

Medicines Management Programme

Lidocaine 5% Medicated Plaster (Versatis®)

Prescribing and Cost Guidance



Medicines Management
Programme

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Table of Contents

1. Background	2
2. Purpose	2
3. Definitions.....	3
4. Mode of action.....	3
5. Posology and administration	3
6. Special warnings and precautions for use	3
7. Undesirable effects	4
8. Clinical evidence for lidocaine 5% plaster (Versatis®)	5
8.1 Clinical evidence to support the use of lidocaine 5% plaster	5
8.2 Cochrane review of ‘Topical lidocaine for neuropathic pain in adults’	7
9. Recommendations for prescribing.....	8
10. Expenditure on lidocaine 5% plaster	9
10.1 Primary Care expenditure	9
10.2 Hospital expenditure.....	10
11. National Centre for Pharmacoeconomics evaluation of lidocaine 5% plaster	10
11.1 Outcome of Health Technology Assessment on lidocaine 5% plaster.....	10
11.2 Health Technology Assessments in other jurisdictions.....	11
12. Alternative topical treatment options and associated costs	11
12.1 Topical treatment options for the treatment of post-herpetic neuralgia	11
12.2 Topical treatment options for the treatment of muscular/rheumatic pain	12
12.3 Cochrane review on ‘Topical NSAIDs for acute musculoskeletal pain in adults’	13
12.4 Cochrane review on ‘Topical NSAIDs for chronic musculoskeletal pain in adults’	14
13. Potential savings	14
14. Conclusion.....	15
15. References	17

List of Tables

Table 1: List of adverse drug reactions associated with lidocaine 5% plaster.....	4
Table 2: Clinical evidence to support the use of lidocaine 5% plaster	6
Table 3: Overview of the utilisation of lidocaine 5% plaster	9
Table 4: Topical products and price comparison of treatments for PHN	12
Table 5: Topical products and price comparisons of treatments for non-PHN indications.....	13

List of Figures

Figure 1: Total expenditure for lidocaine 5% plaster (Versatis®) under the GMS and DPS scheme from January 2012 to December 2015.	9
Figure 2: The potential for cost savings by switching in different scenarios	15

List of abbreviations

BNF	British National Formulary
DPN	Diabetic polyneuropathy
DP	Drug Payment (Scheme)
GMS	General Medical Services
HSE	Health Service Executive
HSE-CPU	Health Service Executive Corporate Pharmaceutical Unit
HTA	Health technology assessment
ICER	Incremental cost effectiveness ratio
MMP	Medicines Management Programme
N	Number of participants
NCPE	National Centre for Pharmacoeconomics
NICE	National Institute of Health and Care Excellence
NRS	Numerical rating scale
NSAID	Non-steroidal anti-inflammatory drug
PBAC	Pharmaceutical Benefits Advisory Committee
PCRS	Primary Care Reimbursement Service
PHN	Post herpetic neuralgia
QALY	Quality adjusted life year
SMC	Scottish Medicines Consortium
SmPC	Summary of product characteristics

1. Background

Lidocaine 5% medicated plaster (Versatis®) is licensed for the symptomatic relief of neuropathic pain associated with previous herpes zoster infection known as post-herpetic neuralgia (PHN) in adults.¹ This plaster has been reimbursed under the community drug schemes in Ireland since 2010.² Total expenditure (including pharmacy fees and VAT) on the General Medical Services (GMS) and the Drug Payment (DP) schemes for this product totalled €28 million in 2015.³ Lidocaine 5% plaster was also ranked 4th on the GMS list of the top 100 products for expenditure by ingredient cost in the same year.⁴

The Medicines Management Programme (MMP) in its remit to promote safe, effective and cost-effective prescribing of medicines in Ireland identified large increases in the utilisation of lidocaine 5% plaster from 2012 to 2014. The Health Service Executive-Corporate Pharmaceutical Unit (HSE-CPU) in accordance with the Health Act 2013, (section 18(4)), requested the National Centre for Pharmacoeconomics (NCPE) to assess the cost-effectiveness of lidocaine 5% plaster and a health technology assessment (HTA) was undertaken in 2015. The NCPE concluded that the cost-effectiveness of lidocaine 5% plaster had not been demonstrated. The NCPE report is explained in detail in section 11.1 (page 10) of this report. Following the HTA report, the HSE negotiated a price reduction for lidocaine 5% plaster from €93.96 to €77.52 in March 2016.

