Comments on the ACD Received from the Public through the NICE Website

Name	[redacted]
Organisation	NHS Nene CCG
Role	NHS Professional
Job Title	[redacted]
Location	England
Conflict	No
Comments on the ACD:	
The first comment relates to the need for "continuous psychosocial support focused on treatment adherence and reducing alcohol consumption", which is part of the marketing authorisation. In practice this may be difficult to achieve and this may depend on whether the drug is intened to be used in a primary care (GP) setting or is intended to be prescribed in a specialist setting, where psychosocial support may be more readily available. It is difficult to see therefore how the drug could be used in a GP setting. It would be useful if NICE is able to comment and provide a steer on this within the TA. The second comment relates to commissioning responsibility for alcohol services. This now sits with Local Authorities / Public Health, rather than with CCGs, so presumably this should also be made clear within the TA. The 3 month timescale for implementation might need to be extended if commissioners have to develop psychosocial support services - if these are not already provided.	
Date	11/07/2014

Name	[redacted]
Organisation	
Role	NHS Professional
Job Title	[redacted]
Location	England
Conflict	No
Comments on the ACD:	
The document does not comment on the lack of testing of the integrity of the double-blind in the 2 studies by Mann et al and by Gual et al. This is critical, because the treatment response in both studies was small in comparison to the size of the placebo response, and the difference could be due to assessor or participant bias, for which there is huge potential given that retrospective accounts of drinking are the basis of the main outcome measures, and such bias could have been possible through guessing who was on nalmefene, perhaps through presence of side effects. That both studies seem to have been sponsored by Lundbeck should add to this concern. The document seems to accept the Lundbeck version of nalmefene's mode of action in reducing drinking. I would be interested to know if participants most affected by nausea drank less. Is it actually an aversive agent? If it works by reducing reward, is this not a pharmacologically induced equivalent to tolerance and isn't tolerance often cited as reason for escalation, not for reduction.	

As an opioid receptor antagonist, nalmefene cannot be expected to have effects specific to drinking behaviour. If it impacts on drinking, it impacts on all rewarding behaviour and thereby, may have very pervasive negative effects in areas such as exercise, hobbies and interests, and, of course, relationships, generally, and sex, perhaps especially.

The document fails to address the psychology of taking a tablet to reduce drinking. In the real world, as opposed to trials, would some people on nalmefene be less interested in psychosocial interventions, purely because they had their tablet to take? Would some people, for anticipating having a drink and taking a tablet, then feel it must be a drinking day because I've taken my tablet, i.e. the tablet could actually increase the probability of some alcohol being consumed. In this respect it is noteworthy that nalmefene per se, is not being promoted as causing more alcohol free days. Could some people think that for not having yet taken a tablet, today must be a binge? These possibilities are based on sound principles of conditioning and expectation.

The document fails to adequately emphasise the high drop out rates in the 2 main studies of nalmefene. I doubt that prescribed nalmefene will be taken at all regularly by most who receive it and in primary care, a psychosocial element to treatment will be offered rarely, and taken up, at best, only as it would have in the absence of the medication. The potential for widespread implementation of psychosocial treatments to reduce alcohol related harm is huge, but it isn't going to happen because of nalmefene.

Given that subgroup analysis of study participants who continued to drink at high risk level, not just medium risk level, produced the more favourable results for nalmefene; why not advocate it for people drinking at very high risk level; especially if they have already had detoxifications and returned to such heavy drinking? The history of 'alcoholism' as a useful cultural concept and the consequent controversies over 'controlled' drinking explain why Lundbeck steered clear of these drinkers. Clearly, the potential for reduction from huge levels of consumption is also huge. After 40 years of having nalmefene, and after who knows how many trial flops (how many of these on drinkers?), Lundbeck has concocted a commercial use for nalmefene.

