NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Overview

Naltrexone for the management of opioid dependence

The overview is written by members of the Institute's team of technical analysts. It forms part of the information received by the Appraisal Committee members before the first committee meeting. The overview summarises the evidence and views that have been submitted by consultees and evaluated by the Assessment Group, and highlights key issues and uncertainties. A list of the sources of evidence used in the preparation of this document is given in appendix A.

1 Background

1.1 The condition

Opioid dependence can cause a wide range of health problems and is often associated with simultaneous misuse of a number of drugs (including alcohol). Opioids are a group of psychoactive substances derived from the poppy plant that includes opium, morphine, codeine, and others. The term 'opiate' is also used for the semi-synthetic drug heroin that is produced from poppy compounds. The term 'opioids' refers to opiates and other semi-synthetic and synthetic compounds with similar properties. Heroin is the most widely misused opiate and dependence on illicit heroin can cause a number of other physical problems as a result of the spread of blood borne viruses (for example, HIV and hepatitis) and the risk of an accidental overdose. Injecting drug users may be exposed to blood-borne infections through the sharing of infected needles, syringes or other injecting paraphernalia. The mortality risk of individuals dependent on heroin is estimated to be around 12 times that of the general population. Psychiatric comorbidity is common in opioid-

dependent populations, particularly anxiety, and affective, antisocial and other personality disorders.

Associated social problems include marital and relationship breakdown, unemployment and homelessness and child neglect, often resulting in children being taken into the care system. There is also a clear association between illicit drug use and crime, although this link can arise in several ways. Many opioid-dependent individuals become involved in crime to support their drug use, but crime may also provide the money and the contacts to buy drugs. It is estimated that half of all recorded crime is drug related, with associated costs to the criminal justice system in the UK estimated as reaching £1 billion per annum in 1996. However, the majority of those who steal to buy drugs were involved in crime before their drug use became a problem for them.

Biological, psychological, social and economic factors influence when and why a person starts taking opioids. Opioid use quickly escalates to misuse (repeated use with adverse consequences) and then dependence (opioid tolerance, withdrawal symptoms, compulsive drug-taking).Dependence has been defined in the Diagnostic and Statistical Manual (DSM) as a maladaptive pattern of substance use, leading to clinically significant impairment or distress. 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, blood pressure and temperature). The body also becomes tolerant to the effects of opioids and therefore the dose needs to be increased to maintain the effect. Getting the next dose can become an important part of each day and may take over people’s lives. It is difficult to stop using these drugs and remain abstinent due to a combination of craving, unpleasant withdrawal symptoms, and the continued or worsening personal circumstances that led to drug use in the first place.

When a dependent opioid user manages to become abstinent, there are usually repeated cycles of cessation and relapse, with extensive treatment

histories extending over decades. Nevertheless, some dependent users may make dramatic changes in their drug use without recourse to formal treatment. The natural histories of heroin users attending treatment services suggest that most individuals develop dependence in their late teens and early twenties, several years after their first use of heroin, 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.

National prevalence estimates, which combine local prevalence data and routinely available indicator data, suggest that in the UK problem drug use is 9.35 per 1000 of the population aged 15–64 years (360,811 people), with 3.2 per 1000 (123,498 people) injecting. The National Drug Treatment Monitoring System (NDTMS) 2004–5 estimates that there were 160,450 people in contact with treatment services in England. As a result of the lack of substitute medications for other drugs (such as crack cocaine and alcohol) the majority of these were dependent on opioids. Data suggest that approximately 70% of people newly presenting for treatment were male. There are approximately 40,000 drug misusers in prison in England and Wales at any one time. In one UK survey, 21% of prisoners had used opiates at some point during their sentence, and 10% of prisoners during the previous week.

1.2 Current management

The UK has a range of treatment services for opioid dependency. Medical and psychosocial interventions are provided in the community and criminal justice system and include inpatient, residential, day-patient and outpatient settings.

There are two broad strategies for the treatment of opiate dependence; maintenance (also known as harm reduction and a substitution regimen), and abstinence (also known as detoxification and withdrawal). In abstinence treatment for opioid drug misuse, an individual who is physically dependent on that drug stops taking it. Individuals receiving treatment may decide to become abstinent, or may initially receive maintenance therapy with a long acting opioid substitute (methadone or buprenorphine) and then progress to abstinence therapy. Maintenance of abstinence can be aided by the use of the opioid antagonist naltrexone.

