Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nicotinell Fruity Mint 1 mg compressed lozenge

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each piece of lozenge contains:

Active substance: 1 mg nicotine (corresponding to 3.072 mg nicotine bitartrate dihydrate).

Excipient(s) with known effect:
aspartame (0.01 g), maltitol (0.9 g), sulphites (0.00005 mg) and sodium (9.8 mg).
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Compressed lozenge

White, fruit-mint flavoured, round biconvex lozenge

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Nicotinell Fruity Mint is indicated in adults.

Treatment of tobacco dependence by providing relief of nicotine withdrawal symptoms including cravings (see section 5.1), thereby facilitating smoking cessation or temporary smoking reduction in smokers motivated to quit smoking. Permanent cessation of tobacco use is the eventual objective.

Patient counselling and support normally improve the success rate.

4.2 Posology and method of administration

Nicotinell Fruity Mint lozenge 1 mg may be used alone or in combination with Nicotinell transdermal patch.

Paediatric population

Nicotinell Fruity Mint could only be used in adolescents (aged 12-17 years) with advice and medical supervision from a physician.

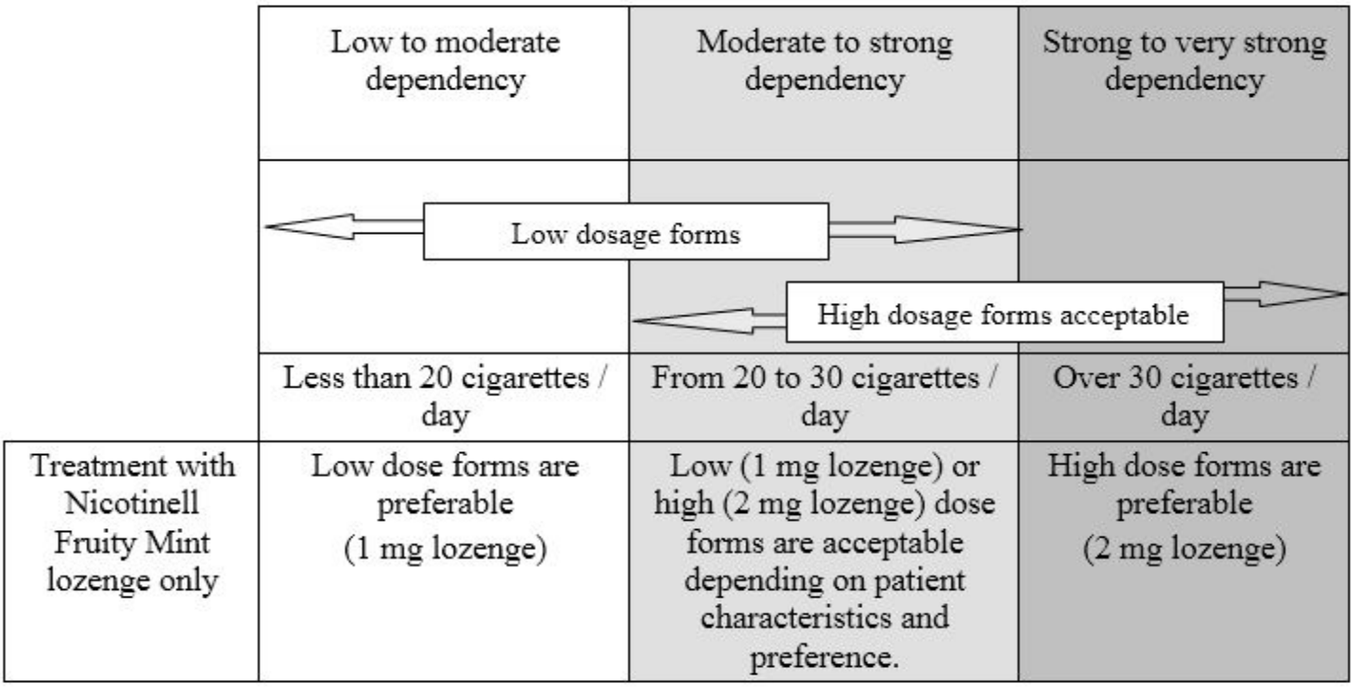
Nicotinell Fruity Mint is not recommended for use in children under 12 years of age. The safety and efficacy of Nicotinell Fruity Mint in children under 12 years of age have not been established. No data are available.

