

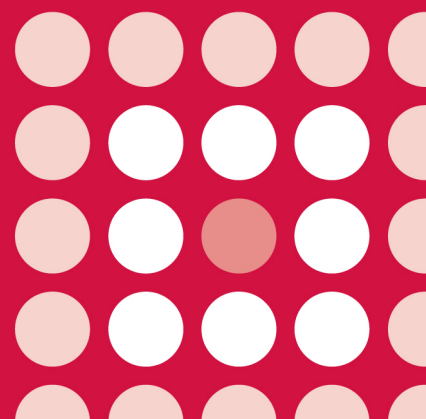


AWMSG SECRETARIAT ASSESSMENT REPORT

Nalmefene (Selincro[®]▼)
18 mg film-coated tablets

Reference number: 1259

FULL SUBMISSION



This report has been prepared by the All Wales Therapeutics and Toxicology Centre (AWTTC), in collaboration with the Centre for Health Economics and Medicines Evaluation, Bangor University.

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AWMSG Secretariat Assessment Report Nalmefene (Selincro[®]▼) 18 mg film-coated tablets

This assessment report is based on evidence submitted by Lundbeck Ltd on 5 July 2013¹.

1.0 PRODUCT DETAILS

Licensed indication under consideration	<p>Nalmefene (Selincro[®]▼) for the reduction of alcohol consumption in adult patients with alcohol dependence who have a high drinking risk level (DRL) without physical withdrawal symptoms and who do not require immediate detoxification.</p> <p>Nalmefene should only be prescribed in conjunction with continuous psychosocial support focused on treatment adherence and reducing alcohol consumption.</p> <p>Nalmefene should be initiated only in patients who continue to have a high DRL two weeks after initial assessment².</p>
Dosing	<p>Nalmefene is to be taken as-needed: on each day the patient perceives a risk of drinking alcohol; one tablet should be taken, preferably 1–2 hours prior to the anticipated time of drinking. If the patient has started drinking alcohol without taking nalmefene, one tablet should be taken as soon as possible. The maximum dose is one tablet per day².</p>
Marketing authorisation date	25 February 2013 ²

2.0 DECISION CONTEXT

2.1 Background

Alcohol dependence (AD) is characterised by craving, tolerance, a preoccupation with alcohol and continued drinking in spite of harmful consequences³. Patients with AD may also experience comorbid mental health disorders (e.g. depression, anxiety disorders and drug misuse) and physical comorbidities (e.g. neurological disorders, cardiovascular disease and gastrointestinal disorders, particularly liver disease)³. The diagnosis of AD is made on the basis of the symptoms and consequences of alcohol misuse³. Based on a prevalence of 5.9% (8.7% for men, 3.3% for women) in England (2007)⁴, the company estimates that there are 139,598 alcohol-dependent adults in Wales, with an incidence of 714 cases per year¹.

For people with mild AD (those scoring ≤ 15 in the Severity of Alcohol Dependence Questionnaire [SADQ]), the National Institute of Health and Care Excellence (NICE) Clinical Guideline (CG) 115 recommends offering psychological intervention focused on alcohol-related cognitions, behaviour, problems and social networks³. For people with moderate to severe AD (SADQ score > 15), NICE CG115 recommends alcohol withdrawal followed by acamprosate or oral naltrexone in conjunction with psychological intervention, focused specifically on alcohol misuse³. Nalmefene is indicated for the reduction of alcohol consumption, rather than withdrawal; the company proposes that it is used in patients with mild AD, as categorised in NICE CG115^{1,3}. Acute alcohol intake results in mesolimbic dopamine release (facilitated by

the release of beta-endorphins), which can provide positive reinforcement⁵. Nalmefene, an opioid system modulator is thought to counteract the reinforcement effects and reduce alcohol consumption, possibly by modulating these cortico-mesolimbic functions⁵.

2.2 Comparators

The comparator included in the company submission was psychosocial intervention¹.

