NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA123: varenicline for smoking cessation

This guidance was issued in July 2007
The review date for this guidance is May 2010

Recommendation

- The guidance should be transferred to the 'static guidance list'.
- The NICE Public Health team has received a remit *"to update existing NICE Guidance (Technology Appraisals and Public Health Guidance) on technologies used in smoking cessation".* The decision to send the guidance to the static list may need to be reconsidered when this project begins.
- That we consult on this proposal.

Consideration of the recommendation

This review proposal has been prepared taking into account the principles outlined in the Department of Health policy document PWG IB (10)05.

If this proposal is agreed following consultation, the decision may need to be reviewed following scoping of the public health guidance. In this instance a further consultation would be required.

Consideration of options for recommendation:

Options	Comment
A review of the guidance should be planned into the appraisal work programme as a potential MTA with nicotine conjugate vaccine (NCV), if NCV is referred to NICE.	At present the evidence does not suggest that a review as a single technology appraisal would change the conclusions of TA123.
The decision to review the guidance should be deferred (until a specified date)	We prefer the option above, in the first instance.

Options	Comment
A review of the guidance should be combined with a review of a related technology and conducted at the scheduled time for the review of the related technology.	The NICE Public Health team have recently received a remit *"to update existing NICE Guidance (Technology Appraisals and Public Health Guidance) on technologies used in smoking cessation".* Because no evidence has been found that would be expected to cause the guidance on varenicline to change, an update of at least that part of the smoking cessation guidance is not required at present. In the light of this, the Centre for Public Health Excellence will focus on the remit for harm reduction approaches before tackling the review of smoking cessation guidance.
A review of the guidance should be combined with a new appraisal that has recently been referred to the Institute.	No related, newly-referred appraisals are in progress.
The guidance should be incorporated verbatim into an on-going public health programme guidance.	The following remit has been referred to the Public Health programme *" to update existing NICE Guidance (Technology Appraisals and Public Health Guidance) on technologies used in smoking cessation"*. For the reasons given above, the Centre for Public Health Excellence will focus on the remit for harm reduction approaches before tackling the review of smoking cessation guidance.
A review of the guidance should be updated into an on-going clinical guideline.	We do not believe that a review is necessary at present. The decision to send the guidance to the static list may need to be reconsidered when this project begins.
The guidance should be transferred to the 'static guidance list'.	**Given that we do not anticipate any substantive change in the evidence base underpinning TA123, this is the preferred option.**

Original remit(s)

To prepare a technology appraisal on the clinical and cost effectiveness of varenicline for smoking cessation.

Current guidance

1.1 Varenicline is recommended within its licensed indications as an option for smokers who have expressed a desire to quit smoking.

1.2 Varenicline should normally be prescribed only as part of a programme of behavioural support.

Relevant Institute work

Published and ongoing

School-based interventions to prevent the uptake of smoking among children. Public Health Guidance PH23. Issued: February 2010. Expected review date: TBC.

Brief interventions and referral for smoking cessation in primary care and other settings. Public Health Guidance PH1. Issued: March 2006. Expected review date: TBC.

Smoking cessation services in primary care, pharmacies, local authorities and workplaces, particularly for manual working groups, pregnant women and hard to reach communities. Public Health Guidance PH10. Issued: February 2008. [This guidance supersedes TA39 'Smoking cessation - bupropion and nicotine replacement therapy'. It cross-references and is consistent with PH1 'Brief interventions and referral for smoking cessation in primary care and other settings', PH5 'Workplace health promotion: how to help employees to stop smoking' and TA123 'Varenicline for smoking cessation']. Expected review date: 2012.

Guidance on preventing the uptake of smoking by children and young people. Public Health Guidance PH14. Issued: July 2008. Expected review date: TBC.

Workplace interventions to promote smoking cessation. Public Health Guidance PH5. Issued April 2007. Expected review date: TBC.

Reducing the rate of premature deaths from cardiovascular disease and other smoking-related diseases: finding and supporting those most at risk and improving access to services. Public Health Guidance PH15. Issued September 2008. Expected review date: TBC.

The most appropriate means of generic and specific interventions to support attitude and behaviour change at population and community levels. Public Health Guidance PH6. Issued October 2007. Expected review date: TBC.

How to stop smoking in pregnancy and following childbirth. Public Health Guidance. Expected issue date: June 2010.

