NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Final Appraisal Determination

Naltrexone for the management of opioid dependence

1 Guidance

1.1 Naltrexone is recommended as a treatment option in detoxified formerly opioid-dependent people who are highly motivated to remain in an abstinence programme.

1.2 Naltrexone should only be administered under adequate supervision to people who have been fully informed of the potential adverse effects of treatment. It should be given as part of a programme of supportive care.

1.3 The effectiveness of naltrexone in preventing opioid misuse in people being treated should be reviewed regularly. Discontinuation of naltrexone treatment should be considered if there is evidence of such misuse.

2 Clinical need and practice

2.1 The term ‘opioids’ refers to opiates and other semi-synthetic and synthetic compounds with similar properties. Opiates are a group of psychoactive substances derived from the poppy plant that include opium, morphine and codeine. The term ‘opiate’ is also used for the semi-synthetic drug diamorphine (heroin), which is produced from poppy compounds. Opioid dependence can cause a wide range of health problems and is often associated with misuse of other drugs (including alcohol). Diamorphine is the most widely misused opiate, and its misuse can lead to accidental overdose. Injecting diamorphine may also be associated with the spread of blood-borne viruses, such as HIV and hepatitis B or C. The mortality risk of people dependent on illicit diamorphine is estimated to be around 12 times that of the

general population. Psychiatric comorbidity – particularly anxiety, but also affective, antisocial and other personality disorders – is common among opioid-dependent people.

2.2 Associated social problems include marital and relationship breakdown, unemployment, homelessness, and child neglect, which often results in children being taken into the care system. There is also a clear association between illicit drug use and crime. Some opioid-dependent people become involved in crime to support their drug use. It is estimated that half of all recorded crime is drug related, with associated costs to the criminal justice system in the UK estimated at £1 billion per annum in 1996.

2.3 Biological, psychological, social and economic factors influence when and why a person starts taking illicit opioids. Use of opioids can quickly escalate to misuse (repeated use despite adverse consequences) and then dependence (opioid tolerance, withdrawal symptoms, compulsive drug-taking). The 'Diagnostic and statistical manual of mental disorders' (fourth edition; DSM-IV) defines dependence as 'a maladaptive pattern of substance use, leading to clinically significant impairment or distress'. Dependence syndrome has been defined in the 'International statistical classification of diseases and related health problems' (10th revision; ICD-10) as a 'cluster of behavioural, cognitive, and physiological phenomena that develop after repeated substance use and that typically include a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal state'. Physical and psychological dependence can develop within a relatively short period of continuous use (2–10 days), and is characterised by an overwhelming need to continue taking the drug in order to avoid withdrawal symptoms such as sweating, anxiety, muscle tremor, disturbed sleep, loss of appetite, and raised heart rate, respiratory rate and blood pressure. The body also becomes tolerant of the effects of opioids and the dose needs to be

increased to maintain the effect. Getting the next dose can become an important part of each day and can take over a person's life. It is difficult to stop using these drugs and remain abstinent because the person experiences a combination of craving, unpleasant withdrawal symptoms, and the continuation or worsening of personal circumstances that led to opioid misuse in the first place.

2.4 When a person manages to remain abstinent, it may be after repeated cycles of cessation and relapse, with extensive treatment histories spanning decades. Nevertheless, some dependent people may make dramatic changes in their drug use without formal treatment. The histories of people using illicit diamorphine who attend treatment services suggest that most people develop dependence in their late teens and early twenties, several years after their first use of illicit opioids, and continue use over the next 10–20 years. Treatment can alter the natural history of opioid dependence, most commonly by prolonging periods of abstinence from illicit opioid misuse, allowing health and social circumstances to improve.

2.5 National estimates, which combine local prevalence data and routinely available indicator data, suggest that in the UK the prevalence of problem drug use is 9.35 per 1000 of the population aged 15–64 years (360,811 people), and that 3.2 per 1000 (123,498 people) inject drugs. The National Drug Treatment Monitoring System (NDTMS) estimates that in 2004–05 there were 160,450 people in contact with drug treatment services in England. Most of the people in treatment were dependent on opioids. There are about 40,000 people in prison in England and Wales at any time who misuse illicit drugs. In one UK survey, 21% of prisoners had used illicit opioids at some point during their sentence, and 10% had used illicit opioids during the previous week.

