



MHRA PUBLIC ASSESSMENT REPORT

The use of nicotine replacement therapy to reduce harm in smokers

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1. INTRODUCTION

(See glossary for explanation of terms used in this document)

The Medicines and Healthcare products Regulatory Agency (MHRA) is the UK government agency responsible for regulating the effectiveness and safety of medicines and medical devices. We produce public assessment reports which evaluate, in addition to safety issues, the suitability of currently available medicines for wider use. This MHRA public assessment report discusses the benefits of expanding the use of nicotine replacement therapy (NRT) to include “harm reduction”; ie, for use as a substitute or partial substitute for smoking tobacco, both for those making an attempt to quit and those not currently intending to make a quit attempt, without any restriction on its duration of use.

Reducing the adverse impact of smoking on health remains a high priority for the government. Over the last 7–8 years there has been a growing consensus to move towards the use of medicinal nicotine to minimise the harm from tobacco smoke^[1–4]. Nicotine is strongly addictive and stopping smoking results in cravings and withdrawal effects, but it is the tobacco smoke that produces the diseases and premature deaths associated with smoking. Providing smokers with access to less harmful forms of nicotine could benefit both them and others who would be exposed to their second-hand smoke.

Nicotine has been licensed as a medicine in the UK since the late 1970s and currently there are six different delivery forms: gum; patch; microtablet; lozenge/pastille; nasal spray; and inhalator (see our [‘stop smoking treatments’](#) webpage for more information). All are General Sales List^a (GSL) products and are readily available from a wide range of non-pharmacy outlets. Until 2005, NRT was only licensed to assist smokers who were making an immediate and complete quit attempt. However following advice from a working group set up by the Committee on Safety of Medicines (CSM), the predecessor of the current [Commission on Human Medicines](#)^b (CHM), NRT can now be used to cut down smoking as a “stepping stone” to quitting completely for smokers unable to stop abruptly^[5].

Over several years the MHRA has been in discussion with the Department of Health (DH) and other interested parties to determine and implement actions necessary for the effective regulation of NRT. This evolving approach has focussed on extending access to new patients and supporting wider access to new formulations of NRT.

The MHRA received an application to expand the use of Nicorette inhalator, an NRT product, to include a “harm reduction” element. Broader indications are proposed so the product would help smokers to:

- quit (abruptly stop)
- reduce smoking, with no limit on the treatment duration, with the aim of quitting when they are ready
- temporarily avoid smoking in front of others, so minimising the risks associated with passive smoking

^a List of approved medicines which can be sold from pharmacies or retail outlet

^b An independent body which gives advice to UK government ministers on the safety, quality and efficacy of medicines

- reduce compensatory smoking (smoking more intensely and/or using higher nicotine content cigarettes) after enforced abstinence (eg in smoke-free environments, during hospitalisation)

In October 2009, this application was reviewed by a specific CHM Working Group on Harm Reduction & NRT. The working group considered the evidence on the safety and efficacy of a harm-reduction element as part of the indication for the Nicorette inhalator, and also advised whether indications including harm reduction are appropriate for other forms of NRT.

2. SUMMARY OF DATA

2.1 Clinical pharmacology

Nicotine acts on specific brain receptors (nicotinic acetylcholine receptors). Low concentrations of nicotine increase the activity of these receptors, and high levels have the reverse effect. Nicotine mimics the effect of the neurotransmitter acetylcholine on these nicotinic receptors, which in turn control the release of other neurotransmitters that influence emotion and cognition. It activates the dopamine systems within the brain; dopamine is the neurotransmitter directly responsible for generating feelings of pleasure. Although nicotine per se has potent pharmacological effects (including increased heart rate and constriction of blood vessels), there is a large body of evidence that medicinal nicotine (in currently licensed forms) is not a significant risk factor for cardiovascular events^[6], and does not cause cancer or respiratory disease.

