MTRAC
Midlands Therapeutics Review and Advisory Committee

Considerations for Commissioners

Lidocaine 5% Medicated Plaster *(Versatis®, Ralvo®)*

For the treatment of localised (focal) neuropathic pain *(UNLICENSED INDICATION)*

This review focusses on the **unlicensed** use of lidocaine 5% medicated plasters for the treatment of localised (focal) neuropathic pain (LNP). In line with the National Institute for Health and Care Excellence (NICE), and the guidance from the General Medical Council (GMC), MTRAC advises that, "It is the responsibility of the prescriber to determine the clinical need of the patient and the suitability of using the product outside its licensed indications".

Commissioning guidance:

Commissioners may wish to bear the following in mind when considering the commissioning of the lidocaine medicated plaster (LMP):

- In the opinion of MTRAC members, there is a place for the use of the LMP in the treatment of people with localised neuropathic pain with allodynia, who are intolerant of first-line systemic and topical therapies, or where these therapies have been ineffective. In line with NHS England guidance on items that should not be routinely prescribed in primary care, treatment initiation should be undertaken in a cooperation arrangement with a multi-disciplinary team and/or other healthcare professional. The committee also felt that a RICaD (Rationale for Initiation, Continuation and Discontinuation) will enable identification of appropriate patients, and facilitate discontinuation of treatment where appropriate.
- The NHS England guidance also advises CCGs to support prescribers in deprescribing lidocaine plasters in all patients and, where appropriate, ensure the availability of relevant services to facilitate this change.
- Guidance on deprescribing the LMP is available from South East London APC. It makes a distinction between use in post-herpetic neuralgia or focal neuropathic pain with allodynia, for which *(weak)* evidence of efficacy exists, and other indications, and includes an algorithm to aid in deprescribing where use is inappropriate.
- The Summaries of Product Characteristics for lidocaine plasters advise re-evaluation of treatment with the plaster every 2-4 weeks, and if there has been no response to treatment stop use, as potential risks may outweigh benefits in this context. Regular review enables re-assessment of the number of plasters to use and the duration of the plaster-free interval.

Strength of the evidence for efficacy: weak

The evidence for the efficacy of the LMP for the treatment of localised neuropathic pain was based on three RCTs. These trials enrolled people with pain with neuropathic features that had persisted longer than three months post-surgery; two small studies with specific populations of patients with post-surgical knee pain (n = 34) or cancer and post-surgical pain (n = 28), and a larger trial of patients with any post-surgical pain (n = 363). Two of the trials evaluated pain intensity and found no significant difference in pain scores for the LMP *vs*. placebo over 12 weeks' treatment. One of the smaller studies found greater improvement in pain due to allodynia with the LMP *vs*. placebo.

MTRAC considered the LMP for this off-label use to assist local commissioners

Description of technology

The lidocaine 5% medicated plaster (Ralvo® and Versatis®)[1,2] has a dual mode of action: lidocaine diffusion into the skin providing an analgesic effect, and mechanical protection of the hypersensitive area. Both products are licensed for the symptomatic relief of neuropathic pain associated with previous herpes zoster infection (post herpetic neuralgia, PHN) in adults. MTRAC considered the lidocaine medicated patch for the licensed indication in 2010, and advised that use was restricted to patients in whom alternative treatments had proved ineffective or were contraindicated[3].

The plaster delivers 700 mg lidocaine and can be applied for up to 12 hours within a 24-hour period; plasters can be cut to size, or up to three used for a larger affected area of skin. The Summaries of Product Characteristics (SPCs)[1,2] state that "treatment outcome should be re-evaluated after 2-4 weeks. If there has been no response to the plaster after this period (during the wearing time and/or during the plaster-free interval), treatment must be discontinued as potential risks may outweigh benefits in this context. Long-term use of the lidocaine plaster in clinical studies showed that the number of plasters used decreased over time. Treatment should be regularly reassessed to determine the number of plasters needed, and the duration of the plaster-free interval."

Background

Guidance from the National Institute for Health and Care Excellence (NICE) on Neuropathic pain in adults: pharmacological management in non-specialist settings (Pub: 2013; updated 2019)[4] advises the use of capsaicin cream for people with localised neuropathic pain who wish to avoid, or who cannot tolerate, oral treatments. An accompanying footnote advises that this is unlicensed use and that "The prescriber should follow

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relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information." The NICE guidance does not include LMPs due to insufficient evidence.

In guidance from NHS England on Items that should not be routinely prescribed in Primary care[5], the LMP is classified as an "Item of low clinical effectiveness, where there is a lack of robust evidence of clinical effectiveness or there are significant safety concerns". The guidance recommends that LMP are not initiated in Primary care, and that arrangements should be in place to enable them to be deprescribed. The third recommendation is that if, in exceptional circumstances, there is a clinical need for lidocaine plasters to be prescribed in primary care, this should be undertaken in a cooperation arrangement with a multi-disciplinary team and/or other healthcare professional.

The British Pain Society stated in 2018[6] that the LMP, like tricyclic antidepressants (also unlicensed for this indication), is one of a range of options that should be available to a person with localised neuropathic pain. Pain services often use short sequential trials of different/several medicines to help each person decide what works best for them.

Clinical evidence for efficacy and safety

The evidence for efficacy of the LMP came from three RCTs (two with < 50 participants) evaluating post-surgical pain relief (n = 363[7], n = 34[8]), or pain relief in people with cancer and post-surgical incisional pain (n = 28[9]). All three trials used a placebo plaster as comparator: two trials were 3-month parallel studies[7,8], and the third[9] had a 1-month crossover design. Eligibility for all three trials required pain that had persisted for at least three months and had neuropathic features (e.g. pain related to gentle brushing). The outcome measures related to the intensity of pain and other symptoms.

The largest trial in 363 people with post-surgical neuropathic pain found no significant difference between LMP and placebo for the primary outcome of change from baseline in 24-hour pain intensity scores after 12 weeks' treatment. There was also no difference for any of the secondary outcomes including quality of life and sleep quality.

The 3-month trial in 34 people with post-surgical knee pain found significantly greater improvements in relief of pain following light brushing of the painful area, and in global pain scores using a numerical rating scale for the lidocaine plaster compared with placebo. There was no significant difference in the results from sleep or quality of life questionnaires for the lidocaine plaster *vs*. placebo[8].

The 1-month crossover trial found no significant difference in pain intensity scores between the LMP and placebo. The trial suffered from the limitations that it was stopped early by the safety monitoring board due to slow recruitment and did not recruit enough participants to achieve the necessary statistical power. The authors commented, however, that the size of the treatment effect seen between the LMP and placebo was so small that they felt no difference would have been seen with a sufficiently well-powered trial.

Adverse events

Two of the RCTs[7,8] reported that treatment-emergent adverse events occurred in about 50% of participants. The most frequently reported adverse events were related to application site reactions; skin-related adverse events occurred in about 16% of participants. Other adverse events reported were pain (7.3% LMP *vs*. 3.9% placebo) and headache (5.6% *vs*. 4.4%). Gastroenteritis (2.8%) and itchiness at the application site (2.8%) were also reported with LMP treatment.

Considerations for cost impact

At current prices, the cost of three months' treatment with a topical treatment for LNP is:

Capsaicin (Axsain®) 0.075% cream	£26.97
LMP (Ralvo®) 700mg plaster	£135.85
LMP (Versatis®) 700mg plaster	£164.18

Source: MIMs January 2020;

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