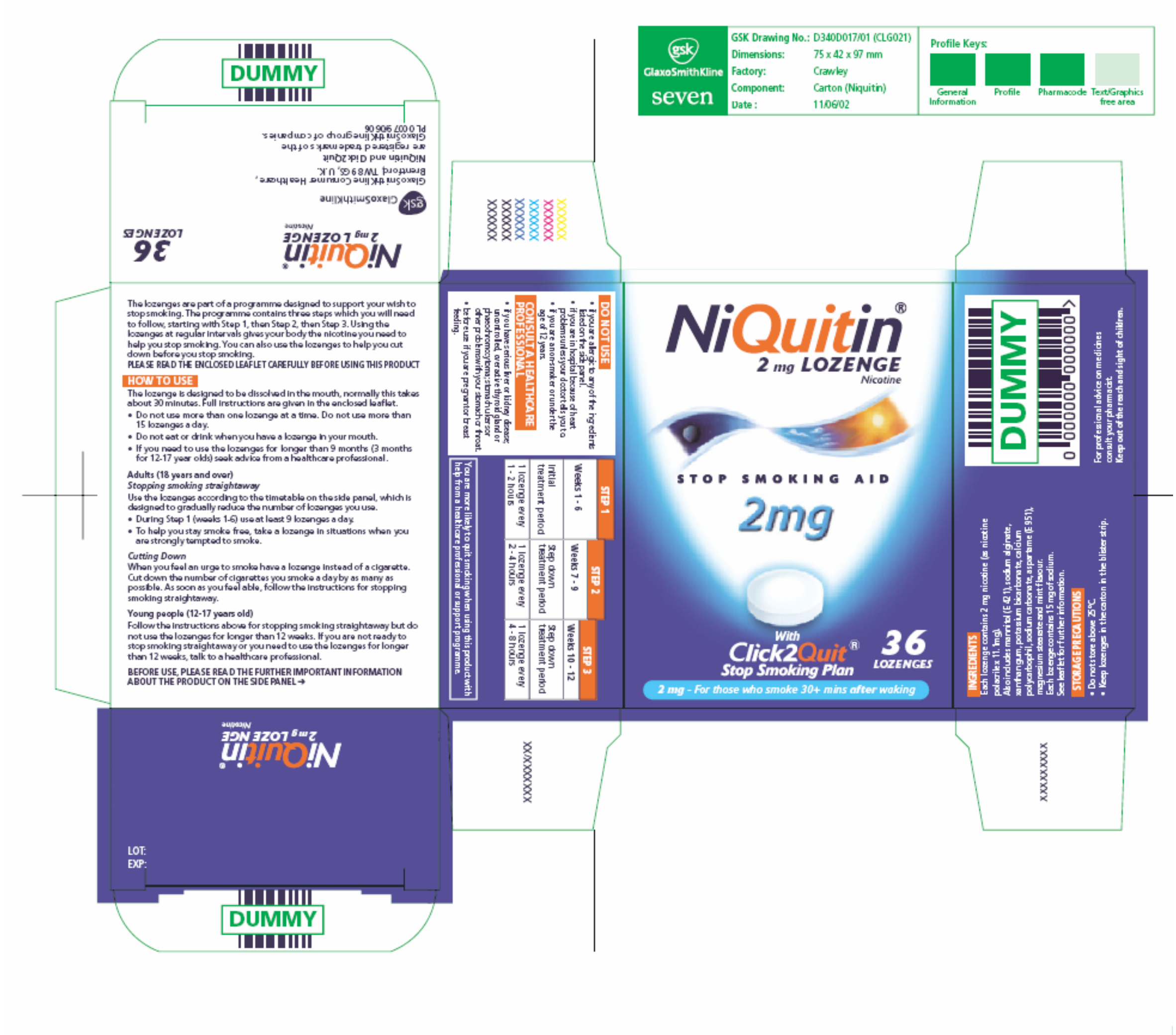
