New Medicine Recommendation
ActiPatch for treatment of pain: Knee Osteoarthritis, Plantar Fasciitis

LMMG recommendation:

Black – ActiPatch is not recommended for treatment of chronic pain (presence of pain for longer than 3 months) associated with knee osteoarthritis and plantar fasciitis.

The evidence was not sufficient to demonstrate the product's efficacy.

Summary of supporting evidence

Knee Osteoarthritis

After 1 month of treatment, there was a 25.5% reduction in VAS pain scores for subjects treated with the Pulsed Electro Magnetic Field (PEMF) device and a 3.6% reduction in those who received placebo, with a standardized effect size of -0.73 (95% CI-1.24 to-0.19) in VAS score. There was a 23.4% reduction in WOMAC pain subscale and 18.4% reduction in WOMAC total score compared with 2.3% reduction for both WOMAC pain and total in the placebo group.

During the study, 8 (26%) of patients in the PEMF group stopped NSAID/analgesic therapy and none started a new therapy for chronic pain, whereas in the placebo group 1 patient (3%) stopped and 3 (10%) started a new therapy for chronic pain.

Within the UK registry study, 66% of subjects suffering from chronic osteoarthritic pain felt they had benefitted from use of the device, with a VAS difference of 4.67 and a pain reduction of 56%.

Plantar Fasciitis

The study group using the active pulsed radiofrequency electromagnetic field (PRFE) device showed progressive decline in morning pain. The day 7 AM-VAS score was 40% lower than the day 1 AM-VAS score. The control group, in comparison, showed a 7% decline.

Medication use in the study group also showed a trend downward, but the use in the control group remained consistent with the day 1 levels.

Details of Review

Name of medicine: ActiPatch Device
Strength and form: Battery powered device, antenna size of 8 or 12 cm providing treatment area of 70 or 100cm^2 respectively. Provides pulse rate of 1000 pulses per second, with a pulsed on duration of 100microseconds.
Dose and administration: ActiPatch provides 720 hours with on/off capability. Recommended use time is initially 24 hours a day. Thereafter 6-24 hours per day as needed.
BNF therapeutic class / mode of action: ActiPatch provides relief from chronic musculoskeletal pain through mitigation of central sensitization, a task accomplished through neuromodulation of afferent nerves.[1]
Licensed indications: BioElectronics currently has FDA OTC clearances for adjunctive treatment of two types of musculoskeletal pain: 1) Knee osteoarthritis 2) Plantar Fasciitis. It is CE marked as a class II device, meaning that it has been cleared for sale in the European Union off the shelf, and it is commercially available in the UK and on prescription.
Proposed use: For treatment of chronic pain (presence of pain for longer than 3 months) associated with knee osteoarthritis and plantar fasciitis

Clinical Evidence

Introduction

Pulsed shortwave therapy (PSWT) devices such as the ActiPatch provide pain relief through prolonged stimulation of incoherent (stochastic) stimuli that the brain cannot interpret. Simply put, a repeated application of a signal at intensity levels too low to consistently trigger a pain response can still initiate a system response because the system is not only exposed to the applied signal, but also to electrical noise in the physiologic environment. This noise in physiological systems, such as neural systems, while ubiquitous, is widely considered to be essential in facilitating information processing in the body. The phenomenon whereby the presence of “noise” in non-linear systems can be used to enhance the detection of sub-threshold stimuli is referred to as “stochastic resonance (SR)”. As stated above, in a situation where there is a detection threshold, such as exists for nerves, a sub-threshold “signal” in the presence of noise may randomly become sufficiently large to exceed the necessary threshold to activate the nerve.

Knee Osteoarthritis Pain Clinical Study

Pulsed electromagnetic fields in knee osteoarthritis: a double blind, placebo-controlled, randomized clinical trial: Bagnato et al; Rheumatology 2016;55:755-762[2]

A double-blind, randomised, placebo-controlled clinical trial, in which patients with radiographic evidence of knee OA and persistent pain higher than 40mm on the visual analogue scale (VAS) were recruited. The trial consisted of a minimum of 12 hour daily

treatment (mainly at night), with the antenna placed over the knee, for 1 month in 60 knee OA patients.

The primary outcome measure was the reduction in pain intensity, assessed through VAS and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores. Secondary outcomes included quality of life assessment through the 36-item Medical Outcomes Study Short-Form version 2 (SF-36 v2), pressure pain threshold (PPT) and changes in intake of NSAIDs/analgesics.

Sixty-six patients were included, and 60 completed the study 3 patients from each group being lost to follow up). Patients were asked, during the enrolment phase, to record wear/hours per day and to report at the end of the study, the hours per day of device use. After 1 month, Pulsed Electro Magnetic Field (PEMF) induced a significant reduction in VAS pain and WOMAC scores compared with placebo. Additionally, pain tolerance, as expressed by PPT changes, and physical health improved in PEMF-treated patients. The pain threshold test was performed twice on the same day, with 2-5 min separating tests. The first test was designated as a trial run, to accustom participants to the testing procedures. The second test was designated as the test run, from which all data were obtained. The tests were performed on the same day to minimize heterogeneity caused by daily changes in environment, disease activity and mental status. To analyse the change in daily intake of NSAIDs per week at baseline and after 4 weeks of treatment patients reported analgesic and anti-inflammatory medications taken in the last week prior to each assessment.

During the study, the rates of compliance with the different devices were similar. Patients from PEMF group reported an average use of 11.3 ± 0.8 h/day, whereas patients treated with the placebo device reported 11 ± 0.7 h/day. No statistically significant difference was observed in daily use of the devices between the two groups.

Primary Outcomes - After 1 month of treatment, there was a 25.5% reduction in VAS pain scores for subjects treated with the PEMF device and a 3.6% reduction in those who received placebo, with a standardized effect size of -0.73 (95% CI-1.24 to-0.19) in VAS score. There was a 23.4% reduction in WOMAC pain subscale and 18.4% reduction in WOMAC total score compared with 2.3% reduction for both WOMAC pain and total in the placebo group. The standardized effect size was -0.61 (95% CI-1.12 to -0.09) for WOMAC pain and -0.34 (95% CI-0.85 to 0.17) for WOMAC total score.

Secondary Outcomes - PPT improved in OA patients after 1 month of treatment with the PEMF device compared with placebo. Physical health scores improved in the PEMF group.

During the study, 8 (26%) of patients in the PEMF group stopped NSAID/analgesic therapy and none started a new therapy for chronic pain, whereas in the placebo group 1 patient (3%) stopped and 3 (10%) started a new therapy for chronic pain.

Limitations – short study duration and small number of patients.

Safety - No adverse events were detected during the study.

Conclusion - These results suggest that PEMF therapy is effective for pain management in knee OA patients and that it also affects pain threshold and physical functioning. The use of a wearable PEMF therapy in knee OA can be considered as an alternative safe and effective therapy in knee OA, providing the possibility for home-based management of pain. Future larger studies, including head-to-head studies comparing PEMF therapy with standard pharmacological approaches in OA, are warranted.

Plantar Fasciitis/Heel Pain Clinical Study

Pulsed Radiofrequency Electromagnetic Field Therapy: A Potential Novel Treatment of Plantar Fasciitis: Brook et al; The Journal of Foot & Ankle Surgery 51 (2012) 312–316[3]

A double-blind, multicentre, randomised, placebo-controlled study was used to evaluate a small, wearable, extended-use pulsed radiofrequency electromagnetic field (PRFE) device as a treatment of plantar fasciitis. A total of 70 subjects diagnosed with plantar fasciitis were enrolled in the study.

The subjects were randomly assigned a placebo (28 patients) or active pulsed radiofrequency electromagnetic field (PRFE) (42 patients) device. The subjects were instructed to wear the PRFE device overnight, record their morning and evening pain using a 0- to 10-point visual analogue scale (VAS), and log any medication use. The primary outcome measure for the study was morning pain, a hallmark of plantar fasciitis.

The study group using the active PRFE device showed progressive decline in morning pain. The day 7 AM-VAS score was 40% lower than the day 1 AM-VAS score. The control group, in comparison, showed a 7% decline. A significantly different decline was demonstrated between the 2 groups ($p = .03$). The PM-VAS scores declined by 30% in the study group and 19% in the control group, although the difference was not significant. Medication use in the study group also showed a trend downward, but the use in the control group remained consistent with the day 1 levels.

Limitations - the length of time that data was collected (7 days), the lack of long-term follow-up and the lack of intercentre analysis. No power analysis was performed to calculate the study size, the sample size being determined by the amount of time the podiatric authors could allot to do the study, which resulted in lower than anticipated recruitment goals.

Safety - The PRFE therapy devices were well tolerated by all the patients, and no adverse effects were noted.

Conclusion - PRFE therapy worn on a nightly basis appears to offer a simple, drug-free, noninvasive therapy to reduce the pain associated with plantar fasciitis. Additional studies are warranted to confirm these initial findings.

Chronic pain study

A UK registry study of the effectiveness of a new over – the -counter chronic pain therapy: Rawe et al; Pain Manag. (2015), 5(6), 413-423[4]

This registry study included 44,000 subjects who tried the device, with 5,000 submitting an assessment. Subjects reported on overage severe baseline pain which was present despite using on average two pain modalities. In the study over 65% reported a clinically meaningful reduction in pain from a wide variety of aetiologies and locations of pain. The average pain reduction reported in these individuals was 57%. The 3 month follow up showed sustained pain relief, decreased oral analgesic medication use and quality of life improvement. The ActiPatch device was considered effective or of benefit when there was a reported 2 or greater visual analogue scale (VAS) point reduction (0-10 scale). Baseline VAS score pain for all the responses was an average of 8.02 despite the use of other pain modalities.

Safety Summary

No major adverse events were reported. Minor issues centred on attachment of the device and a reaction to the adhesive medical tape and occurred in 0.4% of the responses.[4]

Cost Effectiveness Summary

Cost Effectiveness Review

One ActiPatch provides 720 hours with on/off capability. Recommended use time is initially 24 hours a day. Thereafter 6-24 hours per day as needed.

The cost of one ActiPatch =£13.95. If the patch was activated continuously for 24 hours a day, this equates to the cost of 1 months treatment. If used for 12 hours i.e. overnight, then this equates to the cost of two months treatment.

If used continuously, the annual cost per patient = £13.95 x 12 = £167.40.

If used continuously for 1 month and then on a regular overnight basis i.e. 12 hours, the annual cost per patient = £13.95 x 7 = £97.65

In the UK registry study, there was a high baseline pain despite the subjects using on average two concurrent pain therapy modalities (84% reported taking pain medications), demonstrating that many patients respond poorly to a pharmacological approach for chronic pain as shown in previous studies the use of nonsteroidal anti-inflammatories and non-opiate analgesics is associated with a significant impact on primary care workload, with poor efficacy being the trigger for almost as many consultations as poor tolerability.[5]

Drug tariff prices for commonly prescribed anti-inflammatories / analgesics are:

- **Ibuprofen 400mg tablets** = £3.54 / 84 tablets
  (400mg tds = monthly cost £3.54, **annual cost £ 42.48**)
- **Diclofenac 50mg tablets** = £7.94 / 30 tablets
  (50mg tds = monthly cost £23.82, **annual cost = £285.84**)
- **Diclofenac 50mg gastro resistant tablets** = £2.25 / 28 tablets
  (50mg tds = monthly cost £6.75, **annual cost = £81.00**)
- **Celecoxib 200mg capsules** = £1.69 / 30 capsules
  (200mg bd = monthly cost £3.38, **annual cost = £40.56**)

As most patients suffering from chronic pain will be prescribed more than one concurrent pain medication (plus potentially a PPI for gastric protection) the annual cost per patient is likely to be higher than estimated above.

