Versatis®

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Introduction

Herpes zoster infection or "shingles" is one of the most common causes of peripheral neuropathic pain.[1-3] After the shingles rash has cleared, some people may continue to experience pain for several months or even years. This condition is known as postherpetic neuralgia (PHN).[1-3] More than 70% of patients with PHN experience pain evoked by lightly touching the skin, also known as tactile allodynia.[1] Patients with PHN often experience "substantial long-standing debilitating pain", may have a significant loss of function and poor quality of life.[1-4]

5% Lidocaine-medicated plasters have been used for many years, and in many countries, for the management of PHN.[1-7] Lidocaine plasters allow for the continuous diffusion of lidocaine, a local anaesthetic, into the skin.[6] Lidocaine stabilises the neuronal membranes via the down-regulation of sodium channels, which results in a reduction in pain.[5,6]

Versatis® 5% medicated plasters

Each Versatis® plaster contains 700 mg (equivalent to 5% w/w) lidocaine in an aqueous adhesive base. Plasters are packed in re-sealable sachets, each containing five plasters.[5]

Indications

Versatis® plaster is indicated in adults, for the treatment of neuropathic pain associated with previous herpes zoster infection also known as PHN.[5]

Pharmacokinetics

The absorption of lidocaine from the skin, following the application of lidocaine-medicated plaster, is usually low.[4] Approximately 3 ± 2% of the total applied lidocaine dose is systemically available and about 70% is bound to plasma proteins.[5]

Lidocaine and its metabolites do not have a tendency to accumulate and steady-state plasma concentrations are reached within the first four days of application.[5] Lidocaine crosses the blood brain and placental barriers.[5]

Lidocaine and its metabolites are primarily eliminated by the kidneys.[1,5] Less than 10% of the lidocaine dose is excreted unchanged.[5] The elimination half-life is 7.6 hours after multiple applications.[5] In patients with cardiac, hepatic or renal insufficiency, the elimination of lidocaine and its metabolites may be delayed.[5]

Dosing

The plaster should only be applied to intact, dry, non-irritated skin once the shingles has cleared/healed.[5]

Once removed from the sachet, the plaster should be used immediately. Each plaster is 10 cm by 14 cm, and depending on the size of the painful area, up to three plasters may be applied to cover the affected area.[5] Plasters may also be cut into smaller pieces with scissors (if needed); this should be done prior to the removal of the release liner.[5]

The plasters contain water and if there are any plasters left in the sachet, the sachet should be closed tightly in order to prevent them from drying out. The remainder of the plasters in the sachet should be used within 14 days.[5]

Plaster(s) should be applied once daily, for up to 12 hours to the affected/painful area; the plaster(s) should not be worn continuously for longer than 12 hours, this should be followed by a plaster-free interval of at least 12 hours.[5]

Application instructions:

- Hairs in the affected area should be removed with a pair of scissors (not shaved).[5]
- Prior to application, the transparent release liner needs to be removed from the gel surface, while taking care not to touch the sticky part of the plaster.[5]
- The plaster should then be pressed down onto the skin for at least 10 seconds; ensuring that the whole plaster, including the edges, firmly adhere to the skin.[5]

Once removed, the used plaster(s) should be folded in half with the adhesive side inwards. This will prevent the self-adhesive layer, which still contains active ingredient, from being exposed. It should be discarded out of the reach of children.[5]

Treatment should be:

- Reassessed at regular intervals – This will allow one to determine whether the plaster-free period could be extended or whether the amount of plasters needed to cover the affected area could be reduced.[5]
- Discontinued – If there is no response after 2–4 weeks.[5]

Efficacy

Several studies have demonstrated the efficacy of Versatis® plaster in the treatment of PHN.[3,4,6-10]

Binder A *et al*., 2009, evaluated the analgesic efficacy and safety of 5% lidocaine-medicated plaster in 265 patients with post-herpetic neuralgia.[8] 51.7% of patients in the "run-in phase" (open-label phase) responded to treatment and achieved at least moderate pain relief.[6,8]

