National Institute for Clinical Excellence

National Institute for Clinical Excellence

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N0082 1P 50k March 02 (ABA)

Technology Appraisal Guidance - No. 39

NHS

National Institute for Clinical Excellence

Guidance on the use of nicotine replacement therapy (NRT) and bupropion for smoking cessation

March 2002

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Issue date: March 2002
Review date: March 2005

Ordering information
Copies of this guidance can be obtained from the NHS Response Line by telephoning 0870 1555 455 and quoting ref: N0082. A patient version of this document can be obtained by quoting ref: N0084. A bi-lingual patient leaflet is also available, ref: N0085.

Distribution of guidance

This document has been circulated to the following:

- Health Authority Chief Executives in England and Wales
- NHS Trust Chief Executives in England and Wales
- PCG Chief Executives
- Local Health Group General Managers
- Medical and Nursing Directors in England and Wales
- GP Partners in England and Wales
- Chief Pharmacists, Heads of Drug Purchasing, Heads of Drug Information, Pharmaceutical Advisors, GP Prescribing Advisors and Purchase Advisors in England and Wales
- NHS Director Wales
- Chief Executive of the NHS in England
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- Patient advocacy groups
- Commission for Health Improvement
- NHS Clinical Governance Support Team
- Chief Medical, Nursing Officers and Pharmaceutical Officers in England and Wales
- Medical Director & Head of NHS Quality – National Assembly for Wales
- Representative bodies for health services, professional organisations and statutory bodies, Royal Colleges

This guidance is written in the following context:
This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Health professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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Web: www.nice.org.uk

ISBN: 1-84257-163-X
Published by the National Institute for Clinical Excellence
March 2002

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Guidance on the use of nicotine replacement therapy (NRT) and bupropion for smoking cessation

This section (Section 1) constitutes the Institute's guidance on the use of nicotine replacement therapy (NRT) and bupropion for smoking cessation. The remainder of the document is structured in the following way:

A bi-lingual summary is available from our website at www.nice.org.uk or by telephoning 0870 1555 455 and quoting the reference number N0083.

Mae crynodeb ar gael yn Gymraeg ac yn Saesneg ar ein gwefan yn www.nice.org.uk neu drwy ffonio 0870 1555 455 gan ddyfynnu cyfeirnod N0083.

1. Guidance

1.1 Nicotine replacement therapy (NRT) and bupropion are recommended for smokers who have expressed a desire to quit smoking.

1.2 NRT or bupropion should normally only be prescribed as part of an abstinent-contingent treatment (ACT), in which the smoker makes a commitment to stop smoking on or before a particular date (target stop date). Smokers should be offered advice and encouragement to aid their attempt to quit. Ideally, initial prescription of NRT or bupropion should be sufficient to last only until 2 weeks after the target stop date. Normally, this will be after 2 weeks of NRT therapy, and 3-4 weeks for bupropion, to allow for the different methods of administration and mode of action. Second prescriptions should be given only to people who have demonstrated that their quit attempt is continuing on re-assessment.

1.3 It is recommended that smokers who are under the age of 18 years, who are pregnant or breastfeeding, or who have unstable cardiovascular disorders, should discuss the use of NRT with a relevant health-care professional before it is prescribed.

1.4 Bupropion is not recommended for smokers under the age of 18 years, as its safety and efficacy have not been evaluated for this group. Women who are pregnant or breastfeeding should not use bupropion.

1.5 If a smoker's attempt to quit is unsuccessful with treatment using either NRT or bupropion, the NHS should normally fund no further attempts within 6 months. However, if external factors interfere with an individual's initial attempt to stop smoking, it may be reasonable to try again sooner.

1.6 There is currently insufficient evidence to recommend the use of an NRT and bupropion in combination.

1.7 In deciding which of the available therapies to use and in which order they should be prescribed, practitioners should take into account:

- Intention and motivation to quit, and likelihood of compliance
- The availability of counselling or support
- Previous usage of smoking cessation aids
- Contraindications and potential for adverse effects
- Personal preferences of the smoker

2 Clinical need and practice

2.1 In 1997, in the UK there were more than 11 million regular tobacco smokers – about 27% of the adult population. The proportions of men and women who smoke are about the same. Over the past 5 years, the proportion of smokers in the population has stabilised or may even be increasing, as about 25% of 15 year-olds are regular smokers.

2.2 Smoking rates are lowest among socio-economic class A, and rise successively through to classes D and E. Smoking rates are also high among some ethnic groups.

2.3 It is estimated that about 4 million smokers a year attempt to quit but that only 3% to 6% of these (1% to 2% of all smokers) succeed.