Adults and elderly

Posology:

Treatment with Nicotinell Lozenges only
Nicotinell Fruity Mint 1 mg lozenge is recommended in smokers with a low to moderate nicotine dependency. It is not recommended in the case of smokers with a strong or very strong nicotine dependency.

The optimal dosage form is selected according to the following table:



If an adverse event occurs with the use of the high dose form (2 mg lozenge), use of the low dose form (1 mg lozenge) should be considered.

The initial dosage should be individualised on the basis of the patient's nicotine dependence. One piece of lozenge to suck when the user feels the urge to smoke.

Initially, 1 lozenge should be taken every 1-2 hours. The usual dosage is 8-12 lozenges per day. For smoking cessation and smoking reduction with Nicotinell Fruity Mint lozenge, the maximum daily dose is 30 lozenges.

Nicotinell lozenge should primarily be used for smoking cessation.

Smoking cessation:
Users should stop smoking completely during treatment with Nicotinell Fruity Mint lozenge.

The treatment duration is individual. Normally, treatment should continue for at least 3 months. After 3 months, the user should gradually reduce the number of lozenges. Treatment should be discontinued when the dose has been reduced to 1-2 lozenges per day. Use of nicotine medicinal products like Nicotinell Fruity Mint 1 mg lozenge beyond 6 months is generally not recommended. Some ex-smokers may need treatment with the lozenge longer to avoid returning to smoking.

Patients who have been using oral nicotine replacement therapy beyond 9 months are advised to seek additional help and information from health care professionals.

Counselling may help smokers to quit.

Smoking reduction:
Nicotinell Fruity Mint lozenge should be used between periods of smoking in order to prolong smoke-free intervals and with the intention of reducing smoking as much as possible. The number of cigarettes should be gradually replaced by Nicotinell Fruity Mint lozenge. If a reduction of at least 50 % in the number of cigarettes per day has not been achieved after 6 weeks, professional advice should be sought. A quit attempt should be made as soon as the smoker feels ready, but not later than 4 months after start of treatment. After that the number of lozenges should be gradually reduced, for example by quitting one lozenge every 2-5 days. If a quit attempt cannot be made within 6 months after starting treatment, professional advice should be sought. Regular use of Nicotinell lozenge beyond 6 months is generally not recommended. Some ex-smokers may need treatment with the lozenges for longer to avoid returning to smoking.

Counselling may improve the chance for smokers to quit.

Treatment with Nicotinell Fruity Mint Lozenge in combination with Nicotinell transdermal patch

Smoking cessation:
People who have failed when treated with only Nicotinell Fruity Mint Lozenge can use Nicotinell patches together with Nicotinell 1 mg lozenge.

Users should stop smoking completely during treatment with Nicotinell Fruity Mint lozenge in combination with Nicotinell transdermal patch.

The use of Nicotinell patches together with Nicotinell Fruity Mint 1 mg lozenge is recommended for smokers with moderate to very strong dependency, i.e. over 20 cigarettes per day. It is strongly recommended that the combination therapy is used in conjunction with the advice and support from a health care professional.

The maximum total treatment duration is 9 months (for the initial treatment and reduction of nicotine dose)

Initial combination therapy:
Treatment should begin with one patch 21 mg/24 hours in combination with Nicotinell Fruity Mint 1mg lozenge. At least 4 pieces of lozenge (1 mg) per day should be used. In most cases, 5-6 lozenges are enough. Not more than 15 pieces of lozenge a day should be used. In normal cases, the treatment may last for 6-12 weeks. Thereafter, the nicotine dose is reduced gradually.

The patch is applied on a clean, dry, hairless, intact area of skin on the trunk, arms or hips. The patch is pressed against the skin for 10-20 seconds.

To minimize the risk of local irritation the placement of Nicotinell patches should be alternated between different application sites.

Hands should be washed thoroughly after application of transdermal patches to avoid irritation of the eyes with nicotine from the fingers.

Reduction of nicotine dose:
This can be done in two ways.
Alternative 1: Use of the patches of a lower strength, i.e. 14 mg/24 hours patches for 3-6 weeks followed by 7 mg/24 hours for another 3-6 weeks together with the initial dose of Nicotinell 1 mg lozenge. -Thereafter, the number of lozenges is reduced gradually. It is generally not recommended to use Nicotinell Mint lozenge for longer than 6 months. However, some ex-smokers may need treatment for longer to avoid returning to smoking but it should not be more than9 months.
Alternative 2: Discontinuation of the use of the patches and gradual reduction of the number of 1 mg lozenges. It is generally not recommended to use Nicotinell Fruity Mint lozenge for longer than 6 months. However, some ex-smokers may need treatment for longer to avoid returning to smoking but it should not be more than9 months.

