NICOTINE REPLACEMENT THERAPY

GUIDANCE FOR HEALTH PROFESSIONALS ON CHANGES IN THE LICENSING ARRANGEMENTS FOR NICOTINE REPLACEMENT THERAPY

ASH, London, December 2005

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http://www.ash.org.uk/html/cessation/Smoking%20reduction/NRT051229.pdf

The licensing arrangements for NRT have been changed to widen access, ensure consistency across similar products and remove some of the contraindications, warnings and restrictions on their use. ASH supports these changes and has produced this information and guidance for health professionals, in particular smoking cessation specialists. These changes in licensing could result in increased spending on NRT, but NRT is a highly cost effective life-preserving intervention and combating smoking remains a high priority of the government, particularly given that smoking is a key cause of health inequalities. The key messages table shows the changes to the licensing in bold, followed by our recommendations regarding implementation.

Key messages to health professionals

1. All forms of NRT can be used by patients with cardiovascular disease. NRT should be offered in any case where the alternative is the patient resuming smoking. In patients with cardiovascular disease that is not stable or controlled by treatment, the decision to prescribe should be made in consultation with the supervising physician (GP or consultant).

2. All forms of NRT can be used by smokers aged 12 to 17 years. Those prescribing or supplying NRT should check that: a) the young person is dependent enough to warrant use of NRT; b) is committed to stopping smoking.

3. NRT can be used by pregnant smokers. Those prescribing or supplying NRT should ensure that the potential risks and benefits are understood by the patient and that the clinician supervising management of the pregnancy has been consulted. The 24-hour patch should be taken off at night.

4. More than one form of NRT can now be used concurrently. Patients with a history of failure of quit attempts using a single form of NRT should be offered a prescription for combinations of patch plus gum, patch plus inhalator or other combinations, but any smoker who wishes to use a combination and is willing to purchase one of the forms themselves should be encouraged to do so.

5. NRT can now be prescribed for up to 9 months if patients show evidence of a continued need for NRT beyond the initial 8 to 12 week treatment phase. Prescriptions should be issued, and the case reviewed, monthly unless patients wish to purchase the NRT themselves.

6. NRT can now be used while still smoking, with a view to reducing the amount smoked as a prelude to quitting. This approach is only appropriate in cases where it is clear that the smoker is not willing to make an immediate quit attempt. Stop smoking counsellors may offer brief advice on cutting down but should only provide support when smokers want to stop completely.

Background

In 2005 the Committee on Safety of Medicines (CSM) and Medicines and Healthcare Regulatory Authority (MHRA) reviewed the indications for all forms of nicotine replacement therapy (NRT) and proposed new, harmonised rules for NRT use. The purpose of the new rules is to ensure that the benefits of NRT are maximised and that any risks associated with NRT are seen in the context of the far greater harm of continued smoking.

To further these aims, NRT product information has been revised and made consistent across all products. Some contraindications and restrictions have been removed and some new indications approved. These changes are effective immediately, but it will take several months for the new labelling to appear on all NRT.

The changes to the licensing arrangements, which can be seen in full in the report by the CSM working group[1], include the following:

All forms of NRT can now be used by:

1. smokers with cardiovascular disease
2. pregnant smokers
3. young people aged 12 to 17

In addition:

4. combinations of different forms of NRT can be used together
5. three formulations (Nicorette 2mg gum, Nicorette 4mg gum, Nicorette inhalator) can be used to reduce smoking as a step towards stopping completely, by smokers not currently able to stop abruptly – nicotine assisted reduction to stop (NARS)[2]
6. product labelling is being simplified and updated, including the removal of some contraindications.

Given that the best chance of success is achieved through combining medication with specialist support, health professionals dealing with smokers should be liaising with specialists in the NHS stop smoking services to ensure smokers are referred to the services for treatment where appropriate.

Although NRT is available from pharmacists and on general sale, the changes outlined in this guidance should result in increased prescribing of NRT, as it has been shown to be extremely cost-effective in comparison with other life preserving NHS treatments. Even increased prescribing along the lines outlined below will still represent extremely good value for money.

The table lists the products currently available, except ‘own label’ (for example *Boots*) and generic products. In total six different products are available, some with different dosages and flavours. All are available either on prescription or from a pharmacy, and nicotine patches, gum and lozenges are available on general sale from a wide variety of retail outlets.