2.4 Half of all smokers die prematurely of a smoking-related ailment. This represents about 120,000 deaths each year. The decrease in life expectancy for regular smokers under the age of 35 years who do not subsequently quit has been estimated to be about 8 years. Smoking is a major aetiological factor for lung cancer, cardiovascular disease and peripheral vascular disease. It also causes respiratory disease, such as chronic obstructive pulmonary disease, including bronchitis and emphysema. The annual cost to the NHS of treating patients with smoking-related disease is of the order of £1,500 million.

2.5 Stopping smoking has major health benefits. Smokers who quit before the age of about 35 years have a life expectancy only slightly less than those who have never smoked. Even cessation in middle age improves health and substantially reduces the excess risk of death. Quitting at any age provides both immediate and long-term health benefits.

2.6 Inhaled nicotine is strongly addictive. Therefore, stopping smoking results in craving and withdrawal symptoms. Nicotine itself is not a major primary cause of smoking-related disease, but it has marked effects on arterial tone. The main disease-causing element from smoking comes from 'tar', a dark, viscous fluid formed from tobacco smoke, which contains at least 4,000 different chemicals, including over 50 known carcinogens and metabolic poisons. Other disease-causing elements include carbon monoxide, oxides of nitrogen and hydrogen cyanide.

3 The technologies

Nicotine replacement therapy

3.1 Nicotine replacement therapy (NRT) aims to replace the nicotine from cigarettes by other means of delivery: nicotine skin-patches, chewing-gum, lozenges, sublingual tablets, inhalators or nasal spray. NRT provides a background level of nicotine that reduces craving and withdrawal. The products currently licensed in the UK are:

3.1.1 Nicotine transdermal patches

- 5 mg, 10 mg, 15 mg (Nicorette®, Pharmacia)
- 7 mg, 14 mg, 21 mg per 24 hours (NICOTINELLE® TTS 10, TTS 20 and TTS 30, Novartis Consumer Health)
- 7 mg, 14 mg, 21 mg (NiQuitin CQ®, GlaxoSmith Kline (GSK))

3.1.2 Nicotine chewing gum

- 2 mg, 4 mg (Nicorette®, Pharmacia) (Nicotinell®, Novartis Consumer Health)

3.1.3 Nicotine 2 mg sublingual tablet (Nicorette® Microtab, Pharmacia)

3.1.4 Nicotine 1mg lozenge (Nicotinell®, Novartis Consumer Health)

3.1.5 Nicotine 10 mg inhalation cartridge plus mouthpiece (Nicorette® Inhalator, Pharmacia)

3.1.6 Nicotine 0.5 mg per puff metered nasal spray (Nicorette®, Pharmacia)

3.1.7 Nicotine 2 mg and 4 mg lozenge (NiQuitin CQ®, GSK)

3.2 All NRT are available either on general (over-the-counter) sale or on prescription through the National Health Service (NHS). They are available to smokers aged over 18 years of age, and to those under 18 years on the recommendation of a medical practitioner. Smokers with certain conditions (cardiovascular disease, hyperthyroidism, diabetes mellitus, severe renal or hepatic impairment and peptic ulcer) are advised to use an NRT only after careful consideration of risks and benefits and after discussion with a health care professional. Similar advice applies to women who are pregnant or breastfeeding. When giving such advice to people in these groups who have been unable to quit smoking without using a cessation aid, health care professionals should take into account the significant harm associated with continuing to smoke and that it can be expected that NRT will deliver less nicotine (and none of the other potentially disease-causing agents) than would be obtained from cigarettes.

3.3 Dosages of NRT may depend on the number of cigarettes smoked per day. Use should normally be restricted to the licensed duration of the form of NRT used. However, use may continue for up to 3 months in cases of continuing nicotine dependency. (In the case of nicotine patches, use should be reduced after 3 months.) NRT therapy should be discontinued if the user restarts smoking.

3.4 The most common side effects are localised reactions (for example, skin irritation with patches, irritation of the nose, throat and eyes with nasal spray), but minor sleep disturbances occur commonly. These side effects are unlikely to lead to discontinuation of therapy.

Bupropion

3.5 Bupropion sustained release (SR) (Zyban®, GSK) is a prescription-only drug licensed for use in smoking cessation (with motivational support) in the UK. In the USA, bupropion is also used as an antidepressant and licensed as Wellbutrin. Bupropion is a relatively weak but selective inhibitor of the neuronal re-uptake of dopamine and noradrenaline. Although the exact mechanism by which it aids smoking cessation is unclear, it is presumed to work directly on the brain pathways involved in addiction and withdrawal.

3.6 Smokers aged over 18 years should take one 150 mg tablet for the first 6 days, followed by two tablets per day for the following 6 to 8 weeks. They should delay stopping smoking until 7 to 14 days after starting treatment, because the drug needs this period of time to achieve its optimal effect.