Recommended dosage:

Period	**Patches**	**Lozenge 1 mg**
Initial treatment(followed by alternative 1 or 2 below)		
First 6-12 weeks	1 patch 21 mg/24 hours	When necessary, 5-6 lozenges per day is recommended
Reduction of nicotine dose – alternative 1		
Next 3-6 weeks	1 patch 14 mg/24 hours	Continue to use lozenges, when necessary

Following 3-6 weeks	1 patch 7 mg/24 hours	Continue to use lozenges, when necessary
Up to 9 months in total	---	Reduce the number of lozenges gradually
Reduction of nicotine dose – alternative 2		
Up to 9 months in total	---	Continue to reduce the number of lozenges gradually

Method of administration - lozenges:

1. One lozenge to be sucked until the taste becomes strong.

2. The lozenge should then be lodged between the gum and cheek.

3. When the taste fades, sucking of the lozenge should commence again

4. The sucking routine will be adapted individually and should be repeated until the lozenge dissolves completely (about 30 minutes)

Concomitant use of acidic beverages such as coffee or soda may decrease the buccal absorption of nicotine. Acidic beverages should be avoided for 15 minutes prior to sucking the lozenge.

4.3 Contraindications

Hypersensitivity to nicotine or to any of the excipients listed in section 6.1.
Nicotinell Fruity Mint lozenge should not be used by non-smokers.

4.4 Special warnings and precautions for use

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

Nicotinell Fruity Mint lozenges should be used with caution in patients with hypertension, stable angina pectoris, cerebrovascular disease, occlusive peripheral arterial disease, heart failure, diabetes mellitus, hyperthyroidism or pheochromocytoma and with moderate to severe hepatic and/or severe renal impairment.

Patients should initially be encouraged to stop smoking with non-pharmacological interventions (such as counselling).

Swallowed nicotine may exacerbate symptoms in subjects suffering from active oesophagitis, oral and pharyngeal inflammation, gastritis or peptic ulcer.

Doses of nicotine that are tolerated by adult smokers during treatment may produce severe symptoms of poisoning in small children and may prove fatal (please see Section 4.9).

Special warnings about excipients

Nicotinell Fruity Mint lozenges contain sweeteners, including aspartame and maltitol.

Each Nicotinell Fruity Mint 1 mg lozenge contains aspartame (E951), a source of phenylalanine equivalent to 5 mg/dose and may be harmful for people with phenylketonuria.

Because Nicotinell Fruity Mint 1 mg lozenge contains maltitol (E965)**,** a source of fructose:

- patients with rare hereditary conditions of fructose intolerance should not take this medicine,
- patients may experience a mild laxative effect.

Calorific value 2.1 kcal/g maltitol.

Nicotinell Fruity Mint 1 mg lozenge contains 9.8 mg sodium per piece. To be taken into consideration by patients on a controlled sodium diet.

Each Nicotinell Fruity Mint 1 mg lozenge contains 0.00005 mg sulphites, that may rarely cause severe hypersensitivity reactions and bronchospasm.

For special warnings and precautions for the Nicotinell patch, see the Summary of Product Characteristics for the specific product.

4.5 Interaction with other medicinal products and other forms of interaction

Drug Interactions: No information is available on interactions between Nicotinell Fruity Mint lozenge and other medicinal products.

Smoking Cessation: Smoking but not nicotine is associated with increased CYP1A2 activity. After stopping smoking there may be reduced clearance of substrates for this enzyme and increased plasma levels of some medicinal products of potential clinical importance because of their narrow therapeutic window e.g. theophylline, tacrine**,** olanzapine and clozapine.

The plasma concentrations of other active substances metabolised by CYP1A2 e.g. caffeine, paracetamol, phenazone, phenylbutazone, pentazocine, lidocaine, benzodiazepines, warfarin, oestrogen and vitamin B12 may also increase. However the clinical significance of this effect for these active substances is unknown.

Smoking may lead to reduced analgesic effects of propoxyphene, reduced diuretic response to furosemide (frusemide), reduced effect of propranolol on blood pressure and heart rate and reduced responder rates in ulcer healing with H2-antagonists.

Smoking and nicotine may raise the blood levels of cortisol and catecholamines, i.e. may lead to a reduced effect of nifedipine or adrenergic antagonists and to an increased effect of adrenergic agonists.

