SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Nicotine 0.45 mg Inhaler

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pack contains 9 mg nicotine and provides approximately 20 charges of the stick device. Each charge contains approximately 0.45 mg nicotine, equivalent to a delivered dose of 0.43 mg nicotine, except for the first charge, which delivers less than 0.43 mg (range 0.10 – 0.30 mg) due to stick design.

Excipient: ethanol (contains less than 10 mg of ethanol per charged stick).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Pressurised inhalation solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Nicotine 0.45mg Inhaler relieves and/or prevents craving and nicotine withdrawal symptoms associated with tobacco dependence. It is indicated to aid smokers wishing to quit or reduce prior to quitting, to assist smokers who are unwilling or unable to smoke, and as a safer alternative to smoking for smokers and those around them.

Nicotine 0.45mg Inhaler is indicated in pregnant and lactating women making a quit attempt.

4.2 Posology and method of administration

Nicotine 0.45mg Inhaler is for oral inhalation use only.

Posology

Adults over 18 years of age:

Nicotine 0.45mg Inhaler should be used whenever the urge to smoke is felt or to prevent cravings in situations where these are likely to occur.

Smokers willing or able to stop smoking immediately should initially replace all their cigarettes with the Inhaler and as soon as they are able, reduce the number of charges used until they have stopped completely.

Smokers aiming to reduce cigarettes should use the Inhaler, as needed, between smoking episodes to prolong smoke-free intervals and with the intention to reduce smoking as much as possible.

As soon as they are ready, smokers should aim to quit smoking completely.

Maximum daily dose: 2 packs

When making a quit attempt, behavioural therapy, advice and support will normally improve the success rate. Those who have quit smoking, but are having difficulty discontinuing their Inhaler are recommended to contact their pharmacist or doctor for advice.

Each pack lasts for 20 charges. Each charge apart from the first one (see Section 2) provides a comparable number of inhalations to a conventional cigarette, although frequency, puffing/inhalation time and technique vary between individuals.

Paediatric population

Nicotine 0.45mg Inhaler is contraindicated in children and adolescents under the age of 18 years (see Section 4.3).

Method of administration

Charging the Nicotine 0.45mg Inhaler stick:

- Tear away the strip on the pack and remove the cellophane outer wrap completely.
- Peel away the foil strip at the bottom of the pack.
- Click open the side door and remove the Nicotine 0.45mg Inhaler stick.
- Hold the pack upright and away from you.
- Insert the arrowed end of the stick into the base of the pack and push firmly for five seconds to charge.
- The first time you charge a Nicotine 0.45mg Inhaler stick, you need to repeat this charging step and shake well before use.
- If you have not used Nicotine 0.45mg Inhaler for more than two days, repeat this charging step.
- You should only fill the stick before you intend to use it.

If spray comes into contact with skin or eyes, rinse gently with water.

Using the Nicotine 0.45mg Inhaler stick:

- Inhale through the filter end of the stick as you would with a cigarette ensuring you don’t cover the air inlet holes at the filter end of the stick.
- On average each charge apart from the first one provides a comparable number of puffs to a conventional cigarette.
- The stick is empty when you no longer feel the flavoured spray in your mouth.
- Put the Nicotine 0.45mg Inhaler stick back in the pack when not in use.
- The Nicotine 0.45mg Inhaler stick is designed so that proper inhalation does not usually produce a visible vapour exhale. In any event, your exhale during use is harmless both to you and those around you.

Recharging the Nicotine 0.45mg Inhaler stick:

- To recharge the stick follow the relevant instructions in “Charging the Nicotine 0.45mg Inhaler stick”.
- The stick can be charged up to twenty times, sometimes more if the stick is only partially emptied between charges.

To clean the stick, wipe the mouthpiece gently with a dry tissue.

4.3 Contraindications

Hypersensitivity to any component of Nicotine 0.45mg Inhaler.

Nicotine 0.45mg Inhaler is contraindicated in children and adolescents under the age of 18 years.

