Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
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# buprenorphine 5, 10, 15 and 20 microgram/hour transdermal patch (Butec®)

SMC No. (1213/17)

## Qdem Pharmaceuticals Limited

09 December 2016

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 patches (Butec®)** are accepted for restricted use within NHS Scotland.

**Indication under review:** In adults, for the treatment of chronic non-malignant pain of moderate intensity when an opioid is necessary for obtaining adequate analgesia.

**SMC restriction:** for use in elderly patients (over 65 years).

Non-inferiority was demonstrated between buprenorphine weekly patches and twice daily oral tramadol in patients with moderate to severe osteoarthritic pain. Non-inferiority was also demonstrated between buprenorphine weekly patches plus oral paracetamol and co-codamol in patients with severe osteoarthritic pain.

Overleaf is the detailed advice on this product.

**Chairman,**
**Scottish Medicines Consortium**

Published 16 January 2017

## Indication

Treatment of non-malignant pain of moderate intensity when an opioid is necessary for obtaining adequate analgesia. Buprenorphine patches are not suitable for the treatment of acute pain. Buprenorphine patches are indicated in adults.[1]

## Dosing Information

Buprenorphine (Butec®) patches deliver medication over seven days. Initially the lowest dose (5 microgram/hour transdermal patch) should be used. Consideration should be given to the previous opioid history of the patient as well as to their current general condition and medical status. The maximum recommended dose is 40 microgram/hour.

The dose of buprenorphine may be titrated upwards after three days, when the maximum effect of a given dose is established. Subsequent dosage increases may then be titrated based on the need for supplemental pain relief and the patient's analgesic response to the patch. To increase the dose, a larger patch should replace the patch that is currently being worn, or a combination of patches should be applied in different places to achieve the desired dose. It is recommended that no more than two patches are applied at the same time. Patients should be carefully and regularly monitored to assess the optimum dose and duration of treatment. A new patch should not be applied to the same skin site for the subsequent three to four weeks.[1]

## Product availability date

February 2016

## Summary of evidence on comparative efficacy

Buprenorphine is a partial agonist opioid, acting at the mu opioid receptor and also has antagonistic activity at the kappa opioid receptor.[1] Butec® 7-day transdermal patch is a branded generic version of BuTrans®. In 2009, BuTrans® was not recommended by SMC for the treatment of severe opioid-responsive pain conditions which are not adequately responding to non-opioid analgesics. The licensed indication for BuTrans® was subsequently changed but the new indication (which is identical to that of the product under review) has not been assessed by SMC. The submitting company has requested that SMC considers Butec® when positioned for use in elderly patients (over 65 years).

The main clinical evidence is from two phase IV studies investigating the reference product, BuTrans® transdermal patches.[2,3] BUP4004 compared buprenorphine weekly patches plus oral paracetamol (hereafter referred to as buprenorphine/paracetamol) with an oral combination of codeine and paracetamol (co-codamol).[2] BUP4009 compared buprenorphine patches with oral tramadol.[3] Supportive evidence was presented from a retrospective cohort study.[4]

BUP4004 was an open-label, randomised, controlled study that recruited patients ≥60 years of age with osteoarthritis of the knee and/or hip causing severe pain (defined as a score of ≥5 on the box scale-11 [BS-11] pain scale, where 0=no pain and 10=pain as bad as you can imagine).[2] Patients were required to be taking paracetamol at their maximum tolerated daily

dose (≥ four 500mg tablets). They (n=220) were randomised equally, stratified by study site, to receive open label treatment with buprenorphine patches plus oral paracetamol or co-codamol tablets. The medication was titrated for up to 10 weeks to achieve optimum pain relief. The initial dose of buprenorphine was 5 micrograms/hour, increasing by increments of 5 micrograms/hour to a maximum of 25 micrograms/hour, and the dose of concomitant paracetamol was two 500mg tablets four times daily. The initial (four times daily) dose of co-codamol was two 8/500mg tablets, then one 8/500mg tablet plus one 15/500mg tablet, then two 15/500mg tablets, then (again) two 15/500mg tablets, then two 30/500mg tablets. Oral ibuprofen (400mg up to three times daily) was allowed for breakthrough pain, and patients were advised to take 20mg omeprazole on each day that they took ibuprofen, for gastroprotection. Patients in both treatment arms were prescribed an anti-emetic medicine, oral prochlorperazine three times daily, during the first week of the titration period and then as required. Laxatives were prescribed if required. Patients who achieved optimum pain control during the titration period entered the 12-week assessment period. If required, further dosage adjustments were permitted after four and eight weeks to maintain optimum pain control.[2]