The number of patients receiving lidocaine 5% plaster on GMS and DP schemes in December 2015 was 18,802 and this number continues to increase each month.³ The utilisation of and expenditure on lidocaine 5% plaster has been identified as a priority by the MMP.

2. Purpose

This document outlines the available evidence, current guidelines, cost and practice tips for the prescribing and reviewing of lidocaine 5% plaster in adults. Recommendations are also provided on suitable alternative topical preparations where lidocaine 5% plaster has been shown to be ineffective or prescribed for unlicensed indications.

Prescribers should be aware that lidocaine 5% plaster is licensed ONLY in the treatment of neuropathic pain associated with post-herpetic neuralgia (PHN) and should be prescribed ONLY for this indication.

3. Definitions

For the purpose of this report the associated cost refers to the reimbursed cost of the preparation as listed on the HSE Primary Care Reimbursement Service (PCRS) website (www.pcrs.ie).⁵ Only licensed, reimbursable products are included in this review. Versatis® is the only licensed reimbursed topical lidocaine plaster in Ireland. Where alternative therapies are discussed in this review only topical, local-acting agents are considered. Systemic preparations in the treatment of PHN and other forms of neuropathic pain are outside the scope of this document. Costs are correct as of December 2016. This review should be used in conjunction with clinical judgement and decision-making appropriate to the individual patient. Prescribers should refer to sources such as the summary of product characteristics (SmPC) for Versatis® and the British National Formulary (BNF) to inform decisions made with individual patients.

4. Mode of action

Lidocaine 5% plaster exerts its effect by stabilising the neuronal membranes and causing down-regulation of neuronal sodium channels. As a result this impairs the conduction of signals associated with the perception of pain.⁶ The plaster consists of a white hydrogel adhesive material which is applied to a non-woven fabric backing containing lidocaine 5% and covered with a polyethylene terephthalate film used as a release-liner.¹ Lidocaine 5% plaster has a dual mode of action. Firstly, the lidocaine diffuses continuously into the skin providing a local analgesic effect and secondly it exerts a mechanical effect on the pain due to the hydrogel layer contained within the plaster.¹

5. Posology and administration

The painful area should be covered with the lidocaine 5% plaster once daily for up to 12 hours within a 24 hour period.⁷ They may be applied day or night and must be worn for no longer than 12 hours. The minimum number of plasters that demonstrate a therapeutic benefit should be used and no more than three plasters may be used at one time.¹ The plaster may be cut into smaller sizes prior to removal from the liner and should be applied to the skin immediately.⁷ After first opening, the sachet (containing 5 plasters) should be tightly sealed and the plasters should be used within 14 days.¹

6. Special warnings and precautions for use

Lidocaine 5% plaster should be used with caution in severe cardiac, renal and hepatic impairment.¹ The plaster contains propylene glycol which may cause skin irritation. It also contains methyl parahydroxybenzoate and propyl parahydroxybenzoate which may cause allergic reactions and

these effects may be delayed. One of the metabolites of lidocaine, 2,6 xylidine, has been shown to be genotoxic and carcinogenic in rats. Also, secondary metabolites have been shown to be mutagenic. The clinical significance of this is unknown and therefore the long-term treatment with lidocaine 5% plasters is only warranted if there is a therapeutic benefit to the patient.¹

7. Undesirable effects

Approximately 16% of patients can be expected to experience an adverse reaction.¹ These reactions are generally localised due to the nature of the product. The most commonly seen adverse reactions are related to site reactions e.g. burning, dermatitis, erythema, pruritus, rash and skin irritation.¹

Table 1 below lists adverse drug reactions that have been reported in studies of patients with PHN receiving lidocaine 5% plaster.⁸ The adverse-effects are listed by body system and frequency, very common ($\geq 1/10$) and uncommon ($\geq 1/1,000$ to $1 < 100$).