2.6 The UK has a range of treatment services for opioid dependency. Pharmacological and psychosocial interventions are provided in the

community and the criminal justice system, and include inpatient, residential, day-patient and outpatient services.

2.7 The interventions used for opioid-dependent people range from needle exchange to maintenance therapy and abstinence. Pharmacological treatments are broadly categorised as maintenance (also known as 'substitution' or 'harm reduction' therapies), detoxification, or abstinence. The aims of the maintenance approach are to provide stability by reducing craving and preventing withdrawal, eliminating the hazards of injecting and freeing the person from preoccupation with obtaining illicit opioids, and to enhance overall function. To achieve this, a substitution opioid regimen (a fixed or flexible dose of methadone or buprenorphine to reduce and stop illicit use) is prescribed at a dose higher than that required merely to prevent withdrawal symptoms. The aim is for people who are dependent on illicit opioids to progress from maintenance to detoxification and then abstinence (when a person has stopped taking opiods). All detoxification programmes require relapse prevention strategies and psychological support after detoxification because relapse rates are high. Some people can rapidly achieve total abstinence from opioids; others require the support of prescribed medication for longer than a few months. The opioid antagonist naltrexone can be used to help maintain abstinence.

2.8 Psychosocial and behavioural therapies play an important role in the treatment of drug misuse. They aim to give people the ability to resist drug misuse and cope with associated problems. For opioid-dependent people, these therapies are often an important adjunct to pharmacological treatments.

2.9 The government's 'Drug strategy' (2004) aims to reduce the harm caused by illicit drugs by:

- increasing the number of people entering drug treatment programmes through the criminal justice system
- reducing the use of Class A and illicit drugs by people under the age of 25
- increasing enrolment in drug treatment programmes.

2.10 In England, naltrexone treatment accounts for 11,000–14,000 prescriptions per annum and a total annual drug cost of less than £500,000. The majority of naltrexone prescriptions are for opioid dependence, although naltrexone can also be used to treat alcohol dependence and other conditions.

3 The technology

3.1 Naltrexone (Nalorex, Bristol-Myers Squibb Pharmaceuticals Ltd) is an opioid antagonist with a high affinity for opioid receptors. It competitively displaces opioid agonists (for example, diamorphine or methadone), blocking the euphoric and other effects of opioids and thereby minimising the positive rewards associated with their use. The 'Summary of product characteristics' (SPC) states that naltrexone is licensed for use as an adjunctive prophylactic treatment for detoxified formerly opioid-dependent people (who have remained opioid free for at least 7–10 days). There are unlicensed long-lasting formulations of naltrexone in development (depot preparations and implants), but these do not fall within the scope of this appraisal.

3.2 Naltrexone is rapidly absorbed, metabolised by the liver and excreted in the urine with an elimination half-life of 4 hours. Liver function tests are recommended before and during naltrexone treatment to check for liver impairment. The SPC states that 'caution should be observed in administering the drug to patients with impaired hepatic or renal function'.

3.3 Naltrexone is associated with opioid withdrawal symptoms if people are opioid dependent. The SPC recommends challenge testing with naloxone hydrochloride (a shorter-acting injectable opioid antagonist) to screen for the presence of opioids if it is not certain whether the person is detoxified. People may be at risk of a fatal overdose caused by respiratory depression if they relapse while taking naltrexone. This can happen if the person tries a larger dose of diamorphine to achieve euphoria, or if they return to diamorphine use after naltrexone treatment, because of loss of tolerance to diamorphine. For full details of side effects and contraindications, see the SPC.

3.4 The cost of naltrexone is £1.52 per 50-mg tablet excluding VAT ('British national formulary' [BNF], edition 51). People should receive 25 mg naltrexone on day 1 followed by 50 mg daily thereafter for an initial period of 3 months. However, extended treatment may be necessary because time to full recovery from opioid dependence is variable. A three-times-a-week dosing schedule may be considered if it is thought likely to improve compliance with treatment. Costs may vary in different settings because of negotiated procurement discounts.

