Cost Effectiveness of nalmefene (Selincro®) for the reduction of alcohol consumption in adult patients who continue to have a high drinking risk level.

The NCPE has issued a recommendation regarding the use of nalmefene for this indication. The NCPE recommends reimbursement of nalmefene with psychosocial support.

The HSE has asked the National Centre for Pharmacoeconomics (NCPE) to evaluate the manufacturer's (Lundbeck (Ireland) Ltd) economic dossier on the cost effectiveness of nalmefene. The NCPE uses a decision framework to systematically assess whether a technology is cost effective. This includes clinical effectiveness and health related quality of life benefits which the new treatment may provide and whether the cost requested by the pharmaceutical company is justified.

Following the recommendation from the NCPE, the HSE examine all the evidence which may be relevant for the decision; the final decision on reimbursement is made by the HSE. In the case of cancer drugs, the NCPE recommendation is also considered by the National Cancer Control Programme (NCCP) Technology Review Group.

About the National Centre for Pharmacoeconomics

The NCPE are a team of clinicians, pharmacists, pharmacologists and statisticians who evaluate the benefit and costs of medical technologies and provide advice to the HSE. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. Our aim is to provide impartial advice to help decision makers provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has a responsibility for commissioning or providing healthcare, public health or social care services.

National Centre for Pharmacoeconomics **April 2014**

Summary

1. Lundbeck (Ireland) submitted a dossier for nalmefene (Selincro®) on 21st October 2013. Selincro® (nalmefene) is indicated for the reduction of alcohol consumption in adult patients with alcohol dependence who continue to have a high drinking risk level (DRL; alcohol consumption >60 g/day for men and >40 g/day for women according to the WHO DRLs of alcohol consumption), two weeks after initial assessment, without physical withdrawal symptoms and who do not require immediate detoxification. Nalmefene is 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, the patient should take one tablet as soon as possible. The maximum dose is one tablet per day.
   Final clarifications were received on 21 March 2014. The company are seeking reimbursement under the General Medical Scheme (GMS) and the Drugs Payment Scheme (DPS). The perspective of the assessment is that of the Healthcare payer (Health Service Executive). The economic evaluation presented compared nalmefene in combination with psychosocial support to pyschosocial support alone.

1. Clinical trial data was presented from three trials; ESENSE1 and ESENSE2 which were randomised double blind placebo-controlled parallel group studies and a third long term safety study (SENSE). The primary endpoints in the ESENSE studies were the number of Heavy Drinking Days (HDDs) (defined as a day with alcohol consumption ≥60g for men and ≥40g for women); and Total Alcohol Consumption (TAC), defined as mean daily alcohol consumption in g/day over a month (28 days). All participants took part in a psychosocial programme developed on behalf of Lundbeck (BRENDA) to enhance medication and treatment compliance at each visit. This intervention was carried out by GPs and took between 15 and30 minutes to complete.

2. In the ESENSE 1 study the adjusted change from baseline to 6 months in the nalmefene group was -11.2 HDDs (Standard Error (SE) 0.6) and in the

placebo group was -8.9(SE 0.6) which is a mean difference of -2.3HDDs (P=0.0021). The change from baseline in TAC (g/day) was -50.7g/day in the nalmefene group compared to -39.7g/day in the placebo group which is a difference of -11g/day (P=0.0003). Eighteen per cent of patients stopped drinking in the two week screening period which was undertaken in the run in to initiation of the randomised phase. There was also a high rate of treatment discontinuation; 33.9% in the placebo group and 42.9% in the nalmefene group. Withdrawal of consent was the primary reason for withdrawal in both groups but was higher in the nalmefene group (13.3% vs. 15.7% respectively). In ESENSE 2 study the mean change from baseline to 6 months was -12.3 HDDs (SE 0.5) versus -10.5 HDDS (SE 0.5) which is a mean difference of -1.7 HDDs (p=0.12). The change from baseline in TAC (g/day) was -59g/day (SE2.3) in the nalmefene group versus -54.1g/day (SE2.2) in the placebo group. The rate of discontinuation was 38% in the placebo group and 41% in the nalmefene group. In the SENSE study, the mean difference in HDDs from baseline to month 13 was -3.6 days/month (95% CI -6.5,-0.7) (P=0.0164) and in TAC was -17.3g/day (95%CI -30.9,-3.8) (p=0.0129).