In the second part of the study (double-blind phase), 71 patients were randomised to receive either placebo or lidocaine 700 mg medicated plaster. The primary endpoint was the time-to-exit from treatment due of lack of efficacy. They found that patients in the lidocaine plaster group remained in the study for longer periods compared to those who received placebo (14 days vs. 6 days in the per-protocol population).[8] There were 9/36 patients in the lidocaine plaster group and 16/35 patients on placebo who withdrew because of lack of treatment benefit.[6,8]

Results from a long-term efficacy and safety study by Hans G *et al*., 2009, showed that long-term treatment with the 5% lidocaine-medicated plaster resulted in consistent and sustained long-term pain relief (for up to 24 months) in patients suffering from PHN. They also found that 5% lidocaine-medicated plaster was well-tolerated during long-term use.[2,9]

Rehm S *et al*., 2010, compared the efficacy of 5% lidocaine-medicated plaster with pregabalin in 98 patients with PHN. 48 patients received pregabalin and 50 patients applied the plaster. Results suggested that 5% lidocaine-medicated plaster has comparable efficacy to pregabalin for pain relief in PHN with a favourable safety profile ("positive benefit-risk ratio").[10]

Safety of Versatis® plasters

Special warnings and precautions for use

Versatis® plasters are contra-indicated in patients with hypersensitivity reactions to lidocaine, other local anaesthetics of the amide type or to any of the excipients.

Possible reactions may occur as a result of excipients, for example:

- Propylene glycol could cause skin irritation.[5]
- Propyl parahydroxybenzoate and methyl parahydroxybenzoate could cause allergic reactions (possibly delayed).[5]

The plaster should not be applied to mucous membranes, inflamed or injured skin such as active herpes zoster lesions, wounds or atopic dermatitis. In addition, contact with the eyes should be avoided.[5]

Lidocaine 5% plasters are not recommended for use in patients under 18 years of age, in pregnancy or breastfeeding (lidocaine crosses the placenta and is excreted in breast milk)[5]; and the plasters should be used with caution in patients with severe cardiac impairment, renal impairment or hepatic impairment.[5]

Drug interactions

The maximum lidocaine plasma concentration reached following the use of medicated lidocaine patches, is low. As a result, clinically relevant pharmacokinetic drug-drug interactions are unlikely.[5]

However, owing to the possible risk of additive systemic effects, the plaster should be used with caution in patients receiving other local anaesthetics or Class I antidysrhythmic medicines (e.g. tocainide, mexiletine).[5]

Adverse effects

The patches are generally well-tolerated.[1-10] The most commonly reported side effects were typically due to the nature of the patch and were localised reactions such as burning, dermatitis, erythema, pruritus, rash, skin irritation, and vesicles at the administration site. The intensity of the adverse reactions were usually mild to moderate.[5]

Systemic adverse reactions and overdose with the plaster are unlikely, when the plaster is used as indicated, owing to the low systemic concentration of lidocaine.[5]

Important prescribing points

Compared to systemic administration, the topical route offers a "site-specific delivery" to the most painful areas and has a lower risk of possible drug interactions, systemic side-effects and overdose.[1,6,11]

The hydrogel plaster also provides an immediate cooling sensation (known as the "patch effect"), as well as a mechanical protection for the hypersensitive area.[1,6,11]

Lidocaine plasters are considered to have a better benefit-to-risk ratio than systemic analgesic agents, since systemic levels following the application of lidocaine plaster(s) are low, when used as indicated.[1] However, higher than normal plasma concentrations may occur with inappropriate use, for example:

- When a higher number of plasters are used at the same time
- With prolonged application periods or
- When the plaster is applied to broken skin[5]

In the 2012 South African clinical practice guidelines for management of neuropathic pain, the authors mentioned that 5% lidocaine-medicated patches have been included, in several guidelines, as a first-line treatment option for PHN. However, since the lidocaine patches were not available at the time, the panel could not recommend their use "despite strong supporting evidence". They suggested that "the regulatory authorities in South Africa consider approval of these agents for use in neuropathic pain."[7]

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