3.7 The most clinically important adverse events associated with bupropion are seizures, which occur in about 1 in 1000 patients. Bupropion must not be prescribed for smokers with a current seizure disorder or any history of seizure. Smokers with a predisposition towards seizures must not be prescribed bupropion unless the potential benefits of smoking cessation outweigh the increased risks. Factors that may increase the risk of bupropion-associated seizures include concomitant administration of any drug known to lower the seizure threshold, alcohol abuse, head trauma, the use of glucose-lowering drugs or insulin in people with diabetes, and the use of stimulants and drugs to induce anorexia. Additionally, drug interactions between bupropion and several other medicines have been reported.

3.8 Bupropion should be prescribed subject to the contraindications listed in the Summary of Product Characteristics. Women who are pregnant or breastfeeding should not be prescribed bupropion.

3.9 In addition to seizures, about 0.1% of smokers suffer severe hypersensitivity reactions (e.g. angioedema, dyspnoea/ bronchospasm and anaphylactic shock), and a further 3% suffer milder reactions such as rash, urticaria or pruritis. Other adverse events have been reported, most commonly insomnia and dry mouth.

4.1 Clinical effectiveness

Nicotine replacement therapy

4.1.1 There is currently insufficient evidence to conclude that one form of NRT is more effective than another. From a meta-analysis of all six NRT products taken together, containing 97 RCTs involving 38,000 smokers, followed for 6 months after commencing treatment, the odds ratio of smoking cessation of any NRT versus placebo was 1.74 (95% confidence interval 1.64 - 1.86). For 12 months' follow-up from start of treatment, a meta-analysis of all six NRT products, containing 72 RCTs involving 29,000 smokers, indicated that the odds ratio of smoking cessation of any NRT versus placebo was 1.69 (1.57 - 1.82). Analyses or meta-analyses of five of the products taken separately, using 12- month data, yielded estimated odds ratios of 1.61(gum), 1.62 (patch), 2.08 (inhaler), 2.14 (2 mg lozenge), 2.69 (4 mg lozenge) and 2.27 (spray). Studies were taken from various sources, about 75% reporting continuous abstinence, and the rest point abstinence. In terms of percentages of smokers quitting, the average over all trials shows that about 10% had not smoked for the 12 months following placebo therapy, and about 17% had not smoked following NRT.

4.1.2 In the small number of studies undertaken with specific subgroups (smokers with lung disease, cardiovascular disease, peripheral vascular disease, pulmonary disease, or pregnant women), results were generally inconclusive on an individual study basis, but in aggregate were consistent with the overall pooled results.

4.1.3 The odds ratios for those forms of NRT (patch and gum) for which there is clinical trial evidence of effectiveness in different settings (community, primary care, smoking clinic or hospital) were not significantly affected by the setting.

4.1.4 In trials, a combination of two different NRTs was in general more effective than a single NRT.

Bupropion

4.1.5 From a random-effects meta-analysis of ten RCTs involving 3,800 smokers, the odds ratio for smoking cessation of bupropion versus placebo was 2.16 (1.51 – 3.10). This result combines data for smoking cessation for 6 months and 12 months and, in all but one study, measures continuous abstinence. For 12 months of smoking cessation (random-effects meta-analysis involving 3,100 smokers; in all but one study, continuous abstinence), the odds ratio was 2.05 (1.45 –

2.91). In terms of percentages of smokers quitting, the average over all trials shows that about 9% had not smoked for the 12 months following placebo therapy, and about 19% had not smoked following bupropion therapy.

4.1.6 The results for specific subgroups (smokers with pulmonary disease, cardiovascular disease, or those who had failed to quit at least once before they used bupropion) were generally consistent with the overall pooled results.

Bupropion versus NRT

4.1.7 There have been only two head-to-head studies of bupropion versus NRT. The first, a double blind, double dummy, randomised placebo controlled trial, compared bupropion with an NRT patch, and with a combination of bupropion plus NRT patch. For bupropion versus patch, the odds ratio at 12 months for continuous abstinence was 2.07 (1.22 - 3.53) in favour of bupropion, and for bupropion plus patch versus bupropion it was 1.28 (0.82 - 1.99). In the second study, an open-label, non-placebo, randomised controlled trial, bupropion 300mg/day was compared at 12 months (point abstinence) with NRT gum (4 mg). In this unpublished study, there was no significant difference between the treatment groups in quit rates.

Combination of NRT and bupropion

4.1.8 In the single study so far conducted, the result was in favour of the combination of NRT and bupropion against bupropion alone, but the difference was not statistically significant. Other studies are expected to report before the guidance review date.

4.2 Cost effectiveness

4.2.1 A number of cost-effectiveness studies have been reviewed. Outcomes from these studies have been expressed in a variety of ways as cost per long-term 'quitter', cost per life year gained (LYG), or cost per quality-adjusted life year (QALY) gained. Estimates of LYGs ranged from 0.3 to 2.4, depending on the model used and the discount rate. Estimates of QALYs gained from quitting are somewhat higher than LYGs, because the quality of life of a non-smoker is estimated to be on average higher than that of a smoker.