NRT products available in the UK

Product	Manufacturer	Dose	Normal duration of use (see table note)
Gum	Pfizer (Nicorette)	2mg	Up to 3 months then gradually reduce
		4mg	Up to 3 months then gradually reduce
	GSK (NiQuitin)	2mg	Up to 3 months then gradually reduce
		4mg	Up to 3 months then gradually reduce
	Novartis (Nicotinell)	2mg	Up to 3 months then gradually reduce
		4mg	Up to 3 months then gradually reduce
Patch	Pfizer (16 hour)	15mg	8 weeks on 15mg then if abstinent, reduce to
		10mg	2 weeks, then reduce to
		5mg	2 weeks
	GSK (24 hour)	21mg	6 weeks then reduce to
		14mg	2 weeks
		7mg	2 weeks
	Novartis (24 hour)	21mg	Up to 4 weeks then gradually reduce, using lower dose patches up to total of 3 months altogether
		14mg	
		7mg	
Nasal spray	Pfizer	0.5mg per individual spray	Up to 8 weeks as required then reduce use for 4 more weeks
Inhalator	Pfizer	10mg per cartridge	Between 6 and 12 cartridges a day for 8 weeks then halve use over 2 weeks and stop in the next 2 weeks
Sublingual tablet	Pfizer	2mg	Up to 3 months then gradually reduce
Lozenge	GSK	2mg	Maximum use up to 6 weeks then gradually reduce
		4mg	Maximum use up to 6 weeks then gradually reduce
	Novartis	1mg	Three months minimum then gradually reduce
		2mg	Three months minimum then gradually reduce

Table note: these are the manufacturers' recommendations in the product labelling, prior to the changes described in this paper. See section 5 "Long term use of NRT."

1 Use of NRT by smokers with cardiovascular disease

The pharmacology of nicotine suggests that it may have the potential to trigger cardiac events in patients with cardiovascular disease[3]. However there is now a great deal of experience of NRT use in smokers with cardiovascular disease, and in practice it has not been found to pose a risk[4,5,6]. A recent study of a large cohort of general practice patients has also confirmed that the use of NRT is not associated with an increase in the risk of myocardial infarction, stroke or death[7]. Moreover, there is no doubt at all that it is far safer than continuing to smoke [8,9].

Although NRT has not been shown consistently to improve smoking cessation rates in this group, the broader evidence of its effectiveness is overwhelming[9]. Stopping smoking is particularly important in cardiovascular patients. However, most smokers who develop CVD are still smoking a year later. The potential benefits of NRT use by smokers with CVD therefore considerably outweigh the potential risks.

There is no direct evidence concerning how soon after an acute event (such as a stroke, myocardial infarction or surgery to relieve angina) it is safe to use NRT but the need to prevent resumed smoking is so great that it should be offered at *any* stage where it is clear that the alternative is smoking.

Given the theoretical potential of NRT to trigger cardiovascular events in particularly vulnerable patients, it is a sensible precaution to ensure that where a patient is under the active management of a cardiologist or cardiac surgeon, this clinician is involved in the decision to prescribe or dispense NRT. For NHS stop smoking specialists, it is advisable to put in place a simple procedure in which the supervising clinician's signature is obtained to state that s/he has been consulted.

2 Use of NRT by pregnant and breast-feeding smokers

The pharmacology of nicotine suggests that it may contribute to some of the damage to the fetus caused by smoking. However, this contribution is likely to be small and there is no doubt at all that NRT use is much safer than smoking. Experience of NRT use in pregnant women has not so far been associated with significant problems[10,11,12]. Nicotine does pass to the baby through breast milk and so there is a theoretical risk that it could cause harmful effects, however in practice none have been found to date.

There is insufficient evidence to date on the effect of NRT on cessation in pregnant women and new mothers[13,14,15] but the overwhelming evidence for effectiveness generally and the need to stop smoking to protect the baby mean that NRT should be offered to pregnant smokers who have not given up and who feel that they would be unable to give up without it.

It is prudent to offer shorter acting NRT products, such as gum or lozenges rather than patches, to avoid excessive exposure to nicotine over time. However, some pregnant smokers suffering from nausea prefer to use patches, in which case it should be recommended that these not be worn overnight.

It would therefore be sensible to adopt the following precautions in this group before prescribing NRT:

1. To obtain written confirmation from the mother that the risks and benefits have been explained and understood;

2. To have a system in place to ensure that the clinician (who may be the GP) overseeing the management of the pregnancy has been consulted;
3. In the case of nicotine patches to recommend that the patient removes the patch at night to avoid nicotine exposure beyond that which is absolutely necessary.

