How Pharmacists Can Help Patients Reduce Their Alcohol Intake: A Guide To New And Existing Treatments

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Summary
This paper indicates that:
● alcohol is an important topic, responsible for a substantial proportion of admissions worldwide
● addiction is a complex condition requiring input from multiple healthcare professionals to ensure the best outcome for patients
● pharmacists can contribute to the treatment of alcohol addiction since there are various pharmacological treatments shown to effectively supplement psychological treatment
● new treatments are emerging which can hopefully engage a wider patient group.

Introduction
Alcohol misuse is a global problem with almost 4% of all deaths worldwide attributed to alcohol. A figure greater than that of deaths caused by HIV/AIDS, violence or tuberculosis.1

In the UK, the Department of Health estimates that 7% of all hospital admissions are alcohol related, with alcohol misuse costing approximately £2.7 billion annually for an already overburdened NHS.2 Such figures highlight the magnitude of alcohol misuse as a public health issue and the importance of prevention and treatment for patients who are alcohol dependent.

As well as social and economic implications, individual harm from alcohol misuse can manifest both acutely and chronically. Acute events include alcohol-related accidents and injuries as well as acute alcohol withdrawal seizures and delirium tremens, which can be fatal.3,4 Moreover, alcohol consumption can be a contributory factor for the development of chronic conditions including hypertension, stroke, pancreatitis and depression as well as certain types of cancer; notably liver, mouth, oesophageal, bowel and colorectal.3 Moreover, the death rate from liver cirrhosis has quadrupled in the UK over the past 40 years - UK alcohol consumption doubled in that same period.5

The National Institute for Health and Care Excellence (NICE) categorises alcohol dependence as craving, tolerance and continued drinking despite harmful consequences. The Alcohol Use Disorders Identification Test (AUDIT) is a screening tool used to identify early signs of harmful drinking and mild dependence.6 A more detailed interpretation of the severity of alcohol dependence can be achieved using the Severity of Alcohol Dependence Questionnaire (SADQ) score.6 This self-administered 20-item questionnaire was designed by the World Health Organisation and questions users about their drinking habits and the associated consequences. A score of 15-30 indicates moderate dependence and scores of 31 or more are suggestive of severe dependence.4

Strategies recommended to promote abstinence and prevent relapse are intensive and structured systems which encompass appropriate psychological and pharmacological interventions. Psychological interventions include cognitive behavioural therapies and counselling sessions, which target alcohol-related perceptions, individual behaviour and social networks.6 Guidance issued to those wishing to treat alcohol dependence with pharmacological treatment, including that from NICE, advises that psychological treatment be provided concurrently to maximise successful outcomes. Substance dependence and addiction are complex issues and users need to be supported in both the physical addiction as well as addressing the social/psychological pressures.

It has been shown that interventions tend to have a greater impact on those who are classed as severe drinkers.7 However, until recently with the introduction of nalmefene, there has been a lack of pharmacological treatment aimed at those with moderate dependence and who may not have achieved abstinence.

“Substance dependence and addiction are complex issues and users need to be supported in both the physical addiction as well as addressing the social/psychological pressures.”
Current Pharmacological Interventions

Alcohol, as with most dependence-producing drugs, activates the ‘reward’ pathway (i.e. the mesolimbic dopaminergic pathway) and subsequently increases dopamine levels in the brain. This pathway mediates the positive reinforcement or rewarding effects of alcohol. In this way, pharmacological therapies aimed at alcohol dependency tend to act on the central nervous system to alter this activated reward pathway.\(^8\)

In the UK, acamprosate and naltrexone are available pharmacological treatments which, combined with counselling, aim to prevent relapses of alcohol consumption once abstinence has been achieved; usually in patients with severe alcohol dependence.\(^9\)

Acamprosate is a weak agonist at N-methyl-D-aspartate (NMDA) receptors and has been shown to effectively maintain abstinence.\(^9\) It has a chemical structure similar to gamma-aminobutyric acid (GABA), the major inhibitory neurotransmitter in the brain.\(^10\) Treatment with acamprosate is initiated as soon as possible following alcohol withdrawal and achievement of abstinence. The dosage is dependent on the patient’s weight.\(^8\)

The opioid receptor antagonist naltrexone proved effective in studies when the outcome was to reduce alcohol consumption.\(^11\) As with acamprosate, treatment with naltrexone follows successful withdrawal and achievement of abstinence. While naltrexone can be effective for some patients, there are various associated limitations. Throughout treatment, patients must avoid the use of opioid analgesia since it blocks opioid receptor agonists.\(^8\) Furthermore, naltrexone can be hepatotoxic and, as such, severe or acute liver impairment is a contraindication;\(^12\) consequently discounting patients with alcohol liver disease.