The primary outcome was average daily pain scores which were recorded each night by the patient using the BS-11 numeric rating pain scale. A decrease of at least two boxes is considered to be clinically relevant. The primary analysis was in the per protocol (PP) population, defined as patients who received at least one dose of study medication, had at least one primary efficacy measurement after randomisation, had no major protocol violations and completed at least 75% of the assessment period. Efficacy was also assessed in the full analysis population, defined as patients who received at least one dose of study medication and had at least one primary efficacy measurement after randomisation. In the PP population (n=61 in the buprenorphine/paracetamol group and n=56 in the co-codamol group), there was an improvement in both treatment groups from baseline mean BS-11 scores (standard deviation [SD]) of 7.0 (1.31) for buprenorphine/paracetamol and 7.0 (1.1) for co-codamol to 3.4 (1.44) and 3.7 (1.66) for the respective groups at the end of the titration period. This improvement was maintained throughout the assessment period. The pain scores were analysed fortnightly during the assessment period resulting in an estimated treatment difference of -0.02 (95% confidence interval [CI] -0.64 to 0.60). The lower boundary of the CI was greater than the pre-specified limit of -1.5 boxes, therefore non-inferiority of buprenorphine/paracetamol to co-codamol tablets was shown. This result was supported by an analysis in the full analysis set (FAS) (n=107 in the buprenorphine/paracetamol group and n=102 in the co-codamol group). Estimated treatment difference was -0.07 (95% CI: -0.67 to 0.54).[2]

Use of breakthrough medication (oral ibuprofen) was significantly (33%) lower in the buprenorphine/paracetamol group than in the co-codamol group in the PP population: estimated treatment difference -0.98 (95% CI:-1.55 to -0.40); p=0.002. Similar results were seen for the FAS. There was no significant difference between treatment groups in sleep disturbance, quality of sleep or laxative use.[2] There was no significant difference between treatment groups in quality of life assessed using the EuroQol -5D (EQ-5D) and the General Well-being Index. However, the EQ-5D results were analysed post-hoc and showed that patients in both groups had a mean increase in utility scores of 0.2 from baseline.[2]

BUP4009 was an open-label, randomised, controlled, non-inferiority study that recruited patients >18 years of age with a clinical diagnosis of osteoarthritis of the hip and/or knee (American College of Rheumatology [ACR] and radiographic criteria).[3] Pain relief in the primary osteoarthritic joint had to be suboptimal (BS-11 ≥4) in the week before baseline and patients had to have inadequate pain relief from maximal-dose paracetamol during the screening week in which they stopped all current analgesia and were provided with paracetamol only. A total of

135 patients were then randomised equally to receive treatment with buprenorphine 7-day patches (titration doses as for BUP4004) or tramadol prolonged release tablets twice daily, titrated from a daily dose of 150mg to 400mg if required for pain control. The study lasted 12 weeks and incorporated the titration period. Paracetamol (up to four 500mg tablets daily) was permitted as rescue medication. Anti-emetics could be taken as required.[3]

The primary outcome was the mean weekly BS-11 pain score, calculated from the daily scores entered in the patient diaries. Efficacy was analysed in both the FAS (all randomised patients who received at least one dose of study medication) and in the per-protocol analysis set (PPAS) (FAS patients with no major protocol violations). Results were presented as the least squares mean (LSM) change in BS-11 scores from baseline. FAS analysis (n=134): LSM (95% CI) -2.26 (-2.76 to -1.76) for buprenorphine and -2.09 (-2.61 to -1.58) for tramadol; difference between treatments: -0.17 (-0.89 to 0.54). PPAS analysis (n=90): LSM (95% CI) -2.69 (-3.27 to -2.12) for buprenorphine and -2.43 (-3.06 to -1.80) for tramadol; difference between treatments: -0.26 (-1.11 to 0.59). Non-inferiority was demonstrated in both analyses as the treatment difference was less than 1.5 boxes.[3]