4.2.2 Incremental cost effectiveness of NRT over and above brief advice was estimated to be £4,500 per LYG at 1992 product prices and using discount rates of 6% for both costs and benefits, but a later estimate, at 1998

prices, ranged from £350 to £800 per LYG, using a discount rate of 6% for costs and 1.5% for benefits. US figures (using discount rates of 5% or 6% for both costs and benefits) are mostly closer to the higher end of the scale, but would be towards the lower end if benefits were discounted at 1.5%.

4.2.3 The independent model, produced by the authors of the Assessment Report, assumed a quit rate of 4% for advice only or 10% for counselling. The quit rate for the intervention was then estimated from these figures, given an odds ratio for NRT of 1.67 taken from clinical effectiveness studies. For each quitter, it was assumed that 2 discounted life-years were gained. The incremental cost per LYG for advice alone against doing nothing, and for counselling against doing nothing, were both less than £1,000. For either NRT or bupropion in addition to brief advice, the incremental cost per LYG was less than £2,500, and for either NRT or bupropion in addition to counselling, the incremental cost per LYG was not more than £1,000. Some researchers in the area believe the costs per LYG for the interventions quoted above may be even less than the above estimates.

4.2.4 The three manufacturers have performed separate calculations, which also yield low estimates of mean incremental costs per LYG, broadly consistent with those in 4.2.3.

4.3 Consideration

4.3.1 Both bupropion and NRT are considered to be among the most cost effective of all healthcare interventions. The central estimates of cost-effectiveness ratios across all evaluations, considering a range of assumptions, are below, and possibly well below, £3,000 per LYG, and with UK discount rates, are below £2,000 per LYG.

4.3.2 All of the cost-effectiveness models, however, assume that people who quit smoking using NRT or bupropion would otherwise either have never quit, or would have only had a small chance of quitting each year during their lifetime. This assumption may overstate the reality. A preponderance of those who quit using a cessation aid may have been smokers who would otherwise have quit within the next few years without an aid. However, while this might effectively make NRT and bupropion more expensive per unit of benefit gained, they would almost certainly still be cost-effective.

4.3.3 The participants in most, if not all, of the trials may not be representative of the population of smokers as a whole, but of smokers who are motivated to quit and therefore are more likely to volunteer for the trial. The quit rates seen in the trials cannot therefore be readily extrapolated to the total population of smokers. This effect, however, would only alter the cost effectiveness of these treatments if they were given to the whole population of smokers, and would not affect estimates of cost-effectiveness when the treatments are targeted at smokers wishing to quit.

4.3.4 The likelihood that a smoker will be successful in quitting depends on several factors: the smoker's motivation; the extent of the smoker's nicotine dependence; the intensity and quality of the support offered; and the use of pharmacological aids. Motivation, however, is extremely difficult to measure accurately, and consequently the effect of motivation on cessation rates, other than in qualitative terms, is not well known. The importance of motivation in successful smoking cessation was accepted by the Appraisal Committee. The Committee did not consider it appropriate to set criteria for assessing levels of motivation to quit smoking. It was felt appropriate to recommend a limit on the frequency of quit attempts using either NRT or bupropion that should be prescribed under the NHS. The Committee considered it important that, to enable the smoker to regain adequate motivation, at least 6 months should elapse between an unsuccessful attempt to quit and the next prescription of NRT or bupropion, unless external factors are known to have interfered with the initial quit attempt and indicate that an earlier reassessment of motivation is required.

4.3.5 Similarly, the effectiveness of advice and counselling on quit rate are difficult to measure with any accuracy, and studies of these factors show mixed results. Advice and counselling are often given with NRT, and are required when bupropion is prescribed. While it is known that both advice and counselling improve the quit rate for patients receiving NRT, and that NRT is still both clinically and cost effective without advice or counselling, it is not clear how much of the success of smoking cessation aids is due to the increased level of the kind of support that accompanies their use. The Committee therefore considered that the level of advice and support that should be provided to the smoker during a quit attempt was of major importance, but that it was difficult to judge accurately the extent of what should be provided.

4.3.6 Smokers should be offered the option of being referred to a specialist smoking cessation service where this is available. In the absence of such support, consideration should be given to making provision for regular support sessions for smokers wishing to cease smoking.

4.3.7 The abstinent-contingent (ACT) protocol, which is supported by both patient groups and clinicians expert in smoking cessation therapies, and which incorporates limited prescription periods during treatment, was considered to be a useful part of the provision of smoking cessation aids. Within this regimen, the target quit date is a means of focussing smokers' commitment to quit. Prescriptions for NRT or bupropion in the first instance should last only 2, or 3-4 weeks, respectively, to allow further support to be given when the second prescription is written, and to allow potential quit attempts to focus on lasting until the second consultation date. Further, since most quit attempts fail, a first prescription covering a longer time period would in many cases waste NHS resources.