Increased subcutaneous absorption of insulin which occurs upon smoking cessation may necessitate a reduction in insulin dose.

For interactions for the Nicotinell patch, see the Summary of Product Characteristics for the specific product.

4.6 Fertility, pregnancy and lactation

Pregnancy

In pregnant women, complete cessation of tobacco smoking should always be recommended without nicotine replacement therapy.

Nevertheless, in the case of failure in highly dependent pregnant smokers, tobacco withdrawal via nicotine replacement therapy may be recommended. Indeed, foetal risk is probably lower than that expected with tobacco smoking, due to:

- lower maximal plasma nicotine concentration than with inhaled nicotine
- no additional exposure to polycyclic hydrocarbons and carbon monoxide
- improved chances of quitting smoking by the third trimester.

Smoking continued during the third trimester may lead to intra-uterine growth retardation or even premature birth or stillbirth, depending on the daily amount of tobacco.

Tobacco withdrawal with or without nicotine replacement therapy should not be undertaken alone but as part of a

medically supervised smoking cessation program.

In the third trimester nicotine has haemodynamic effects (e.g. changes in foetal heart rate) which could affect the foetus close to delivery. Therefore, after the sixth month of pregnancy, the lozenge should only be used under medical supervision in pregnant smokers who have failed to stop smoking by the third trimester.

Lactation

Nicotine is excreted in breast milk in quantities that may affect the child even in therapeutic doses. The lozenge, like smoking itself, should therefore be avoided during breast-feeding. Should smoking withdrawal not be achieved, use of the lozenge by breast feeding smokers should only be initiated after advice from a physician. Where nicotine replacement therapy is used whilst breast-feeding, the lozenge should be taken just after breast-feeding and not during the two hours before breast-feeding.

4.7 Effects on ability to drive and use machines

There is no evidence of any risks associated with driving or operating machinery when the lozenge is used following the recommended dose. Nevertheless one should take into consideration that smoking cessation can cause behavioural changes.

4.8 Undesirable effects

Nicotinell Fruity Mint lozenge can cause adverse reactions similar to those associated with nicotine administered by smoking. These can be attributed to the pharmacological effects of nicotine, which are dose-dependent. Non dose-dependent adverse reactions are as follows: hypersensitivity, angioneurotic oedema and anaphylactic reactions.

Most of the adverse reactions which are reported by patients occur generally during the first 3-4 weeks after initiation of therapy.

Nicotine from lozenges may sometimes cause a slight irritation of the throat and increased salivation at the start of the treatment. Excessive swallowing of nicotine which is released in the saliva may, at first, cause hiccups. Those who are prone to indigestion may suffer initially from minor degrees of dyspepsia or heartburn; slower sucking will usually overcome this problem.

Excessive consumption of lozenges by subjects who have not been in the habit of inhaling tobacco smoke, could possibly lead to nausea, faintness and headache.

Increased frequency of aphthous ulcer may occur after abstinence from smoking.

Adverse reactions are listed below, by system organ class and frequency. Frequencies are defined as: *very common* (≥1/10), *common* (≥1/100 to <1/10), *uncommon* (≥1/1,000 to <1/100), *rare* (≥1/10,000, <1/1,000) or *very rare* (<1/10,000).

Nervous system disorders:
Common: dizziness, headache

Gastrointestinal disorders:
Common: nausea, flatulence, hiccups, gastritis, dry mouth, stomatitis and oesophagitis.

Cardiac disorders:
Uncommon: Palpitations
Rare: atrial arrhythmia

Immune system disorders:
Rare: hypersensitivity, angioneurotic oedema and anaphylactic reactions.

Certain symptoms which have been reported such as dizziness, headache and insomnia may be ascribed to withdrawal symptoms in connection with smoking cessation and may be due to insufficient administration of nicotine.

Cold sores may develop in connection with smoking cessation, but any relation with the nicotine treatment is unclear.

The patient may still experience nicotine dependence after smoking cessation.

For undesirable effects for the Nicotinell patch, see the Summary of Product Characteristics for the specific product.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie

4.9 Overdose

In overdose, symptoms corresponding to heavy smoking may be seen.

The acute lethal oral dose of nicotine is about 0.5 – 0.75 mg per kg body weight, corresponding in an adult to 40 – 60 mg. Even small quantities of nicotine are dangerous in children, and may result in severe symptoms of poisoning which may prove fatal. If poisoning is suspected in a child, a doctor must be consulted immediately.