There was no significant difference in the number of paracetamol tablets (rescue medication) taken by either treatment group. There was no significant difference between treatment groups in sleep disturbance or in quality of sleep. Global impression of pain relief (patients' and investigators' ratings) of study medication compared with pre-study medication was significantly higher for buprenorphine patches than oral tramadol (patient rating, p=0.039; investigator rating p=0.020). There were no significant differences between treatment groups for any Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index subscale scores. There was a significantly lower incidence of anxiety and depression at study completion in the tramadol group compared with the buprenorphine group. There were no significant differences between treatment groups in EQ-5D, mobility, self-care, usual activities, and pain/discomfort or EQ-visual analogue scale. At the end of the study, patients were asked: "Imagine equal pain relief - what would you prefer as a basic analgesic treatment for your osteoarthritis pain in the future: a patch applied once a week or a tablet taken twice daily?" Of those that responded, 70% (90/128) would prefer a patch.[3]

In a retrospective cohort study using UK data from the General Practice Research Database (GPRD), patients in the buprenorphine 7-day patch cohort (n=4,968) were matched by age, sex, and practice with comparator cohorts prescribed oral codeine, dihydrocodeine, or tramadol.[4] Most (64%) patients in the buprenorphine cohort were over 65 years; the most common indication (49%) was osteoarthritis. The mean patch strength prescribed over the 20-month assessment period was 10 to 12 micrograms/hour. Treatment persistence (based on repeat prescribing within 90 days after the expected end of a prescription) over six months was significantly higher with buprenorphine patches than with codeine, dihydrocodeine, or tramadol (28.9%, 22.4%, 24.4%, and 23.8%, respectively; p<0.01). Persistence over 12 months was significantly higher with buprenorphine patches (18.5%, 16.1%, 18.0%, and 17.6%, respectively; p<0.01). After 12 months, the differences were not statistically significant.[4]

## Summary of evidence on comparative safety

In BUP4004 treatment-emergent adverse events were reported in 86% (95/110) of patients in the buprenorphine/paracetamol group and in 82% (89/109) of patients in the co-codamol group. Most were of mild or moderate intensity. A higher proportion of patients in the

buprenorphine/paracetamol group than in the co-codamol group discontinued the study due to adverse events: 34% (38/110) versus 22% (24/109), respectively. The most common treatment-emergent adverse events were: constipation (26% versus 32%) in the buprenorphine/paracetamol group versus the co-codamol group; nausea (40% versus 25%); erythema at application site (27% versus 0); pruritus at application site (17% versus 0); dizziness (14% versus 5.5%) and vomiting (11% versus 8.3%). Erythema was categorised as moderate in six patients and severe in two patients, and pruritus was categorised as moderate in two patients and severe in two patients. Three patients (2.7%) in the buprenorphine/paracetamol group reported a total of six serious adverse events (including chest pain, peripheral oedema, fall, patella fracture and dyspnoea) compared with one patient (0.9%) in the co-codamol group (arthritis).[2]

In BUP4009, adverse events were reported in 88% (61/69) of patients on buprenorphine (total of 226 events) and in 78% (51/65) of patients on tramadol (total of 152 events). There was one serious adverse event that was considered to be possibly related to study treatment, a subendocardial myocardial infarction in a patient receiving tramadol. Discontinuations due to adverse events occurred in 14% (10/69) of patients on buprenorphine and in 29% (19/65) of patients on tramadol. The most common adverse events were: nausea (30% versus 25%) in the buprenorphine versus tramadol groups; constipation (19% versus 7.7%); dizziness (16% versus 4.6%); pain (14% versus 12%); hyperhidrosis (14% versus 6.2%); fatigue (13% versus 18%); vertigo (13% versus 1.5%) and headache (12% versus 11%).[3]

In the GPRD study, the safety profile (Cox proportional hazards regression models) for the buprenorphine cohort was significantly worse ($p<0.05$) than the other opioid cohorts, with higher rates of constipation, dizziness, nausea and vomiting.[4]

## Summary of clinical effectiveness issues

Chronic pain is a difficult condition to treat. There is no definitive treatment path and there are risks associated with using opioid medicines in the elderly. Buprenorphine transdermal patch (Butec®) was the first branded generic version of BuTrans® to receive a UK marketing authorisation. Butec® and BuTrans® transdermal patches are identical.[5] BuTrans® was not recommended by SMC in 2009 for the treatment of severe opioid responsive pain conditions which are not adequately responding to non-opioid analgesics. Subsequently the licensed indication for BuTrans® was changed and now corresponds with that of Butec®.[6] This indication has not been reviewed by SMC. Several other generic buprenorphine 7-day patch products have recently been licensed in the UK.

