APPENDIX A

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Naltrexone as a treatment for relapse prevention in drug misusers

Final scope

Appraisal objective

To appraise the clinical and cost effectiveness of naltrexone (Nalorex, Bristol-Myers Squibb Pharmaceuticals Ltd) as an adjunctive treatment for relapse prevention for drug misusers. Further objectives are: to identify those groups of drug misusers (in the community and prison settings) who are most likely to benefit from being prescribed naltrexone, to advise on the optimum care package required for effective outcomes, and to provide guidance to the NHS in England and Wales[1].

Background

Opiate is a collective term for analgesics that are derived from the naturally occurring compound opium. This includes diamorphine (heroin), morphine and codeine. The term 'opioid' denotes a broader group that includes opiates plus synthetic analgesics with agonist, partial agonist, or mixed agonist and antagonist activity at opioid receptors.

Opiates are used therapeutically as painkillers, but also produce euphoria and are therefore abused. Physical and psychological dependence can also 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 taken needs to be increased to maintain the effect.

Opioid misuse can be defined as the compulsive use of opioids despite physical, psychological, and social harm to the user. Most individuals who meet the criteria of opioid misuse and continue to use opioids go on to fulfil the criteria of opioid dependence.

Opioid dependence can cause a wide range of health problems and is often associated with simultaneous abuse of a number of drugs (including alcohol). Heroin is the most widely abused opiate and dependence on illicit heroin can

[1] The Department of Health and Welsh Assembly Government remit to the Institute: To appraise the clinical and cost effectiveness of naltrexone as a treatment for relapse prevention for drug misusers and to identify those groups of drug misusers (in the community and prison settings) who are most likely to benefit from being prescribed naltrexone. Also to advise on the optimum care package that needs to be available to those prescribed naltrexone to secure effective outcomes, and to provide guidance to the NHS in England and Wales.

cause a number of other physical problems due to the spread of blood borne viruses and an increased risk of an accidental overdose. The mortality risk of individuals dependent on heroin is estimated to be around twelve times that of the general population. Associated social problems include marital and relationship breakdown, unemployment, homelessness, and criminal activity.

Estimates suggest there are around 280,000 dependent drug misusers in the UK, with approximately 160,000 in treatment at some point during the year. 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% during the previous week.

There are two broad strategies for the treatment of opiate dependence. The first is harm reduction (which can include taking the individual off illicit street drugs and administering an opiate substitute in a maintenance regimen) to enable the individual to achieve social stability. Factors that might be necessary to achieve maintenance on opiate substitutes include; decisions being made on appropriate doses for individuals, enhancing outcomes with counselling and other psychosocial interventions, and engaging and retaining clients in drug treatment.

The second is abstinence (taking the individual off the drug altogether using detoxification and withdrawal). Choice of strategy is influenced by individual circumstances and occasionally an individual's preference.

The technology

Naltrexone is a specific, high-affinity, long-acting competitive antagonist at opioid receptors. It has negligible opioid agonist activity and tolerance does not develop with prolonged use. The Summary Product Characteristics (SPC) states that it is indicated "as an adjunctive prophylactic therapy in the maintenance of detoxified, formerly opioid-dependent patients". The route of administration is oral. Treatment should only be considered in patients who have been opioid-free for a minimum of 7-10 days. Treatment should be initiated in a drug addiction centre and supervised by suitably qualified physicians. The SPC also states that "safe use in children has not been established" and that "there is no experience of use in the elderly".

Nalorex is the only formulation currently available on the NHS. Naltrexone in the form of subcutaneous implants and depot injectable microcapsules are still in product development stage and are not currently licensed in the UK.

There is currently lack of agreement on the evidence for oral naltrexone for abstinent opiate dependent drug users and there is significant variation in practice between different services, between prisons and the community. There is also a lack of clarity for whom oral naltrexone is most appropriate and in what supportive care package.

Intervention(s)	Naltrexone (oral)
Population(s)	Detoxified, formerly opioid-dependent individuals
Standard comparators	Any current treatment strategies in the maintenance of detoxified, formerly opioid-dependent individuals without naltrexone.
Outcomes	Outcome measures include: • Changes in illicit drug use • Proportion of individuals being maintained opioid-free • Drug-related morbidity and mortality • Concordance with and retention to treatment • Adverse effects of treatment • Quality of life
Economic analysis	Ideally, the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The time horizon of the economic evaluation should be an appropriate time period over which the costs and benefits of this technology can be expected to be experienced. The appraisal will consider both the short and the longer term costs and benefits of treatment. Costs and benefits for the base case will be considered from an NHS and Personal Social Services perspective. Sensitivity analysis will also be undertaken to include the wider societal costs and benefits including societal function, criminal activity, public health and safety and costs to the prison service. Sensitivity analysis will also be undertaken to include the costs/benefits of different service delivery strategies.

Other considerations	The intervention will be appraised according to its licensed indication. Guidance will only be issued in accordance with the marketing authorisation. Where evidence allows, the appraisal will examine subgroups of individuals for whom naltrexone (oral) may be particularly appropriate or inappropriate. Where evidence allows, the appraisal will advise on the optimum care package required to secure effective outcomes. The appraisal will consider the wider implications of the use of naltrexone for relapse prevention in drug misusers. For example societal costs and benefits including societal function, criminal activity, public health and safety and costs to the prison service.
Related NICE recommendations	Related Technology Appraisals: None Related Guidelines (in development): Drug misuse: psychosocial management of, drug misusers in the community and prison settings. Drug misuse: opiate detoxification management of, drug misusers in the community, hospital and prison settings.