3. A Markov model was presented which had two phases; a short term phase (up to one year based on clinical trials of nalmefene); and a long term phase (beyond one year within trial time horizon and up to five years). The cycle length in the short term phase is one month (28 days) and for the long term phase a one year cycle length is applied. The time horizon for the model is five years. The short term phase accounts for treatment efficacy and patients' adherence as measured in clinical trials. It also includes alcohol-attributable harmful events and deaths. The long term phase models the maintenance of treatment effects, patient progression and incidence of alcohol-attributable deaths.

4. Adverse effects were experienced commonly in both placebo and nalmefene groups in the Lundbeck studies (approximately 75% of the nalmefene group and 63% of the placebo group experienced adverse effects). Dizziness, nausea and insomnia/sleep disorders occurred about 3-4 times more often in subjects receiving nalmefene. Psychiatric disorders such as confusion, abnormal

thinking, and hallucination occurred in 2.9% of subjects receiving nalmefene, about three times more often than in the placebo group. Depressive symptoms were reported in 3.2% of patients in the nalmefene group and 2.8% of patients in the placebo group.

5. The model includes utilities for drinking level health states and for alcohol attributable harmful events. The EQ-5D and the Short Form 36 (SF-36) were both collected in the three trials ESENSE 1, 2 and SENSE. The EQ-5D data was used to derive utilities for the cost-effectiveness model. Utilities are applied to alcohol-attributable harmful events using data gathered for the Sheffield alcohol policy model.

6. The incremental cost effectiveness ratio presented by Lundbeck is €7,813/QALY (incremental costs €551 and QALYs 0.0705) versus pyschosocial support alone. The basecase is presented for a 5 year time horizon.

7. Applying a shorter time horizon had most impact on the ICER by increasing it to €32,106/QALY for 1 year. The model was sensitive to the number of medical visits per month for patients treated with nalmefene (when increased by 25% the ICER increased to €10,578/QALY), year 1 QALY (AUC utility) gain with psychosocial support (when decreased by 5% the ICER increased to €17,575/QALY), year 1 QALY (AUC utility) gain with nalmefene (when decreased by 5% the ICER increased to €18,035/QALY) and the number of medical visits for pyschosocial support (when increased by 25% the ICER increased to €9,968/QALY). The probability of cost effectiveness at a threshold of €45,000 is 100%.

8. The annual drug treatment costs based on full pack monthly dispensing would be €1,425 (i.e. patient would take nalmefene every day). The company have assumed that approximately 50% of the total amount of drug will be used (i.e. patients will only take nalmefene on 50% of days) and have therefore estimated the annual treatment costs to be less at €800.50 on GMS scheme. The company have estimated that in 2014 there will be 518 new patients

started on nalmefene, increasing to 1,048 in 2015, 1,724 in 2016, 2.281 in 2017 and 2,716 in 2019. The gross budget impact (BI) based on approx 50% usage (daily usage (100% usage) was calculated by the NCPE and in brackets) is estimated to be €419,303 (€748,755) in 2014, €848,669 (€1,515,481) in 2015, €1,395,637 (€2,492,208) in 2016, €1,846,964 (€3,298,150) in 2017 and €2,198,974 (€3,926,739) in 2018. A net drug BI was not presented but it is unlikely that this product will displace other pharmacological treatments.

9. One of the key uncertainties for this product is whether the benefit from the trial will be reproduced in the real life setting. This is primarily due to the lack of provision of formal psychosocial intervention as a treatment in Ireland. The NCPE consider this to be a cost effective product for the defined patient population and in combination with psychosocial intervention.