Overdose with Nicotinell Fruity Mint 1 mg lozenge may only occur if many pieces are sucked simultaneously. Nicotine toxicity after ingestion will most likely be minimised as a result of early nausea and vomiting that occur following excessive nicotine exposure.

General symptoms of nicotine poisoning include: weakness, perspiration, salivation, throat burn, nausea, vomiting, diarrhoea, abdominal pain, hearing and visual disturbances, headache, tachycardia and cardiac arrhythmia, dyspnoea, prostration, circulatory collapse, coma and terminal convulsions.

Treatment of overdose:

Treatment of overdose should be immediate as symptoms may develop rapidly. Emesis is usually spontaneous. Administration of oral activated charcoal and gastric lavage should be considered as soon as possible and within 1 hour of ingestion. Monitor vital signs and treat symptomatically.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: N07B A01
Pharmacotherapeutic group: Drugs used in nicotine dependence

Nicotine, the primary alkaloid in tobacco products and a naturally occurring autonomous substance, is a nicotine receptor agonist in the peripheral and central nervous systems and has pronounced CNS and cardiovascular effects. On consumption of tobacco products, nicotine has proven to be addictive, resulting in craving and other withdrawal symptoms when administration is stopped. This craving and these withdrawal symptoms include a strong urge to smoke, dysphoria, insomnia, irritability, frustration or anger, anxiety, concentration difficulties, agitation and increased appetite or weight gain. The lozenge replaces part of the nicotine that would have been administrated via tobacco and reduces the intensity of the withdrawal symptoms and smoking urge.

5.2 Pharmacokinetic properties

The absorbed amount of nicotine depends on the amount released into the mouth and absorbed through the buccal mucosa.

The main part of nicotine in Nicotinell Fruity Mint 1 mg lozenge is absorbed through the buccal mucosa. A proportion, by the swallowing of nicotine-containing saliva, reaches the stomach and intestine where it is inactivated. Due to the first-pass effect in the liver, the systemic bioavailability of nicotine is low. Consequently, in the treatment with Nicotinell Fruity Mint 1 mg lozenge the high and quick systemic nicotine concentration, as seen when smoking, is rarely obtained.

Distribution volume after intravenous administration of nicotine is approximately 2-3 1/kg and the half-life is 2 hours. Nicotine is metabolised principally in the liver and the plasma clearance is approximately 1.2 l/min; nicotine also metabolises in the kidney and lungs. Nicotine crosses the blood-brain barrier.

More than 20 metabolites have been identified, all believed to be less active than nicotine. The main metabolite is cotinine which has a half-life of 15-20 hours and with approximately 10 times higher plasma concentration than nicotine. Nicotine's plasma-protein binding is less than 5%. Changes in nicotine binding from the use of concomitant medicinal products or due to altered disease state are not expected to have significant effect on nicotine kinetics. The main metabolite in urine is cotinine (15% of the dose) and trans-3-hydroxy cotinine (45% of the dose).

About 10% of the nicotine is excreted unchanged. Up to 30% may be excreted with urine in increased diuresis and the acidity under pH 5.

The peak value for the plasma concentration of Nicotinell Fruity Mint 1 mg lozenge after a single dose is approximately 4 ng per ml and the maximal concentration at steady state is approximately 10.6 ng per ml (average plasma concentration of nicotine after smoking one cigarette is 15-30 ng per ml). Peak plasma concentration is reached after about 45 minutes following sucking of a single lozenge and after about 30 minutes at steady state.

5.3 Preclinical safety data

Nicotine was positive in some in vitro genotoxicity tests but there are also negative results with the same test systems. Nicotine was negative in standard in-vivo tests.

Animal experiments have shown that nicotine induces post-implantation loss and reduces the growth of foetuses.

The results of carcinogenicity assays did not provide any clear evidence of a tumorigenic effect of nicotine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maltitol (E965)
Sodium carbonate anhydrous
Sodium hydrogen carbonate
Polyacrylate dispersion 30 per cent
Xanthan gum
Colloidal anhydrous silica
Levomenthol
Peppermint oil
Aspartame (E951)
Magnesium stearate
Guarana flavour (including sulphites)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

24 or 72 (3 x 24) lozenges in polypropylene bottle. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Consumer Healthcare (Ireland) Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0678/142/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 8th August 2016

10 DATE OF REVISION OF THE TEXT

October 2016