4.3.8 NRT in general is associated with few adverse events. Users of bupropion, however, will sometimes suffer adverse events, occasionally serious, and which now appear to be relatively well known. Concern about these adverse events will deter many smokers from using bupropion. However, for some smokers, who are unable to quit using NRT, bupropion will enable them to cease smoking. (Conversely, some patients who have been unable to quit using bupropion may be successful with NRT.) While both sets of drugs are effective compared with no cessation aids, the majority of smokers who are prescribed them will still fail to quit at any single attempt. While this is often disappointing to prescribers of smoking cessation aids as well as for smokers themselves, the relatively low success rates are still a highly cost-effective use of NHS resources.

4.3.9 Practitioners' time for advice plus the writing of an increased number of prescriptions when this guidance has been put into practice has an implicit cost, the size of which will depend on the increase in workload. This is likely to amount to between £3 million and £9 million.

5 Implications for the NHS

5.1 The estimated budget impact for the NHS in England and Wales depends on:

i the number of additional quit attempts that will be made when the price to the smoker of cessation aids is lowered (since, when taken on prescription, most of the drug cost will in future be paid by the NHS), and

ii the number of courses of NRT that would have been paid for, over-the-counter, by the smoker and will now be mostly paid for by the NHS.

If the number of additional prescriptions written is in the range of 500,000 to 1.4 million per year, this will give rise to additional drug costs of between £20 million and £56 million per year, based on £40 per prescription.

5.2 It is likely that each GP would, on average, see approximately one new patient requesting advice for smoking cessation every 2 weeks. If counselling is also offered, the potential impact is estimated to be one group session per week for the average GP practice, with each session comprising between 3 and 8 patients. Costs of additional support groups set up by GP practices may add an extra £3 million to the cost of provision of smoking cessation therapy, on the basis of 60,000 sessions (of an average of 5 patients each) at a cost of £50 per session.

6 Further research

6.1 Since there are only two head-to-head trials of bupropion against NRT, only one of which shows a significant difference between the treatments, further such studies comparing these methods of smoking cessation should be carried out. Combination therapy of bupropion and NRT should be considered as one arm.

6.2 Optimal use of resources to maximise health gains from smoking cessation strategies requires more detailed knowledge than is currently available. Important areas where more information is required are the roles of advice/counselling and smoker motivation in conjunction with NRT or bupropion, and the relationships between smoking cessation aids and smoking dependency, age, social support systems, and their interactions.

6.3 Since smoking cessation therapies are such cost effective means of providing health care, the extension of these therapies to smokers who are less motivated to quit may also be cost effective. Innovative strategies to encourage quitting should be investigated.

7 Implementation

7.1 NHS Trusts, primary care teams, local health groups, community pharmacists, hospital-based clinical services and health authorities should review policies and practices regarding smoking cessation to take account of the guidance set out in Section 1.

7.2 Local guidelines or care pathways, particularly those on cardiac or respiratory conditions should incorporate consideration of action to be taken for the patient who is a smoker.

7.3 Arrangements should be made to ensure that smoking cessation advice and support is available to patients at both community and hospital locations.

7.4 To measure compliance locally with the guidance set out in Section 1, the following criteria should be used:

7.4.1 NRT and bupropion are available for prescription for smokers who have expressed a desire to quit smoking.

7.4.2 Smokers who are under the age of 18 years, who are pregnant or breastfeeding or who have unstable cardiovascular disorders discuss the use of NRT with a relevant health-care professional before it is prescribed.

7.4.3 Bupropion is not prescribed for people under the age of 18 year or for women who are pregnant or breast-feeding.

7.4.4 Initial prescriptions are for 2 weeks only (for NRT) and for 3-4 weeks only (for bupropion), if minimum pack size permits, or one month otherwise. A second prescription for the remaining period of treatment is given only to people whose quit attempt is continuing at re-assessment.

7.4.5 Advice and encouragement is available to smokers who are trying to stop smoking

7.4.6 When a smoker's attempt to quit is unsuccessful with either NRT or bupropion, ordinarily no further prescriptions are funded under the NHS within 6 months of the last prescription.

7.5 Patient Group Directions (PGDs) for bupropion and NRT could be considered in situations where responsibility for smoking cessation lies with appropriately trained non-physician health care professionals (e.g. nurse or pharmacist), and access to a medical practitioner for prescriptions is limited. This would enable convenient and timely provision of smoking cessation pharmacotherapies to patients in accordance with a strict protocol. For NRT, nurse prescribing is also an option.

7.6 Local clinical audits on the prescription of NRT and bupropion could include measurement of whether or not patients are routinely asked if they smoke, whether or not smoking status is routinely recorded in patient records, whether or not patients are advised about smoking cessation and assisted to stop smoking if they wish to, and of other performance indicators specified in the National Service Framework Coronary Heart Disease.