4.4 Special warnings and precautions for use

Any risks that may be associated with the use of nicotine are substantially outweighed by the well-established dangers of continued smoking.

Underlying cardiovascular disease: In stable cardiovascular disease, Nicotine 0.45 mg Inhaler presents a lesser hazard than continuing to smoke. However, dependent smokers currently hospitalised as a result of myocardial infarction, unstable or worsening angina including Prinzmetal's angina, severe dysrhythmia or CVA and who are considered to be haemodynamically unstable and/or who have uncontrolled hypertension should be encouraged to stop smoking with non-pharmacological interventions. If this fails, Nicotine 0.45 mg Inhaler may be considered, but as data on safety in this patient group are limited, initiation should only be under medical supervision.

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

GI disease: Swallowed nicotine may exacerbate symptoms in patients suffering from oesophagitis, gastritis or peptic ulcers and oral NRT preparations should be used with caution in these conditions. Ulcerative stomatitis has been reported.

Renal or 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.

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.

Phaeochromocytoma and uncontrolled hyperthyroidism: As nicotine causes release of catecholamines, Nicotine 0.45 mg Inhaler should be used with caution in patients with uncontrolled hyperthyroidism or phaeochromocytoma.

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

Stopping smoking: Polycyclic aromatic hydrocarbons in tobacco smoke induce the metabolism of drugs metabolised by CYP 1A2 (and possibly by CYP 1A1). When a smoker stops smoking, this may result in slower metabolism and a consequent rise in blood levels of such drugs. This is of potential clinical importance for products with a narrow therapeutic window, e.g. theophylline, clozapine and ropinirole.

Lung Disease: Patients with obstructive lung disease may find use of the Inhaler difficult. Nicotine 0.45 mg Inhaler should be used with caution in patients with chronic throat disease and bronchospastic disease.

Allergic Reactions: Susceptibility to angioedema and urticaria.

Potential choking hazard: When not in use, the stick should be kept in the pack. This reduces the potential for contamination with dirt or fluff which, if inhaled, may cause choking.

Excipients: This medicinal product contains small amounts of ethanol (alcohol), less than 10 mg per charged stick. This medicine contains 54mg propylene glycol (E1520) in each pack, equivalent to 2.7mg in each full charge of the stick.

4.5 Interaction with other medicinal products and other forms of interaction

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

4.6 Fertility, Pregnancy and lactation

Pregnancy

Stopping smoking is the single most effective intervention for improving the health of both the pregnant smoker and her baby, and the earlier abstinence is achieved the better. Ideally smoking cessation during pregnancy should be achieved without NRT. However, if the mother cannot (or is considered unlikely to) quit without pharmacological support, NRT may be used as the risk to the foetus is lower than that expected with smoking tobacco. Stopping completely is by far the best option but if this is not achievable Nicotine 0.45 mg Inhaler may be used in pregnancy as a safer alternative to smoking. Because of the potential for nicotine-free periods, intermittent dose forms are preferable, but patches may be necessary if there is significant nausea and/or vomiting. If patches are used they should, if possible, be removed at night when the foetus would not normally be exposed to nicotine.

Lactation

The relatively small amounts of nicotine found in breast milk during NRT use are less hazardous to the infant than second-hand smoke. Intermittent dose forms would minimise the amount of nicotine in breast milk and permit feeding when levels were at their lowest.

Fertility

In females, tobacco smoking delays time to conception, decreases in-vitro fertilization success rates, and significantly increases the risk of infertility.

In males, tobacco smoking reduces sperm production, increases oxidative stress, and DNA damage. Spermatozoa from smokers have reduced fertilizing capacity.

The specific contribution of nicotine to these effects in humans is unknown.

4.7 Effects on ability to drive and use machines

Nicotine 0.45mg Inhaler has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Effects of smoking Cessation

Some symptoms may be related to nicotine withdrawal associated with stopping smoking. These can include: irritability/aggression, dysphoria/depressed mood, anxiety, restlessness, poor concentration, increased appetite/weight gain, urges to smoke (cravings), night-time awakenings/sleep disturbance and decreased heart rate.