The submitting company has requested that SMC considers Butec® when positioned for use in elderly patients (over 65 years).

Clinical experts consulted by SMC considered that there is unmet need in this therapeutic area, namely in some elderly patients who require low dose opioids, but cannot tolerate currently available treatment options. They have advised that BuTrans® is currently being prescribed widely in Scotland and this is confirmed with NHS Scotland prescribing data.[7]

In patients with osteoarthritis, non-inferiority was demonstrated between buprenorphine weekly patches/paracetamol and co-codamol in patients with severe pain and between buprenorphine weekly patches and twice daily oral tramadol in patients with moderate to severe pain.[2,3] There

was less use of breakthrough medication in the buprenorphine/paracetamol group compared with the co-codamol group.[2] For the comparison of buprenorphine versus tramadol, global impression of pain relief (patients' and investigators' ratings) of study medication compared with pre-study medication was significantly higher for buprenorphine patches than oral tramadol; however, there was a significantly lower incidence of anxiety and depression at study completion in the tramadol group compared with the buprenorphine group. Although patient preference was for patches over tablets, no evidence of improved quality of life was demonstrated.[3]

Limitations of the evidence are that only osteoarthritic pain was investigated in the controlled studies. No randomised controlled study evidence was provided for the efficacy of buprenorphine patches in other types of non-malignant pain in elderly patients. The studies were open-label in design. The assessment period in both studies was 12 weeks, which is too short to determine long-term efficacy and safety in patients with chronic pain. The pivotal studies investigated patients in severe pain and in moderate to severe pain, whereas the licensed indication is for moderate pain. Only 43% of the study population in BUP4009 was over 65 years.[3] The submitting company has claimed that patient compliance would be increased but there is no robust comparative evidence for this. Compliance was not reported for either pivotal study. In BUP4004, all patients receiving buprenorphine patches also took concomitant paracetamol (two tablets four times daily), so there was no advantage with respect to reduced oral medication (pill burden) compared with the group taking co-codamol.[2]

Clinical experts consulted by SMC considered that the place in therapy of buprenorphine weekly patches is in frail elderly patients with additional risk factors including co-morbidities, swallowing difficulty, polypharmacy and cognitive impairment. Buprenorphine may provide a benefit in patients with renal impairment as no special dose adjustment is required.[1] Tramadol and codeine should be used with caution in renal impairment.[8,9]

## Summary of comparative health economic evidence

The submitting company provided a cost-minimisation analysis comparing buprenorphine to BuTrans® for use in elderly patients. As noted above, prescribing data indicates that BuTrans® is being used in NHS Scotland, and thus could be considered a relevant comparator in the population of interest. The company also submitted a cost- utility analysis comparing buprenorphine to co-codamol and tramadol for use in elderly patients.

In terms of the methods used for the cost-minimisation analysis which compared buprenorphine to BuTrans® (the reference product for buprenorphine as a branded generic), comparable efficacy was assumed between treatments and the analysis included only medicines costs. Costs were calculated according to a weighted average approach (whereby the proportion of patients receiving each dose was derived from study BUP4004).

For the cost-utility analysis (CUA), a two state Markov model was provided which included the health states ‘on treatment’ (consisting of a titration phase and maintenance phase) and ‘off treatment’. Patients moved through the model according to the probability of withdrawal and were assumed to withdraw due to adverse events or lack of efficacy. Once in the ‘off treatment’ health state, patients could not return to the ‘on treatment’ state and were assumed to receive rescue treatment only. The time horizon used in the analysis was five years.