8 Review of guidance

8.1 This guidance will be reviewed by the Institute in March 2005.

Andrew Dillon
Chief Executive

March 2002

APPENDIX A

Appraisal Committee members

The Appraisal Committee is a statutory committee whose members sit for 3 years. Two meetings are held per month and the majority of members attend one or the other. Declared interests may also exclude a member from individual technology appraisals. The committee are supplemented by technology specific experts as indicated in Appendix B.

Professor R. L. Akehurst
Dean, School of Health Related Research
Sheffield University

Professor David Barnett (Chairman)
Professor of Clinical Pharmacology
University of Leicester

Professor Sir Colin Berry
Professor of Morbid Anatomy
St Bartholomew's and Royal London School of Medicine

Dr Sheila Bird
MRC Biostatistics Unit,
Cambridge

Professor Martin Buxton
Director of Health Economics Research Group
Brunel University

Dr Karl Claxton
Lecturer in Economics
University of York

Professor Sarah Cowley
Professor of Community Practice Development
Kings College, London

Mr Chris Evennett
Chief Executive
Mid-Hampshire Primary Care Group

Professor Terry Feest
Clinical Director and Consultant Nephrologist
Richard Bright Renal Unit and
Chairman of the UK Renal Registry

Ms Jean Gaffin
Formerly Executive Director
National Council for Hospice and Specialist Palliative Care Service

Mrs Sue Gallagher
Chief Executive
Merton, Sutton and Wandsworth Health Authority

Dr Trevor Gibbs
Head, Global Clinical Safety & Pharmacovigilance
GlaxoSmithKline
(Although a member of this Committee, Dr Gibbs took no part in this appraisal topic, due to conflict of interest: GSK manufactures both NRTs and bupropion.)

Mr John Goulston
Director of Finance
The Royal Free Hampstead NHS Trust

Professor Philip Home
Professor of Diabetes Medicine
University of Newcastle

Dr Terry John
General Practitioner
The Firs, London

Dr Diane Ketley
Research into Practice Programme Leader
NHS Modernisation Agency

Dr Mayur Lakhani
General Practitioner, Highgate Surgery, Leicester and Lecturer,
University of Leicester

Mr M Mughal
Consultant Surgeon
Chorley and South Ribble NHS Trust

Mr James Partridge
Chief Executive
Changing Faces

Professor Philip Routledge
Professor of Clinical Pharmacology
University of Wales

Professor Andrew Stevens (Vice Chairman)
Professor of Public Health
University of Birmingham

Dr Cathryn Thomas
General Practitioner/Senior Lecturer
Department of Primary Care & General Practice
University of Birmingham

APPENDIX B

Sources of evidence

1. The following documents were made available to the Committee in their discussions of the appraisal of nicotine replacement therapy (NRT) and bupropion for smoking cessation.

a. Assessment Report:

- prepared by the NHS Centre for Reviews & Dissemination, University Of York and Department of Public Health & Epidemiology, University of Birmingham *(A rapid and systematic review of the clinical and cost effectiveness of bupropion and nicotine replacement therapy (NRT) for smoking cessation,* 24 August 2001).

b. Professional/specialist, patient and trade group submissions:

- Action on Smoking Health, British Lung Foundation and Cancer Research Campaign (joint submission)
- Health Development Agency
- Imperial Cancer Research Fund
- Institute of Psychiatry (Tobacco Research Section)
- Pharmacy Health Care
- Roy Castle Lung Cancer Foundation
- Royal College of Physicians and British Thoracic Society (joint submission)

c. Manufacturer/sponsor submissions:

- GlaxoSmithKline
- Novartis Consumer Health
- Pharmacia

d. Other:

- Department of Health and National Assembly for Wales

e. External experts:

- John Stapleton, Senior Lecturer in Tobacco Studies & Medical Statistics, Tobacco Research Section, Institute of Psychiatry, London
- Gay Sutherland, Lecturer and Clinical Psychologist, Institute of Psychiatry, University of London (also on behalf of QUIT)

APPENDIX C

Patient information

Guidance on the use of nicotine replacement therapy and bupropion for people who want to stop smoking

The patient information in this appendix has been designed to support the production of your own information leaflets. You can download it from our website at www.nice.org.uk where it is available in English and Welsh. If you would like printed copies of the leaflets please ring the NHS Response Line on 0870 1555 455 and quote reference number N0084 for the English patient leaflet and N0085 for the bi-lingual patient leaflet.

What is NICE guidance?

The National Institute for Clinical Excellence (NICE) is a part of the NHS. It produces guidance for both the NHS and patients on medicines, medical equipment, diagnostic tests and clinical and surgical procedures and where they should be used.

When the Institute evaluates these things, it is called an appraisal. Each appraisal takes around 12 months to complete and involves the manufacturers of the drug or device, the professional organisations and the groups who represent patients.

NICE was asked to look at the available evidence on nicotine replacement therapy (NRT) and buproprion and provide guidance that would help the NHS in England and Wales decide where they should be used to help people to give up smoking.