Date	17/07/2014

Name	[redacted]
Organisation	Turning Point
Role	Healthcare other
Job Title	[redacted]
Location	England
Conflict	No

Comments on the ACD:

Turning Point is a leading health and social care organisation working in over 200 locations across England and Wales. We have been operating for 50 years, providing specialist and integrated services that meet the needs of individuals, families and communities. We are a social enterprise reinvesting its surplus to provide the best services in the right locations for those that need them most across mental health, learning disability, substance misuse, the criminal justice, primary care and employment.

Turning Point welcomes the opportunity to feed in to this consultation on the use of Nalmafene for reducing alcohol consumption in people with alcohol dependence.

Feedback to the consultation questions has been gathered by Turning Point's Clinical Management team and responses are set out below.

The key points from our response are:

ï‚§ Not all evidence related to the use of Naltrexene has been taken into account.

ï‚§ There are issues related to the level of complexity of psychosocial interventions needed in the client group for which Nalmefene has the marketing authorisation

ï‚§ There are no issues related to discrimination against certain groups.

ï‚§ We do not foresee issues with ability to offer Nalmefene within the normal three month timescale after NICE recommendation.

Question 1: Has all of the relevant evidence been taken into account?

We have identified that there is relevant evidence that has not been taken into account. The first is that there has been a lack of economic comparison with the medication Naltrexone. The second aspect of evidence that is lacking is related to recovery capital and the complexity of the psychosocial interventions required for the client group for which Nalmefene has marketing authorisation.

The Committee identified that Naltrexene plus psychosocial intervention was not an appropriate comparator to Nalmafene as it was not part of the established treatment for the reduction of alcohol consumption. We believe that there is a need for economic modelling of Naltrexene and a comparison to Nalmafene. The reasons for this are identified below:

ï‚§ Regarding the issue of Naltrexene not being an established treatment in England (para 4.6), it is important to understand that the reason why services typically have difficulty providing this level of treatment• (para 4.1) is because services for non-dependent drinkers are not currently funded by the NHS such clients are signposted by the NHS to non-statutory and voluntary, community and social enterprise (VCSE) sector services for brief interventions only. This is despite evidence that this group benefit from reduced alcohol consumption as reducing high risk drinking reduces the morbidity of numerous physical diseases.

ï‚§ We believe that Naltrexone is suitable to be used in comparison to Nalmafene. The unlicensed use of Naltrexone for alcohol should be compared in an economic analysis to the licensed use of Nalmefene. Naltrexone in dependent drinkers has a large evidence base, and paragraph 3.12 refers to three Randomised Control Trials (RCTs) of Naltrexone in alcohol dependence. There are also three studies of Naltrexone used on an as needed basis similar to that for Nalmefene, although these studies were not RCTs.

ï‚§ The document quotes NICE clinical guideline 115 that oral Naltrexone does not have UK marketing authorisation for this indication (for alcohol) (paragraphs 4.1 and 4.6). In fact there was a generic oral Naltrexone which did have a marketing authorisation for alcohol post-detox licensed in the UK in March 2010 by Accord Healthcare (PL 20075/0144), which incidentally was prior to CG115 being issued in

Feb 2011.

ï‚§ Some services nationally have been using Naltrexone to assist in the treatment of non-dependent drinkers. However specific funding for pharmacological interventions in those not having structured psychosocial interventions is not recognised either by the Commissioners of NHS services or by Public Health England. This is a problem for services, which therefore have to fund such Tier 2 medication interventions as added value in order to improve outcomes in this group. Commissioners have only recently identified that this non-dependent group as requiring psychosocial interventions, and have not as yet recognised that some of this group also may benefit from medication interventions such as Nalmefene or Naltrexone.

ï‚§ Because Naltrexone and Nalmefene are so pharmacological similar, we disagree with the statement that Naltrexone would be used in practice to treat a different patient group than those included in the Nalmefene trials, with abstinence as the treatment goal. Due to funding issues within services, providers may choose to make use of medication outside of their license, based on the costing of the medication.

Question 1: Has all of the relevant evidence been taken into account?

