Scottish Medicines Consortium

buprenorphine transdermal patch 5, 10 and 20 microgram/hour (BuTrans®) No. (234/06)

Napp Pharmaceuticals

6 January, 2006

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHS Scotland. The advice is summarised as follows:

ADVICE: following a full submission

Buprenorphine transdermal patch (BuTrans®) is not recommended for use within NHS Scotland for the treatment of severe opioid responsive pain conditions which are not adequately responding to non-opioid analgesics.

There was a lack of evidence of comparative efficacy with a clinically relevant treatment for chronic pain available in the UK. The economic case has not been demonstrated.

The licence holder has indicated their decision to resubmit.

Overleaf is the detailed advice on this product.

Chairman
Scottish Medicines Consortium

Licensed indication under review

Treatment of severe opioid responsive pain conditions which are not adequately responding to non-opioid analgesics.

Dosing information under review

Transdermal patches of 5, 10 or 20 microgram per hour applied every seven days. It is recommended that no more than two patches are applied at the same time.

UK launch date

30th September 2005

Comparator medications

Buprenorphine transdermal 72 hour patches, buprenorphine sublingual, dihydrocodeine prolonged release, co-dydramol and co-codamol.

Cost per treatment period and relevant comparators

Medicine	Dose	Cost per month (30 days)
Transdermal buprenorphine	**5-20 mcg/hour over a period of 7 days**	**£19 - £64**
Transdermal buprenorphine	35-52.5mcg/hour for 72 hours	£58 - £87
Co-dydramol 30/500	2 tablets four times daily	£27
Buprenorphine sublingual tablets	200 – 400mcg 3 – 4 times daily	£10 - £26
Co-codamol 30/500	2 tablets four times daily	£17
Dihydrocodeine prolonged release	60 – 120mg twice daily	£6 - £12

Doses are shown for general comparison and do not imply therapeutic equivalence.

Summary of evidence on comparative efficacy

The usually accepted definition of chronic pain is pain of at least three to six months duration which has persisted beyond the point at which healing would be expected to be complete or that occurs in disease processes in which healing does not take place. Chronic pain affects around 18% of the Scottish population. Buprenorphine is an opioid with mixed agonist-antagonist properties; it has partial agonist activity at the mu opioid receptor and antagonistic activity at the kappa opioid receptor.

The company submitted seven clinical trial reports, two in osteoarthritis pain, two in chronic back pain, two in chronic non-malignant pain and one long-term study in chronic pain of differing aetiologies. All studies used buprenorphine 5,10 or 20 microgram/hour patches and only three have active comparators.

Other data were also assessed but remain commercially confidential.*

Summary of evidence on comparative safety

No new safety concerns were raised during the studies with buprenorphine patches 5,10 and 20 micrograms /hour. Most adverse events were mild to moderate in intensity. Those most commonly reported were nausea, dizziness, vomiting, somnolence, headache, constipation and asthenia.

Summary of clinical effectiveness issues

Of seven clinical trial reports submitted, only three had an active comparator, two of which are not licensed in the UK and the third, sublingual buprenorphine tablets, is not considered standard treatment for chronic pain. The lack of an appropriate comparator reflecting the usual standard of care in Scotland, the variety of trial design, employing prior screening and different titration methods, different background analgesia and relatively small patient numbers with often significant discontinuation rates makes assessment difficult. In addition, most of the studies were of relatively short duration.

Summary of comparative health economic evidence

The manufacturer presents a cost utility analysis of buprenorphine 7 day transdermal patch plus current therapy against current therapy alone. Two time horizons are considered: 44 days and 250 days. The source of clinical evidence is a placebo controlled non-malignant pain trial among 107 elderly US nursing home residents.

Pain scores on an 11 point (0-10) scale were collected three times weekly during the trial. These are converted to utilities through analysis of the same scale having been used in conjunction with the EQ-5D within two studies of buprenorphine 7 day transdermal patch in chronic back pain.

For the elderly respondents within the trial the average utilities estimated are 0.510 for the buprenorphine plus usual care patients and 0.481 for those under usual care, a net average gain of around 0.03.

The average cost per patient during the 44 day trial was £61 equivalent to an annual cost of around £500 per patient. Coupling this with the average gain in quality of life results in a cost effectiveness estimate of £17,100/QALY. The manufacturer within an extrapolated one year analysis provides an additional estimate of the cost effectiveness of buprenorphine of £29,000/QALY on the basis of the utility increment declining linearly to zero over 250 days.

These figures do not include any consideration of possible adverse events and their treatment costs, though the manufacturer indicates in an additional communication that this might add around £6 to the net cost of buprenorphine. Another transdermal opioid or oral opioid combination analgesic might also have been a contender for the comparator arm of the analysis, rather than the usual care arm of the trial.

Within the trial population under consideration, elderly nursing home care residents, the cost effectiveness of buprenorphine 7 day transdermal patch has not been demonstrated. The cost effectiveness of buprenorphine within the wider population group indicated by the licence has not been considered.

Patient and Public involvement

Patient Interest Group Submission: Pain Concern
Patient Interest Group Submission: Pain Association Scotland

Budget impact

The manufacturer estimates the gross cost of buprenorphine 7 day transdermal patch at £344,000 in year one, rising to £1.1m in year five.

Guidelines and protocols

Recommendations for the appropriate use of opioids for persistent non-cancer pain, a consensus statement prepared on behalf of the Pain Society, the Royal College of Anaesthetists, the Royal College of General Practitioners and the Royal College of Psychiatrists, March 2004.

Additional information

In August 2004 the Scottish Medicines Consortium (SMC) concluded that buprenorphine 72 hour patch (Transtec) was not recommended for use within NHS Scotland for the treatment of moderate to severe cancer pain and severe pain that does not respond to non-opioid analgesics.

In January 2003 the SMC concluded that fentanyl transdermal patch (Durogesic) was recommended for restricted use within the NHS Scotland and should be considered as a second-line alternative for patients with intractable pain due to non-malignant conditions. It should be reserved for patients whose pain has initially been controlled by oral means, the pain being relatively stable. Its use should focus on such patients who have difficulty swallowing or have problems with opiate induced constipation. Transdermal patches are significantly more expensive than oral therapy.

In August 2005 the SMC recommended that oxycodone prolonged release (Oxycontin) was accepted for restricted use within NHS Scotland for the treatment of severe non-malignant pain requiring a strong opioid analgesic. It was restricted to use in patients in whom controlled release morphine sulphate is ineffective or not tolerated.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

This assessment is based on data submitted by the applicant company up to and including 16 December 2005.

** Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:* http://www.scottishmedicines.org.uk/

Drug prices are those available at the time the papers were issued to SMC for consideration.

The references supplied with the submission remain commercial in confidence.