Studies have shown that both acamprosate and naltrexone are effective therapies for the treatment of alcohol dependence.\(^11\) Interestingly, a study which examined a combination of naltrexone and acamprosate failed to find any advantages of dual therapy over mono-drug therapy.\(^13\)

Disulfiram is an alternative treatment but should only be used where acamprosate and naltrexone are unsuitable. While acamprosate and naltrexone are generally well tolerated in those who continue to misuse alcohol, disulfiram is associated with potentially severe adverse events in individuals who continue to drink.\(^14\)

Used as an aversion therapy, disulfiram inhibits the breakdown of acetaldehyde (a metabolite of ethanol) which precipitates a severe reaction including flushing, tachycardia, hyperventilation and considerable distress following alcohol consumption.\(^8\) The treatment can encroach on patients’ everyday activities since they should be cautious of perfume or aerosols containing alcohol as well as certain mouthwashes and medicines which contain alcohol. Treatment should be started at least 24 hours after consuming the last alcoholic drink at a typical dose of 200mg daily, which is up-titrated to a dose which causes an unpleasant reaction to alcohol (maximum 500mg daily).\(^9\)

Some studies have shown 5-HT 3 receptor antagonist, ondansetron, to be efficacious in the treatment of early onset alcohol dependency by reducing the craving for alcohol.\(^15\) It is postulated that early stage alcohol misuse is associated with a greater serotonergic abnormality than that of chronic alcohol misuse.\(^14\) Ondansetron inhibits serotonin action on 5-HT 3 receptors, which decreases alcohol-induced dopamine release and, therefore, alters the reward pathway associated with alcohol misuse.

When combined with psychosocial treatment in the form of counselling, the pharmacological interventions described above can be effective for reducing alcohol misuse and maintaining abstinence. Nonetheless, the limitations of current pharmacological therapies include the requirement to achieve abstinence prior to treatment and poor compliance. Factors contributing to poor compliance include the associated side effects (particularly with disulfiram) as well as disengagement with the addiction treatment due to the stigma associated with addiction. In light of these issues, pharmacists are appropriately placed within the community and in hospitals or
clinics to engage with such patients and empower them to partake with their treatment. By initiating such discussions, either upon initiation or while dispensing a repeat prescription, pharmacists can open the dialog for patients to discuss their treatment freely in a supportive and confidential environment.

**Nalmefene**

Until recently, (with the exception of ondansetron, which is unlicensed) the pharmacological treatments available for alcohol dependence targeted those with severe alcohol dependency. However, in November 2014, the NICE Technology Appraisal (TA325) of nalmefene brought new scope to the treatment of alcohol misuse. Clinicians are able to consider treating alcohol dependency before it reaches the severe stages and before abstinence has been established.

Nalmefene differs from other pharmacological treatments since it is aimed at those with moderate alcohol dependency who do not require immediate detoxification. Suitability of the drug is established after an initial assessment where the patient reports their level of alcohol dependence and alcohol consumption. The patient must then record his/her own alcohol consumption for approximately two weeks from the initial visit. If they have a high level of alcohol consumption within the two week period (>7.5 units/day for men and >5 units/day for women), then nalmefene treatment can be started.

Patients are encouraged to take nalmefene if they anticipate a risk of alcohol consumption, ideally 1-2 hours before alcohol intake. However, if the patient has already started drinking, nalmefene should be taken as soon as possible. Concurrent intake of alcohol and nalmefene does not prevent its intoxicating effects. The ‘when required’ dosing schedule may be more user-friendly to integrate with patients’ lives without the need to remember to take a daily treatment.

Similar to naltrexone, nalmefene has affinity at opioid receptors; notably antagonist action at \(\mu\) and \(\delta\) receptors and partial agonist action at \(\kappa\) receptors. It has a longer duration of action compared to naltrexone due to its slower dissociation from the opioid receptors and is less hepatotoxic.

**Evidence**

In the ESENSE1 and ESENSE2 studies evaluated by NICE in the Technology Appraisal [TA325], nalmefene was found to effectively reduce total alcohol consumption and the number of heavy drinking days when compared to placebo after 6 months of treatment. Furthermore, improvements in liver function, notably \(\gamma\)-glutamyltransferase (GGT) and ALAT, were also noted.

Psychosocial support was provided in both treatment and placebo arms of the studies in the form of BRENDA, which resembles the current psychosocial support available in the UK. The BRENDA approach is valuable to use in conjunction with pharmacological interventions since it has the general aim of enhancing medication and treatment compliance. BRENDA consists of the six components shown in Box 1. Although the components are undertaken by trained professionals, pharmacists can also contribute to the provision of BRENDA. Through treatment counselling upon initiation of medication and through MURs within community, pharmacy staff often establish if the treatment adequately addresses the patient’s needs, direct advice regarding the management of potential side-effects can be given and an assessment can be made regarding the success of the treatment upon follow-up. Upon initiation of medication for substance dependence (or any critical medication) it is important to recognise the need for adequate communication between pharmacists and patients to discuss their treatment freely in a supportive and confidential environment.

