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[Intervention Review]

# Nicobrevin for smoking cessation

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## ABSTRACT

### Background

Nicobrevin is a proprietary product marketed as an aid to smoking cessation. It contains quinine, menthyl valerate, camphor and eucalyptus oil.

### Objectives

The objective of this review was to assess the effects of Nicobrevin on long-term smoking cessation

### Search methods

We searched the Cochrane Tobacco Addiction Group trials register. Most recent search was January 2009.

### Selection criteria

Randomized trials comparing Nicobrevin to placebo or an alternative therapeutic control, which reported smoking cessation with at least six months follow up.

### Data collection and analysis

Data were sought on the outcome, method of randomisation, and completeness of follow up.

### Main results

We identified no trials meeting the full inclusion criteria including long-term follow-up.

### Authors' conclusions

There is no evidence available from long-term trials that Nicobrevin can aid smoking cessation.

## PLAIN LANGUAGE SUMMARY

### Does Nicobrevin help people to stop smoking

Nicobrevin is a proprietary product containing quinine, menthyl valerate, camphor and eucalyptus oil marketed as an aid to smoking cessation. No randomised trials with long-term follow-up of smoking status were identified, so there was no evidence to assess efficacy.

## BACKGROUND

A range of products are marketed to smokers trying to quit. There is good evidence that some products can increase the chance of a successful quit attempt, by reducing the urge to smoke or reducing the feelings of craving and withdrawal. Effective products include all forms of nicotine replacement therapy, and some antidepressant pharmacotherapies. Other products such as those containing silver acetate, or lobeline, have not been shown to be effective in high quality clinical trials. A large number of proprietary remedies are marketed to smokers even though they do not contain ingredients established to be effective. A list of such products, with detailed information on each, is maintained by the Campaign for Tobacco-Free Kids ([TobaccoFreeKids 2005](#)).

Nicobrevin is marketed as a smoking cessation aid in 11 countries including the UK, New Zealand and Germany. The formulation marketed in the UK contains four 'active' ingredients; quinine 15mg, menthyl valerate 100mg, camphor 10mg and eucalyptus oil 10mg ([Nicobrevin 2006](#)). The manufacturers claim that quinine may reduce craving, camphor and eucalyptus can relieve respiratory congestion and gastrointestinal disturbance and menthyl valerate has a sedative effect.

## OBJECTIVES

To assess the evidence for the effectiveness of Nicobrevin in assisting long-term smoking cessation.

The hypothesis tested was that Nicobrevin was more effective than placebo, or an alternative treatment, in achieving long-term smoking cessation.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

Randomized studies using a placebo or an alternative therapeutic control.

#### Types of participants

Smokers wishing to quit.

#### Types of interventions

Treatment with Nicobrevin (a 28-day course of tablets).

#### Types of outcome measures

Smoking cessation, assessed at follow up at least six months from the start of treatment, following the recommendations of the Russell Standard ([West 2005](#)).

### Search methods for identification of studies

We searched the Tobacco Addiction Review Group specialised register for trials, using the term 'Nicobrevin' in the title, abstract or keyword. This register has been developed from electronic searching of databases including MEDLINE, EMBASE, PsycINFO and Web of Science, together with handsearching of specialist journals, conference proceedings and reference lists of previous trials and overviews. We also made contact with the English Department of Health to obtain data submitted for the product licensing

of Nicobrevin in the UK. Our most recent electronic search for 'Nicobrevin' in title, abstract or keyword was January 2009.

## Data collection and analysis

Trials using a relevant intervention were identified by one author and checked by a second. For trials meeting the inclusion criteria the number of quitters at the longest follow up would be extracted. Quitting would be based on the strictest available criteria to define cessation, using sustained abstinence in preference to point prevalence if both were presented. In studies which used biochemical validation of cessation, only those subjects meeting the criteria for biochemically confirmed abstinence would be regarded as having stopped smoking. Participants in any group lost to follow-up would be regarded as being continuing smokers. Data would be extracted by one reviewer and checked by a second. In the event of there being more than one eligible trial, meta-analysis would be used to derive a typical odds ratio and its associated confidence intervals, using the Mantel-Haenszel method and a fixed-effect model.

## RESULTS

### Description of studies

We found no studies meeting all the inclusion criteria. Only two trials of Nicobrevin have been published and neither had long-term follow-up. One assessed patients at the end of four weeks treatment ([Dankwa 1988](#)) and the other after three months ([Schmidt 1974](#)).

### Risk of bias in included studies

Lack of long-term follow-up was a reason for exclusion of both known trials.

### Effects of interventions

Due to the lack of trials there is no evidence to support an effect of Nicobrevin on long-term cessation.