4 Evidence and interpretation

The Appraisal Committee (appendix A) considered evidence from a number of sources (appendix B).

4.1 Clinical effectiveness

4.1.1 The review identified 17 studies of the clinical effectiveness of naltrexone treatment: 1 systematic review (Cochrane review), 13 randomised controlled trials (RCTs) and 3 non-randomised comparative studies. None of the studies were conducted in the UK. The length of follow-up varied in the RCTs from 20 days to 1 year. The RCTs and comparative studies evaluated the effectiveness of naltrexone treatment in a total of 1269 people and reporting was of poor quality (for example, randomisation was not adequately reported in most RCTs). Two of the RCTs were conducted in a prison setting (parolees or probationers), and seven included various psychosocial therapies in both arms of the trials (for example, twice-weekly drug counselling, psychotherapy and behavioural therapy).

4.1.2 In addition to the 17 studies of the clinical effectiveness of naltrexone treatment, 9 RCTs studied the effectiveness of different strategies to improve retention on naltrexone treatment. Three of these RCTs assessed reward with incentive vouchers for treatment compliance (one also included relationship counselling), four RCTs evaluated psychosocial therapies and two RCTs examined the effectiveness of pharmaceutical agents. These were of poor to

moderate quality (the methods of randomisation were not adequately described and intention-to-treat analyses were not performed in most of the trials).

4.1.3 The main effectiveness outcomes reported in the RCTs were retention, relapse rates (opioid use) and re-incarceration of parolees or probationers.

Effectiveness of naltrexone compared with control treatment

4.1.4 Retention on treatment was reported in the Cochrane review and seven RCTs. The Cochrane review showed no significant difference in retention for people treated with naltrexone and adjunctive psychosocial therapy compared with psychosocial therapy alone (risk ratio [RR] 1.08; 95% confidence interval [CI], 0.74 to 1.57). Six of the seven RCTS (three of which included adjunctive psychosocial therapy in each arm) reported no significant difference in retention with naltrexone treatment. One trial reported a significant improvement in retention on naltrexone treatment compared with psychosocial therapy (RR 0.66; 95% CI, 0.43 to 0.93). A fixed-effect meta-analysis of all seven RCTs conducted by the Assessment Group showed no difference in retention on treatment with naltrexone, with a RR of stopping treatment of 0.94 (95% CI, 0.84 to 1.06) and a hazard ratio (HR) from five RCTs of 0.90 (95% CI, 0.69 to 1.17). However, a fixed-effects model was not the most appropriate method of meta-analysis because heterogeneity between trials was found. A random-effects meta-analysis gave a RR of stopping treatment of 0.90 (95% CI, 0.55 to 1.48).

4.1.5 Relapse rates (assessed by the presence of opioids in urine samples) were reported in the Cochrane review and six RCTs. The Cochrane review showed a significant reduction in illicit diamorphine use (RR 0.72; 95% CI, 0.58 to 0.90). Of the six RCTs that reported relapse rates, three included adjunctive psychosocial therapy in each arm. Five of the six RCTs reported no statistically significant differences in relapse rates with naltrexone treatment. One RCT reported a statistically significant improvement in relapse rates with

naltrexone treatment (RR 0.41; 95% CI, 0.21 to 0.74). Pooled analysis of relapse rates in the six RCTs showed a statistically significant reduction in the risk of opioid use with naltrexone compared with placebo; the RR of relapse was 0.72 (95% CI, 0.58 to 0.90), with a HR of 0.53 (95% CI, 0.34 to 0.82) and a number needed to treat (NNT) of eight people to prevent one opioid relapse. One trial reported the number of people who were opioid free as a proportion of people retained on treatment. This trial showed no difference in the number of opioid-free people treated with naltrexone compared with psychosocial therapy over 26 weeks (statistical significance was not reported).