Remit referred in the 23rd wave. 'To produce public health guidance for commissioners and providers on the development and implementation of policies on smoke free homes and smoke free private cars and other vehicles.' Expected issue date: TBC

Remit referred in the 23rd wave. 'To produce public health guidance for PCTs and Local Authorities on multi agency partnership working to combat markets in illicit tobacco products.' Expected issue date: TBC

Remit referred in the 23rd wave. 'To produce public health guidance for commissioners and providers on delivering cessation services for users of smokeless tobacco.' Expected issue date: TBC

Remit referred in the 23rd wave. 'To produce public health guidance for retail and community pharmacists and other retailers on providing support and information to customers buying OTC nicotine replacement products.'

Remit referred in the 23rd wave. 'To update existing NICE Guidance (Technology Appraisals and Public Health Guidance) on technologies used in smoking cessation.'

Remit referred in the 23rd wave. 'To produce public health guidance for PCTs and NHS smoking cessation services on the use of harm reduction approaches to smoking cessation.

Remit referred in the 23rd wave. 'To produce public health guidance for NHS secondary care providers on smoking cessation services for patients in hospital and in the community with long term and chronic conditions Expected issue date: TBC.

In topic selection:

[redacted]

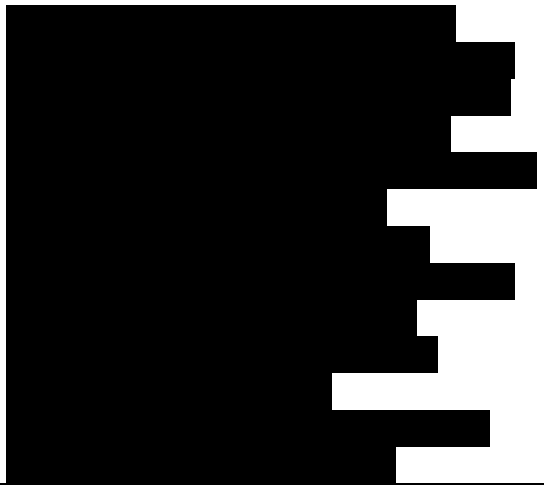
Safety information

The MHRA started intensively monitoring varenicline in 2007 following concerns of serious psychological side effects. A possible effect on driving ability has also been mooted. The SPC has been amended to alert doctors to these possibilities following a review of the available data in 2008 (source: NELM). Similar action has also been taken in the United States (source: NELM).

Details of new indications

Drug (manufacturer)	Details
Varenicline (Pfizer)	None. [redacted]

Details of new products

Drug (manufacturer)	Details
Nicotine conjugate vaccine (Nabi)	Phase III. 

On-going trials

Trial name and contact	Details
Varenicline Treatment for Smoking Cessation in Patients With Bipolar Disorder	Not yet open for recruitment Phase IV Estimated primary completion date: June 2012
Evaluation of Varenicline (Champix) in Smoking Cessation for Patients Post-Acute Coronary Syndrome (EVITA) Trial	Not yet open for recruitment Phase III Estimated primary completion date: August 2012
Varenicline (Champix®) Special Investigation (Regulatory Post Marketing Commitment Plan)	Ongoing Phase IV Estimated primary completion date: October 2014
Varenicline Versus Transdermal Nicotine Patch for Smoking Cessation in Patients With Coronary Heart Disease	Currently recruiting Phase IV Estimated primary completion date: February 2010
Improving Varenicline Adherence and Outcomes in Homeless Smokers	Phase IV Ongoing Estimated primary completion date: May 2011
Measuring Smoking Behaviors While Using Varenicline	Currently recruiting Phase IV Estimated primary completion date: September 2010
Drug Use Investigation Of Varenicline (Regulatory Post Marketing Commitment Plan)	Enrolling by invitation Phase IV observational follow up of participants in previous RCT Expected primary completion date: April 2013