Various psychosocial (or behavioural) therapies are often given as part of abstinence and maintenance strategies and aim to give patients the skills for resisting substance use and coping with related problems. These include relapse prevention; and cognitive, dynamic, group, and aversion therapies.

Relapse prevention highlights important concepts and techniques, for example identification and avoidance of high-risk situations, understanding the chain of decisions leading to drug use, and changing one's lifestyle. Cognitive therapy helps individuals to identify complex behaviours and thought processes central to drug misuse, such as positive and negative drug-related beliefs and spontaneous flash backs to situations immediately before giving in to the actual drug use. Dynamic psychotherapy helps people to become aware of underlying unconscious psychological conflicts at the root of drug misuse and develop coping mechanisms and healthier methods of resolving intrapsychic conflict. Group therapy targets the social stigma attached to substance misuse with other group members providing support and suggesting alternative methods of maintaining abstinence. Narcotics Anonymous (NA), a form of group therapy, is based on principles similar to those of Alcoholics Anonymous (AA), including progression through 12 steps of recovery. Some patients have difficulty engaging in the AA/NA approach to recovery; however, these programmes do help some people and can provide much-needed support for those attempting abstinence. Aversion therapy involves pairing aversive stimuli with cognitive images of opioid use and conversely inducing images of socially appropriate behaviours such as employment and education with non-drug-related behaviour.

Psychosocial and behavioural therapies play an important role in the treatment of drug misusers; the therapies aim to give patients the ability to resist substance use and cope with problems related to drug use. For opiate users they are often an important adjunct to pharmacological treatments. A NICE clinical guideline due for publication in July 2007 will evaluate the place of psychosocial interventions in the treatment of drug misuse.

The government's 'Drug strategy' (2004) aims to reduce the harm caused by illegal drugs (including treatment through the criminal justice system), increase enrolment in drug treatment programmes, and reduce the use of class A and illicit drugs.

2 The technology

Table 1 Summary description of naltrexone

Generic name	Naltrexone hydrochloride
Proprietary name	Nalorex
Manufacturer	Bristol-Myers Squibb Pharmaceuticals Ltd
Dose	25 mg initially and then 50 mg/day
Acquisition cost excluding VAT ('BNF' edition 51)	£1.52 per 50-mg tablet

Naltrexone is licensed as an adjunctive prophylactic therapy for use in detoxified formerly opioid-dependent patients (who have remained opioid-free for at least 7–10 days). Patients are initially treated (on day one) with 25 mg followed by 50 mg daily thereafter for an initial period of 3 months, although extended treatment may be necessary as 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.

Naltrexone is an opioid antagonist with a high affinity for opioid receptors. It competitively displaces opioid agonists (for example, heroin or methadone), blocking the euphoric and other effects of opioids and thereby minimising the positive rewards associated with their use. Naltrexone is rapidly absorbed, metabolised by the liver and excreted in urine with an eliminated half-life of 4.5 hours. Liver function tests are recommended prior to and during naltrexone treatment to check for liver impairment. The 'Summary of product characteristics' states that 'caution should be observed in administering the drug to patients with impaired hepatic or renal function'.

The antagonist activity of naltrexone leads to an increased risk of death from overdose. Patients who relapse while on naltrexone treatment are at risk of

overdose because a larger dose of heroin is required to overcome the blockade and achieve a pleasurable effect. While on naltrexone treatment, patients lose their tolerance to opioids. Patients who discontinue naltrexone treatment may be unaware of the loss of tolerance and be at risk of fatal overdose if they inject the dose of heroin they were previously accustomed to. The National Coronial Information Service reported 32 naltrexone-related deaths in Australia between 2002 and 2003. This corresponds to a mortality rate of 10.1 per 1000 treatment episodes; 22.1 per 100 person–years during the initial 2-week high-risk period of treatment, and 1 per 100 person–years during the rest of treatment.

Naltrexone is associated with withdrawal symptoms if patients are opioid dependant. Naloxone hydrochloride challenge is recommended to screen for the presence of opioids if uncertainty exists as to whether patients are detoxified.