4.1.6 Two small RCTs reported re-incarceration rates of parolees or probationers having naltrexone treatment compared with placebo, with adjunctive psychosocial therapy in each arm. Pooled analysis showed a significant reduction in re-incarceration in favour of naltrexone (RR 0.50; 95% CI, 0.27 to 0.91).

4.1.7 Mortality was not reported in any of the trials. A retrospective study in the USA examined the number of deaths in people who had received naltrexone treatment over a period of 2 years (n = 1196) and in people who had not received naltrexone treatment (total number not reported). Diamorphine overdose resulted in 21 out of 33 (64%) deaths in the naltrexone group and 71 out of 96 (74%) deaths in people not being treated with naltrexone.

4.1.8 The National Coronial Information Service reported 32 naltrexone-related deaths in the period from 2000–2003 in Australia. The mortality rate was estimated at 1 per 100 person years during naltrexone treatment and 22.1 per 100 person years during the first 2 weeks post treatment.

4.1.9 Nine RCTs evaluated the effectiveness of different strategies to increase retention on naltrexone treatment (incentive vouchers, psychosocial therapy and pharmaceutical agents). The length of follow-up in these trials ranged from 12 to 52 weeks. Pooled analysis of the effect of adjunctive psychosocial therapies on compliance with naltrexone treatment in six trials reported a

significant improvement of 19% with adjunctive psychosocial therapy compared with naltrexone treatment alone.

4.1.10 In summary, the small evidence base reported conflicting results. The quality of the studies was poor and randomisation was not adequately reported in RCTs. One trial reported a significant improvement in retention and relapse rates with naltrexone treatment, but the majority of RCTs reported no significant difference between naltrexone and control treatment. When the results from these trials were pooled, naltrexone was associated with a significant reduction in relapse, but not a difference in retention on treatment compared with control treatment. Adverse events reported in two trials showed no difference in mortality between naltrexone and control treatment. Although useful data for the comparison of adverse events were not reported in the majority of the RCTs, mortality data from the USA showed no difference in mortality rates with naltrexone compared with non-naltrexone treatment.

4.2 Cost effectiveness

4.2.1 No published economic evaluations of the cost effectiveness of naltrexone treatment were identified. The manufacturer did not submit evidence for this appraisal.

4.2.2 The Assessment Group developed a decision analytical model to assess the cost effectiveness of naltrexone plus psychosocial support compared with placebo plus psychosocial support (psychosocial support alone). The model estimated costs and outcomes from a National Health Service (NHS) perspective. Costs were based on estimates of resource use including a daily dose of 50 mg naltrexone, counselling sessions, monitoring of treatment, GP visits, emergency department visits, inpatient hospital stays, outpatient mental health appointments and inpatient mental health admissions. The time horizon of the model was limited to 12 months. This was because of the length of follow-up in the trials, and clinical advice that people are not retained on naltrexone treatment in the long term.

4.2.3 Data on retention on treatment at 2, 6, 13 and 25 weeks and 12 months were included in the model. Data on this endpoint for naltrexone (with or without psychosocial therapy) compared with placebo treatment (with or without psychosocial therapy) was based on the meta-analysis of five RCTs (pooled HR 0.90; 95% CI, 0.69 to 1.17). This HR was applied to the survival curve for naltrexone treatment to generate an estimate of retention on psychosocial treatment alone. Data on the proportion of opioid-free people retained on treatment was based on a single RCT, which reported little difference between the naltrexone arm (84% opioid-free people) and the control arm (86% opioid-free people). Data from the 'National treatment outcome research study' (NTORS) were used to inform the proportion of drug-taking people who were injecting or not injecting.

4.2.4 Health outcomes were expressed as quality adjusted life years (QALYs). In the absence of published data on quality of life associated with drug misuse, the Assessment Group obtained health-related utility data from a panel of members of the public. Average QALYs were calculated for people retained on naltrexone treatment and psychosocial therapy, people retained on psychosocial therapy alone, and people not retained on treatment. People retained on naltrexone treatment gained fewer QALYs than those retained on control treatment, based on evidence from one RCT that showed that a higher number of people relapsed on naltrexone. The total QALYs associated with each treatment arm were then determined by different retention rates.

