NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Nalmefene for reducing alcohol consumption in people with alcohol dependence

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: Dr Chris Daly

Name of your organisation Greater Manchester West Mental Health FT

Are you (tick all that apply):

- ✓ a specialist in the treatment of people with the condition for which NICE is considering this technology?

  a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?

- ✓ an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)?

  other? (please specify)

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?

Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

Alcohol dependence treatment varies widely across the UK in terms of service provision and treatments delivered. Broadly alcohol dependence is treated in Primary and Secondary care with both generalist and specialist staff involvement depending on severity of dependence and inherent complexity. The treatment approaches include a variety of psycho-social interventions and psychopharmacological approaches. There are differences in opinion between professionals as to treatment. The NICE clinical guideline 115 has comprehensively reviewed the evidence base for treatment in Alcohol dependence.
Nalmefene offers a novel psychopharmacological approach to treatment of alcohol dependence in that it is used to support a goal of controlled drinking rather than abstinence which the other pharmacological interventions are identified as adjuncts for. Therefore the treatment paradigm and outcomes from the treatment are different from the outset the primary goal of treatment with nalmefene being reduction in drinking level from hazardous or harmful. As with other pharmacological interventions in this field nalmefene should only be considered in treatment alongside psychosocial interventions.
The sub-groups identified from research evaluation for use of nalmefene are also different. The patient should have a goal of controlled drinking, have mild alcohol dependence, high drinking risk level but not have physical withdrawal symptoms. It is not suitable for those who require immediate detoxification.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

The medication is not suitable for individuals taking opiod based analgesia, those dependent on opiods, those with previous history of severe alcohol withdrawals or those with significant liver/ renal impairment.
The drug could be used in either primary or secondary care significant proprtions of patients identified with mild dependence will be managed in primary care and therefore the use in this area must be considered. The provision of additional PSI is essential in the successful use of this technology.
The technology is available and licensed for use in the UK the use across the country varies. I am aware that the technology has been appraised in Scotland and Wales and the use there is more common place than elsewhere in the UK
Please see
Scottish Medicines Consortium and All Wales Medicines Strategy Group links below
These include relevant clinical guidelines for the use of the technology

http://www.scottishmedicines.org.uk/files/briefing-notes/2013/BN_October_2013.pdf

http://www.awmsg.org/

The evidence base is to be found as follows:

1. Mann K, Bladstrom A. Extending the treatment options in alcohol dependence: a randomised controlled study of as-needed nalmefene. Biol Psychiatry 2012;epub:[1-0737]. 4
2. Gual A, He Y. A randomised, double-blind, placebo-controlled, efficacy study of nalmefene, as-needed use, in patients with alcohol dependence. European Neuropsychopharmacology 2013;epub:[1-0797]. 5
3. van den Brink W, Aubin H-J, Bladstrom A. Efficacy of as-needed nalmefene in alcohol-dependent patients with at least a high drinking risk level: results from a subgroup analysis of two randomized controlled 6-month studies. Alcohol and Alcoholism 2013;48 (5):570-578 [1-0909]. 6
4. Sinclair J, Chick J, Sorensen P, Gual A. As-needed use of nalmefene in the treatment of alcohol dependence: subgroup analysis of patients with high drinking risk level. Poster presented at 26th ECNP Congress, Barcelona, Spain, 5-9 October 2013 2013;[1-0957].7
5. Nutt David, Sorensen P, Torup L. Clinical relevance of nalmefene in the treatment of alcohol dependence: subgroup analysis of patients with high drinking risk level. Poster presented at 26th ECNP Congress, Barcelona, Spain, 5-9 October 2013 2013; [1-0956].8
6. van den Brink W, Sorensen P. Long-term efficacy, tolerability, and safety of nalmefene as needed in alcohol dependence: a randomised, double-blind, placebo-controlled study. Poster presented at 35th RSA Scientific Meeting 2012; San Francisco, USA June 23-27:[1-0599].10

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

No direct current alternatives in terms of pharmacological agents used to support controlled drinking goals. However will be interesting to evaluate against naltrexone and its observed benefits in patients at high risk of lapsing to drinking and compare whether there are additional benefits to using nalmefene or naltrexone in these individuals

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

There may be issues in terms of its use as required when the patient perceives they are at risk of drinking. Explaining this to the patient will need to be considered and also the appropriate PSI intervention to use alongside nalmefene.
In the original trials patients required assessment as follows
1 Diagnosis of alcohol dependence of mild severity (SADQ or alternative)
2 Alcohol intake assessment > 6 heavy drinking days in preceeding 28 days using a drinking diary
3 Liver Function Test (ALT/ AST < 3x upper limit of normal),
4 Assessment of Alcohol Withdrawal severity (using CIWA-Ar) <10 i.e less than moderate alcohol withdrawals
5 Breathylzer Alcohol reading < 0.02%
6 Exclusion of use of concomitant medications that could interact especially opiate agonist/ partial agonists

There is a requirement for ongoing assessment of Liver Function Test

Limited UK experience with no direct clinical experience of its use so far. The clinical trials excluded a number of individuals for whom this medication may be considered in routine clinical practice and the level of assessment and intervention may vary considerably from the trial conditions. The practical use of nalmefene in routine clinical practice must be considered

The outcome measures used in the trials followed internationally accepted standards in terms of Heavy Days Drinking and Total Alcohol Consumed and have clinical applicability. The change in these over placebo will need to be considered in relation to whether this difference is clinically relevant. Data is available for 6 and 12 month outcomes longer term data is not available to my knowledge

Side effects more commonly associated with nalmefene over placebo were nausea, dizziness, insomnia, hyperhidrosis mostly these were of mild to moderate severity.
I am unaware of any further adverse reactions reported in clinical practice

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Equality and Diversity

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that this appraisal:

- Could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed;
- Could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- Could lead to recommendations that have any adverse impact on people with a particular disability or disabilities

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts

There may be issues of consent in certain populations in terms of cognitive decline and learning disability. Issues relating to reading and writing in terms of receiving information must be considered

Any additional sources of evidence

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Implementation issues

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

I am not aware of any supply issues for nalmefene this this currently available and stocked
There will be training requirements for generalist and specialist staff and consideration by the various bodies responsible for medicines management I would envisage that this could be in place within the required timescales for implementation
Additional resources in terms of the cost of the nalmefene need to be considered
It may be that initially the medication will need to be started in specialist prescribing clinics with associated cost implications