Table 1: List of adverse drug reactions associated with lidocaine 5% plaster

Body system	Adverse Drug Reaction	Frequency
General disorders and administration site conditions	Administration site reactions	<i>Very common</i>
Skin and subcutaneous tissues disorders	Skin lesion	<i>Uncommon</i>
Injury, poisoning and procedural complications	Skin injury	<i>Uncommon</i>

8. Clinical evidence for lidocaine 5% plaster (Versatis®)

Summary of the clinical evidence for lidocaine 5% plaster

- The evidence to support the use of lidocaine 5% plaster in the treatment of post-herpetic neuralgia (PHN) is limited due to the lack of comparative data to show clinical effectiveness.
- The evidence to support the use of lidocaine 5% plaster for other types of pain is uncertain due to lack of available evidence.
- The evidence assessing the effectiveness of lidocaine 5% plaster in relieving the symptoms of allodynia, hyperalgesia and dysesthesias in localised neuropathic pain conditions is limited.
- The clinical trials were conducted using enriched populations defined as responders and had small numbers of patients with a short follow-up period, leading to a high risk of bias.

A detailed evaluation of the evidence is discussed below.

8.1 Clinical evidence to support the use of lidocaine 5% plaster

Table 2 describes the main Phase III studies supporting the use of lidocaine 5% plaster in clinical practice for the treatment of PHN and painful diabetic polyneuropathy (DPN).

Table 2: Clinical evidence to support the use of lidocaine 5% plaster

Name of study	Type of study	N [†]	Time	Primary endpoint	Comparator	Conclusion
1. Study KF 10004/H32 ⁹	Double-blind, randomised, crossover study.	32	14 days	“Time to exit”	Lidocaine plaster vs. placebo	The median time to exit was 14 days for lidocaine and 3.8 days for placebo (p<0.0001).
2. Study KF 10004/01 ¹⁰	Double-blind randomised, parallel group.	71	2-14 days	“Time to exit due to lack of efficacy for 2 consecutive application days”	Lidocaine plaster vs. placebo	9/36 on lidocaine withdrew and 16/35 on placebo withdrew due to lack of efficacy.
3. 5% lidocaine plaster vs. pregabalin in PHN & diabetic poly-neuropathy ¹¹	Open-label, two-stage adaptive, non-inferiority	96 ^{††}	4 week	“Response rate at 4 weeks”	Lidocaine plaster vs. pregabalin	Lidocaine 5% plaster numerically better than pregabalin 62.2% vs. 46.5%.

[†]N=Number of participants PHN=Post-herpetic neuralgia

^{††}with a PHN indication

The first study (KF10004/H32) was a randomised, double-blind, placebo-controlled, two-period crossover trial consisting of 32 patients with PHN. Patients who were recruited were regular users of lidocaine 5% plaster from open-label extension studies. Patients were assigned to receive 14 days of lidocaine 5% plaster followed by 14 days of placebo or vice versa with no washout period. The primary end-point was the “time to exit” where patients withdrew because their pain relief was two points lower than their normal response on a six-point categorical verbal rating scale of pain relief (worse, no pain relief, slight relief, moderate relief, a lot of relief and complete relief). The median time to exit was 14 days for lidocaine 5% plaster and 3.8 days for placebo (p<0.001).⁹ The secondary endpoint was the patient’s preference between treatments. Three patients (9.4%) preferred the placebo plaster compared with 25 (78.1%) patients who preferred the lidocaine 5% plaster.⁹

The second study (KF10004/01) was an open-label, randomised, double-blind, parallel group, withdrawal design which examined a subgroup of patients with PHN who were known to respond to the lidocaine 5% plaster. Patients initially received an 8 week open-label lidocaine 5% plaster treatment and only those with a positive response to treatment after this time were entered into the randomised withdrawal treatment phase. Of the 265 patients who entered the 8 week open-

label phase, 137 (52%) were classified as responders with at least moderate relief with lidocaine 5% plaster treatment. The primary end-point was “time to exit” during the double-blind treatment phase due to “lack of efficacy during two or more consecutive days” of treatment because their relief was two points lower than their normal response on a six-point categorical verbal rating scale of pain relief (worse, no pain relief, slight relief, moderate relief, a lot of relief and complete relief). A total of 71 patients were randomised to either receive lidocaine 5% plaster (36 patients) or placebo (35 patients) for 2-14 days. Nine out of the 36 patients on lidocaine 5% plaster and 16 out of the 35 on placebo withdrew due to lack of efficacy.¹⁰