2.3 Guidance and related advice

- NICE CG115. Alcohol-use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence (2011)³.
- European Medicines Agency (EMA). Guideline on the development of medicinal products for the treatment of alcohol dependence (2010)⁶.
- NICE Public Health Guidance 24 Alcohol-use disorders: preventing harmful drinking (2010)⁷.
- NICE CG100. Alcohol-use disorders: Diagnosis and clinical management of alcohol-related physical complications (2010)⁸

3.0 SUMMARY OF EVIDENCE ON CLINICAL EFFECTIVENESS

The company submitted results from three clinical trials: two 24-week trials ESENSE1 (12014A) and ESENSE2 (12023A), which evaluated the clinical efficacy of nalmefene, and SENSE (12013A), a 52-week study which evaluated the long term safety of nalmefene⁹⁻¹¹. All three trials compared the use of nalmefene with psychosocial intervention versus the use of placebo with psychosocial intervention¹. ESENSE1, ESENSE2 and SENSE were carried out in an outpatient setting with 604 participants (nalmefene, n = 306; placebo, n = 298), 718 participants (nalmefene, n = 358; placebo, n = 360) and 675 participants (nalmefene, n = 509; placebo, n = 166) respectively⁹⁻¹¹. The company submission is focused on comparative clinical efficacy within the licensed population, which is a subset of the full trial population in ESENSE1, ESENSE2 and SENSE, namely those with a high or very high drinking risk level (DRL; see glossary) at baseline and at randomisation i.e. the patients judged to benefit most from nalmefene treatment¹. The full trial population is however, considered in the comparative safety section (section 3.2).

3.1 Comparative efficacy

The ESENSE1 and ESENSE2 trials were 24-week, randomised, double-blind, multicentre, parallel-group, placebo-controlled phase III trials, designed to determine the efficacy of nalmefene in patients > 18 years with diagnosed AD (≥ 6 heavy drinking days [HDD, see glossary], an average alcohol consumption ≥ WHO medium DRL and ≤ 14 consecutive abstinent days in the four weeks preceding screening)^{9,10}. SENSE was a 52-week phase III, randomised, double-blind, multicentre, parallel-group, placebo-controlled trial, designed to determine the safety of nalmefene⁵. The ESENSE trials consisted of four sequential periods: a one to two week screening period, a 24-week double-blind treatment period, a four-week double-blind placebo-controlled run-out in each treatment arm (in which nalmefene treated patients were randomised 1:1 to receive either nalmefene or placebo to evaluate discontinuation effects) and a four week safety follow-up^{9,10}. In all three studies, patients in the treatment and placebo arms received motivational and adherence-enhancing psychosocial intervention sessions, BRENDA (see glossary) which was provided by trained personnel (such as investigators, nurses and psychologists)⁵.

At monthly intervals, patients provided retrospective estimates of the number of standard drinks consumed each day in the previous month, which were subsequently converted into grams of alcohol/day. Patient's took a maximum of one tablet per day if

they perceived a risk of drinking alcohol. If the patient started drinking without having taken a tablet, they were advised to take one tablet as soon as possible⁵.

The coprimary endpoints for the ESENSE studies were the changes from baseline in the monthly number of HDDs, and total alcohol consumption (TAC) at month six. A large proportion of patients (18% in ESENSE1 and 33% in ESENSE2) almost entirely finished drinking during the period between screening and randomisation, offering limited space for further improvement. Therefore, the applicant company conducted a post-hoc analysis of patients with a high or very high DRL at baseline and at randomisation. Nalmefene was subsequently licensed for this subgroup of patients⁵. In patients receiving nalmefene and psychosocial intervention within the subgroup, mean monthly HDDs decreased from 23 at baseline in both studies to 11 in ESENSE1 and 10 in ESENSE2 and mean TAC decreased from 102 g/day to 44 g/day in ESENSE1 and from 113 g/day to 43 g/day in ESENSE2⁵. This corresponds to the equivalent of a decrease of 160 HDDs per year and 330 fewer wine bottles consumed per year compared to baseline⁵. The differences in the reduction in HDDs (2.7–3.7) and TAC (10.3–18.3 g/day) between nalmefene- and placebo-treated patients in the subgroup are presented in Table 1. This corresponds to approximately 1½ months fewer HDDs per year and almost 80 bottles of wine less per year with nalmefene compared with placebo⁵.