Trial name and contact	Details
Relapse Prevention With Varenicline	Currently recruiting Phase IV Estimated primary completion date: August 2010
Varenicline Treatment in Alcohol and Nicotine Dependent Patients With Schizophrenia	Currently recruiting Phase IV Estimated primary completion date: June 2010
Safety and Efficacy of 12 Weeks of Varenicline for Smoking Cessation in Smokers With Depression	Currently recruiting Phase IV Estimated primary completion date: June 2010
Use of Varenicline for 4-Weeks Prior to Quitting	Not yet open for recruitment Phase IV Estimated primary completion date: April 2009
Post Marketing Surveillance Study to Observe Safety and Efficacy of Champix® Tablets	Enrolling by invitation Phase IV Estimated primary completion date: March 2010
Efficacy and Safety of Varenicline Among HIV-infected Patients	Phase III Currently recruiting Estimated primary completion date: March 2012
Smoking Cessation Study for Patients With Schizophrenia or Schizoaffective Disorder	Phase III Estimated primary completion date: February 2010
Smoking Cessation Program in the Preadmission Clinic	Ongoing Phase IV Estimated primary completion date: June 2010
Pharmacogenetics, Emotional Reactivity and Smoking	Currently recruiting Phase III Estimated primary completion date: December 2010
Smoking Cessation Treatment for Methadone Maintenance Patients	Currently recruiting Phase IV Estimated primary completion date: August 2014
Efficacy and Cost-Effectiveness of Cost-free Pharmacotherapy for Smoking Cessation for High-risk Smokers With Cerebrovascular Disease	Currently recruiting Phase IV Estimated primary completion date: June 2011
EUROACTION PLUS intensive smoking intervention (varenicline)	Ongoing Anticipated end date: December 2010

Proposed Timing for updating the guidance

If the proposal is accepted then the guidance will be incorporated into public health guidance. TA 123 will remain extant alongside the public health guidance.

New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from December 2006 onwards were reviewed. The results of the literature search are discussed in the 'Appraisals comment' section below.

Implementation

A submission from Implementation is attached at the end of this paper.

Equality and diversity issues:

Various trials are being conducted on the use of varenicline for smoking cessation within specific groups, including (but not limited to): those with HIV (1 trial); bipolar disorders (1 trial); schizophrenia (2 trials); depression (1 trial) and those undergoing treatment for substance abuse (1 trial). None of the studies have reported.

Appraisals comment:

The studies provided by the manufacturer were largely focussed on population groups in Japan, Taiwan, Korea, China, Singapore and Thailand. They indicate that the continuous abstinence rate (CAR) were higher for varenicline treated versus placebo. Three of these studies look at CAR for weeks 9 through 52 (12 week treatment phase) which can provide some indication of the long term effectiveness of varenicline with particular reference to relapse rates after completion of treatment. The manufacturer also provided results on two trials evaluating the effectiveness of varenicline in patients with COPD and cardiovascular disease. Both indicate that the continuous abstinence rate was higher for varenicline than placebo and that adverse events were limited to the side-effect profile of varenicline.

The updated literature search identified studies comparing varenicline with nicotine patches, buproprion and placebo were also identified which reported higher continuous abstinence rates for varenicline. As these results are consistent with the evidence included in the initial appraisal, they are unlikely to provide the basis for a reversal of the recommendation. One trial assessing the effect of varenicline on neuropsychiatric symptoms was also identified and though it is complete, results are not available yet.

The updated literature searches and information provided by the manufacturer (Pfizer) suggest that, although there are new studies on the use of varenicline

for smoking cessation, there is no new evidence that would lead to a change in the recommendations of the guidance.

It is noted that Public Health have received a referral (as part of the 23rd wave) to update existing NICE Guidance (Technology Appraisals and Public Health Guidance) on technologies used in smoking cessation.

Summary

The NICE Public Health team have received a remit "to update existing NICE Guidance (Technology Appraisals and Public Health Guidance) on technologies used in smoking cessation" in the 23rd wave. This will include a review of TA123 as well as the guidance on nicotine replacement and buproprion that is now within public health guidance (PH10 'Smoking cessation services: guidance'). No new or forthcoming evidence has been found that would cause the guidance on varenicline to change, therefore an update of at least that part of the smoking cessation guidance is not required at the present time. In the light of this, the Centre for Public Health Excellence will focus on the remit for harm reduction approaches first and will postpone work on the remit for smoking cessation technologies to a later date.

Based on the current evidence base, the technology appraisal guidance for varenicline in smoking cessation can be moved to the static list.

GE paper sign off: Janet Robertson, 31 August 2010

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NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE
IMPLEMENTATION DIRECTORATE

Guidance Executive Review

Technology appraisal 123: Varenicline for smoking cessation.