The key efficacy parameters used within the cost-utility analysis were the probability of withdrawal and the proportion of patients assumed to stabilise on treatment. The model included withdrawal probabilities for each treatment at the end of the titration phase (week 10), maintenance phase (week 22) and cycle 3 onwards. Based on data from the pivotal studies (BUP4004, BUP 4009) and the GPRD retrospective cohort study, buprenorphine resulted in the lowest probability of withdrawal during the titration phase (39.1% compared to 42.7% and 47.9% for co-codamol and tramadol respectively). However, by cycle 3 buprenorphine resulted in the highest probability of withdrawal (19.2% compared to 14.5% and 13.5% for co-codamol and tramadol respectively). This was based on the proportion of patients remaining on treatment between week 22 and month 12 of the GPRD study. Long term treatment persistence data were derived from 20 month Kaplan-Meier curves. Based on the GPRD study, the proportion of patients assumed to stabilise on treatment were 19%, 16.5% and 17.8% for buprenorphine, co-codamol and tramadol respectively. However, these results were not statistically significant.

In terms of medicines acquisition costs in the CUA, these were based on a weighted average approach, whereby the proportions of patients were derived from BUP4004. It was also assumed that patients with uncontrolled pain ie those in the 'off treatment' health state, would receive 2000mg of paracetamol per day only. These patients were also assumed to incur a monthly GP visit (£38). Adverse event costs were not included.

Utility values were derived from the published literature. For patients in the 'on treatment' (controlled pain) health state a value of 0.59 was applied, while those in the 'off treatment' (uncontrolled pain) health state were estimated to have a utility value of 0.41. The model also accounted for utility within the titration phase of the model. Based on a mean time to optimum pain control of 20.7 days (from study BUP4004) and a titration phase of 10 weeks, 70.6% of patients were assumed to have controlled pain.

For the cost-minimisation analysis, based on a weighted average cost per patient per day of £1.22 and £0.55 for BuTrans® and buprenorphine respectively, buprenorphine resulted in incremental savings of £245 over one year compared to BuTrans®.

In the comparison versus co-codamol, buprenorphine plus paracetamol resulted in a base case incremental cost effectiveness ratio (ICER) of £7,751, based on an incremental cost of £63 and an incremental quality adjusted life year (QALY) gain of 0.0081. When compared to tramadol, buprenorphine resulted in a base case ICER of £4,688, based on an incremental cost of £109 and an incremental QALY gain of 0.0232. The relatively minor incremental cost versus both comparators stemmed primarily from drug costs alone, while the small QALY gain was a result of a higher proportion of patients remaining on buprenorphine treatment i.e. more patients remained in the controlled pain health state (accruing a higher utility).

Given the simplicity of the cost-minimisation analysis, no sensitivity analysis was provided. Sensitivity analysis on the CUA results showed that the ICERs were upwardly sensitive to changes in the values for key parameters (eg withdrawal probabilities, utility values for controlled pain and the proportion of patients stabilising on treatment), which in some cases led to buprenorphine being dominated (more expensive and less effective). For example, when the proportion of patients stabilising on treatment was set to 19% for all treatments (in line with the buprenorphine rate), buprenorphine was dominated by co-codamol and produced an ICER of £7,401 compared to tramadol. Also, when the utility value for the uncontrolled pain state was increased to 0.53, the ICERs increased to £24,477 compared to co-codamol and £14,803 compared to tramadol. Some of these sensitivity analyses stemmed weaknesses associated with the CUA (eg lack of statistical significance for the results in terms the key efficacy

parameters on withdrawal rates and the proportion of patients remaining on treatment).

Despite these weaknesses, the economic case was considered demonstrated.

## Summary of patient and public involvement

A Patient Group Submission was not made.

## Additional information: guidelines and protocols

In 2014, the National Institute for Health and Care Excellence published Clinical Guideline no. 177 which provides guidance on the care and management of adults with osteoarthritis. The recommendations on pharmacological management in the original 2008 guideline (CG59) remained unchanged. These state that: the evidence supporting the use of opioid analgesia in osteoarthritis is poor, and it must be noted there are virtually no good studies using these agents in peripheral joint osteoarthritis patients. There is little evidence to suggest that dose escalation of these agents is effective. There are also few data comparing different opioid formulations or routes of administration. Toxicity remains a concern with opioid use, especially in the elderly. However, it also states: If paracetamol or topical non-steroidal anti-inflammatory drugs are insufficient for pain relief for people with osteoarthritis, then the addition of opioid analgesics should be considered. Risks and benefits should be considered, particularly in elderly people.[10]