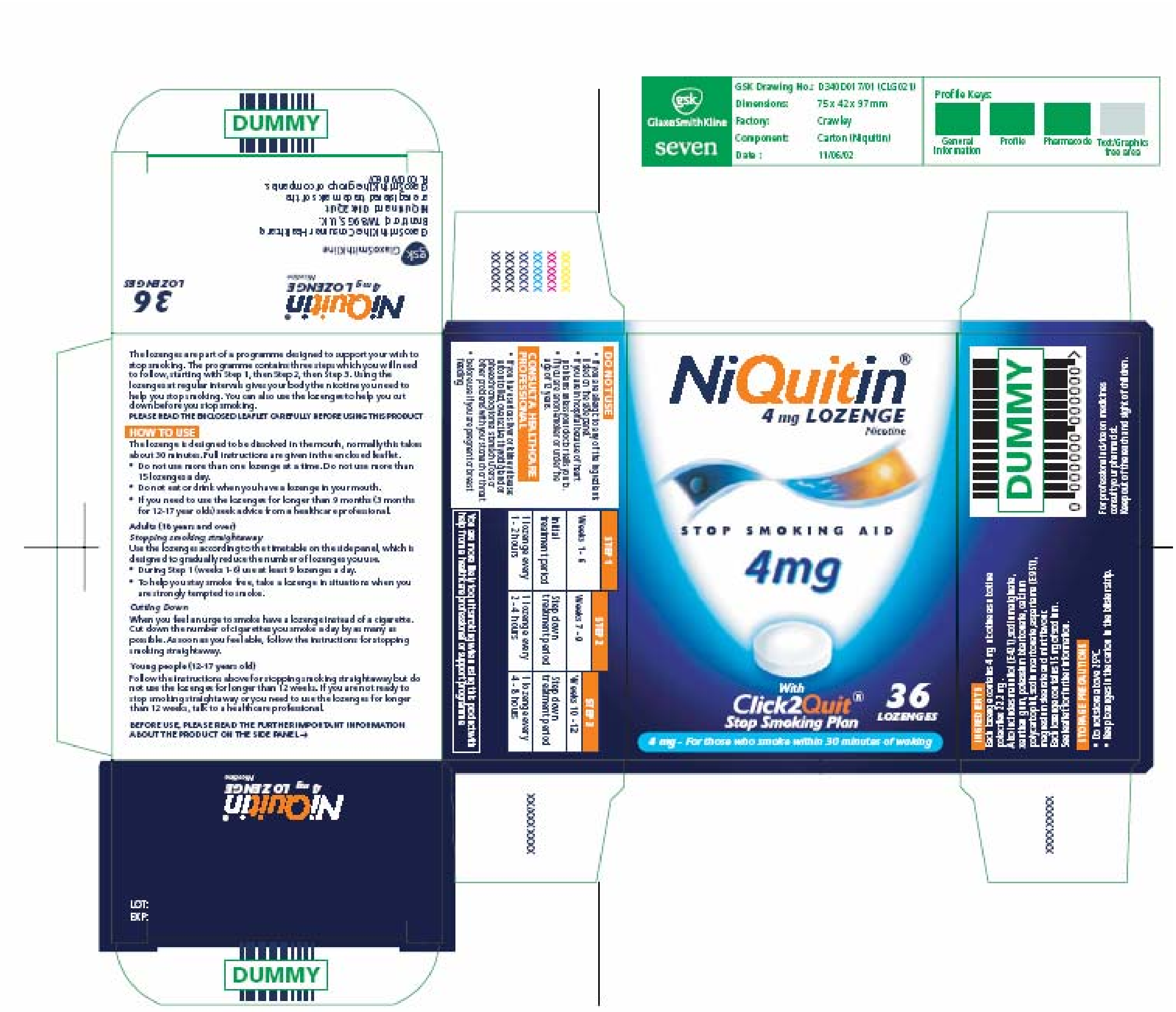