Increased frequency of aphthous ulcer may occur after abstinence from smoking. The causality is unclear.

Adverse Drug Reactions

Nicotine 0.45 mg Inhaler may cause adverse reactions similar to those associated with nicotine given by other means, including smoking, and these are mainly dose-dependent. At recommended doses, nicotine has not been found to cause any serious adverse effects. Excessive use of nicotine by those who have not been in the habit of inhaling tobacco smoke could possibly lead to nausea, faintness or headaches.

Most of the undesirable effects reported by the patient occur during the first weeks after starting treatment. About 40% of users experience mild local reactions such as cough and irritation in the mouth and throat.

Allergic reactions (including symptoms of anaphylaxis) occur rarely during use of this product.

The adverse reactions below are listed by system organ class (SOC).

Frequencies are defined in accordance with current guidance, as: Very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1 000, <1/100); rare (≥1/10 000, <1/1 000); very rare (<1/10 000), Not known - cannot be estimated from the available data.

Reported adverse events associated with inhaled nicotine include:

System Organ Class	Incidence	Reported Adverse Event
Immune System Disorders	Common	Hypersensitivity[a]
	Not known	Anaphylactic reaction[a]
Psychiatric disorders	Uncommon	Abnormal dreams[c]
Nervous System Disorders	Very Common	Headache[a#]
	Common	Burning sensation[b]
	Common	Dizziness
	Common	Dysgeusia
	Common	Paraesthesia[a]
Eye Disorders	Not known	Blurred Vision
	Not known	Lacrimation increased
Cardiac Disorders	Uncommon	Palpitations[a]
	Uncommon	Tachycardia[a]
	Very Rare	Reversible atrial fibrillation
Vascular Disorders	Uncommon	Flushing[a]
	Uncommon	Hypertension[a]
Respiratory, Thoracic and Mediastinal Disorders	Very Common	Cough*
	Very Common	Throat irritation
	Common	Nasal Congestion
	Uncommon	Bronchospasm
	Uncommon	Dysphonia
	Uncommon	Dyspnoea[a]
	Uncommon	Sneezing
	Uncommon	Throat tightness
Gastrointestinal Disorders	Very Common	Nausea[a]
	Very Common	Stomatitis
	Very Common	Hiccups
	Common	Abdominal pain
	Common	Diarrhoea**
	Common	Dry mouth

	Common	Dyspepsia
	Common	Flatulence
	Common	Salivary hypersecretion
	Common	Vomiting[a]
	Uncommon	Eructation
	Uncommon	Glossitis
	Uncommon	Oral mucosal blistering and exfoliation
	Uncommon	Paraesthesia oral**
	Rare	Dysphagia
	Rare	Hypoaesthesia oral**
	Rare	Retching
	Not known	Dry throat
	Not known	Gastrointestinal discomfort[a]
	Not known	Lip pain
Skin and Subcutaneous Tissue Disorders	Uncommon	Hyperhidrosis[a]
	Uncommon	Pruritus[a]
	Uncommon	Rash[a]
	Uncommon	Urticaria[a]
	Not known	Angioedema[a]
	Not known	Erythema[a]
General Disorders and Administration Site Conditions	Common	Fatigue[a]
	Uncommon	Asthenia[a]
	Uncommon	Chest discomfort and pain[a]
	Uncommon	Malaise[a]

[a] Systemic effects;
[b] At the application site
[c] Identified if formulation was used at night
*Higher frequency observed in clinical studies with inhaler formulation.
**Reported the same or less frequently than placebo
Although the frequency in the active group is less than that of the placebo group, the frequency in the specific formulation in which the preferred term was identified as a systemic ADR was greater in the active group than the placebo group.

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 the Yellow Card Scheme (www.mhra.gov.uk/yellowcard).