2.2 Efficacy

It is well established that the Nicorette inhalator can reduce the cravings and withdrawal symptoms that occur when stopping smoking^[7,8], and, as with other forms of NRT, can increase the likelihood of a successful outcome in those motivated to abruptly quit^[9]. In addition, there are data indicating that both the Nicorette inhalator and NRT can, in those who cut down the amount they smoke but who do not at the time intend to stop smoking altogether, increase the chances of a future quit attempt^[10-16]. Although there are no robust data indicating the health benefits of cutting down smoking, rather than quitting completely, a systematic review^[17] suggests that a substantial reduction in smoking improved several cardiovascular risk factors, and respiratory symptoms.

2.3 Safety

If a smoker continues to smoke they are subjecting themselves to an increased risk of death and disease; half of all smokers die prematurely of a smoking-related disease. Stopping smoking has major health benefits, with smokers who quit before the age of 35 years having a life expectancy only slightly less than a non-smoker. In addition, passive smoking is responsible for a substantial burden of disease, disability and mortality particularly in infants and children. Any adverse effects associated with the use of NRT need to be seen in the context of the substantial risks of continuing to smoke.

There is a well-established favourable benefit-to-risk balance for Nicorette inhalator with the current indication. With the expanded indication, some individuals may use the product long term, and others may use NRT while continuing to smoke. However, there are data, some directly relating to long-term NRT and some to other non-smoked sources of nicotine^[6,18], that give no indication of an association with cardiovascular illness or other serious side effects; although there was a degree of inconsistency in the studies^[19-25] as to whether concurrent NRT and smoking increases nicotine levels, even if this were to be the case there would not appear to be any major safety issues.

3. CONCLUSIONS

Having considered available data, the CHM Working Group concluded that the Nicorette inhalator has been shown to:

- relieve craving (such as the urge to smoke; the feeling of 'missing' cigarettes)
- relieve withdrawal symptoms (such as irritability; impatience; difficulty in concentrating)
- improve the likelihood of a successful abrupt quit attempt
- reduce the amount smoked in those not immediately motivated to quit

Consequently, they advised that the following indication should be included in the product information:

“Nicorette Inhalator 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.”

In addition, the Working Group recommended a “harm reduction” element was appropriate for the indications of all other currently authorised forms of NRT.

4. REFERENCES

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5. GLOSSARY

Abstinence

Refraining from consuming certain substances (eg, cigarettes) or acting on certain behaviours (eg, smoking)

Acetylcholine

A **neurotransmitter** found in the body and brain, which activates muscles and sustains attention

Addictive

A substance that the body forms a **dependence** on, due to habitually taking it

Cardiovascular

Related to the heart and blood vessels

Cognition

Mental processes involved in behaviour and acquiring knowledge

Constriction

Narrowing (of blood vessels)

Craving

An intense desire for a particular substance

Dependency

A compulsion to keep taking a substance

Dopamine

A **neurotransmitter** found in the body and brain, which generates feelings of pleasure

Indication

Any of the conditions for which a particular medicine may be prescribed, as defined by its licence

Mortality

The incidence of death in a population over a given period

Neurotransmitter

An important chemical messenger located in the nerves and brain

Nicorette inhalator

A type of **nicotine replacement therapy**

Nicotine

A drug found in tobacco, that acts on nicotinic **acetylcholine receptors**, causing an increase in blood pressure and heart rate

Nicotine replacement therapy

A method to help people quit smoking

Passive smoking

Where a non-smoker involuntarily inhales smoke from a smoker's cigarette nearby

Pharmacological

Related to the science of drugs and their effect on the body

Premature

Occurring before the assigned or correct time

Receptor

An area on a cell surface to which specific substances bind. This causes a change in the cell, that in turn affects the body

Respiratory

Related to breathing

Withdrawal symptoms

Feeling of being unwell, caused by not taking (or withdrawing from) an **addictive** substance