GSK Drawing No.: D340D017/01 (CLG021)
Dimensions: 75 x 42 x 97 mm
Factory: Crawley
Component: Carton (Niquitin)
Date: 11/06/02
GlaxoSmithKline
seven
Profile Keys:
General Information
Profile
Pharmacode
Text/Graphics free area
DUMMY
NiQuitin 2 mg LOZENGE Nicotine
36 LOZENGES
GlaxoSmithKline
The lozenges are part of a programme designed to support your wish to stop smoking. The programme contains three steps which you will need to follow, starting with Step 1, then Step 2, then Step 3. Using the lozenges at regular intervals gives your body the nicotine you need to help you stop smoking. You can also use the lozenges to help you cut down before you stop smoking.
PLEASE READ THE ENCLOSED LEAFLET CAREFULLY BEFORE USING THIS PRODUCT
HOW TO USE
The lozenge is designed to be dissolved in the mouth, normally this takes about 30 minutes. Full instructions are given in the enclosed leaflet.
• Do not use more than one lozenge at a time. Do not use more than 15 lozenges a day.
• Do not eat or drink when you have a lozenge in your mouth.
• If you need to use the lozenges for longer than 9 months (3 months for 12-17 year olds) seek advice from a healthcare professional.
Adults (18 years and over)
Stopping smoking straightaway
Use the lozenges according to the timetable on the side panel, which is designed to gradually reduce the number of lozenges you use.
• During Step 1 (weeks 1-6) use at least 9 lozenges a day.
• To help you stay smoke free, take a lozenge in situations when you are strongly tempted to smoke.
Cutting Down
When you feel an urge to smoke have a lozenge instead of a cigarette. Cut down the number of cigarettes you smoke a day by as many as possible. As soon as you feel able, follow the instructions for stopping smoking straightaway.
Young people (12-17 years old)
Follow the instructions above for stopping smoking straightaway but do not use the lozenges for longer than 12 weeks. If you are not ready to stop smoking straightaway or you need to use the lozenges for longer than 12 weeks, talk to a healthcare professional.
BEFORE USE, PLEASE READ THE FURTHER IMPORTANT INFORMATION ABOUT THE PRODUCT ON THE SIDE PANEL →
NiQuitin 2 mg LOZENGE Nicotine
LOT:
EXP:
DO NOT USE
CONSULT A HEALTHCARE PROFESSIONAL
STEP 1
Weeks 1 - 6
Initial treatment period
1 lozenge every 1 - 2 hours
STEP 2
Weeks 7 - 9
Step down treatment period
1 lozenge every 2 - 4 hours
STEP 3
Weeks 10 - 12
Step down treatment period
1 lozenge every 4 - 8 hours
You are more likely to quit smoking when using this product with help from a healthcare professional or support programme.
NiQuitin®
2 mg LOZENGE
Nicotine
STOP SMOKING AID
2mg
With Click2Quit® Stop Smoking Plan
36 LOZENGES
2 mg - For those who smoke 30+ mins after waking
INGREDIENTS
STORAGE PRECAUTIONS

NiQuitin®
4 mg LOZENGE Nicotine
GlaxoSmithKline Consumer Healthcare
XXXXXXX/XX XXXXXXX

NiQuitin®
4 mg LOZENGE Nicotine
GlaxoSmithKline Consumer Healthcare
XXXXXXX/XX XXXXXXX

NiQuitin®
4 mg LOZENGE Nicotine
GlaxoSmithKline Consumer Healthcare


GSK Drawing No.: D340D01 7/01 (CLG021)
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NiQuitin®
4 mg LOZENGE
Nicotine
STOP SMOKING AID
4mg
With
Click2Quit®
Stop Smoking Plan
36
LOZENGES
4 mg - For those who smoke within 30 minutes of waking
LOT:
EXP: