VERDICT & SUMMARY

Lidocaine 5% plaster *(Versatis®)*

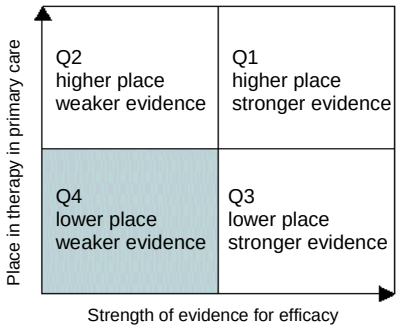
For the treatment of postherpetic neuralgia

Committee's Verdict: CATEGORY B (Q4) **BNF: 15.2**

Prescribing of the lidocaine 5% plaster in primary care should be restricted to patients diagnosed with postherpetic neuralgia, in whom alternative treatments have proved ineffective or where such treatments are contraindicated, and in line with NICE guidance.

Category B: *suitable for restricted prescribing under defined conditions*

Q4 rating: Based on the findings of four published, randomised, controlled trials, the evidence for the efficacy of the lidocaine 5% plaster was considered to be weak. Outcomes were inconsistent in two studies measuring 'time-to-exit' (based on deterioration in pain relief using a verbal rating scale) in patients who had previously responded to treatment with the plaster. In an open-label comparative study with pregabalin, the criteria for non-inferiority of the lidocaine plaster were not clearly met. The fourth trial assessed lidocaine plaster for two 12-hour periods only. The lidocaine plaster is considered to have 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.*

MTRAC reviewed this drug because it is a new product with potential for prescribing in primary care.

Licensed indication considered

Lidocaine 5% plaster is indicated for the symptomatic relief of neuropathic pain associated with previous herpes zoster infection (postherpetic neuralgia, PHN).[1]

Background information

PHN is a defined as prolonged neuropathic pain persisting for more than 90 days after an acute attack of herpes zoster (shingles).[2] The pain, which results in large part from viral damage to sensory nerves, can be of a burning, shooting or stabbing nature. Areas of the skin may become abnormally sensitive to touch, a phenomenon termed allodynia. It is not uncommon for the distressing pain of PHN to interfere with sleep and daily activities, and patients with PHN may become clinically depressed.

The risk of developing herpes zoster approximately doubles every decade after age 50.[3] The incidence of herpes zoster infection was reported to be 5.23 cases per 1,000 person-years in individuals in the UK aged 50 or above, with 13.7% of patients developing PHN within three months of the initial diagnosis.[3]

Lidocaine 5% plaster and capsaicin 0.075% cream are licensed as topical treatments for PHN. Agents approved for the treatment of neuropathic pain, including PHN, are gabapentin and pregabalin. The tricyclic antidepressants amitriptyline and nortriptyline, and the antiepileptic carbamazepine may also be used, although these drugs are not licensed for either neuropathic pain. Opioids (morphine, methadone, tramadol and oxycodone) may be considered when other treatments fail.[4]

Lidocaine 5% plaster was launched in the UK in 2007.

NICE guidance

The National Institute for Health and Clinical Excellence (NICE) published guidance on the management of neuropathic pain in March 2010. It recommended pregabalin or amitriptyline as first-line treatments for non-diabetic neuropathic pain, and either a combination of the two treatments or a switch to the other drug as second-line therapy.[5] Topical lidocaine (licensed for post-herpetic neuropathic pain) may be considered as third-line therapy in patients unable to take oral medication because of medical conditions or disability, whilst awaiting referral to a specialist pain service or condition-specific service. Oral tramadol, in combination with or instead of second-line treatment, may also be considered as a third-line treatment option whilst waiting for referral.

Clinical efficacy

Five randomised controlled trials have assessed the efficacy and safety of lidocaine 5% plasters in patients with PHN,[6-10] of which four are fully published.[6-9]

One trial was a double-blind, two-period, crossover study in patients already using the plaster who reported at least 'moderate pain relief' whilst using the plaster.[6] Patients (n = 33) were randomised to receive either the lidocaine 5% plaster or a placebo plaster for up to 14 days, before switching to the alternate treatment. The mean duration of use of the plaster prior to the study was 3.3 years and most patients used three plasters per day. The primary outcome was the median 'time-to-exit', with 'exit' required from each treatment period following a specified deterioration in pain relief using a verbal rating scale. The median time-to-exit was significantly higher with the lidocaine plaster compared with the placebo plaster (> 14 days *vs.* 3.8 days, p < 0.001).