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**Box 1: Components of BRENDA**

<table>
<thead>
<tr>
<th>Biopsychosocial evaluation, whereby a series of questions</th>
<th>Report of findings; evaluation and feedback given to the patient throughout treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>establish the individual’s physical, psychological and social issues upon initiation of treatment</td>
<td>empathy; patients’ treated in an open, non-judgemental environment</td>
</tr>
<tr>
<td>report of findings; evaluation and feedback given to the patient throughout treatment</td>
<td>Needs of the patient are addressed</td>
</tr>
<tr>
<td>Empathy; patients’ treated in an open, non-judgemental environment</td>
<td>direct advice is given</td>
</tr>
<tr>
<td>Needs of the patient are addressed</td>
<td>Assessment of the patient throughout treatment</td>
</tr>
</tbody>
</table>

Do not hallucinate.
primary and secondary care providers in order for complex patients to be adequately followed up and reviewed.

NICE concluded that nalmefene plus BRENDA reduced the number of heavy drinking days and total alcohol consumption compared with BRENDA alone.\textsuperscript{24} In the more recent SENSE study, patients were evaluated after 6 months and 13 months of nalmefene versus placebo treatment.\textsuperscript{22} Upon enrolment, patients had an average of 14 heavy drinking days per month and consumed on average 68 grams of alcohol per day which is approximately 8.75 alcohol units. After one year, total alcohol consumption was reduced by 67% in the nalmefene group. Self-reported alcohol consumption data was supported by clinician-based judgments and liver function tests.

A recent BMJ analysis used data obtained from the three clinical trials (ESENSE 1, ESENSE 2 and SENSE) and, rather unsurprisingly, supported the conclusions of the clinical trials.\textsuperscript{23} It was found that the use of nalmefene plus psychosocial support considerably reduced the number of patients in the high and very high drinking-risk level groups compared with psychosocial support alone. Additionally, the number of patients in the low and abstinence groups increased with nalmefene uptake.

**Cost effectiveness**

The BMJ analysis, as well as NICE, considers nalmefene to be cost effective when costs and effects were compared over 1 and 5 years.\textsuperscript{21} Nalmefene is priced at £42.42 for a pack of 14 tablets or £84.84 for a pack of 28 tablets.\textsuperscript{17} As part of its analysis of cost effectiveness, NICE offset the price of nalmefene against various cost parameters including the cost of a GP visit as well as second-line treatment for assisted withdrawal using naltrexone or acamprosate. The cost of treatment varies dependent on whether abstinence is established by home-based assisted withdrawal (£596), secondary care outpatient-assisted withdrawal (£606) or secondary care inpatient-assisted withdrawal (£4145). Cost-effective analysis also included societal costs related to crime and productivity, as specified in the remit to NICE from the Department of Health.\textsuperscript{18} It is worth noting that effectiveness of nalmefene has been established with the concomitant provision of psychosocial support and therefore commissioners must also weigh the cost of psychological therapy here.

**Side effects**

In the aforementioned studies, adverse events were more common in the nalmefene group than placebo, most events were mild-moderate and transient in nature. Nalmefene readily crosses the blood-brain barrier and, consequently, psychiatric adverse effects such as insomnia, confusion, restlessness and loss of libido are reflective of the pharmacological profile of the drug. Other reported side effects include nausea, dizziness and decreased appetite although trial data suggests that, generally, nalmefene is well tolerated.\textsuperscript{17}

**Discussion**

Addiction is a complex issue; compliance and uptake with interventions tend to be relatively low in such patients. This can be due to a variety of contributing factors including user profile, the social stigma of addiction, forgetfulness, lack of faith in the available treatments and inability to identify addiction/dependence. Nalmefene, like any other pharmacological therapy, will not be the panacea for addressing alcohol addiction. Treatment should be considered on a case-by-case basis and, as guidance recommends, supplemented with psychosocial support and counselling.\textsuperscript{17,18} There is opportunity for healthcare professionals, including pharmacists to engage with such a complex patient group by understanding the treatments available and ensuring patients can access the adequate support through-out their treatment by confirming this every time a patient of this group is encountered; whether in community pharmacy or addiction clinic or hospital ward.