4.9 Overdose

Symptoms: The minimum lethal dose of nicotine in a non-tolerant man has been estimated to be 40 to 60 mg. Symptoms of acute nicotine poisoning include nausea, salivation, abdominal pain, diarrhoea, sweating headache, dizziness, disturbed hearing and marked weakness. In extreme cases, these symptoms may be followed by hypotension, rapid or weak or irregular pulse, breathing difficulties, prostration, circulatory collapse and terminal convulsions.

Management of an overdose: All nicotine intake should stop immediately and the patient should be treated symptomatically. Artificial respiration should be instituted if necessary. Activated charcoal reduces the gastro-intestinal absorption of nicotine.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Drugs used in nicotine dependence.

ATC code: N07B A01

Nicotine 0.45mg Inhaler facilitates the rapid uptake of nicotine into the systemic circulation. The amount taken up alleviates the craving symptoms caused by the absence of nicotine from smoking.

Clinical data demonstrate a rapid reduction in craving following use of the Nicotine 0.45mg Inhaler. After inhaling the contents of a single stick the reduction in craving lasts for several hours.

Increased appetite is a recognised symptom of nicotine withdrawal and post-cessation weight gain is common. Clinical trials have demonstrated that NRT can help control weight following a quit attempt.

5.2 Pharmacokinetic properties

Nicotine given intravenously (i.v.) has a volume of the distribution of 2 or 3 l/kg with a half-life of 1-2 hours. Average plasma clearance is about 1-2 l/min mainly in the liver. More than 20 metabolites are known, all less active than nicotine: cotinine, with a half-life of 15-20 hours and concentrations ten times that of nicotine is the main one.

Plasma binding of nicotine below 5% means significant displacement of drugs or nicotine is unlikely. Nicotine is excreted in the urine principally as cotinine (15%), 3-hydroxycotinine (45%), nicotine (10%).

After inhaling Nicotine 0.45mg Inhaler at a rate of one puff every 15 seconds for up to 4 minutes, nicotine rapidly enters the arterial bloodstream. Arterial nicotine concentrations are expected to increase as early as 2 minutes after the start of inhalation, reaching a maximum concentration approximately 7 minutes after the start of inhalation. Venous concentrations would reach a peak approximately 18 minutes after the start of inhalation. After inhaling one complete charge of the Nicotine 0.45mg Inhaler every hour for 12 hours, steady state plasma nicotine concentrations in the region of 8 ng/ml are expected. This is substantially less than the concentrations seen with cigarette smoking. The rapid appearance of nicotine in arterial blood after oral inhalation is consistent with pulmonary absorption. Aerosol impaction in the mouth and throat is also likely to result in some degree of oromucosal absorption.

Because the pattern of use is decided by the patient up to a limit of 2 packs per day to relieve craving, therapeutic levels of nicotine are individual and dictated by the level of dependence.

5.3 Preclinical safety data

None stated

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol

Ethanol

Saccharin

Levomenthol

HFA134a

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

12 Months.

Once opened discard Nicotine Inhaler within 7 days.

6.4 Special precautions for storage

Store below 25°C

Do not expose to temperatures higher than 50°C.

Store away from heat or direct sunlight.

As with most inhaled medications in aerosol canisters, the therapeutic effect of this medication may decrease when the canister is cold.

The canister contains a pressurised liquid, do not puncture, break or burn even when empty.

Do not attempt to light the stick.

6.5 Nature and contents of container

Polybutylene terephthalate inhalation stick-shaped device with breath operated valve and a pressurised aluminium canister with a continuous valve. One pack contains 1 stick device and 1 canister. A canister contains twenty charges for the stick.

Pack sizes: 1 pack, 2 x 1 packs, 5 x 1 packs.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Because of residual nicotine and the potential choking hazard, used packs and sticks may be a hazard to children, animals and fish and so should never be left lying around. The stick should be kept in the pack and disposed of with household rubbish or at an appropriate recycling facility.

7 MARKETING AUTHORISATION HOLDER

Ayrton Saunders Ltd
Parliament Business Park, Ayrton House, 38 Commerce Way Liverpool, L8 7BA, United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 16431/0208

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11/09/2014 / 31/05/2019

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27/10/2023