Derbyshire Medicines Management UPDATE

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Buprenorphine Patches – a high price for convenience?

Date Produced: March 2017

WHAT IS THE PROBLEM?

Buprenorphine is a strong opioid similar to morphine. Although it has both opioid agonist and antagonist properties this makes little difference to its clinical use. It is generally used like other opioids in chronic pain.
Buprenorphine patches cost several times more than oral morphine in equivalent doses. In the last year (February 2016 – January 2017), Derbyshire CCGs spent over **£700k** on buprenorphine patches, at an average cost of around £30 per item.
The majority of prescribing **(£621,461)** was for the weaker strength (Butrans®, Butec® and Reletrans®), which are similar in efficacy to co-codamol or tramadol.

If half of this had been prescribed as codeine or tramadol, over £300,000 could have been available to spend on other treatments.

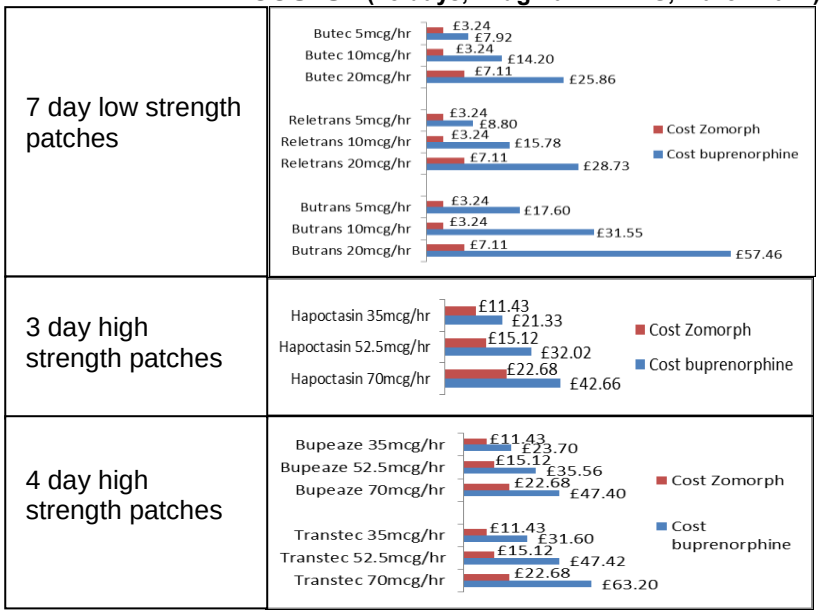
MAJOR CONSIDERATIONS

- Patches containing buprenorphine are available as either:
  - **low strength** patches (e.g. Butrans®, Butec® and Reletrans®) which are applied for **7 days** at a time, or,
  - **higher strength** patches (e.g. Hapoctasin®, Transtec® and Bupeaze®) which are applied for **either 3 or 4 days** at a time. The higher strength patches are **not interchangeable** as the time each patch is applied for is different – 3 days for Hapoctasin®, and 4 days for Transtec® and Bupeaze®. It is important that patients receive the same brand each time and understand the application instructions. Check individual SPC carefully.
- **To avoid confusion buprenorphine patches should be prescribed by brand name. The preferred brand of low strength patch is Reletrans®. If all prescriptions written generically or as Butrans® had been written as Reletrans®, over £300,000 could have been available to spend on other treatments.**
- The patches are not suitable for titrating the dose upwards in acute or unstable pain due to a delay in achieving higher blood levels. It may take up to 72 hours after a dose change for blood levels to reach a new stable level. After removal of a patch, a reservoir of active drug may remain in the skin and continue to be absorbed for several days and can cause difficulties in switching to alternative analgesics.
- A review of trials involving lower dose buprenorphine patches for chronic non cancer pain found that efficacy was similar to tramadol or co-codamol and that the patches have a considerable placebo effect. Data on equivalent doses for these agents are lacking.

Dose equivalents of oral morphine and buprenorphine patches
NB These doses are a guide only. They are based on a ratio of 100:1 potency, though this may not be applicable to all patients. **This data should not be used to switch treatments.**

Buprenorphine 5 micrograms/hr	12mg morphine in 24 hours
Buprenorphine 10 micrograms/hr	24 mg morphine in 24 hours
Buprenorphine 20 micrograms/hr	48 mg morphine in 24 hours
Buprenorphine 35 micrograms/hr	84 mg morphine in 24 hours
Buprenorphine 52.5 micrograms/hr	125 mg morphine in 24 hours
Buprenorphine 70 micrograms/hr	168 mg morphine in 24 hours

WHAT ARE THE COSTS? (28 days, Drug Tariff/MIMS, March 2017)



Comparison of cost of commonly prescribed buprenorphine patches at each dose with approximate equivalent dose of Zomorph®. NB Patients should be monitored closely if any changes in dose or formulation are made. List of products is not exhaustive.