## DISCUSSION

There are many smoking cessation remedies available which have been not subjected to the same process of clinical testing as those pharmacological cessation aids for which effectiveness is well established. Nicobrevin includes active pharmaceutical ingredients, but none of these has been tested independently for an effect on smoking cessation and there is no strong rationale to believe that they have a specific effect on overcoming nicotine addiction. At best their respiratory and digestive system effects are most likely to relieve some of symptoms that smokers experience whilst abstaining from cigarettes. At the doses used they are unlikely to cause harm.

If trials with short-term outcomes had been included, both the identified trials would have had some methodological concerns. [Dankwa 1988](#) was unusual in that the smokers were not asked to try to quit, and numbers of cigarettes smoked on the last day of therapy was the primary outcome. Levels of blood carbon monoxide were measured, but not related to smoking status so could not be used to validate self reported quitting.

In the second study ([Schmidt 1974](#)) a variety of smoking cessation products were tested in a single trial. Participants received their

allocated therapy by post. The placebo group received a placebo matched to the characteristics of another active therapy rather than to Nicobrevin, and there was no validation of self reported quit rates.

It has been argued that requiring evidence of efficacy after long-term follow-up is unnecessary to assess whether a product is of benefit, since smoking is a chronic condition and repeated quit attempts are generally needed. However since the benefits of quitting are only likely to come from sustained cessation, products that have not been shown to increase long-term quit rates cannot be recommended. It is possible that relapse rates may be relatively higher in actively treated groups after the end of treatment, so that the net benefit of treatment is eroded.

The UK product licence for Nicobrevin was withdrawn in 2011 ([MHRA 2011](#)). No new research has been identified since [Dankwa 1988](#), therefore we do not plan to continue updating this review.

## **AUTHORS' CONCLUSIONS**

### **Implications for practice**

We found insufficient clinical evidence for the effectiveness of Nicobrevin as an aid to sustained smoking cessation.

### **Implications for research**

Well designed randomised controlled trials with long-term follow-up could test the effectiveness of Nicobrevin as a non-nicotinic aid to smoking cessation.

## **ACKNOWLEDGEMENTS**

We thank Matt Barry and Adrian White for reading and commenting on earlier drafts of this review.

## REFERENCES

### References to studies excluded from this review

#### Dankwa 1988 {published data only}

Dankwa E, Perry L, Perkins A. A double-blind, placebo-controlled study to determine the efficacy of Nicobrevin anti-smoking capsules. *British Journal of Clinical Practice* 1988;**42**(9):359-63.

#### Schmidt 1974 {published data only}

Schmidt F. Medical support of nicotine withdrawal. report on a double blind trial in over 5000 smokers [Medikamentöse unterstützung der raucherentwöhnung: bericht über versuche an über 5000 rauchern im doppelblindversuch]. *München Med Wochenschr* 1974;**116**(11):557-64.

### Additional references

#### Nicobrevin 2006

Nicobrevin/home page. <http://www.nicobrevin.com> (accessed 2/2/2006) 2006.

#### TobaccoFreeKids 2005

Campaign for Tobacco-Free Kids. QuiTIP - Other Cessation products. <https://secure.tobaccofreekids.org/Cessation/ListOther.asp> (accessed 7/2/2006) 2005.

#### West 2005

West R, Hajek P, Stead L, Stapleton J. Outcome criteria in smoking cessation trials: proposal for a common standard. *Addiction* 2005;**100**:299-303.

## CHARACTERISTICS OF STUDIES

### Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
<a href="#">Dankwa 1988</a>	Only four weeks follow-up, and abstinence was not the primary outcome.
<a href="#">Schmidt 1974</a>	Only three months follow-up, with placebo matched to a different active therapy.

## WHAT'S NEW

Date	Event	Description
31 January 2013	Review declared as stable	Review has no included studies, and no research identified since 1988; product licence withdrawn from UK in 2011.
31 January 2013	Amended	Information regarding UK withdrawal added.

## HISTORY

Protocol first published: Issue 2, 2006

Review first published: Issue 2, 2006

Date	Event	Description
8 January 2009	New search has been performed	No new trials found
28 October 2008	Amended	Converted to new review format.

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## CONTRIBUTIONS OF AUTHORS

Both authors contributed equally to the suggestion for the review, to the data extraction and evaluation of the studies, and to the discussion and conclusions. Lindsay Stead performed the electronic and handsearching for trials.

## DECLARATIONS OF INTEREST

None known

## SOURCES OF SUPPORT

### Internal sources

- Department of Primary Health Care, Oxford University, UK.
- National School for Health Research School for Primary Care Research, UK.

### External sources

- NHS Research and Development Programme, UK.

## INDEX TERMS

### Medical Subject Headings (MeSH)

\*Smoking Cessation; \*Smoking Prevention; Pentanoic Acids [\*therapeutic use]; Quinine [\*therapeutic use]; Terpenes [\*therapeutic use]

### MeSH check words

Humans