The second aspect of evidence that we believe is lacking is related to recovery capital and the complexity of psychosocial interventions required. There are a number of points related to this highlighted below:

ï‚§ Non-dependent drinkers typically have high recovery capital: Nalmefene is targeted at high risk drinkers, rather than dependent drinkers. This subgroup of drinkers have both less severe problems and a higher level of recovery capital (personal, social and community assets) than clients with alcohol dependence - who may have much lower levels of recovery capital and who may require treatment with medical and psychological interventions by addiction services. The reason that this is significant is because it helps determine the level of psychosocial intervention required. A high level of psychosocial intervention is typically required for more dependent drinkers or those with a lower level of recovery capital, whereas only a relatively low level of psychosocial intervention is required for non-dependent drinkers and those with a high level of recovery capital. The recovery research suggests that brief interventions or self-help interventions may be all that is required for those with high recovery capital. Hence low level support would be typical of physical health medications, such as periodic assessment of compliance, side-effects and efficacy may be all that is required. Computerised CBT as with www.reduceyourdrinking.com (12 sessions) and Breaking Free Online are likely to be sufficient for the majority of patients. The requirement for continuous psychosocial support focussed on treatment adherence and reducing alcohol consumption would I think be met by this, although it would be helpful to clarify this in the guidance.

ï‚§ Amber vs Green traffic lighting where high recovery capital and no dependence means only a low level of psychosocial support is required: This means that the situation is very different from the current situation with Naltrexone, Acamprosate and Disulfiram, which are used in alcohol dependence and rated as amber drugs drugs that should be started by specialists (or specialist generalists),

but which may be continued by any doctor including the GP. The reason these drugs are rated amber is because of the need for significant psychosocial support, because of the presence of the dependency syndrome. Now the situation with Nalmefene is quite different because the population is quite different. Nalmefene only requires a low level of psychosocial support for its licenced indication, and can be taken as needed in this patient population, and therefore can be rated green i.e. it can be initiated by any doctor including GPs.

ï‚§ BRENDA as a complex psychosocial intervention for use in primary care: Although BRENDA was used in the industry funded studies, which is a fairly intensive intervention to use in primary care, Nalmefene does not appear to require this level of intervention from the clinical point of view as explained above. Indeed such an intervention is likely to have reduced rather than increased the apparent medication effect of the nalmefene. Although the industry funded evidence base is only generalisable if BRENDA is used, BRENDA is highly likely to be unnecessary overkill for use in the NHS in general.

Question 2: Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

YES, but what is missing is a cost-effectiveness comparison with Naltrexone, and consideration of the non-licensed use of Naltrexone.

Question 3: Are the provisional recommendations sound and a suitable basis for guidance to the NHS?

YES, but need to take account of the issues about Naltrexone above. In a cost conscious NHS, we would tend to use a product outside its licensed indication first line if it is considerably cheaper, and use the more expensive product second line.

Question 4: Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

NO

Question 5: Given the requirement for relevant health bodies (clinical commissioning groups, NHS England and local authorities) to provide funding to ensure that the health technology is available within 3 months, from the date the recommendation is published by NICE (see section 5.1), is an extension to this normal period appropriate because any of the following circumstances apply:

5.1: The health technology cannot be appropriately administered until training is in place?

ï‚§ NO, as minimal training is required for prescribers and psychosocial interventions

5.2: The health technology cannot be appropriately administered until certain health service infrastructure requirements including goods, materials or other facilities are in place?

ï‚§ NO, as urine screening tests for opioids are available in primary care (for morphine, methadone and buprenorphine, but not tramadol typically)

5.3: The health technology cannot be appropriately administered until other appropriate health services resources, including staff, are in place?

ï‚§ NO, as no special resources or staff are required. There is already computerised CBT available specifically for alcohol (Reduce Your Drinking), and for drugs and alcohol in general (Breaking Free Online). Both require access codes, but the first is free and done by the manufacturer of Nalmefene, and the second is paid for but is increasingly being paid for by commissioners. Both are good quality CBT packages, and neither recommends specific drugs.