Currently, the decision about which drug treatment to offer is based on local availability, on the individual's previous history, current situation, social support network and expressed wishes. Treatment decisions are taken together with the person and based on the clinician's judgment of the required degree of structure, monitoring and support.

In England naltrexone treatment accounts for 11,000–14,000 prescriptions per annum and a total annual drug cost of less than £500,000. Expenditure on naltrexone treatment is stable compared with maintenance treatments for drug misusers (methadone and buprenorphine) which are increasing annually.

3 The evidence

3.1 Clinical effectiveness

The review identified 17 studies of the effectiveness of naltrexone treatment: 1 systematic review (Cochrane review), 13 randomised controlled trials (RCTs) and 3 non-randomised comparative studies. The Cochrane Review included 10 RCTs in 696 individuals and was of good quality. The RCTs and

comparative studies evaluated the effectiveness of naltrexone treatment in a total of 940 individuals and were of poor quality (randomisation was not adequately reported in most RCTs). Two of the RCTs were conducted in a prison setting (parolees or probationers), and seven RCTs included various psychosocial treatments in both arms of the trials (bi-weekly drug counselling, psychotherapy and behavioural therapy).

In addition to the 17 studies of the effectiveness of naltrexone treatment, 9 RCTs studied the effectiveness of different strategies to improve retention on naltrexone treatment. Three studies assessed contingency management (vouchers as a reward for treatment compliance), four studies evaluated psychosocial therapies and two trials examined the effectiveness of pharmaceutical agents for improving patient retention in naltrexone treatment. These studies were of poor quality (methods of randomisation and blinding were not adequately described and intention-to-treat analysis was not performed in most of the trials). A quality assessment of all the RCTs is provided in the assessment report (pages 106–108)

3.1.1 The effectiveness of naltrexone treatment

The effectiveness of naltrexone treatment was assessed using the outcomes of retention, relapse rates (opioid use), re-incarceration of parolees or probationers and risk taking behaviour. The length of follow-up varied in the RCTs from 20 days to 1 year. Most results were expressed as relative risks (RRs); however, the Assessment Group noted that hazard ratios (HRs) may be better indicators of effect because of the differences in the length of follow-up between the trials. A summary of the evidence is given in table 2.

The Cochrane review identified 10 studies of naltrexone treatment (with or without psychosocial therapy) compared with placebo treatment (with or without psychosocial therapy) in 696 patients. Combined analysis showed a significant reduction in heroin use (RR 0.72; 95% confidence interval [CI], 0.58 to 0.90) but no difference in treatment retention (RR 1.08; 95% CI, 0.74 to 1.57) with naltrexone and adjunctive psychosocial treatment compared with psychosocial therapy alone.

Treatment retention was reported in seven RCTs (three of these included adjunctive psychosocial therapies). Six of the seven RCTs reported no difference in retention with naltrexone treatment. One trial reported a significant improvement in retention with naltrexone treatment (RR 0.66; 95% CI, 0.43 to 0.93). Meta-analysis of seven studies showed no difference in treatment retention with naltrexone compared with placebo (RR of stopping treatment 0.94; 95%CI, 0.84 to 1.06). A similar finding was observed when the Assessment Group pooled the results of five of the trials for which HRs were available (HR 0.90; 95%CI, 0.69 to 1.17).

Relapse rates (opioid use) of individuals on naltrexone treatment compared with placebo were reported in six RCTs (three of these included adjunctive behavioural therapies). Five of the six RCTs reported no statistically significant differences in relapse rates with naltrexone treatment. One trial reported a statistically significant improvement in relapse rates with naltrexone treatment (RR 0.41; 95% CI, 0.21 to 0.74). Pooled analysis of six of the studies showed a statistically significant reduction in the risk of opioid use with naltrexone compared with placebo (RR 0.72; 95%CI, 0.58 to 0.90). A pooled analysis of HRs from three studies also showed a showed a statistically significant reduction in opioid use with naltrexone treatment (HR 0.53; 95%CI, 0.34 to 0.82). One RCT compared the number of drug-free patients retained in treatment with naltrexone plus psychosocial therapy compared with psychosocial therapy alone (see figure 10 in the assessment report, page 55). There was no statistically significant difference in relapse rates between the two arms, with an average of 84% drug-free patients in naltrexone treatment arm compared with 86% in the control arm (personal communication from the Assessment Group).