3 Use of NRT by adolescents

There is no reason to believe that NRT use carries a significant health risk for adolescents. Studies in which NRT has been used by adolescents have found no significant problems[16,17,18]. It is also apparent that some adolescent smokers are addicted to cigarettes[19]. There is insufficient evidence on whether NRT can help this specific group to stop smoking but evidence on its effect in the general population is overwhelming and the risk associated with its use are minimal so there is no reason for it to be contraindicated in adolescents. Hanson and colleagues found that NRT reduced craving in adolescents (compared with placebo) and concluded that although larger trials were needed on efficacy, NRT was a promising treatment for adolescents[17].

Adolescent smokers are different from older smokers in that their motivation to stop smoking tends to be more unstable. It is sensible, therefore, to check that they are fully committed to trying to stop smoking permanently before offering them NRT, and to attempt to establish that they are dependent, according to earlier guidance: "In the meantime, we suggest that health professionals should assess motivation and readiness to quit and dependency with adolescent smokers similar to their assessment of adult smokers before offering treatment. Dependence in adolescent smokers may be harder to assess than in adults, as there may be constraints on time to first cigarette of day and daily cigarette consumption, two of the standard dependency measures used with adults; nevertheless, these questions plus additional questions such as difficulty perceived in going without cigarettes, should give some indication of dependence."[20]

Given that many NHS stop smoking services are working at full capacity we do not recommend that they actively seek adolescent smokers to treat, given the limited evidence with this age group. However we encourage all health professionals routinely to advise adolescent smokers to stop and suggest that those satisfying the criteria outlined here be offered NRT under an abstinent contingency protocol. Some services may be able to offer specialist support including NRT to these adolescent smokers. The MHRA has recommended that adolescent smokers using NRT should seek advice from a health professional after 12 weeks treatment.

4 Use of more than one NRT product concurrently

There are no grounds for believing that concurrent use of different NRT products poses a significant health risk and there is evidence that it can increase cessation rates above those obtained with one NRT form alone[21]. The combination that appears to make most sense is patch plus an acute delivery form such as gum or inhalator. The steady nicotine delivery of the patch is enough to reduce the background withdrawal while the acute delivery system enables the user to respond to surges in craving that may arise in particular situations or at particular times.

Although any combinations of NRT are now permitted, Pfizer Consumer Healthcare has been granted a specific licence for the 15mg Nicorette patch and 2mg Nicorette chewing gum (Nicorette Combi) as a combination package.

Health professionals should consider prescribing combination therapy in cases where one product has failed in the past or a particular urgency in stopping smoking. In other cases, patients may be prescribed one NRT product and be advised to purchase another one.

5 Long-term use of NRT

NRT has no known adverse health effects from long-term use. A significant minority of smokers stopping with the aid of NRT feel it necessary to continue beyond the previously recommended (see table) 8 to 12 week treatment period[22,23]. There is some evidence of increased relapse when NRT treatment is discontinued[24]. While research with nicotine patches has not shown a clear benefit with extended use[25], there have not been adequately powered studies specifically in smokers who still feel a need for medication.

Given the safety of NRT and the clinical experience of need for continued NRT beyond the acute treatment period, it is sensible to permit smokers who feel they need it to use NRT for longer than 8 to 12 weeks. The MHRA has stipulated a new limit of 9 months but it makes sense to consider each case individually. For reasons of cost, NHS prescriptions may need to be limited to 9 months but there is no reason to prohibit smokers from purchasing NRT after that time.

6 Smoking whilst using NRT to cut down

ASH guidance on Nicotine Assisted Reduction to Stop (NARS)[2] was published in October 2005 and is available, with this guidance, on the ASH website. Three NRT formulations are licensed specifically for this new indication and the contraindication of using NRT whilst still smoking has now been removed from all NRT products. The NARS guidance recommends that smokers who are clearly unwilling to make a quit attempt be advised to cut down using NRT with a view to quitting later. Stop Smoking Services may provide brief advice of this kind but should not be involved in attempting to support smokers until they are ready to stop completely.

7 Other changes

Several other changes have been made to the indications, including that smokers with diabetes mellitus should be advised to monitor their blood sugar levels more closely than usually when NRT is initiated because catecholamine release can affect carbohydrate metabolism and vasoconstriction may delay/reduce insulin absorption, and that NRT should be used with caution in patients with moderate to severe hepatic impairment and/or severe renal impairment as they may be at risk of increased adverse effects. Because of theoretical risk associated with these conditions[26,27,28] as with patients undergoing treatment for cardiovascular disease, the clinician responsible for the management of the patient should be consulted. We recommend that the CSM report[1] be consulted for a complete list of these other changes.

Further reading

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