Table 1. Coprimary endpoints for population subgroup (patients with high or very high DRL at baseline and who maintained a high or very high DRL at randomisation) in ESENSE studies^{1,5}

Study	Coprimary endpoints	Mean difference versus placebo (95% CI)	p value
ESENSE1			
Nalmefene (n = 171)	Mean difference in the change from baseline to month six in HDD	-3.7 days/month (-5.9, -1.5)	0.001
Placebo (n = 167)	Mean difference in the change from baseline to month six in TAC	-18.3 g/day (-26.9, -9.7)	< 0.001
ESENSE2			
Nalmefene (n = 148)	Mean difference in the change from baseline to month six in HDD	-2.7 days/month (-5.0, -0.3)	0.025
Placebo (n = 155)	Mean difference in the change from baseline to month six in TAC	-10.3 g/day (-20.2, -0.5)	0.040
CI: confidence interval; HDD: heavy drinking day; n: number of participants at baseline; TAC: total alcohol consumption			

In the ESENSE studies, the three secondary endpoints proposed by EMA guidance, were not statistically powered to separate nalmefene-treated patients from placebo-treated patients^{1,5}. The mean SF-36 and EQ-5D quality of life scores relative to baseline were numerically higher in the nalmefene arm than in the placebo arm in the licensed population. These increases were statistically significant in the ESENSE1 study for the EQ-5D VAS score but not for the EQ-5D utility index score or for the SF-36 scores. Statistically significant improvement versus placebo was shown in the ESENSE2 study for the SF-36 scores but not for the EQ-5D scores¹. Pooling the results from ESENSE1 and ESENSE2 resulted in statistically significant improvements relative to placebo in SF-36 and EQ-5D VAS and utility index scores¹.

Efficacy analyses were secondary endpoints in the SENSE safety study. In the subgroup (nalmefene, n = 141; placebo, n = 42), the number of HDDs/month was reduced by 3.6 (p = 0.0164) and TAC was reduced by 17.3 g/day (p < 0.0129) for nalmefene versus placebo¹².

3.2 Comparative Safety

The full population data from the three studies, ESENSE1, ESENSE2 and SENSE were pooled in order to analyse the safety of nalmefene (nalmefene, n = 1144 ; placebo, n = 797)⁵. High levels of patient withdrawal were seen; 34% in the placebo group and 43% in the nalmefene group. Withdrawal of consent was the primary reason for discontinuation for 13.3% of the patients in the placebo group and 15.7% of the patients in the nalmefene group⁵. Withdrawal due to adverse events (AEs) occurred in 10.5% of nalmefene-treated patients and in 3.8% of placebo-treated patients. Treatment-emergent AEs (TEAEs) leading to withdrawal occurred earlier in patients receiving nalmefene (median seven days) than in patients receiving placebo (median 63 days). TEAEs occurred in 855/1144 (75%) patients in the nalmefene arm and in 500/797 (63%) patients in the placebo arm. The most prevalent TEAEs, dizziness, nausea and insomnia, occurred approximately 3–4 times more often in patients receiving nalmefene than in placebo-treated patients⁵. Psychiatric disorders such as confusion, abnormal thinking and hallucination occurred in 2.9% of patients receiving nalmefene, which was approximately three times more often than in patients receiving placebo. The Committee for Medicinal Products for Human Use (CHMP) concluded that there were no serious AEs causing major concern⁵.