One RCT of naltrexone compared with placebo (with adjunctive counselling in each arm) included a self-assessment of risk taking behaviour (injected drug use in the previous 30 days and risky sexual behaviour in the previous 6 months). Statistically significant decreases in risk scores were observed at 3 and 6 months following randomisation in both the naltrexone and placebo

groups. However, there were no statistically significant differences between the treatment groups.

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

Mortality data was not reported in any of the trials. A retrospective audit of clinical records, toxicology reports and coronial findings in the USA examined the number of deaths in people who had received naltrexone treatment for over 2 years (n = 1196) and in people who had not received naltrexone treatment (total number not reported). Of 33 deaths in the naltrexone group, 21 (64%) were the result of a fatal heroin overdose as were 71 out of 96 (74%) deaths in people not exposed to naltrexone.

Table 2 Summary of the effectiveness of naltrexone treatment (RCTs)

Outcome	Studies (n)	Patient numbers	Measure of effect (pooled RR or HR [95% CI])	Favour
Retention	7	378	RR 0.94. (0.84, 1.06)	Naltrexone
	5	259	HR 0.90 (0.69, 1.17) – fixed effects	Naltrexone
Relapse rate (opioid use)	6	249	RR 0.72 (0.58, 0.90)	Naltrexone
Relapse rate (relapse free individuals)	3	130	HR 0.53 (0.34, 0.82) – fixed effects	Naltrexone
Re-incarceration rate	2	8	RR 0.50 (0.27, 0.91)	Naltrexone
CI, confidence interval; HR, hazard ratio; RCT, randomised controlled trial; RR, relative risk.				

3.1.2 The effectiveness of adjunctive therapies (psychosocial and pharmaceutical) to enhance compliance with naltrexone treatment

Nine RCTs evaluated the effectiveness of different strategies to increase retention with naltrexone treatment; three trials of incentive vouchers, four trials of behavioural therapy and two trials of pharmaceutical agents

(fluoxetine and sertaline). The length of follow-up in these trials ranged from 12 to 52 weeks.

Three RCTS investigated the effect of incentive vouchers that rewarded patients for compliance with naltrexone treatment (consecutive doses of naltrexone or consecutive opiate-free urine samples) and could be exchanged for goods or services. The monetary value of vouchers varied from US$0.80 per ‘clean’ urine sample to US$2.50 for each consecutive dose of naltrexone. The data from one trial were of limited value because results were not presented for the different randomised groups. The other two trials reported a statistically significant increase in treatment retention (an additional 5.1 weeks in one study and 1.8 weeks in the other, p = 0.02 and 0.05, respectively). One trial reported a reduction in opiate use (increase in the number of opiate-free urine samples with incentive vouchers). Incentive vouchers were associated with a mean of 19 opiate-free urine samples compared with a mean of 14 opiate-free urine samples in the control arm, p = 0.04).

Four RCTs assessed the effect of different behavioural therapy strategies (behavioural therapy, cognitive behavioural therapy, behavioural family counselling and cognitive group counselling) on compliance with naltrexone treatment. Three of these trials reported improvements in the effectiveness of adjunctive behavioural therapy for outcomes of retention, opioid use and medication compliance.

Two RCTs assessed the effect of adjunctive pharmaceutical treatments (fluoxetine and sertraline) on compliance with naltrexone treatment. One small trial of sertraline in 13 patients did not demonstrate any clinically important effects. The other trial, in 112 patients, showed a statistically significant improvement in compliance at 6 months with adjunctive fluoxetine treatment (RR of continued treatment 1.63; 95% CI, 1.00 to 2.70), but not at 12 months (RR 1.31; 95%CI, 0.97 to 1.81).

All of the above strategies (which can be described as enhanced-care packages) showed some evidence of effectiveness. Pooled analysis of the combined effect of enhanced -care packages at 12 weeks showed a

statistically significant improvement in treatment compliance (RR of stopping treatment 0.81; 95% CI, 0.71 to 0.94), which corresponds to a 19% improvement in treatment retention with enhanced care compared with naltrexone alone.