The clinical studies cited in this paper have demonstrated that patients using the ActiPatch device have decreased the amount of concurrent pain medication they use and so the associated medication costs would be expected to decrease.

A healthcare utilisation study carried out by BioElectronics (which was considered by the NHS when approving Actipatch on prescription), looking at the decreased utilisation of healthcare services by subjects in the study and the decreased analgesic medication costs, concluded that the total cost for providing chronic pain treatment reduced by 41% for those subjects using Actipatch.

Relevant Guidance

NICE CKS Plantar fasciitis; most people with plantar fasciitis will make a complete recovery within 6 months of starting conservative treatment.

Strengths and Limitations of the Evidence

Strengths

Knee Osteoarthritis Pain Clinical Study: This was a randomised, double blind, placebo controlled trial. In addition to the self-reported pain scores, such as the VAS and WOMAC scores, pain threshold was measured using pressure algometry, which is the most

commonly used quantitative and objective sensory testing method used in rheumatic diseases.

Plantar Fasciitis/Heel Pain Clinical Study: This was a randomised, double blind, multi centred, placebo controlled trial. This is the first study using this form of therapy for plantar fasciitis heel pain and demonstrates a decrease in pain within the 7 days, whilst conservative forms of treatment, including nonsteroidal anti-inflammatory drugs, heel pads or orthotics, physical therapy, stretching of the gastrocnemius-soleus, and corticosteroid injections, have a longer interval of resolution and have additional associated drawbacks and adverse effects.

Chronic Pain Study: The registry data come from 58 separate assessments that generate remarkably consistent results when grouped on a month by month basis. Baseline pain scores vary by only a few tenths between each of the sets of data collected, as does the extent of reported benefit in terms of both the level of and average pain reduction, and the effectiveness of the device. The data were also nonresponse bias tested.

Limitations

Knee Osteoarthritis Pain Clinical Study: There was a small (60 completed) number of patients included in the study and the primary end point for assessment of efficacy was set at 1 month.

Plantar Fasciitis/Heel Pain Clinical Study: There was a small number of patients (70) included in the study and the primary end point for assessment of efficacy was set at 1 week**,** with no long term follow up. The results from the study indicate that additional studies are warranted to confirm these initial findings.

Chronic Pain Study: This large (44,000 subjects tried the device, with 5,000 submitting an assessment) study involved participants who self-selected into the sample and thus may not represent a random sample of all chronic pain sufferers. In addition, the results were based only on users who responded to a survey. Although non-response bias testing did not reveal evidence of responder bias, it is still possible that bias could have been present.

Due to the open nature of the study, it could be argued that the reported benefit is due to a strong placebo effect. However, three published randomized controlled trials using placebo controls indicate that the placebo effect is minimal with this medical device.

Prescribing and risk management issues:

Prescribing of device may occur before other conservative treatment options have been explored for a sufficient period of time.

For patients suffering from chronic pain, the ActiPatch device could potentially be used as an adjunct to analgesic / anti-inflammatory treatment and intake of analgesics / anti – inflammatory treatment monitored.

Commissioning Considerations

Comparative Unit Costs

Drug	Example regimen	Pack cost	Cost per patient per year
Actipatch: Back, Knee and Muscle & Joint	Apply for up to 720 hours	£13.95[6]	£167.40 (if used continuously)

Costs based on MIMS online June 2018 and the Drug Tariff online, June 2018, excluding VAT.