1. NICE Implementation uptake report

NICE implementation uptake report: Smoking cessation drugs. Available from: http://www.nice.org.uk/media/D79/42/UptakeReportSmokingCessationPublication.pdf

Summary

Overall, the numbers of prescription items for NRT and bupropion have fallen since 2006. This coincides with an increase in the number of prescription items for varenicline, which was first marketed in the UK in December 2006 and subsequently recommended by NICE in July 2007. In the 12 months to November 2009 the prescribing cost of smoking cessation drugs in primary care was £61,487,877, an increase of 10% compared to the previous 12 months. While bupropion decreased in volume by 18%, varenicline and NRT increased in prescription items by 19% and 8% respectively.

Both the proportion of patients prescribed each drug and the market share by prescription cost, showed a considerable decrease for NRT and a slight decrease for bupropion. This coincides with a large increase in the uptake of varenicline. Varenicline has increased its market share level at a faster rate than anticipated in the NICE costing report.

2. External literature

2.1 ERNIE

2.1.1 The Information Centre for Health and Social Care (2009) Hospital Prescribing, 2008: England

http://www.ic.nhs.uk/webfiles/publications/Primary%20Care/Prescriptions/hospre08/Hospital_prescribing_2008_report2.pdf

Cost (£000s)	Primary care	% growth primary	FP10HP *	% growth	Hospital	% growth hospital	Total	% growth total
Varenicline	**24,089.6**	**50.97**	**96.8**	**-24.3**	**23.4**	**99.4**	**24,209.7**	**50.4**

*FP10HP = prescriptions written in hospitals but dispensed in the community

The data shows that almost all prescribing for varenicline is carried out in a primary care setting.

2.1.2 Use of NICE appraised medicines in the NHS in England - Experimental Statistics, The Information Centre, 2009.

http://www.ic.nhs.uk/webfiles/publications/niceappmed/Use%20of%20NICE%20appraised%20medicines%20in%20the%20NHS%20in%20England.pdf

Overview

Varenicline is a selective nicotine receptor partial agonist used as an aid for smoking cessation.

• Varenicline is recommended within its licensed indications as an option for smokers who have expressed a desire to quit smoking.

• Varenicline should normally be prescribed only as part of a programme of behavioural support

Since the NICE guidance on varenicline was issued in July 2007, the EMEA and MHRA have also issued statements to prescribers to increase awareness of cases of suicidal ideation and suicide attempts reported in patients using this drug.

Expected Number of Eligible Patients

The following assumptions were used in the calculation of the expected number of eligible patients. The assumptions are taken from data on existing practice, research and the views of experts in the field used in the NICE

costing template (for further detail see: http://guidance.nice.org.uk/TA123/CostTemplate/xls/English).

Assumption and Evidence / Source

Assumption	Evidence / Source
Number of smokers setting a quit date by age band – actual rates provided, National average = 6.3% of smokers	Information interpolated from 'Statistics on NHS stop smoking services in England, April 2005 to March 2006' annual bulletin
Estimated number of smokers setting a quit date receiving pharmacological interventions = 65%	Current prescribing practice derived from 'Prescription cost analysis' 2006
Proportion prescribed varenicline = 16%	Varenicline Single Technology Appraisal submission 17th January 2007 - Pfizer UK Ltd

There is considerable regional variation in the rates of smokers and the reported proportion that attempt to quit. The warnings from the EMEA and MHRA may have made prescribers more cautious about the use of this drug and this is not taken into account by the estimates which are based only on evidence available at the time of the appraisal.

Observed uptake

Use of varenicline in hospitals is extremely low (less than £24,000 in 2008 compared with community spend of over £24 million) and so only community data has been used, taken from the two versions of ePACT. The starter pack contains both 500 mcg tablets (11 of them) and 1 mg tablets (14 of them). In order to convert this to daily doses we have regarded this as 14 days treatment following the BNF advice of 500 mcg for 3 days, 500 mcg twice daily for 4 days and 1 mg twice daily thereafter. For all other formulations we have used the WHO DDD of 2 mg although this may underestimate the number of days of treatment.

Note that this medicine may be supplied via Smoking Cessation Clinics and such use would not appear in our data.