4.2.5 The base-case analysis demonstrated that naltrexone plus psychosocial therapy is associated with an incremental cost-effectiveness ratio (ICER) of £42,500 per QALY gained. This is based on the assumption of a slightly higher (non-significant) proportion of people relapsing with naltrexone plus psychosocial therapy compared with psychosocial therapy alone.

4.2.6 Data on the proportions of opioid-free people in each arm of the model was based on one trial. A one-way sensitivity analysis that assumed the same

proportion of people taking opioids in both arms reduced the ICER to £34,600 per QALY gained.

4.2.7 A probabilistic sensitivity analysis around the base-case analysis was also undertaken. The probability of naltrexone being cost effective does not rise much above 50%, regardless of the willingness to pay for an additional QALY. This is because of the uncertainty in the estimates of clinical effectiveness reported in the RCTs.

4.2.8 An analysis that included the costs of the criminal justice system and victims of crime was also performed. Costs to victims of crime included the costs of increased security measures and the direct costs of material or physical damage. The results of this analysis found that naltrexone plus psychosocial therapy dominates psychosocial therapy alone because it is less costly and more effective. The dominance of naltrexone therapy is driven by the reduction in costs to the victims of crime in the naltrexone arm, because of the increased retention on treatment and the associated reduction in crime. A one-way sensitivity analysis that excluded the costs to the victims resulted in an ICER of approximately £51,000 per QALY.

4.3 Consideration of the evidence

4.3.1 The Committee reviewed the data available on the clinical and cost effectiveness of naltrexone, having considered evidence on the nature of the condition and the value placed on the benefits of naltrexone by people who are dependent on opioids, those who represent them, and clinical experts. It was also mindful of the need to take account of the effective use of NHS resources.

4.3.2 The Committee was persuaded of the likely clinical effectiveness of naltrexone as a disincentive for opioid use in people following detoxification because of their understanding of the pharmacological basis of its action; that is, naltrexone blocks the receptors responsible for the euphoric effects of opioids.

4.3.3 The Committee considered the quality and outcomes of the RCTs. The Committee heard from clinical experts that the most important effectiveness outcome for naltrexone treatment is relapse prevention (continued abstinence from taking illicit opioids). Experts advised that retention on treatment is problematic as an outcome of effectiveness because it is primarily a measure of treatment compliance (taking naltrexone medication) and noted that people who do not wish to remain in contact with drug treatment services may still be compliant in taking naltrexone. The Committee noted that most of the studies showed that naltrexone therapy resulted in no significant difference in retention on treatment, although pooled analysis of the RCTs showed a lower rate of relapse to illicit opioid use compared with control treatment. The Committee was persuaded by the experts' testimony that, in clinical practice, naltrexone therapy was often associated with dramatic improvements in abstinence from opioid use, which is the principal aim of treatment. The Committee considered that mortality in people retained on naltrexone treatment was likely to be reduced specifically because of the lower relapse rate to illicit opioid use. The Committee additionally concluded that the reduction in opioid use could lead to substantial improvements in overall quality of life for those people retained on naltrexone treatment.

4.3.4 The Assessment Group and experts raised concerns regarding the external generalisability of the RCTs, none of which were conducted in the UK and which involved people with differing patterns of opioid misuse. The Committee heard from experts that naltrexone is usually only prescribed following an initial clinical assessment for people who are highly motivated to remain in an abstinence programme, who have been fully informed of the potential adverse effects and the benefits of treatment, and for whom an abstinence programme is judged to be appropriate based on initial clinical assessment. Experts also noted that none of the RCTs were conducted in the UK, and the degree of supervision of naltrexone administration was likely to be variable, whereas adequate supervision is currently recommended as best clinical practice in the UK. The Committee was persuaded that close monitoring is particularly