3.3 AWTTTC critique

- The Scientific Advisory Group (SAG), convened by CHMP, confirmed that although modest, the effect size of nalmefene was clinically meaningful; CHMP considered, by majority decision, that the risk-benefit balance was favourable⁵.
- CHMP observed that, although the withdrawal rate was high (48% and 36% in the nalmefene arms of ESENSE1 and ESENSE2), the proportion of patients who withdrew from the studies was comparable to that in other placebo-controlled studies conducted in patients with alcohol dependence over the last ten years⁵. The SAG recognised the validity of post-hoc analysis, which is commonly used for psychiatric drugs due to high discontinuation rates⁵.
- In their submission, the applicant company has not provided a comparison between nalmefene and acamprosate, disulfiram or naltrexone. The company reported that they included comparison against psychological interventions as this is the preferred treatment option in the population of mild alcohol dependent patients in NICE clinical guideline CG115³. Acamprosate and disulfiram are not indicated for patients continuing to drink alcohol^{13,14}, and naltrexone, a support treatment in abstinence, is not specifically indicated for alcohol reduction¹⁵. NICE clinical guideline CG115 states that acamprosate or naltrexone, in conjunction with psychological intervention, may be considered for use in people with mild AD who have not responded to psychological intervention alone, or who have requested a pharmacological intervention, although neither medication is licensed for this indication³.
- No data was available for the use of nalmefene beyond 13 months; the Summary of Product Characteristics (SPC) advises caution if prescribed for more than one year².
- The company have noted in their submission that nalmefene does not require specialist initiation¹.
- The use of BRENDA, in the ESENSE and SENSE trials, was in line with EMA guidelines, which advises that standardised psychosocial interventions at a low and constant level should be permitted in AD studies^{5,6}.
- Nalmefene is the first medicine licensed for the reduction of alcohol consumption in adult patients with alcohol dependence. Nalmefene does not require patients to achieve and maintain complete abstinence¹⁰. The SAG acknowledged that a reduction in alcohol consumption is an appropriate goal in a subgroup of alcohol dependent patients with high/very high DRL without physiological signs of withdrawal and not requiring any immediate detoxification procedure⁵.

- The company is developing an on-line psychosocial support tool which will be free of charge to the NHS¹.

4.0 SUMMARY OF THE EVIDENCE ON COST-EFFECTIVENESS

4.1 Cost-effectiveness evidence

4.1.1 Context

The company submission describes a cost-utility analysis of nalmefene in conjunction with psychosocial intervention for the treatment of adult patients with alcohol dependence that have a high DRL, without physical withdrawal symptoms, who do not require immediate detoxification, and who continue to have a high DRL two weeks after initial assessment which corresponds to the subgroup of the trial population (ESENSE1, ESENSE2 and SENSE) and to the licensed indication. The comparator treatment is psychosocial intervention alone¹.

The resource use and cost data used in the model were largely obtained from the nalmefene phase III studies, assumptions about clinical practice, NICE CG115³, the Sheffield Alcohol Policy Model¹⁶ and published cost sources¹⁷. The model uses a Markov approach to estimate the incremental costs and health outcomes over a five-year period, consisting of a short-term (one-year) and long-term (four years) phase. The short-term phase of the model consists of five health states based on DRLs: very high risk, high risk, medium risk, low risk and abstinence (based on daily alcohol consumption). Patients enter the model in either the very high or high drinking risk level (alcohol consumption > 60 g/day for men, and > 40 g/day for women), in line with the nalmefene licence, and cycle among the model health states at monthly intervals during the first year. Pooled data from the three phase III nalmefene studies provided the transition probabilities for the short-term phase of the model. The long-term phase of the model consists of three drinking level health states: high and very high risk, medium risk, and controlled drinking. In addition, there is a tunnel state for second line alcohol withdrawal with pharmacological treatment linked to the high and very high risk health states. Patients enter the long-term phase of the model in the health state associated with their drinking risk level at the end of the nalmefene phase III clinical trial (SENSE) and cycle among these health states on a yearly basis. The annual transition probabilities for the long-term phase of the model were derived from the nalmefene phase III studies (using months 6–12 of the trial data for transition probabilities for years 2–5), NICE CG115³ and the published literature^{18,19}.

In addition, the model has two event-related health states: serious event and death. There is also a tunnel state for temporary events. Each patient's risk of experiencing these events is based on their DRL. Patients can have an event during either the short-term or long-term phase of the model. Patients who die or experience a serious event stay in that health state for the remaining duration of the model. Patients who experience a temporary event and survive stay in the tunnel health state for one month before returning to their pre-tunnel health state.