In a second trial, following eight weeks' open-label treatment with up to three lidocaine 5% plasters per day, 71 patients meeting the defined criteria for having responded to treatment were randomised for a two-week, double-blind phase of either continued lidocaine plaster treatment or a switch to a placebo plaster.[7] In the intention-to-treat population, the median time-to-exit was 13.5 days with the lidocaine plaster compared with 9.0 days with the placebo plaster; the difference between the two groups was not statistically significant (p = 0.151).

An open-label, non-inferiority study randomised patients with either PHN or diabetic polyneuropathy to four weeks' treatment with the lidocaine 5% plaster (up to three plasters per day, n = 157) or pregabalin (up to 600 mg/day, n = 154).[8] The lidocaine plaster did not meet the applied statistical criteria for non-inferiority for the outcome of 'response rate' in the per protocol group (comprising all randomised patients who had complied with the protocol and had at least one post-baseline assessment of pain intensity), which was the more robust group for non-inferiority testing. The criteria for non-inferiority were met only in a larger group including patients who had protocol violations.

In a fourth study, the lidocaine 5% plaster was assessed in each of 35 patients in two 12-hour periods compared with a placebo plaster in one 12-hour period and observation only in a fourth 12-hour period, the sequence of the periods being randomly allocated.[9] Lidocaine was associated with significantly greater reductions from baseline values in pain intensity scores at time points between four and 12 hours post-application compared with the placebo plaster. The maximum reduction in pain intensity was observed at four hours after application of the lidocaine plaster, after which time pain intensity increased.

Limited information is available for a fifth, unpublished trial.[10] Patients with PHN were randomised to approximately four weeks' double-blind treatment with the lidocaine 5% plaster (n = 110) or a placebo plaster (n = 57). The reported reductions in visual analogue scale scores for pain intensity with the lidocaine plaster were not statistically different from those with the placebo plaster.[10]

Adverse events

The most common adverse events reported in the above trials related to localised reactions to the lidocaine 5% plaster. See the Summary of Product Characteristics for further details.[1]

Additional information

- Up to three lidocaine 5% plasters may be applied for up to 12 hours within a 24-hour period.[1]
- The current cost of one year's treatment with three plasters per day is £2,643.

References

1. Versatis 5% Medicated Plaster: Summary of Product Characteristics. Grünenthal Ltd. 2010. http://emc.medicines.org.uk/ <accessed 1/2010>
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3. Gauthier A, Breuer J, Carrington D *et al*. Epidemiology and cost of herpes zoster and post-herpetic neuralgia in the United Kingdom. *Epidemiol Infect* 2009;**137:**38-47.
4. British National Formulary. 58. September. 2009.
5. Neuropathic pain: pharmacological management. National Institute for Health and Clinical Excellence. 2010. http://guidance.nice.org.uk/CG96 <accessed 4/2010>
6. Galer BS, Rowbotham MC, Perander J *et al*. Topical lidocaine patch relieves postherpetic neuralgia more effectively than a vehicle topical patch: results of an enriched enrolment study. *Pain* 1999;**80:**533-8.
7. Binder A, Bruxelle J, Rogers P *et al*. Topical 5% lidocaine (lignocaine) medicated plaster treatment for postherpetic neuralgia: results of a double-blind, placebo-controlled, multinational efficacy and safety trial. *Clin Drug Investig* 2009;**29:**393-408.
8. Baron R, Mayoral V, Leijon G *et al*. 5% lidocaine medicated plaster versus pregabalin in postherpetic neuralgia and diabetic polyneuropathy: an open-label, non-inferiority two-stage RCT study. *Curr Med Res Opin* 2009;**25:**1663-76.
9. Rowbotham MC, Davies PS, Verkempinck C *et al*. Lidocaine patch: double-blind controlled study of a new treatment method for post-herpetic neuralgia. *Pain* 1996;**65:**39-44.
10. Versatis 5% plaster: public assessment report. Medicines and Healthcare Products Regulatory Agency. 2007. http://www.mhra.gov.uk/home/groups/par/documents/websiteresources/con2032998.pdf <accessed 01/2010>

Launch date: 2007 *Manufacturer: Grünenthal Ltd* *PL 21727/0016*

WARNING: This sheet should be read in conjunction with the Summary of Product Characteristics

This guidance is based upon the published information available in English at the time the drug was considered. It remains open to review in the event of significant new evidence emerging.

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