APPENDIX A

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Methadone and buprenorphine as opiate substitutes

Draft scope

Appraisal objective

To appraise the clinical and cost effectiveness of oral methadone (Physeptone, Hillcross (AAH Pharmaceuticals Ltd) and Martindale Pharmaceuticals Ltd; Metharose, Rosemont Pharmaceuticals Ltd; Methadose, Rosemont Pharmaceuticals Ltd) and sublingual buprenorphine (Subutex, Schering-Plough Ltd) as substitute opiates for the management of opiate misusers, 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. 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, anorexia, and raised heart rate, respiratory rate, blood pressure and temperature). The body also becomes tolerant to the effects of opiates and therefore the dose taken needs to be increased to maintain the effect.

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

Opiate dependence can cause a wide range of health problems, such as liver and neurological disorders, and is associated with simultaneous abuse of a number of drugs (including alcohol). Mortality risk of heroin abusers is

[1]The Department of Health and Welsh Assembly Government remit to the Institute: To appraise the clinical and cost effectiveness of oral methadone and sublingual buprenorphine as substitute opiates for the management of opiate misusers and to identify those groups of misusers (in the community and prison settings) who are most likely to benefit from being prescribed oral methadone and those most likely to benefit from sublingual buprenorphine. Also to advise on the optimum doses and context of care required to secure effective outcomes, and to provide guidance to the NHS in England and Wales.

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 250,000 dependent drug users in the UK, with approximately 160,000 in treatment at some point during the year. The scale of opiate misuse in prisons is not easy to estimate. General drug misuse in prisons in England and Wales is estimated to be between 15% and 29%. In one UK survey, 20% of prisoners had used opiates at some point during their sentence, and 10% during the previous week.

There are two main strategies for the treatment of opiate dependence. One is harm reduction (taking the individual off illicit street drugs and administering an opiate substitute in a maintenance regimen) to enable the individual to achieve social stability. The second is abstinence (taking the individual off the drug altogether using detoxification and withdrawal). Choice of strategy is influenced by individual preference and circumstances. To improve prognosis, both strategies are used in conjunction with other psychological, social and medical interventions.

The technologies

Methadone and buprenorphine are synthetic opioids with a powerful analgesic action in addition to their psychoactive effects. Methadone is an opioid agonist and buprenorphine is an opioid partial agonist. They cause less euphoria than heroin and have a longer duration of action and can be given orally. Oral methadone and sublingual buprenorphine are both licensed as an adjunct in the treatment of opioid dependence and can be used in strategies aimed at both harm reduction and abstinence. There is however controversy over the most appropriate dose that should be used.

Interventions	Methadone (oral) and buprenorphine (sublingual)
Population	Opiate dependent individuals
Standard comparators	The interventions are adjuncts to current treatment strategies and therefore the comparator is treatment strategies without methadone (oral) or buprenorphine (sublingual). The interventions will be compared to each other.

Outcomes	Outcome measures include: • Relapse rates • Mortality • Compliance with treatment • Adverse effects of treatment • Health-related quality of life • Criminal activity • Unemployment.
Economic analysis	Ideally, the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. 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/benefits including unemployment, criminal activity and costs to the prison service.
Other considerations	Where the evidence allows, the appraisal will examine subgroups of individuals for whom oral methadone and sublingual buprenorphine may be particularly appropriate or inappropriate. Where the evidence allows, the appraisal will consider the use of oral methadone and sublingual buprenorphine in both community and prison settings. Where the evidence allows, the appraisal will consider the impact on the clinical and cost-effectiveness of the prescribed dose and the context of care.
Related NICE recommendations	Related Technology Appraisals: None Related Guidelines: 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.