The SIGN clinical practice guidelines on the management on chronic pain (SIGN 136) (2013) recommend that strong opioids (which includes buprenorphine in the guideline) should be considered as an option for pain relief for patients with chronic low back pain or osteoarthritis, and only continued if there is ongoing pain relief. Regular review is required. It is noted in the guideline that some of the newer formulations of strong opioids allow very low dosing, with an equivalent effect to weak opioids. The guideline also notes that transdermal buprenorphine is useful if oral administration is problematic, and that there is minimal active metabolite accumulation in renal impairment. The guideline notes that there is no clear evidence that any particular opioid is better than any other in terms of efficacy for pain relief.[11]

The British Geriatrics Society/British Pain Society guidance on the management of pain in older people (2013) notes that opioids have demonstrated efficacy in the short term for non-cancer patients, but long-term data are lacking. The guidance recommends that opioids should be considered if the pain is causing functional impairment or is reducing the patient's quality of life. It emphasises that opioid therapy must be individualised and carefully monitored. Patients with continuous pain should be treated with modified release oral or transdermal opioid formulations aimed at providing relatively constant plasma concentrations. The guideline notes that there are limited data on the use of buprenorphine patches in the elderly but cites a post-marketing surveillance study in over 13,000 patients (mean age 68 years) that showed efficacy and sustained and dose-dependent pain relief. It also notes that the pharmacokinetics of buprenorphine are not altered in patients with renal failure and that the convenience of a transdermal preparation that requires to be replaced weekly reduces administration time and staffing requirements in residential and nursing homes.[12]

In May 2009 NICE published CG88 'Low back pain in adults: early management'. The guidelines advise that no opioids have a UK marketing authorisation for treating low back pain, but that weak opioids may be offered when paracetamol alone doesn't provide sufficient pain relief. Strong opioids may be considered for short-term use in severe pain.[13]

In 2008, Osteoarthritis Research Society International published its recommendations for the management of hip and knee osteoarthritis. It does not mention buprenoprphine. Its main general recommendation is that the "optimal management of osteoarthritis requires a combination of non-pharmacological and pharmacological modalities". Twenty-five recommendations were issued. Guide number 20 proposes that "weak opioids and narcotic analgesics can be considered for the treatment of refractory pain in patients, where other pharmacological agents have been ineffective, or are contra-indicated". Also "benefits associated with the use of opioids were limited by the frequency of side effects. Overall in the reviewed studies, 25% of patients withdrew from the studies." The guideline highlights the lack of long-term studies of the use of opioids in treating patients with osteoarthritis.[14]

## Additional information: comparators

The economic case presents a cost minimisation analysis against BuTrans®. Other licensed weekly buprenorphine patch products are included in the cost table for completeness. BuTrans® has not been reviewed by SMC for this indication. Butec® patches have also been compared with tramadol and, when used with concomitant paracetamol, they have been compared with co-codamol, both of which are considered to be "weak" opioids.[17]

## Cost of relevant comparators

| Drug | Dose Regimen | Cost per 12 weeks (£) |
|---|---|---|
| **Buprenorphine 7-day patch (Butec®)** | Transdermally, 5 to 40 micrograms/hour. Patch(es) to be replaced once weekly. | **24 to 155** |
| Buprenorphine 7-day patch (BuTrans®) | | 53 to 345 |
| Buprenorphine 7-day patch (Alliance Healthcare) | | 53 to 345 |
| Buprenorphine 7-day patch (AAH) | | 53 to 345 |
| Buprenorphine 7-day patch (Reletrans®) | | 33 to 215 |
| Buprenorphine 7-day patch (Panitaz®) | | 30 to 193 |
| Buprenorphine 7-day patch (Sevodyne®) | | 24 to 155 |
| Co-codamol | Orally two tablets (comprising codeine [8mg, 15mg or 30mg] plus paracetamol 500mg) every four to six hours up to four times daily. | 24 to 47 |

| | | |
|---|---|---|
| Tramadol | 50mg to 100mg every four to six hours up to a maximum daily dose of 400mg | 11 to 23 |

Doses are for general comparison and do not imply therapeutic equivalence. Costs on 02 October 2016; from eVadis for all medicines except buprenorphine (AAH), Reletrans® and Sevodyne® from eMC dm&d website and Butec® from company submission. Co-codamol cost range is based on maximal doses of 8/500, 15/500 and 30/500 formulations.