About smoking

In 1997, in the UK there were more than 11 million regular tobacco smokers – this represents about 27 people in every 100. The numbers of men and women who smoke are about the same. Over the past 5 years, the number of smokers has stabilised or may even be going up, as about 25 out of every 100 15 year olds are regular smokers.

It is estimated that about 4 million smokers a year attempt to quit but that only 3 to 6 out 100 of these succeed.

Half of all smokers die early because of a smoking-related illness. This represents about 120,000 deaths each year. Smoking causes lung cancer, heart disease, and lung diseases such as chronic obstructive pulmonary disease, including bronchitis and emphysema. It costs the NHS about £1500 million a year to treat patients who have a smoking-related disease.

Stopping smoking has major health benefits. Smokers who quit before the age of about 35 can expect to live very nearly as long as people who have never smoked. Even stopping smoking in middle age improves health and substantially reduces the risk of an early death. Quitting at any age provides both immediate and long-term health benefits.

Inhaled nicotine is strongly addictive, and so people who stop smoking can have a craving to smoke and suffer withdrawal symptoms. The main disease-causing part of cigarettes is 'tar', a dark fluid formed from tobacco smoke, which contains at least 4000 different chemicals, including over 50 known cancer-causing agents and poisons. Other components of tobacco smoke that cause disease include carbon monoxide, oxides of nitrogen and hydrogen cyanide.

What are nicotine replacement therapy and bupropion?

Nicotine replacement therapy (NRT)

NRT aims to replace the nicotine a smoker gets from cigarettes in other ways, for example through nicotine-containing patches, chewing-gum, lozenges, tablets, inhalators or nasal spray. NRT provides a small amount of nicotine that reduces craving and withdrawal. There are several NRT products currently licensed in the UK.

NRT products are available either 'over-the-counter' from the chemist or on prescription through the NHS. They are available to smokers aged over 18 years of age, and to smokers under 18 years on the recommendation of a healthcare professional. People with conditions such as heart disease, over active thyroid, diabetes, severe kidney or liver disease and stomach ulcers are advised to use NRT only after they have carefully considered the risks and benefits of the treatment and after discussion with a healthcare professional. Similar advice applies to women who are pregnant or breastfeeding.

Bupropion

Bupropion (also known as Zyban) is only available on prescription. Bupropion affects some of the chemical messages in the brain and it is thought to work on the parts of the brain involved in addiction and withdrawal.

Smokers aged over 18 years should take one 150 mg tablet for the first 6 days, followed by two tablets every day for the following 6 to 8 weeks. They should not stop smoking until 7 to 8 days after starting treatment, because the drug needs this time to be working at its best.

The most important side effects associated with bupropion are seizures (fits), which occur in about 1 in 1000 patients. Bupropion must not be prescribed for smokers who have a current seizure disorder (for example epilepsy) or any history of seizure. Smokers who are at risk of seizures must not be prescribed bupropion unless the benefits of smoking cessation are likely to outweigh the risks of taking the drug. There are other factors that may increase the risk of seizures in people taking bupropion, including taking other drugs that are known to increase the risk of seizures, alcohol abuse, or head injury. People with diabetes who are using glucose-lowering drugs or insulin and people who are using drugs to treat anorexia may also have a higher risk of seizures with bupropion.

What has NICE recommended about the use of NRT and bupropion?

NICE has made the following recommendations.

It is recommended that NRT and bupropion should be available to you on prescription if you are a smoker who has said that you want to quit smoking.

NRT or bupropion should normally only be prescribed when you have made a commitment to stop smoking on or before a certain date (which is called your 'target stop date'). Healthcare professionals should offer you advice and encouragement to help you quit. Ideally, your first prescription of NRT or bupropion should only be enough to last until 2 weeks after your target stop date. Normally, this will be 2 weeks for NRT. For bupropion it will be 3–4 weeks, because bupropion should be taken for about 1 week before your target stop date. You should only be given a second prescription for NRT or bupropion if you can show that you are still trying to stop smoking.

It is recommended that if you are under the age of 18 years, pregnant or breastfeeding, or you have unstable heart conditions, you should discuss the use of NRT with a doctor or nurse before starting treatment.

Bupropion is not recommended for smokers under the age of 18 years, because it is not licensed for use by people in this age group. Women who are pregnant or breastfeeding should not use bupropion.

If your attempt to quit is unsuccessful, your healthcare professional should not usually prescribe NRT or bupropion for another attempt within 6 months. However, if external factors interfere with your initial attempt to stop smoking, it may be reasonable to try again sooner. (For example, if a particularly stressful event occurred after you had started your initial attempt to quit.)

There is currently not enough evidence to recommend the use of NRT and bupropion together.