The introduction of nalmefene use within current clinical practice provides alcohol dependent patients with another treatment option. The ability to take the medication when required is a novel step in substance addiction and may appeal to those who struggle to comply with a set regime (i.e. acamprosate which requires three times a day dosing). In this way, nalmefene treatment can involve alcohol-dependent patients, whom may not have sought help otherwise. Since there is no requirement for abstinence, nalmefene engages patients who may have been deterred by alternative methods which require abstinence from alcohol. It allows patients to define the parameters of their treatment goal by allowing different levels of reduced alcohol consumption. Pharmacists are appropriately placed to identify potential patients who may have tried other medications unsuccessfully. With adequate and up-to-date knowledge, pharmacists can appropriately signpost patients to seek specialist advice and perhaps commence nalmefene; a potential life-saving intervention.

“Pharmacists are appropriately placed to identify potential patients who may have tried other medications unsuccessfully.”
## AUDIT ALCOHOL SCREENING TOOL

**UNIT GUIDE**

1 unit is typically:

- Half-pint of regular beer, lager or cider; 1 small glass of low ABV wine (9%); 1 single measure of spirits (25ml)

The following drinks have more than one unit:

- A pint of regular beer, lager or cider, a pint of strong /premium beer, lager or cider, 440ml regular can cider/lager, 440ml “super” lager, 175ml glass of wine (12%)

### Questions

<table>
<thead>
<tr>
<th>Question</th>
<th>Scoring system</th>
<th>Your score</th>
</tr>
</thead>
<tbody>
<tr>
<td>How often do you have a drink containing alcohol?</td>
<td>Never</td>
<td>0</td>
</tr>
<tr>
<td>How many units of alcohol do you drink on a typical day when you are drinking?</td>
<td>1-2</td>
<td>0</td>
</tr>
<tr>
<td>3-4</td>
<td>5-6</td>
<td>7-9</td>
</tr>
<tr>
<td>10+</td>
<td></td>
<td>Daily or almost daily</td>
</tr>
<tr>
<td>How often have you had 6 or more units if female, or 8 or more if male, on a single occasion in the last year?</td>
<td>Never</td>
<td>0</td>
</tr>
<tr>
<td>How often during the last year have you failed to do what was normally expected from you because of your drinking?</td>
<td>Never</td>
<td>0</td>
</tr>
<tr>
<td>How often during the last year have you needed an alcoholic drink in the morning to get yourself going after a heavy drinking session?</td>
<td>Never</td>
<td>0</td>
</tr>
<tr>
<td>How often during the last year have you had a feeling of guilt or remorse after drinking?</td>
<td>Never</td>
<td>0</td>
</tr>
<tr>
<td>How often during the last year have you been unable to remember what happened the night before because you had been drinking?</td>
<td>Never</td>
<td>0</td>
</tr>
<tr>
<td>Have you or somebody else been injured as a result of your drinking?</td>
<td>No</td>
<td>Yes, but not in the last year</td>
</tr>
<tr>
<td>Has a relative or friend, doctor or other health worker been concerned about your drinking or suggested that you cut down?</td>
<td>No</td>
<td>Yes, during the last year</td>
</tr>
</tbody>
</table>

### Scoring:

- 0 – 7 Lower risk
- 8 – 15 Increasing risk
- 16 – 19 Higher risk
- 20+ Possible dependence

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**Figure 1: Alcohol Use Disorders Identification Test (AUDIT)**
Pharmacists in all areas are at the forefront of patient care and have the opportunity to interact with many patients over a short space of time. In this way, they can play a key role in promoting alcohol awareness to a wider audience and signpost patients to the available treatments if necessary. The AUDIT (Alcohol Use Disorders Identification Test) questionnaire (available on the Public Health England website) can be used to determine patients’ drinking ‘risk’ by asking relevant questions (see Figure 1). An important consideration is that the majority of the patients enrolled in the nalmefene clinical trials had never received any treatment for their alcohol addiction despite their alcohol problems having started more than 10 years before; it is clear that interventions to engage such patients are desperately required.

Formulary and commissioning groups should be aware that the evidence from clinical trials regarding the efficacy of nalmefene is limited since study data is placebo controlled. Comparative studies with nalmefene and current pharmacological treatments such as acamprosate and naltrexone are required to effectively provide robust, relative evidence.

**Conclusion**

The NHS ‘Five Year Forward View’ agenda of 2014 recognises that, as a nation, one in five adults still smoke, a third drink excess levels of alcohol and just under two thirds are overweight or obese.25 The agenda alludes to the need for national action against such public health risks, with alcohol being one of the major concerns. In this way, perhaps nalmefene can contribute within a wider, robust public health initiative required to engage alcohol misusers within primary care and secondary care. As nalmefene is still relatively new, the anecdotal evidence upon its efficacy and tolerability in patients is absent. However, in order to maximise the use of this drug; as well as other treatments for alcohol addiction, patient-facing healthcare professionals need to become more involved with engaging and supporting these patients throughout this complex treatment.

**Declaration of interests**

- None.

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**REFERENCES**

7. Academy of Medical Sciences, Calling time: the nation’s drinking as a major health issue. 2014.