3.2 Cost effectiveness

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

3.2.1 Assessment Group's model

The Assessment Group developed a decision analytical model to assess the cost effectiveness of naltrexone plus psychosocial support compared with psychosocial support alone. The model estimated costs and outcomes from a National Health Service and Personal Social Services perspective (NHS/PSS). 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 patients are not retained on naltrexone treatment in the long term. Diagrams of the model structure can be found on pages 100–101 of the assessment report.

The main effectiveness parameter of the model is treatment retention, which is estimated at 2, 6, 13 and 25 weeks and 12 months. Data on patient retention with 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 with psychosocial treatment alone. Data on the proportion of opioid-free patients retained on treatment was based on a single RCT, which reported no difference between the naltrexone (84% opioid-free patients) and the control arm (86% opioid-free patients). Data from the 'National treatment outcome treatment research study' (NTORS) were used to inform the proportion of drug-taking patients who were injecting and not injecting. Of the drug-using individuals not on treatment, 61% were injecting

(39% were not injecting); of the drug-using individuals on treatment, 44% patients were injecting (56% were not injecting).

In the absence of published data on quality of life associated with drug misuse, the Assessment Group obtained health-related utility data from the Value of Health Panel. Five health states were defined by the Assessment Group in collaboration with a clinician. The different health states described scenarios for individuals who were retained in treatment (drug free, reduced drug use [injectors] and reduced drug use [non-injectors]), and not retained in treatment (drug misusers [injectors], drug misusers [non-injectors]), in the naltrexone or placebo arms of the model. Members of the general public valued the health states using the standard gamble method to generate utility values (for further information, see appendix 1, page 96 of the assessment report). Average quality-adjusted life years (QALYs) were calculated for patients retained on treatment with naltrexone and psychotherapy, patients retained on treatment with psychotherapy alone and patients not retained on treatment. These were estimated for each of the groups by applying the health-related utility values to the proportions of patients that were drug free, injectors and non-injectors. The average QALYs were 0.835 (SD 0.161) for patients retained on naltrexone treatment for 1 year, 0.838 (SD 0.160) for patients retained in the control arm for 1 year and 0.64 (SD 0.21) for patients who were not retained in treatment for 1 year. Patients retained on naltrexone treatment gain fewer QALYs than those retained on control treatment, based on evidence from one RCT which showed a higher number of patients taking opiate drugs with naltrexone (see assessment report page 55). The total QALYs associated with each treatment arm were then determined by different retention rates.

The reference case analysis assumed that patients attended one counselling session per week, had one urine test per fortnight to monitor treatment success and received a daily dose of 50 mg naltrexone in the naltrexone treatment arm. Other health service resource use was based on data from the NTORS and included GP visits, accident and emergency visits, inpatient

hospital stays, outpatient mental health visits, inpatient mental health visits. Further details are provided on page 77 of the assessment report.

An analysis from a societal (non-reference case) perspective was also provided, which included the costs of the criminal justice system and victims of crime. The NTORS provided information on the costs of drug arrests, arrests for theft, time spent in police custody, court appearances and prison stays and victim costs (see page 80 of the assessment report). Victim costs associated with criminal behaviour represent an average of the costs incurred by victims of crime (costs of increased security measures and direct costs of material or physical damage). These costs were considerably lower per patient for successful treatment than for unsuccessful treatment. Criminal justice service costs excluding victim costs were higher for patients in treatment than those out of treatment, which may be because of closer follow-up of patients in treatment.

Cost-effectiveness results

Naltrexone plus psychosocial therapy is associated with an incremental cost effectiveness ratio (ICER) of £42,500 per QALY gained (see table 3).

Data on the relative numbers of patients that are drug free, injecting drug misusers and non-injecting drug misusers were based on a single study. Differences in the relative numbers of patients in each category would have an impact on the QALYs generated. A one-way sensitivity analysis was performed which assumed the same average QALY for patients successfully retained on treatment with naltrexone and psychosocial therapy as for patients successfully retained on treatment psychosocial therapy alone. The ICER for this analysis was reduced from £42,500 per QALY gained in the base case to £34,500 per QALY gained (see table 3).

The Assessment Group conducted a probabilistic sensitivity analysis around the base case analysis which simultaneously varied all of the key parameters of the model (details are given on page 83 of the assessment report). The incremental cost effectiveness plane shows great uncertainty in the incremental cost and QALY gains associated with naltrexone treatment.

