NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Methadone and buprenorphine for the management of opioid dependence

Final scope

Appraisal objective

To appraise the clinical and cost effectiveness of oral methadone (Physeptone, Martindale Pharmaceuticals Ltd; Metharose, Rosemont Pharmaceuticals Ltd; Methadose, Rosemont Pharmaceuticals Ltd; Generics AAH Pharmaceuticals Ltd and Thornton & Ross Ltd) and sublingual buprenorphine (Subutex, Schering-Plough Ltd) as substitute opiates for the management of opioid dependent individuals, 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.

[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.

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 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 opioid 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 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 and antagonist. They cause less euphoria than heroin and have a longer duration of action and can be given orally. Both drugs are 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.

The Summary Product Characteristics (SPC) for methadone states that it is indicated for "use in the treatment of opioid drug addictions (as a narcotic abstinence syndrome suppressant)". The SPC for buprenorphine states that it is indicated for "substitution treatment for opioid drug dependence, within a framework of medical, social and psychological treatment".

Although both drugs are available in more than one formulation, the appraisal will be restricted to oral methadone and sublingual buprenorphine as per the remit.

Interventions	Methadone (oral) and buprenorphine (sublingual)
Population	Opioid dependent adults (16 years and over)
Standard comparators	The interventions are adjuncts to current treatment strategies and therefore the comparator is treatment strategies without methadone (oral) and/or buprenorphine (sublingual).
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 in 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, including dispensing fees.

Other considerations	The appraisal will consider the use of oral methadone and sublingual buprenorphine within their licensed indications. Guidance will only be issued in accordance with the marketing authorisations. 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 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 impact on the clinical and cost-effectiveness of the prescribed dose and the context of care. The appraisal will consider the wider implications of the use of oral methadone and sublingual buprenorphine in drug misusers. For example societal costs and benefits including societal function, criminal activity, public health and safety and costs to the prison service. Where the evidence allows, the appraisal will consider substance substitution effects.
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.