Nalmefene: first drug for reducing alcohol consumption

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Nalmefene (Selincro) is the first drug approved for the reduction of alcohol consumption. In our New products review, Steve Chaplin presents the data relating to its efficacy and adverse events, and Professor Jonathan Chick discusses its place in therapy.

The NICE clinical guideline on the management of alcohol-use disorders states that the appropriate treatment goal may be abstinence or moderation of alcohol use, depending on the severity of dependence, harmful drinking and co-morbidities.¹ The WHO defines high drinking risk level (DRL) as 61–100g (7.7–12.7 UK units) of alcohol per day for men and 41–60g (5.2–7.6 units) for women, and very high DRL as >100g (12.7 units) per day for men and >60g (7.6 units) for women.²

Recommended interventions include assisted withdrawal with a benzodiazepine and psychological therapies and, for individuals who have successfully withdrawn, treatment with psychological therapies plus acamprosate (Campral EC), naltrexone (Adepend) or disulfiram (Antabuse) to maintain abstinence.

Nalmefene

Nalmefene (Selincro) is a selective opioid receptor antagonist at the mu and sigma receptors and a partial agonist at the kappa receptor. It appears to modulate corticomesolimbic functions to reduce the reinforcing effects of alcohol. It is licensed for the reduction of alcohol consumption in adults with alcohol dependence who have a high drinking risk level, without physical withdrawal symptoms and who do not require immediate detoxification. It should only be prescribed with continuous psychosocial support focused on treatment adherence and reducing alcohol consumption, and only in patients who continue to have a high DRL two weeks after initial assessment.

One tablet of nalmefene (18mg) is taken when the patient perceives a risk of drinking alcohol, preferably one to two hours prior to the anticipated time of drinking. If the patient has started drinking, one tablet should be taken as soon as possible. No dose adjustment is recommended for older people or patients with mild or moderate renal or hepatic impairment, but treatment should be used cautiously in these groups.

Nalmefene is contraindicated in patients with severe renal or hepatic impairment, a recent history of acute alcohol withdrawal syndrome, current or recent opioid addiction or recent opioid use.

KEY POINTS

- Nalmefene (Selincro) is a selective opioid receptor antagonist for the reduction of alcohol consumption in adults with alcohol dependence who have a high drinking risk level.
- It is available as an 18mg tablet; 14=£42.42, 28=£84.84.
- 1 tablet to be taken daily when the patient perceives a risk of drinking alcohol, preferably 1–2 hours before anticipated drinking.
- Compared with placebo, it reduces the number of heavy drinking days by 2.7–3.7 per month and reduces alcohol consumption by around 80 bottles of wine per year in individuals with a high drinking risk level.
- It was also associated with greater improvement than placebo in measurements of serum liver enzymes, objective markers of excessive drinking.
- About half of patients withdrew prematurely from the key clinical trials.
- Common adverse effects include nausea, dizziness and insomnia.
**Clinical trials**

The efficacy of nalmefene has been evaluated in two six-month trials of similar design (ESSENSE 1 and 2); a 12-month trial primarily evaluated safety.

The efficacy studies (n=604, 718) were conducted in different European countries (none in the UK). People diagnosed with alcohol dependence and reporting within the preceding four weeks at least six heavy drinking days – HDDs, defined as alcohol consumption >60g (7.6 units) per day for men and >40g (5.1 units) for women – 14 or fewer abstinent days and who were at least at medium DRL, were randomised to receive placebo or nalmefene as needed. All participated in a psychosocial programme to promote motivation and adherence. The primary end-points were the change from baseline in the number of HDDs and total alcohol consumption over 28 days.

About 80 per cent of participants in each study had a high or very high DRL, with 22–23 HDDs per month and a mean total alcohol consumption 99–113g (12.5–14.3 units) per day (see Figure 1). Patients took nalmefene on 50–60 per cent of days during the trials.

Approximately 40 per cent of patients withdrew from each study. This was most frequently due to withdrawal of consent but in one study more patients using nalmefene withdrew due to adverse events (20 vs 6 per cent with placebo compared with 4 vs 1 per cent in the second study).

The treatment effect was larger in the patients with a high or very high DRL at baseline, and the European Medicines Agency (EMA) concluded that this should be the target patient population. In this subgroup, the mean number of HDDs decreased from 23 days per month to 10–11 and mean total alcohol consumption decreased from 102–113g (12.9–14.3 units) per day to 43–44g (5.4–5.6 units) at six months. Most of this gain was achieved after four weeks and was broadly maintained after 12 months.

Compared with placebo, nalmefene reduced the number of HDDs by 2.7–3.7 days per month and total alcohol consumption by 10–18g (1.3–2.3 units) per day. This is equivalent to almost 80 bottles of wine fewer per year with nalmefene compared to placebo.

**Figure 1.** Pooled data from ESENSE 1 and 2 showing adjusted mean change from baseline in heavy drinking days (A) and total alcohol consumption (B) for nalmefene vs placebo; after reference 3

**Adverse effects**

Overall, 75 per cent of patients taking nalmefene and 63 per cent assigned to placebo reported adverse events during clinical trials. The most common adverse reactions were nausea (19 per cent), dizziness (16 per cent) and insomnia (13 per cent), occurring three to four times more frequently than with placebo. Nausea and dizziness mostly occurred during the first month of treatment.

**References**


**Declaration of interests**

None to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics
Place in therapy

Is total abstinence the only route out of alcoholism? ‘Twelve-step facilitation’, which links patients to Alcoholics Anonymous, improves drinking outcomes and helps thousands achieve abstinence.¹ However, many do not achieve abstinence; of these, some drink but without accruing further problems.²,³ Furthermore, reluctance to consider abstinence is the main reason why people do not seek treatment.⁴

In a UK trial of psychological treatments, patients entering with a goal of reduction achieved a good outcome as often as those whose goal had been abstinence.⁵ Both NICE¹ and the EMA⁶ recognise that reduced drinking is an appropriate goal for some.

Nalmefene is the first drug approved for reduction of alcohol consumption. The EMA, endorsed by the Scottish Medicines Consortium, restricts its prescription to those still drinking at high DRL two weeks following a brief intervention (recognising that some heavy drinkers cut back after a single session of advice). ‘Continuous psychosocial support focused on treatment adherence and reducing alcohol consumption’ is recommended in the prescribing information. This need not be specialist therapy.

Compared with placebo, among patients seeking help for alcohol dependence nalmefene reduced drinking by a further 80 bottles of wine per year.⁷ This was achieved mainly by a reduction in the number of days when heavy drinking occurred (and it is those days when problems arise!). Nalmefene was associated with greater improvement than placebo in measurements of the serum liver enzymes, objective markers of excessive drinking. Adverse effects include nausea, dizziness and insomnia.

References


Declaration of interests

Professor Chick has received consultancy and speaker’s fees from nalmefene’s licence holder Lundbeck.

Jonathan Chick is a consultant psychiatrist, medical director of Castle Craig Hospital, Scotland, and honorary professor at Queen Margaret University, Edinburgh.