Conclusion

In summary we agree with the Committees conclusion that Nalmefene plus psychosocial intervention is an important addition to the treatment pathway. However we would suggest that there is a cost-effectiveness comparison with Naltrexone for potential use with the same client group. A low complexity psychosocial intervention is all that is needed in this treatment group with high recovery capital and non-dependent drinking. We do not foresee any issues related to discrimination against certain groups or that there would be issues related to offering Nalmafene within the normal three month period.

Date	29/07/2014

Name	[redacted]
Organisation	British Association for Counselling and Psychotherapy (BACP)
Role	Professional body
Job Title	[redacted]
Location	England
Conflict	No
Declaration	The British Association for Counselling & Psychotherapy (BACP) is recognised by legislators, national and international organisations and the public, as the leading professional body and the voice of counselling and psychotherapy in the United Kingdom, with over 40,000 members working to the highest professional standards in a wide range of settings, including the NHS.
Comments on the ACD:	

The introduction to the consultation document refers to the requirement for health bodies to provide funding to ensure that the health technology is available within three months of the date the recommendation is published by NICE.

However the Appraisal Committees first preliminary recommendation is that Nalmefene is recommended within its marketing authorisation as an option for reducing alcohol consumption.

We would be grateful for clarification of how these two statements interact, i.e. is it intended that Nalmefene would be merely an option, rather than a requirement, for clinicians treating patients in the target group, but that local health authorities would be required to make the technology available to clinicians?

The consultation document quotes the technology's marketing authorisation that:

Nalmefene should only be prescribed in conjunction with continuous psychosocial support focussed on treatment adherence and reducing alcohol consumption.•

The consultation document incorrectly states that NICE clinical guideline 115 recommends that psychosocial interventions be delivered by a clinical psychologist. There is in fact no such reference in the guidance, which states (Introduction, p9) rather that:

All interventions for people who misuse alcohol should be delivered by appropriately trained and competent staff.

Many thousands of counsellors and psychotherapists work in the NHS. They should be considered trained and competent to deliver psychosocial support for alcohol misuse, with brief top-up training where necessary in the specific interventions, if they meet the Department of Health's required standards for psychological therapists, namely:

To have completed one-year of recognised full-time (or equivalent part-time) psychological therapy or counselling training leading to a qualification, certification or accreditation recognised by a relevant professional or regulatory body; to have achieved a competency level that fulfils the requirements of the regulatory, accrediting or professional body; to be a member of a relevant professional or regulatory body, and continue to fulfil any accreditation or membership criteria, including meeting requirements for continuing professional and personal development, regular supervision and codes of practice; and to have gained the supervised therapy experience required by the regulatory or professional body encompassing assessment, formulation, engagement, developing the therapeutic relationship, using relevant therapeutic interventions, working collaboratively with clients, and working to end therapy.

BACP is the largest professional body for counsellors and psychotherapists in the UK, with over 40,000 members, including many thousands in the NHS, and is among the professional bodies recognised by the Department of Health in relation to the above standards, which all BACP Registered Members and BACP Accredited Members meet.

The psychosocial interventions in guideline 115 do not therefore necessarily require delivery by a clinical psychologist, and we are concerned that the propagation of this misunderstanding to clinicians could exacerbate current difficulties in delivering

psychosocial support, leading to worse outcomes for patients. We are also concerned at the prospect that recommendations arising from this technology appraisal could be worded to require delivery of psychosocial support by clinical psychologists, rather than by any trained and competent psychological therapist meeting the Department of Health's definition. The consultation document makes several references to NICE clinical guideline 115, the current guidance on alcohol-use disorders available to clinicians. We would be grateful for clarification on how the recommendations arising from the technology appraisal of Nalmefene interact with this guidance, specifically whether NICE clinical guideline 115 will be automatically updated as a result, and if not, how clinicians would be advised to treat patients presenting with relevant alcohol-use disorders following publication of the new recommendations.	
Date	29/07/2014