important when naltrexone treatment is initiated because of the higher risk of fatal overdose at this time. In addition, the Committee understood that discontinuation of naltrexone may be associated with an increase in inadvertent overdose from illicit opioids. The Committee therefore considered that supervision of naltrexone administration is important for continued compliance with medication, in order to maximise retention on treatment and abstinence from illicit opioid use, and to minimise the adverse effects of treatment. The Committee was also aware of two uncontrolled studies that reported higher effectiveness of naltrexone in highly motivated people. The Committee was convinced that effectiveness outcomes for retention on treatment and abstinence from opioid use are likely to be higher in clinical practice than reported in the RCTs, because treatment is targeted to motivated people who have expressed a preference for an abstinence programme. The Committee concluded that adequate supervision of treatment is likely to lead to further improvements in the effectiveness of naltrexone treatment over and above that seen in the RCTs.

4.3.5 The Committee considered the personal statements and testimonies of patient experts on the adverse effects of naltrexone treatment. The Committee heard that people taking naltrexone often experience adverse effects of unease (dysphoria), depression and insomnia, which can lead to relapse to illicit opioid use while on naltrexone treatment, or failure to continue on treatment. Experts advised that adverse effects may be caused by either withdrawal from illicit drugs or by the naltrexone treatment itself, and stressed the importance of prescribing naltrexone as part of a care programme that includes psychosocial therapy and general support. The Committee noted the importance of patients and carers being fully informed of the potential adverse effects as well as the benefits of naltrexone treatment, and considered psychosocial therapy to be instrumental in some people remaining on naltrexone treatment.

4.3.6 The Committee considered the uncertainties relating to the external generalisability of the effectiveness evidence used in the economic model and the consequent uncertainties in interpreting the ICERs. The Assessment Group advised that for the purpose of economic modelling, the rate of relapse to illicit opioids used in their assessment was based on a small study that reported no significant difference in relapse rates between naltrexone and control treatment. The Committee noted that this was contrary to the pooled analysis of relapse rates reported in three RCTs (HR 0.53; 95% CI, 0.34 to 0.82), which showed a significant reduction in relapse with naltrexone compared with control treatment. The Committee concluded that the model may have underestimated the reduction in relapse to opioid use, and therefore also underestimated the cost effectiveness of naltrexone treatment on the basis of potential improvements in both quality of life and mortality.

4.3.7 The Committee further considered the base (reference) case ICER of £42,500 per QALY for adjunctive naltrexone treatment plus psychosocial therapy compared with psychosocial therapy alone. The Committee considered that this ICER was based on data on the effectiveness of adjunctive naltrexone treatment compared with psychosocial therapy alone in a general population of drug misusers. The Committee was persuaded that this ICER was a conservative figure that underestimated the cost effectiveness of naltrexone in people who were highly motivated to remain abstinent and who were enrolled in a supervised treatment programme. The Committee was persuaded that for these people, the ICER for naltrexone treatment would be substantially lower than the base case, principally because of the factors outlined in sections 4.3.4 and 4.3.6.

4.3.8 In summary, the Committee was convinced of the clinical effectiveness of naltrexone treatment in a selected, highly motivated group of people. The Committee concluded that for people who preferred an abstinence programme, who were fully informed of the potential adverse effects and

benefits of treatment, and who were highly motivated to remain on treatment, naltrexone treatment would fall within acceptable cost-effectiveness limits.

5 Implementation

5.1 The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health' issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by NICE technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.

5.2 'Healthcare Standards for Wales' was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.

5.3 NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/TAXXX). *[Note: tools will be available when the final guidance is issued]*

6 Recommendations for further research

6.1 None.

7 Related guidance

7.1 NICE is in the process of producing the following guidance.

Community-based interventions to reduce substance misuse among the most vulnerable and disadvantaged young people. *NICE public health intervention guidance* (publication expected February 2007).

Drug misuse: opiate detoxification management of drug misusers in the community and prison settings. *NICE clinical guideline.* Publication expected July 2007.

Drug misuse: psychosocial management of drug misusers in the community and prison settings. *NICE clinical guideline.* Publication expected July 2007.

Methadone and buprenorphine for the management of opioid dependence. *NICE technology appraisal.* Publication expected March 2007.