Associated additional costs or available discounts:

N/A

Productivity, service delivery, implementation:

Allows patient self-care

Anticipated Patient Numbers and Budget Impact

A healthcare utilisation study carried out by BioElectronics (which was considered by the NHS when approving Actipatch on prescription), looking at the decreased utilisation of healthcare services by subjects in the study and the decreased analgesic medication costs, concluded that the total cost for providing chronic pain treatment reduced by 41% for those subjects using Actipatch.

There is little consensus regarding the burden of pain in the UK.

A systematic review and meta-analysis of population studies looking at the prevalence of chronic pain in the UK, concluded that chronic pain (pain that lasts for 3 months or longer) affects between one-third and one-half of the population of the UK.[7] However, this includes chronic pain of aetiologies other than the licensed indications being considered.

The prevalence of knee osteoarthritis in the UK has been estimated by Arthritis Research UK to be approximately 1 in 5 adults over the age of 45 i.e. 20%.[8]

The lifetime prevalence of plantar fasciitis has been estimated at 10%.[9] However, a NICE CKS states that most people with plantar fasciitis will make a complete recovery within 6 months of starting conservative treatment.

The population of Lancashire and South Cumbria is estimated at 1,663,273 with an adult population aged 44years and over of 758,545.

Within the Lancashire and South Cumbria geography it would therefore be estimated that approximately 151,709 adults over the age of 44 would suffer from knee osteoarthritis. If 10% (15,171) of this patient population were to receive Actipatch and were to use it continually on an overnight basis i.e. 12 hours / day, this would equate to an annual cost of £13.95 x 6 x 15,171 = £1,269,813. However, it would be expected that prescribing costs of analgesics / anti-inflammatories and NHS appointments would decrease

With the lifetime prevalence of plantar fasciitis estimated at 10%, this would equate to a population within Lancashire of 166,327 patients. If 10% of this patient population i.e. 16,633 were to use Actipatch for 12 hours per day for 6 months (as per NICE CKS) this would incur an annual cost of £13.95 x 3 x 16,633 =£696,091.

Innovation, need, equity:

Allows patient self-care

References

1. Actipatch Mechanism of Action and Clinical Evidence Packet. [Accessed online on 5 June 2018: http://www.actipatch.com/actipatch/wp-content/uploads/2014/11/ActiPatch-Mechanism-of-Action-and-Clinical-Evidence-Packet.pdf]

2. Pulsed electromagnetic fields in knee osteoarthritis: a double blind, placebo-controlled, randomized clinical trial: Bagnato et al; Rheumatology 2016;55:755-762

3. Pulsed Radiofrequency Electromagnetic Field Therapy: A Potential Novel Treatment of Plantar Fasciitis: Brook et al; The Journal of Foot & Ankle Surgery 51 (2012) 312–316

4.A UK registry study of the effectiveness of a new over-the-counter chronic pain therapy. Rawe et al; Pain Manag. (2015) 5(6), 413–423 .

5.Belsey J. Primary care workload in the management of chronic pain: a retrospective cohort study using a GP database to identify resource implications for UK primary care. J. Med. Econ. 5, 39–50 (2002).

6.Drug Tariff online Part IX June 2018 [Accessed online 4 June 2018: https://www.nhsbsa.nhs.uk/sites/default/files/2018-03/Drug%20Tariff%20Part%20IX%20April%202018.pdf]

7.Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies. Fayaz et al; . BMJ Open 2016;6:e010364. doi:10.1136/bmjopen-2015-01036 https://bmjopen.bmj.com/content/bmjopen/6/6/e010364.full.pdf

8.Arthritis Research UK, Musculoskeletal calculator; https://www.arthritisresearchuk.org/arthritis-information/data-and-statistics/musculoskeletal-calculator.aspx

9.Diagnosis and management of plantar fasciitis in primary care. Thing et al; Br J Gen Pract 2012; 62 (601): 443-444 http://bjgp.org/content/62/601/443

Midlands and Lancashire Commissioning Support Unit,
Jubilee House, Lancashire Business Park, Leyland, PR26 6TR