4.1.2 Results

Results of the base case analysis of nalmefene in conjunction with psychosocial intervention versus psychosocial intervention alone are summarised in Table 2. The analysis shows that treatment with nalmefene in conjunction with psychosocial intervention was estimated to be both less costly and more effective than psychosocial intervention alone i.e. dominant. The results are largely due to the higher proportion of responders (controlled drinking) at year one, the consequent reduction in events and fewer patients requiring abstinence treatment.

Table 2. Company-reported results of the base case analysis

	Nalmefene plus psychosocial intervention	Psychosocial intervention alone	Difference
Cost of medical treatments	£1,396	£1,246	£150
Nalmefene related cost	£618	n/a	£618
Cost of harmful events	£871	£1,085	-£214
Cost of secondary abstinence treatment	£1,707	£2,647	-£940
Total costs	£4,591	£4,978	-£387
Total life-years	4.427	4.419	0.008
Total QALYs	3.623	3.550	0.0725
ICER (£/QALY gained)	Nalmefene plus psychosocial intervention dominates		
ICER: incremental cost effectiveness ratio; QALY: quality-adjusted life-year			

A number of one-way sensitivity analyses have been conducted by the company to address uncertainty in model parameters. Of the 135 parameters included in the sensitivity analysis, the ones having most impact on cost-effectiveness are: the number of medical visits per month (for both treatments), the proportion of high and very high risk drinkers having new treatment, the utility value used and the cost of the relapse prevention programme. The results remain cost saving to changes in all these parameters except medical visits per month for the nalmefene arm¹.

Scenario analyses have been conducted based on different time horizons and nalmefene intake (everyday versus as-needed). The three different scenarios conducted were: (i) one year time horizon, nalmefene taken as-needed; (ii) five year time horizon, nalmefene taken everyday; and (iii) five year time horizon, nalmefene taken as-needed and no second-line treatment. All three scenarios resulted in nalmefene plus psychosocial intervention no longer dominating psychosocial intervention alone; scenario (i) resulted in the highest cost/QALY gained of £24,000.

Probabilistic sensitivity analysis undertaken for the base case analysis indicates that the probability that nalmefene plus psychosocial intervention is cost-effective compared to psychosocial intervention alone is 100% at cost-effectiveness thresholds of both £20,000 and £30,000 per QALY gained.

4.1.3 AWTTTC critique

Based on the evidence available, it is possible that the use of nalmefene in conjunction with psychosocial intervention would reduce alcohol consumption in alcohol dependent adults, reduce alcohol-related harms and improve patient quality of life at the same time as providing considerable cost offsets. However, there is uncertainty associated with extrapolating beyond one year. There is no direct evidence on the treatment pathway, resource use or costs, or major events and utilities associated with alcohol dependence in Wales beyond the 12 months of the nalmefene phase III studies.

Strengths of the company's economic evidence include:

- The model structure is clear and largely in line with other models related to AD.
- The company has made an effort to quantify the impact of AD in terms of harmful events through (i) the micro-simulation model submitted to the European Medicines Agency as part of the regulatory package; and (ii) the estimation and inclusion of alcohol-related events in the model.
- The company has included utilities collected in the nalmefene phase III trials despite some issues highlighted about the lack of sensitivity of generic quality of life instruments in AD.

Limitations of the economic evidence include:

