Committee’s Verdict: CATEGORY B (Q4)

Category B: suitable for restricted prescribing under defined conditions

(The committee did not consider guidance for the use of transdermal buprenorphine for cancer-related pain because this was considered to be restricted to specialist care.)

Commissioning and prescribing considerations

- When commissioning a pain management service, commissioners should consider specifying criteria for patients who may need to use patches for analgesia, for example:
  - patients who cannot tolerate tablet formulations, or have difficulty swallowing (although liquid formulations and subcutaneous morphine may be suitable for some of these patients)
  - patients with mental health problems
  - patients with compliance issues or for those who are socially isolated with limited access to care
- Buprenorphine should be initiated by a specialist or a specialist pain management service, given the range of alternative treatments available for the management of chronic non-cancer pain. Continued prescribing can then occur in primary care.
- Patients receiving buprenorphine patches should be assessed frequently, e.g. after two weeks, to assess the efficacy of the treatment, improvements in functional status, tolerability of side effects, and compliance. Patients should be counselled about correct and safe use of the patches.

Q4 rating: The evidence for the efficacy of the buprenorphine transdermal system (BTDS) was relatively weak. Nine randomised, double-blind trials compared BTDS (seven-day and four-day patches) with placebo, and three open-label trials used active comparators, one with morphine sustained-release (SR). The outcome measures were subjective in all trials. The results showed a considerable placebo effect, even in the five trials in which only patients were included who had previously shown response to BTDS or sublingual buprenorphine. The cost of BTDS compared with oral morphine SR gives it a low place in therapy.

The Q rating relates to the drug’s position on the effectiveness indicator grid. The strength of the evidence is determined by the quality and quantity of studies that show significant efficacy of the drug compared with placebo or alternative therapy. Its place in therapy in primary care takes into account safety and practical aspects of using the drug in primary care, alternative options, relevant NICE guidance, and the need for secondary care input.

Description of technology

Buprenorphine is a strong opioid analgesic. The transdermal system is available in two formulations. Butrans® releases 5, 10 or 20 µg/hour for seven days and is licensed for the treatment of non-malignant pain of moderate intensity when an opioid is necessary for obtaining adequate analgesia. Transtec® releases 35, 52.5 or 70 µg/hour for four days and is licensed for the treatment of moderate to severe chronic cancer pain and severe pain unresponsive to non-opioid analgesics. BTDS was launched in the UK in 2002.

Background information

The World Health Organisation (WHO) recommends the use of strong opioids (e.g. oxycodone or morphine) for the management of moderate to severe pain due to cancer, at step three of the WHO three-step analgesic ladder. Strong opioids are also sometimes used to manage chronic severe non-malignant pain although their use has been controversial as repeated administration may cause dependence and tolerance.

NICE issued a draft Clinical Guideline for consultation in December 2011 on the use of strong opioids for pain management in palliative care. Oral morphine SR was recommended as first-line maintenance therapy. NICE recommended that transdermal preparations may be considered for patients in whom oral opioids are unsuitable and analgesic requirements are not changing rapidly, supported by specialist advice where needed. The final guideline is expected in May 2012.

MTRAC reviewed the buprenorphine transdermal system because of concern about inappropriate prescribing.
Clinical efficacy

Nine placebo-controlled, double-blind, randomised trials were identified that assessed BTDS for the management of pain in a total of 1,914 patients with a variety of conditions and severities of pain.\(^5\) in addition, three open-label trials compared BTDS with either oral tramadol\(^1\) (134 patients), oral codamol\(^5\) (220 patients) or oral morphine SR\(^6\) (52 patients). Seven trials used the lower-dose and five the higher-dose preparation of BTDS (note that the higher-dose patch was used for three days instead of four days as described in the Summary of Product Characteristics). The designs and quality of the trials varied considerably. Five trials only included patients who had responded to BTDS or sublingual buprenorphine in a prior run-in phase.\(^5\),\(^7\),\(^8\),\(^9\),\(^10\),\(^11\) The main primary outcome measures were the proportion of patients classified as treatment responders, using score ratings or amount of rescue medication needed, or actual pain scores on 5- or 11-point scales or a 100 mm-VAS scale. All the outcome measures were recorded or reported by patients.

Results

For the primary outcomes in the placebo-controlled trials, generally more patients using BTDS than placebo were classified as responders or had lower pain scores, except in one trial in which no differences were found.\(^5\) There were few significant differences for the secondary outcomes between BTDS and placebo groups. Compared with tramadol in a trial of patients with osteoarthritis, BTDS was found to be non-inferior for the change in a pain score.\(^1\) In a second trial of patients with osteoarthritis, BTDS plus paracetamol was found to be non-inferior to cocodamol.\(^5\) In a trial of patients with cancer-related pain, BTDS was associated with a significantly lower mean pain score than morphine SR (3.9 vs. 5.1 on an 11-point scale).\(^6\) There was generally a large placebo effect on the outcomes studied.

Adverse effects

The most common adverse events in these trials were nausea, dizziness, somnolence and vomiting, occurring in over 20% of patients using BTDS in most trials. One trial reported a significantly higher incidence of adverse events overall with BTDS than with placebo.\(^6\)

For additional information about adverse effects, refer to the Summaries of Product Characteristics.\(^1\),\(^2\)

Additional information

- At current prices, the costs of one year’s treatment are:
  - buprenorphine 7-day patch 5 to 20 µg/h £229 to £746
  - buprenorphine 4-day patch 35 to 70 µg/h £410 to £820
  - morphine SR (Morphgesic) 10 to 100 mg twice daily £47 to £347

References