In deciding which of the available therapies to use and in which order they should be prescribed, your doctor should take the following factors into account:

- Your intention and motivation to quit, and how likely it is you will follow the course of treatment as prescribed.
- Whether counselling and support are available to help you quit.
- Whether you have used treatments to attempt to stop smoking in the past.
- Whether there are medical reasons why you should not be prescribed NRT or bupropion, and whether you are likely to experience adverse effects with either treatment.
- Which treatment you would prefer to use.

What should I do?

If you smoke, or someone you care for smokes, then you can discuss this advice with your doctor.

Will NICE review its guidance?

Yes. The guidance will be reviewed in March 2005.

Further information:

Further information on NICE, and the full guidance issued to the NHS is available on the NICE website (www.nice.org.uk).

The guidance can also be requested from 0870 555 455, quoting reference N0082.

If you have access to the Internet and would like to find out more about giving up smoking visit the NHS Direct website: www.nhsdirect.nhs.uk. If you would like to speak to NHS Direct, please phone 0845 46 47.

APPENDIX D

Technical detail on the criteria for audit of the use of NRT and bupropion for smoking cessation

Possible objectives for the audit

An audit on the appropriateness of prescription of NRT and bupropion for smoking cessation could be carried out to ensure that:

- NRT and bupropion are offered to people who are regular smokers and who have expressed a desire to quit smoking
- The continuation of prescriptions for NRT and bupropion is cost effective for the NHS
- People who want to stop smoking have access to advice and support

Possible patients to be included in the audit and time period for selection

In a primary care setting, all patients who are smokers and who are being seen for any purpose over a sensible period of time for audit data collection, for example, one to three months

In a hospital setting, all patients who are smokers and who are being treated as inpatients or outpatients in a clinical service over a sensible period of time for audit data collection, for example, one to three months

Patients to be included in an audit will have to have been identified as smokers. If whether or not a patient is a regular smoker is not asked routinely or not recorded routinely, a change in practice will be needed before smokers can be identified on the basis of existing record-keeping practices

Measures to be used as a basis for the audit

The measures that can be used in an audit of the appropriateness of prescribing of NRT and bupropion are as follows:

Criterion	Standard
1. A patient who is a smoker is offered NRT or bupropion on the NHS when the following conditions have been met: a. The patient is a regular smoker **and** b. The patient has expressed a desire to quit	Local teams should agree on the target % of patients recorded as regular smokers and who want to quit who should be offered therapy on the NHS
2. NRT is prescribed as follows: a. Initial prescription is only for 2 weeks after the target stop date b. Second prescription is provided only to a patient whose quit attempt is continuing at reassessment	100% of patients given initial prescription of NRT 100% of patients given initial prescription of NRT and whose quit attempt is continuing
3. Bupropion is prescribed as follows: a. Initial prescription is for only 3-4 weeks after the target stop date b. Second prescription is provided only to a patient whose quit attempt is continuing at reassessment	100% of patients given initial prescription of bupropion 100% of patients given initial prescription of bupropion and whose quit attempt is continuing
4. NRT or bupropion is prescribed on the NHS for a patient whose quit attempt is unsuccessful with either therapy within the last 6 months of a prescription	0% of patients who request prescription after unsuccessful attempt
5. Advice and support is available to patients who are trying to stop smoking	Local teams should agree on the target % of patients recorded as smokers who should be offered access to support

Calculation of compliance with the measure

Compliance with each measure described in the table is calculated as follows:

$$\frac{\text{Number of patients whose care is consistent with the } \textbf{Criterion} \textit{ plus} \text{ plus number who meet any of the Exceptions listed}}{\text{Number of of patients in the audit to whom the } \textbf{Measure} \text{ applies}} \times \mathbf{100}$$

Exception	Definition of Terms
A. NRT is prescribed in the following circumstances only after discussion with a relevant health-care professional: (1) The patient is under 18 years of age (2) The patient is pregnant or breast-feeding (3) The patient has an unstable cardiovascular disorder B. Bupropion is not ordinarily prescribed in the following circumstances: (1) The patient is under the age of 18 years (2) The patient is pregnant (3) The patient is breast-feeding	Clinicians should agree locally on how the patient's motivation to quit is to be determined for audit purposes. Considerations could include previous use of smoking cessation aids, potential adverse effects and personal preferences of the smoker
None None	Target stop date = the particular date by which the individual makes a commitment to stop smoking. For audit purposes, clinical teams should agree how the patient's continuing assessment is recorded, and whether or not the team wants to make any exceptions.
None None	See above for definitions.
None	Clinical teams should agree on how success will be recorded, for audit purposes, and whether or not the team wants to make any exceptions
A. The patient refuses referral to smoking cessation support	Clinical teams should agree locally on what constitutes advice and/or support for audit purposes

Clinicians should review the findings of measurement, identify if practice can be improved, agree on a plan to achieve any desired improvement and repeat the measurement of actual practice to confirm that any desired improvement is being achieved.