- There is a lack of data on long-term treatment of AD after initial treatment with nalmefene plus psychosocial intervention. This relates to how patients move between the different health states in the long-term phase of the model. In particular, there are no direct data on what happens after the 12 month nalmefene treatment period. The company uses months 6–12 of the nalmefene trial data for transition probabilities for years 2–5 for patients continuing nalmefene treatment. Whilst the company has varied these transition probabilities (using only the last month of the SENSE study) in a scenario analysis, this does not address the issue of whether these values are relevant over the longer term.
- The company has assumed that psychosocial intervention utilised in clinical practice in Wales will deliver similar results as demonstrated through BRENDA in the nalmefene phase III studies. In reality, the psychosocial support provided may not be as intensive.
- Nalmefene is licensed on an as-needed basis. As-needed dosing may be every day. The company uses data on dosing from the indicated population of the nalmefene phase III trials in the base case analysis. It also includes a scenario for nalmefene taken every day. However, this scenario is only conducted for the five year time horizon. In addition, the company has not adequately addressed the impact of adherence on dosing in the real world setting.
- The company has not addressed whether the withdrawal rates observed in the nalmefene phase III studies are reflective of routine care in the UK. This group of patients have difficulty adhering to both pharmacological and psychosocial treatment.
- The company's analysis only included direct medical costs to the NHS in Wales and did not include costs to Personal and Social Services in Wales, which given the nature of AD, could be significant.
- The company did not include a pharmacological comparator in the economic analysis. Whilst there are no other pharmacological treatments licensed for the nalmefene patient population, there appears to be some off-label use of acamprosate or naltrexone in this patient population in Wales¹.

4.2 Review of published evidence on cost-effectiveness

AWTTC did not identify any published cost-effective studies of nalmefene for the treatment of adult patients with AD.

5.0 SUMMARY OF EVIDENCE ON BUDGET IMPACT

5.1 Budget impact evidence

5.1.1 Context and methods

As the main data sources for Wales provide data for alcohol problems and dependence rather than the specific indication for nalmefene, the company first estimated the number of patients with AD and then the number of patients specifically relevant to the nalmefene indication. To estimate the number of adult patients with AD, a prevalence rate of 5.9%⁴ was applied to the estimated Welsh adult population (2,366,063), derived from Office of National Statistics 2011 census figures²⁰. This resulted in an estimate of 139,598 adults in Wales with AD. In addition, the company accounted for annual incidence through population growth of 0.51% per annum in Wales. After accounting for alcohol-related mortality, the company then estimated the number of patients for the specific indication through data from NICE CG115³ and the nalmefene phase III trials as 33,576 in year one¹. However, as only a small minority of people with AD receive treatment or any kind of intervention, this was further reduced by assuming 6% (or 2,015 patients) will receive treatment in the first year. Of these, it was assumed that 20% (or 403 patients) will be treated with nalmefene in the first year and that this will increase to 60% (or 2,879 patients) in year five. Given an annual discontinuation rate

of 17.5%, this results in a total of 332 patients treated with nalmefene in the first year, increasing to 2,375 patients in year five. Only medicine acquisition costs are included in the company's assessment of budget impact¹.

5.1.2 Results

The estimated number of patients and the associated costs as described by the company are summarised in Table 3. The annual medicine (nalmefene) cost per patient is based on nalmefene treatment for 127 days each year. The company stated that the introduction of nalmefene would not result in any additional NHS or social work costs or savings.

Table 3. Company-reported costs associated with use of nalmefene for the reduction of alcohol consumption in patients with AD

	Year 1 (2013)	Year 2 (2014)	Year 3 (2015)	Year 4 (2016)	Year 5 (2017)
Number of eligible patients (Indication covered in this submission)	33,576	33,749	33,922	34,096	34,271
Treated (%)	6%	8%	10%	12%	14%
Treated patients	2,015	2,700	3,392	4,092	4,798
Uptake (%)	20%	30%	40%	50%	60%
Number of patients eligible to receive nalmefene plus psychosocial intervention	403	810	1,357	2,046	2,879
Withdrawals	17.5%	17.5%	17.5%	17.5%	17.5%
Number of patients treated with nalmefene plus psychosocial intervention	332	668	1,119	1,688	2,375
Net costs					
Medication cost per patient	£384.81	£384.81	£384.81	£384.81	£384.81
Total Cost	£127,913	£257,138	£430,763	£649,459	£913,907

Scenario analyses of resource implications presented by the company included (i) varying the annual incidence of AD; and (ii) the treatment rate for AD in Wales not increasing over the five-year period. The first scenario resulted in only a minimal change to the budget impact. The second scenario resulted in a large change to the budget impact in the later years.