8 Review of guidance

8.1 The review date for a technology appraisal refers to the month and year in which the Guidance Executive will consider whether the technology should be reviewed. This decision will be taken in the light of information gathered by the Institute, and in consultation with consultees and commentators.

8.2 The guidance on this technology will be considered for review in March 2010.

David Barnett
Chair, Appraisal Committee
October 2006

Appendix A. Appraisal Committee members and NICE project team

A. Appraisal Committee members

The Appraisal Committee is a standing advisory committee of the Institute. Its members are appointed for a 3-year term. A list of the Committee members who took part in the discussions for this appraisal appears below. The Appraisal Committee meets twice a month except in December, when there are no meetings. The Committee membership is split into three branches, with the chair, vice-chair and a number of other members attending meetings of both branches. Each branch considers its own list of technologies and ongoing topics are not moved between the branches.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each Appraisal Committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Dr Darren Ashcroft
Senior Clinical Lecturer, School of Pharmacy and Pharmaceutical Sciences, University of Manchester

Professor David Barnett
Professor of Clinical Pharmacology, University of Leicester

Dr Peter Barry
Consultant in Paediatric Intensive Care, Leicester Royal Infirmary

Mr Brian Buckley
Lay Member

Professor John Cairns

Public Health and Policy, London School of Hygiene and Tropical Medicine

Professor Mike Campbell

Statistician, University of Sheffield

Professor David Chadwick

Professor of Neurology, Walton Centre for Neurology and Neurosurgery, Liverpool

Dr Mark Chakravarty

Industry Member

Dr Peter I Clark

Consultant Medical Oncologist, Clatterbridge Centre for Oncology, Merseyside

Dr Mike Davies

Consultant Physician, University Department of Medicine & Metabolism, Manchester Royal Infirmary

Mr Richard Devereaux-Phillips

Industry Member

Professor Jack Dowie

Health Economist, London School of Hygiene

Dr Fergus Gleeson

Consultant Radiologist, The Churchill Hospital, Oxford

Ms Sally Gooch

Independent Healthcare Consultant

Mr Sanjay Gupta

Stroke Services Manager, Basildon and Thurrock University Hospitals NHS Trust

Professor Philip Home

Professor of Diabetes Medicine, University of Newcastle upon Tyne

Dr Peter Jackson

Clinical Pharmacologist, University of Sheffield

Professor Peter Jones

Professor of Statistics & Dean Faculty of Natural Sciences, Keele University

Dr Mike Laker

Medical Director, Newcastle Hospitals NHS Trust

Dr George Levvy

Chief Executive, Motor Neurone Disease Association, Northampton

Ms Rachel Lewis

Nurse Advisor to the Department of Health

Mr Terence Lewis

Lay Member

Professor Jonathan Michaels

Professor of Vascular Surgery, University of Sheffield

Dr Neil Milner

General Medical Practitioner, Sheffield

Dr Ruairidh Milne

Senior Lecturer in Health Technology Assessment, National Coordinating Centre for Health Technology

Dr Rubin Minhas

General Practitioner, CHD Clinical Lead, Medway PCT

Dr Rosalind Ramsay

Consultant Psychiatrist, Adult Mental Health Services, Maudsley Hospital, London

Mr Miles Scott

Chief Executive, Bradford Teaching Hospitals NHS Foundation Trust

Dr Lindsay Smith

General Practitioner, East Somerset Research Consortium

Mr Roderick Smith

Director of Finance, Adur, Arun and Worthing PCT

Dr Ken Stein

Senior Lecturer, Peninsula Technology Assessment Group (PenTAG), University of Exeter

Professor Andrew Stevens

Professor of Public Health, University of Birmingham

The following individual(s) representing the National Collaborating Centre for Mental Health, which is responsible for developing the Institute's clinical guidelines on detoxification and psychosocial interventions for drugs misuse, were invited to attend the ACD meeting as observers and to contribute as advisers to the Committee.