Cost-effectiveness acceptability curves demonstrate that the probability of naltrexone being cost effective does not rise much beyond 50%, and there is 50% probability that naltrexone treatment is cost effective compared with placebo at a willingness to pay of between £30,000 per QALY and £100,000 per QALY gained (see table 3).

Naltrexone plus psychosocial therapy dominates (is less costly and more effective) psychotherapy alone when costs of the criminal justice system are taken into account. The dominance of naltrexone therapy is driven by the victim costs which are reduced in the naltrexone arm because of the increased treatment retention and the associated reduction in crime. A one-way sensitivity analysis of the societal perspective in which the victim costs were excluded resulted in an ICER of approximately £51,000 per QALY gained (see table 3).

Table 3. Cost effectiveness results

Analysis	Cost (£)	Cost difference (£)	QALYs	QALY difference	ICER (£/QALY)
Reference case					
Placebo + psychosocial therapy	1271		0.7105		
Naltrexone + psychosocial therapy	1510	239	0.7161	0.0056	42,500
Sensitivity analysis (alternative QALY assumptions)					
Placebo + psychosocial therapy	1271		0.7105		
Naltrexone + psychosocial therapy	1510	239	0.7174	0.0069	34,600
Societal perspective (including criminal justice and victim costs)					
Placebo + psychosocial therapy	31716		0.7105		Dominated
Naltrexone + psychosocial therapy	31244	–473	0.7161	0.0056	Dominant

Societal perspective (excluding victim costs)					
Placebo + psychosocial therapy	8799		0.7105		
Naltrexone + psychosocial therapy	9085	286	0.7161	0.0056	51,071

4 Issues for consideration

There are very few studies, using only small numbers of patients, which can be used to assess the effectiveness of naltrexone treatment. In addition, the Assessment Group reported that the quality of most of the studies was low.

The cost effectiveness of naltrexone compared with control treatment is dependant on differential retention rates, the proportion of patients retained in treatment that are taking drugs, and of those taking drugs the relative proportions of patients injecting compared with non-injecting. Retention rates in the model were based on the pooled estimate from the systematic review, which showed no significant difference between naltrexone and the control. Opioid use of retained patients used in the model was based on one study, which showed no significant difference between naltrexone and control treatment. However, it should be noted that the pooled estimate of six RCTs demonstrated a significant reduction in opioid use with naltrexone treatment for all randomised patients (not just those who were retained in treatment).

The economic analysis highlighted a lot of uncertainty in the data inputs and the results. Small differences in the QALYs used and the inclusion of victim costs can have a large impact on ICERs.

There is uncertainty about the reliability of the information about costs to the criminal justice system and victim costs.

The Assessment Group found two uncontrolled studies of naltrexone treatment in motivated individuals (one in 20 people and another in 114 people). These studies showed better abstinence rates in motivated patients

(business executives and healthcare professionals) than those reported in the RCTs. However, the Assessment Group also noted that these data were inconclusive.

A consultee reported that retention on treatment is not a good indicator of abstinence because patients may achieve abstinence without naltrexone treatment; care should be taken to interpret evidence with this in mind.

Consultees highlighted significant variation in practice between different services, prisons and the community. However the Assessment Group reported that there were insufficient data to perform subgroup analyses of the effectiveness of naltrexone treatment in different settings.

Other related NICE guidance includes the technology appraisal ‘Methadone and buprenorphine for the management of opioid dependence’ (due for publication in March 2007) and the clinical guideline ‘Drug misuse: psychosocial management of drug misusers in the community and prison’ (due for publication in July 2007).

5 Author

Eleanor Donegan

Health Technology Analyst, NICE Appraisal Team

May 2006

Appendix A: Sources of evidence considered in the preparation of the overview

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

B Submissions from the following organisations:

I Manufacturers/sponsors:

- None

II Professional/specialist and patient/carer groups:

- Royal Collage of General Practitioners
- Royal College of Nursing

III Commentator organisations (without the right of appeal):

- None

A Additional references used:

- Singleton N, Pendry E, Simpson T et al (2005) 'The impact and effectiveness of mandatory drug testing in prisons.' Home Office: Findings 223.