## Additional information: budget impact

The submitting company presented two different scenarios for the estimation of budget impact; one scenario assumed co-codamol and tramadol would be the displaced medicines of interest and one scenario assumed the displaced medicine would be BuTrans®.

Base case versus BuTrans®

The submitting company estimated there would be 4,514 patients eligible for treatment with buprenorphine transdermal patch in year 1 and 5,873 patients in year 5. The estimated uptake rate was 70% in year 1 (2,505 patients), rising to 90% in year 5 (3,260 patients) with a discontinuation rate of 44.5% applied.

The gross impact on the medicines budget was estimated to be £502k in year 1, rising to £653k in year 5. As medicines were assumed to be displaced, the net medicines budget impact was estimated to be a saving of £614k in year 1, rising to a saving of £799k in year 5.

Base case versus co-codamol and tramadol

The submitting company estimated there would be 488 patients eligible for treatment with buprenorphine transdermal patch in year 1 and 2,468 patients in year 5. The estimated uptake rate was 0.5% in year 1 (271 patients), rising to 2.5% in year 5 (1,370 patients) with a discontinuation rate of 44.5% applied.

The gross impact on the medicines budget was estimated to be £54k in year 1, rising to £274k in year 5. As medicines were assumed to be displaced, the net medicines budget impact was estimated to be £23k in year 1, rising to £117k in year 5.

References

The undernoted references were supplied with the submission.


1. Buprenorphine 5, 10 and 20 micrograms/hour transdermal patch (Butec®) Summary of product characteristics. Qdem Pharmaceuticals Limited. Electronic Medicines Compendium www.medicines.org.uk. Last updated 07 June 2016.

2. Conaghan PG, O'Brien CM, Wilson M et al. Transdermal buprenorphine plus oral paracetamol vs an oral codeine-paracetamol combination for osteoarthritis of hip and/or knee: A randomised trial. Osteoarthritis Cartilage 2011;19: 930-8.

3. Karlsson M, Berggren AC. Efficacy and safety of low-dose transdermal buprenorphine patches (5, 10, and 20 µg/h) versus prolonged-release tramadol tablets (75, 100, 150, and 200mg) in patients with chronic osteoarthritis pain: A 12-week, randomized, open-label, controlled, parallel group noninferiority study. Clin Ther 2009;31 (3):503-13.

4. Gallagher AM, Leighton-Scott J, van Staa TP. Utilization characteristics and treatment persistence in patients prescribed low-dose buprenorphine patches in primary care in the United Kingdom: A retrospective cohort study. 2009;31 (8):1707-15.

5. Medicines and Healthcare Products Regulatory Agency United Kingdom Public Assessment Report (UKPAR) for buprenorphine 5, 10, and 20 micrograms/hour transdermal patch (Butec®) PL 40431/0024-0026

6. Buprenorphine 5, 10, 15 and 20 micrograms/hour transdermal patch (BuTrans®) Summary of product characteristics. Napp Pharmaceuticals Limited. Electronic Medicines Compendium www.medicines.org.uk. Last updated 26 February 2016.

7. Information Services Division Prescription cost analysis 2015/16 https://www.isdscotland.org

8. Tramadol 50mg capsules Summary of product characteristics. Aurobindo Pharma-Milpharm Ltd. Electronic Medicines Compendium www.medicines.org.uk. Last updated 16 September 2015.

9. Boots Paracetamol and Codeine Capsules (Co-Codamol) Summary of product characteristics. The Boots Company plc. Electronic Medicines Compendium www.medicines.org.uk. Last updated 20 August 2015.

10. The National Institute for Health and Care Excellence (NICE). Clinical guideline 177: Osteoarthritis care and management. 12 February 2014. www.nice.org.

11. Scottish Intercollegiate Guidelines Network (SIGN) national clinical guideline on the management of chronic pain. SIGN 136. December 2013. www.sign.ac.uk.

12. British Geriatrics Society and British Pain Society. Guidance on the management of pain in older people. Age Ageing 2013; 42:i1–i57.

13. The National Institute for Health and Care Excellence (NICE). Clinical guideline 88 Low back pain; Early management of persistent non-specific low back pain. 2009. www.nice.org.

14. Zhang W, Moskowitz RW, Nuki G *et al.* OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis Cartilage 2008; 16:137-62

This assessment is based on data submitted by the applicant company up to and including 10 November 2016.

Drug prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

***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.*