The company later provided data for two additional scenarios: (i) nalmefene treatment for 204 days per year; and (ii) nalmefene treatment every day for a 365 day period. The first scenario results in an estimated budget impact in Wales of £205,467 in year 1 rising to £1,468,008 in year 5. The second scenario results in an estimated budget impact in Wales of £367,624 in year 1 rising to £2,626,582 in year 5.

The company also later considered the inclusion of other health care costs. The analysis was based on nalmefene use for 127 days per year and 11.57 health care professional consultations per year (50% at general practitioner level and 50% at specialist level). This increased the cost per patient per year to £1,415.

5.1.3 AWTTTC critique

The company has taken a pragmatic approach to estimate the number of eligible patients given the paucity of available data. A range of assumptions have been necessary which has introduced a degree of uncertainty in these estimates.

In particular, the company analyses highlighted the impact on the budget estimates for Wales due to potential variability in as-needed dosing. The company provided three scenarios which estimate the budget impact for Wales. However, as these are based on different levels of 'as needed' dosing, it is not clear which scenario will be the most relevant in the real world.

5.2 Comparative unit costs

The example costs of regimens for the treatment of adult patients with alcohol dependence for a 28-day period are shown in Table 4. This includes scenarios for nalmefene for both as-needed use and every day use. Assumptions of 10 days and 16 days treatment in a 28-day period is made for as-needed use of nalmefene. This is based on the company's estimate of 127 days and 204 days over a one-year period.

Table 4. Example of cost per patient per 28-day period for the reduction of alcohol consumption in patients with AD

Regimens	Example doses*	Approximate 28-day costs†
Nalmefene (Selincro®▼) 18 mg tablet	One tablet each day if there is a risk of drinking alcohol (10 days per 28 day treatment period*)	£30.30
	One tablet each day if there is a risk of drinking alcohol (16 days per 28 day treatment period**)	£48.48
	One tablet per day	£84.84
Acamprosate (Campral EC®) 333 mg tablet	Weight < 60 kg: 666 mg once daily and 333 mg twice daily	£19.20
	Weight ≥ 60 kg, 666 mg three times daily	£28.80
Naltrexone (Nalorex®) 50 mg tablet	50 mg daily	£22.34
NOTE: Only nalmefene is licensed for use in this patient population		
* Based on as-needed dosing – 127 days of nalmefene treatment during the one-year period		
** Based on as-needed dosing – 204 days of nalmefene treatment during the one-year period		
† Costs are based on British National Formulary (BNF) list prices as of September 2013 ²¹		

6.0 ADDITIONAL INFORMATION

6.1 Prescribing and supply

AWTTTC is of the opinion that, if recommended, nalmefene (Selincro®▼) may be appropriate for prescribing by all prescribers within NHS Wales for the indication under consideration.

6.2 Ongoing studies

The company submission did not highlight any ongoing studies that are likely to be available within 6–12 months.

6.3 AWMSG review

This assessment report will be considered for review three years from the date of Ministerial ratification (as disclosed in the Final Appraisal Recommendation).

6.4 Evidence search

Date of evidence search: 5 August 2013

Date range of evidence search: No date limits were applied to database searches.

GLOSSARY

Heavy Drinking Day (HDD)

Defined as a day with alcohol consumption ≥ 60 g for men and ≥ 40 g for women^{1,6}

Drinking Risk Levels (DRL, WHO criteria for risk of consumption on a single drinking day)²²

Risk Level	Males	Females
Low risk	1–40 g	1–20 g
Medium risk	41–60 g	21–40 g
High risk	61–100 g	41–60 g
Very high risk	101+ g	61+ g

BRENDA²³

A psychosocial intervention consisting of six components:

- Biopsychosocial evaluation;
- Report to the patient on assessment;
- Emphatic understanding of the patient's situation;
- Needs collaboratively identified by the patient and the treatment provider;
- Direct advice to the patient on how to meet those needs;
- Assess reaction of the patient to advice and adjust as necessary for best care.

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