KEY MESSAGES

- **Buprenorphine patches at lower doses are broadly as effective as codeine or tramadol but much more expensive. Oral analgesics should generally be preferred as first line therapy in chronic non-cancer pain.**
- **Buprenorphine patches should be prescribed by brand name. The preferred brand of low strength patch is Reletrans®.**
- **The patches are unsuitable for acute or unstable pain due to the need for slow titration of doses; it may take up to 72 hours to achieve a stable blood level after a change in dose.**
- **Exposure of patches to heat while being worn may lead to increased absorption of the drug and consequent adverse effects. Patients should be warned of the symptoms of excessive absorption including respiratory depression, sedation, drowsiness, and nausea and vomiting (see SPC).**

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Efficacy

See MTRAC review.[1] Trials in non-cancer pain (often back pain) found the patches to be superior to placebo and in a trial comparing low dose buprenorphine patches (Butrans) with tramadol MR, non-inferiority of the patches was found[2]. In a further trial[3] involving osteoarthritis patients, where buprenorphine patches were used together with paracetamol, the patches were found to be non-inferior to co-codamol (using doses of codeine in the co-codamol group up to 60mg).

Prescribing Considerations

The SPC for Butrans recommends not increasing the dose for 3 days when starting on a patch, during this time supplemental analgesia will be needed to maintain analgesic effect for a patient switching from other analgesics.

During discontinuation, additional opioids should not be given for the first 24 hours after removal of a patch as a reservoir of active drug may remain in the skin and continue to be absorbed for over 24 hours. This can cause difficulties in switching to alternative analgesics.

Dose Equivalence

The data is based on a ratio of 100:1compared with morphine, a ratio suggested by the Palliative care Formulary (PCF-4[4]). For example 12mg morphine in 24 hours = 0.5mg per hour = 500mcg per hour, which is equivalent to buprenorphine 5mcg/hr. Clearly these should be treated with caution, particularly at higher doses. Dose equivalents for buprenorphine patches with other opioid analgesics such as tramadol or codeine are not available.

Cost comparisons

*Actual spend on buprenorphine patches was **£716,061.40** on **23,953**items (£29.89 per item). During the same period the average cost per item for tramadol and codeine was £4.23. So, if half the items had been prescribed as tramadol or codeine equally, new cost for buprenorphine patches would have been £358,030.70 and the cost for the tramadol and codeine would have been 11,977 x £4.23 = £50,662.71. So new total spend = £408,693.41, a saving of £307,367.99.*
Spend on low strength generic buprenorphine patches and Butrans patches was £600,232.83. Reletrans patches are 50% cheaper, a saving of £300,116.42

The cost chart compares the cost of buprenorphine patches at each dose with approximate equivalent dose of Zomorph®. The costs of the Zomorph have been calculated from the nearest practicable dose (e.g. the 12mg dose cost is calculated on 20mg daily). Costs of Transtec and Bupeaze calculated using 2 patches per week as suggested in SPC. Costs of Hapoctasin calculated using one patch every 3 days (≈9 patches per 28 days) as suggested in SPC.
NB Patients should be monitored closely if any changes in dose or formulation are made. Morphine has been used as comparator drug for these costings because of the lack of availability of dose equivalents for weaker opioids.

References

1. *MTRAC Review. Buprenorphine transdermal patch for the treatment of chronic non-cancer pain. January 2012.*
2. *Karlsson M & Berggren AC. Efficacy and safety of low-dose transdermal buprenorphine patches (5, 10, and 20 microg/h) versus prolonged-release tramadol tablets (75, 100, 150, and 200 mg) in patients with chronic osteoarthritis pain: a 12-week, randomized, open-label, controlled, parallel-group noninferiority study. Clin ther 2009; 31:503-13.*
3. *Conaghan PG et al. Transdermal buprenorphine plus oral paracetamol vs an oral codeine-paracetamol combination for osteoarthritis of hip and/or knee: A randomised trial. Osteoarthritis and Cartilage 2011;19:930-8.*
4. *Buprenorphine monograph in Palliative Care Formulary (PCF-4). Eds Twycross R & Wilcock A, Pallitivedrugs.com Ltd, 2011, p381.*