Results

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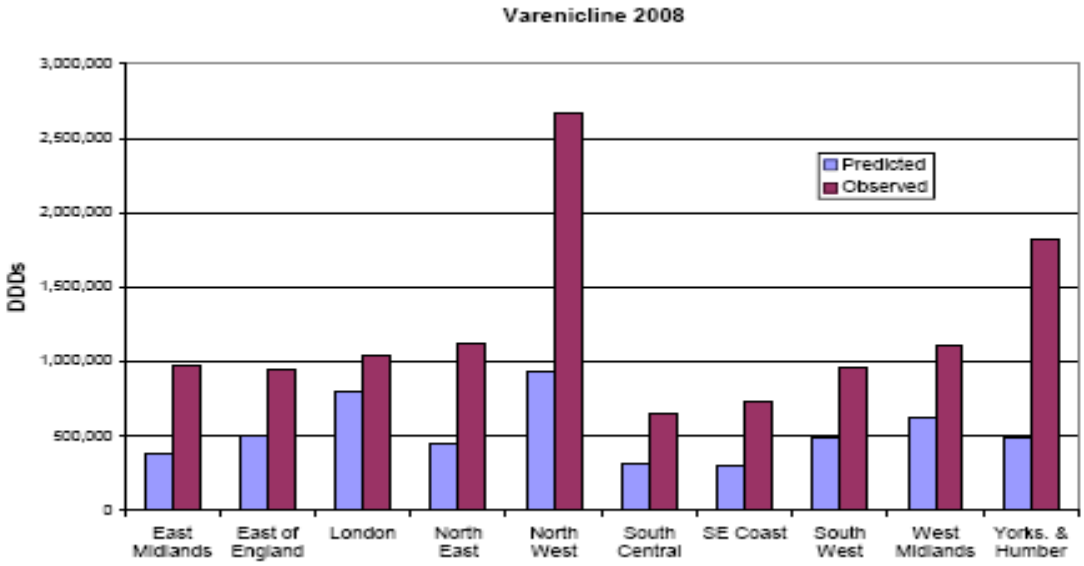
The NICE costing template expected an annual number of 62.4 thousand patients 2008. The BNF recommends a 12 week treatment course. This gives a predicted use of 5,245.2 thousand doses per year. The observed use in 2008 was 12,028.5 thousand defined daily doses, a ratio of 2.3 to 1.

The table below shows the data at SHA level.

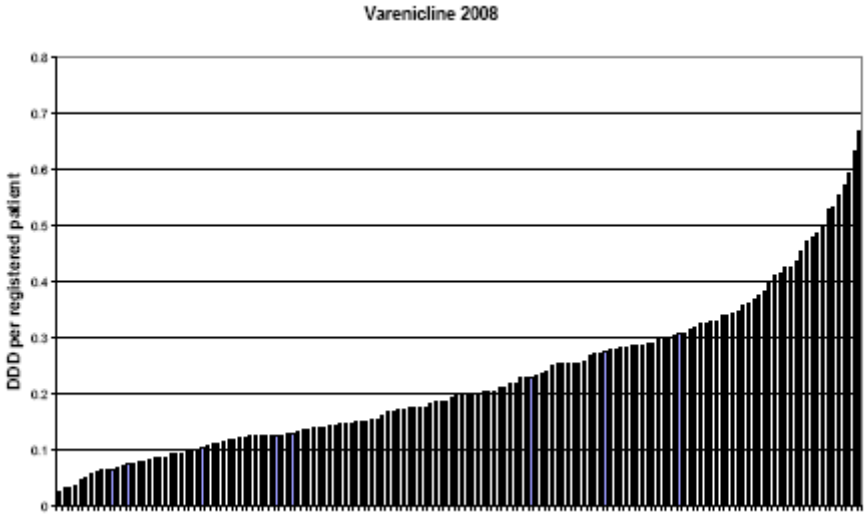
SHA	Expected eligible patients (from NICE) in thousands	Predicted DDDs in thousands	Observed DDDs in thousands	Ratio
East Midlands	5	381	970	2.5
East of England	6	502	947	1.9
London	10	800	1,041	1.3
North East	5	441	1,113	2.5
North West	11	927	2,663	2.9
South Central	4	314	651	2.1
South East Coast	3	292	729	2.5
South West	6	481	962	2.0
West Midlands	7	620	1,110	1.8
Yorkshire and the Humber	6	487	1,816	3.7

The chart below compares predicted and observed use, measured by DDDs, in 2008 by SHA.

Commercial in confidence information has been removed



The graph below shows the number of DDDs per registered patient by PCT for 2008. The data has been taken from the primary care ePACT system. Such use accounts for over 99% of use by cost.



The graph below shows the national (England) expenditure per quarter. Hospital use is very low, so has not been included.

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