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HEALTH TECHNOLOGY BRIEFING
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Buprenorphine for Opioid Dependence

NIHRIO ID	5112	**NICE ID**	10596
Developer/Company	Accord Healthcare Limited	**UKPS ID**	659681

Licensing and market availability plans	Currently in phase III/II clinical trials.

SUMMARY

Buprenorphine is indicated for substitution treatment of opioid dependence in clinically stable adult patients. Opiod dependence is characterised by a strong desire or sense of compulsion to take opioids; difficulty in controlling use; a physiological withdrawal state when opioid use has ceased or been reduced; evidence of tolerance; progressive neglect of alternative pleasures and interests; and persistence with opioid use despite clear evidence of overtly harmful consequences. Buprenorphine is currenly administered orally or via prolonged release injection, however, evidence shows that buprenorphine implant provides improved compliance and convenience, reduced illicit opioid use and increased quality of life measures.

Buprenorphine is a partial opioid agonist, which means that it acts like an opioid but less powerfully. Buprenorphine can therefore be used in a controlled way to help prevent withdrawal symptoms and reduce the urge to misuse other opioids. If licensed, buprenorphine via the implant route will offer an additional treatment option for clinically stable adult patients with opioid dependence.

PROPOSED INDICATION

Substitution treatment of clinically stable adult patients with opioid dependence who require no more than 8mg/day of sublingual buprenorphine within a framework of medical, social and psychological treatment.[a]

TECHNOLOGY

DESCRIPTION

Buprenorphine (Sixmo 74.2mg implant) is a partial agonist at the mu receptor, meaning that it only partially activates opiate receptors. It is also a weak kappa receptor antagonist and delta receptor agonist. It is a potent analgesic that acts on the central nervous system (CNS). The partial agonism at the mu receptor is a unique quality to buprenorphine and the feature that gives it its many unique properties, specifically that its analgesic effects plateau at higher doses, and then its effects become antagonistic.[1-3]

Buprenorphine is available as an implant to be inserted under the skin, which continuously releases buprenorphine into the body. The patient receives four implants, which are inserted under local anaesthesia in the inner side of the upper arm and kept in place for 6 months.[2] Each implant contains buprenorphine hydrochloride equivalent to 74.2 mg of buprenorphine.[4]

INNOVATION AND/OR ADVANTAGES

In contrast to XR-naltrexone, which requires patients to be fully withdrawn before the medicine can be initiated, buprenorphine only requires patients to manifest at least mild withdrawal symptoms, at which point the medication can be started.[1]

Buprenorphine is preferred by some patients because it is less sedating than methadone hydrochloride; for this reason it may be more suitable for employed patients or those undertaking other skilled tasks such as driving. Buprenorphine is safer than methadone hydrochloride when used in conjunction with other sedating drugs, and has fewer drug interactions. Dose reductions may be easier than with methadone hydrochloride because the withdrawal symptoms are milder, and patients generally require fewer adjunctive medications; there is also a lower risk of overdose. Buprenorphine can be given on alternate days in higher doses and it requires a shorter drug-free period than methadone hydrochloride before induction with naltrexone hydrochloride for prevention of relapse.[5]

Evidence also shows that buprenorphine implant is considered favourable in comparison to sublingual buprenorphine. The key benefits of improved compliance and convenience, reduced illicit opioid use and quality of life measures outweigh the key risks related specifically to the implant formulation.[6]

[a] Information provided by Accord Healthcare Limited on UK PharmaScan

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Buprenorphine has marketing authorisation in the UK/EU for the substitution treatment for opiod drug dependence within a framework of medical, social and psychological treatment. The most common side effects with buprenorphine (which may affect up to 1 in 10 people) include headache, constipation and difficulty sleeping. The most common side effects related to the insertion and removal of the implant are pain, itching, bruising, bleeding, reddening of the skin and rash at the site of the implant.[2,7]

Buprenorphine is in phase II/III clinical development for over 270 indications including:[8]

- Neonatal Abstinence Syndrome
- Rotator Cuff Tear and Injury
- Sickle Cell Disease
- Chronic pain
- Depression
- Osteoarthritis
- Suicidal Ideation
- Head and Neck Squamous Cell Carcinoma
- Post-Traumatic Stress Disorders
- End Stage Renal Disease
- Alcohol abuse
- Chemotherapy Induced Mucositis