- Dr Clare Gerada, Royal Collage of General Practitioners, Chair of the Guideline Development Group on drug misuse (detoxification)
- Professor John Strang, Professor of Psychiatry of Addictions, National Addiction Centre (Institute of Psychiatry), Chair of the Guideline Development Group on drug misuse (psychosocial management)
- Mr Steve Pilling, Director, National Collaborating Centre for Mental Health

B. NICE Project Team

Each technology appraisal is assigned to a team consisting of one or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Eleanor Donegan
Technical Lead

Louise Longworth
Technical Adviser

Emily Marschke
Project Manager

Appendix B. Sources of evidence considered by the Committee

A The assessment report for this appraisal was prepared by West Midlands Health Technology Assessment Collaboration.

- Burls A, Yaser A, Juarez-Garcia A et al (2006). Oral naltrexone as a treatment for relapse prevention in formerly opioid dependent drug users – a systematic review and economic evaluation. *West Midlands Health Technology Assessment Collaboration*.

B The following organisations accepted the invitation to participate in this appraisal. They were invited to make submissions and comment on the draft scope, assessment report and appraisal consultation document. Consultee organisations have the opportunity to appeal against the final appraisal determination (FAD).

I Manufacturers/sponsors:

- Bristol-Myers Squibb Pharmaceuticals Ltd

II Professional/specialist and patient/carer groups:

- Addiction
- Addiction Recovery Foundation
- ADFAM
- Alliance (formerly the Methadone Alliance)
- Association of Nurses in Substance Abuse (ANSA)
- British Association for Psychopharmacology
- Families Anonymous
- Federation of Drug and Alcohol Professionals
- Lifeline

- National Drug Prevention Alliance
- National Pharmaceutical Association
- Pharmaceutical Services Negotiating Committee
- Rehabilitation for Addicted Prisoners Trust (RAPt)
- Release
- Royal College of General Practitioners
- Royal College of Nursing
- Royal College of Physicians
- Royal College of Physicians of Edinburgh
- Royal College of Psychiatrists
- Royal Pharmaceutical Society
- Specialist Clinical Addiction Network (SCAN)
- Substance Misuse Management in General Practice (SMMGP)
- UK Harm Reduction Alliance
- Turning Point

III Consultee (others)

- Department of Health
- East Leeds PCT
- Great Yarmouth PCT
- Welsh Assembly Government

IV Commentator organisations (without the right of appeal):

- Action on Addiction
- British National Formulary
- Centre for Research on Drugs and Health Behaviour (Imperial College)

- Department of Addictive Behaviour (St George's Hospital Medical School)
- DrugScope
- Drugs Misuse – Psychosocial Guidelines Development Group
- Drugs Misuse – Detoxification Guidelines Development Group
- HM Prison Service
- Independent Drug Monitoring Unit (IDMU)
- National Addiction Centre (Institute of Psychiatry)
- National Coordinating Centre for Health Technology Assessment
- National programme on substance abuse deaths, St George's Hospital Medical School
- National Treatment Agency for Substance Misuse (NTA)
- NHS Confederation
- NHS Purchasing and Supplies Agency
- NHS Quality Improvement Scotland
- Society for the Study of Addiction
- West Midlands Health Technology Assessment Collaboration

C The following individuals were selected from clinical specialist and patient advocate nominations from the professional/specialist and patient/carer groups. They participated in the Appraisal Committee discussions and provided evidence to inform the Appraisal Committee's deliberations. They gave their expert personal view on naltrexone for the management of opioid dependence by attending the initial Committee discussion and/or providing written evidence to the Committee. They were also invited to comment on the ACD.

- Dr Chris Ford, GP Clinical Lead, nominated by Substance Misuse Management in General Practice (SMMGP) – clinical specialist
- Dr Judith Myles, Consultant Psychiatrist, nominated by Royal College of Psychiatrists – clinical specialist

- Dr Duncan S Raistrick, Consultant in Addiction Psychiatry, nominated by Specialist Clinical Addiction Network (SCAN) –,clinical specialist
- Mr Peter McDermott, nominated by The Alliance – patient expert
- Ms Moya Pinson, nominated by Release – patient expert
- Mr Gary Sutton, Head of Drug Advice Team, nominated by Release – patient expert