PATIENT GROUP

DISEASE BACKGROUND

Opioid dependence develops after a period of regular use of opioids, with the time required to develop the dependence varying according to the quantity, frequency and route of administration, factors of individual vulnerability and the context in which drug use occurs. The key elements of opioid dependence include a strong desire or sense of compulsion to take opioids; difficulty in controlling use; a physiological withdrawal state when opioid use has ceased or been reduced; evidence of tolerance; progressive neglect of alternative pleasures and interests; and persistence with opioid use despite clear evidence of overtly harmful consequences.[9]

Some of the risk factors for opioid dependence include: misunderstanding between the patient and provider, unauthorised self-medication of pain, mood, or sleep problems, desire to avoid symptoms of abstinence syndrome, desire for euphoria or other psychoactive reward, compulsive use due to addiction and illegal diversion for the financial gain.[10]

Most individuals begin to use opioids for euphoric feelings or pain relief; then, tolerance develops due to the desensitisation of opioid receptors, leading to an uncontrolled intake. The symptoms of opioid tolerance and withdrawal, with uncontrolled intake and craving, are the core symptoms of opioid addiction. The withdrawal symptoms include severe muscle ache, bone pain, tearing, runny nose, yawning, diarrhoea, abdominal cramps, agitation,

anxiety, and sweating. Many addicted individuals used opioids again to alleviate these intolerable feelings.[11]

Complications of opiod use and dependence include: overdose which can result in death, infections such as human immunodeficiency virus (HIV) and hepatitis C (especially from using shared injection equipment), and social problems such as homelessness and crime.[9]

CLINICAL NEED AND BURDEN OF DISEASE

There were 268,251 adults in contact with drug and alcohol services in in England in 2018/19. Over half (52%) of them received treatment for problems with opiates, which takes the total number of people using services due to problems with opiates to 139,490. The median age was 41 years, and majority were males.[12]

According to Hospital Episodes Statistics (HES) (ICD-10: F10-F19) data in 2019-20, in England, there were 50,531 hospital admissions, resulting in 296,321 FCE bed days of primary diagnosis of mental and behavioural disorders due to psychoactive substance.[13]

It is estimated that 2,160 opiate related deaths occurred between 2018 and 2019, in England, of which 332 were drug related poisonings that were suicides (210 males and 122 females).[14]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

The National Institute for Health and Care Excellence (NICE) recommends that all practitioners assess and manage people with opioid dependence within their competence and confidence, and refer people for specialist assessment when required (for example, for initiation of prescribing, for more complex physical or mental health diagnostic assessments or for other complex assessments such as complex polypharmacy). Furthermore, a multidisciplinary approach to the management of people with opioid dependence is recommended as people who use drugs have multiple needs and the level of expertise required to manage the person may alter over time. This could include other primary care practitioners, practice nurses, pharmacists, practitioners with a special interest and addiction specialists.[15]

Non-pharmacological treatments of opioid dependence include behavioural and psychosocial interventions to address psychological and social aspects of drug use include brief interventions, structured psychological therapies, motivational interventions, contingency management, and behavioural couples therapy. They are often used in conjunction with pharmacological interventions. Also there are self-help and mutual aid groups which teach cognitive, behavioural and techniques of self-management without formal professional guidance.[16]

CURRENT TREATMENT OPTIONS

NICE recommends:

- Naltrexone[17]

- Methadone and buprenorphine (oral formulations) for the management of opioid dependence in adults[18]

PLACE OF TECHNOLOGY

If licensed, buprenorphine via implant will offer an additional treatment option for clinically stable adult patients with opioid dependence.

ESTIMATED COST

Cost of buprenorphine was confidential at the time of producing this briefing.

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal. Methadone and buprenorphine for the management of opioid dependence (TA114). January 2007.
- NICE technology appraisal. Naltrexone for the management of opioid dependence (TA115). January 2007.
- NICE clinical guideline. Drug misuse in over 16s: opioid detoxification (CG52). July 2007.
- NICE evidence summary. Opioid dependence: buprenorphine prolonged-release injection (Buvidal) (ES19). February 2019.
- NICE guideline. Drug misuse prevention: targeted interventions (NG64). February 2017.

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- No relevant guidance identified

OTHER GUIDANCE

- European Monitoring Centre for Drugs and Drug Addiction. Guidelines for the treatment of drug dependence: a European perspective. 2011.[19]

ADDITIONAL INFORMATION

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