The third study was a two-stage adaptive, open-label, multicentre, non-inferiority study of lidocaine 5% plaster versus pregabalin. This non-inferiority study aimed to compare the efficacy of 5% lidocaine plaster to pregabalin in patients with PHN and painful diabetic peripheral polyneuropathy (DPN), an unlicensed indication in Ireland. Patients were included if the neuropathic pain was present for ≥ 3 months after healing of the herpes zoster skin rash. There were two phases to this study. The first phase of the trial lasted 4 weeks in which adults with PHN or painful DPN received either 5% lidocaine plaster or twice daily pregabalin capsules titrated according to the SmPC. The response was compared in terms of efficacy, quality of life, safety and tolerability. The primary endpoint of the comparative phase was the response rate at four weeks defined as at least 2 points or an absolute value of 4 points or less on the 11-point Numerical Rating Scale (NRS-3) after four weeks of treatment. Secondary endpoints included pain intensity scores, changes from baseline, allodynia severity rating and quality of life parameters. In the second phase, patients with adequate responses to monotherapy continued their previous therapy while those with insufficient response received combination therapy, i.e. the lidocaine 5% plaster with pregabalin. Alternatively, patients received pregabalin and were titrated again according to the SmPC. There were 96 patients who were treated for PHN and 204 patients with painful DPN. The results showed that lidocaine 5% plaster was found to be numerically better than pregabalin for PHN in terms of response rate (62.2% lidocaine 5% plaster vs. 46.5% pregabalin). In patients with DPN the response rate was comparable (66.7% lidocaine 5% plaster vs. 69.1% pregabalin). In the overall mixed population of patients with PHN or DPN included in this study lidocaine 5% plaster was found to be non-inferior to pregabalin in the full analysis set (PHN and DPN), but not in the per protocol group following statistical testing.¹¹

8.2 Cochrane review of ‘Topical lidocaine for neuropathic pain in adults’

The Cochrane Library preformed a review (July 2014) on ‘Topical lidocaine for neuropathic pain in adults’ to assess the analgesic efficacy of topical lidocaine 5% plaster for chronic neuropathic pain in

adults and to assess the associated side-effects. This review involved 12 small studies with 508 participants in total that tested topical lidocaine 5% plaster against topical placebo for a number of weeks. The limited information from single studies mainly in PHN indicated that topical lidocaine 5% plaster may be effective in treating neuropathic pain in a small number of patients and is well tolerated, at least in the short-term. There was no clear evidence of an effect on the incidence of adverse effects or withdrawals. However, the reviewers noted that the studies included 'very low quality evidence' and all had a 'high risk of bias' due to small size and incomplete outcome data.¹²

9. Recommendations for prescribing

Prescribers should ensure that lidocaine 5% plaster is restricted to patients with PHN, in whom alternative treatments have proved ineffective or where such treatments are contraindicated. The initiation of lidocaine 5% plaster for PHN should be reviewed after 2-4 weeks and stopped if ineffective or the relieving effect is solely due to protection of the hypersensitive area by the hydrogel layer within the plaster.

Patients prescribed lidocaine 5% plaster for unlicensed indications should be reviewed and have their therapy discontinued.

Prescribers should ensure all patients are aware of how to use the plaster and have at least 12 hours treatment free period each day.

Long-term therapy with lidocaine 5% plaster should be assessed for continued need and should be discontinued if deemed appropriate. Alternatively, aim to have a longer plaster-free interval between treatments with a plan to discontinue if the patient remains pain-free.¹³

MMP recommendations for the prescribing of lidocaine 5% plaster

- ✓ Prescribing of lidocaine 5% plaster should be restricted to patients with post-herpetic neuralgia (PHN) ONLY.
- ✓ Treatment should be reviewed after 2-4 weeks and stopped if ineffective or if the relieving effect is solely due to protection of the area by the plaster.
- ✓ Patients prescribed lidocaine 5% plaster for unlicensed indications should be reviewed and treatment discontinued.
- ✓ Prescribers should ensure all patients are using the patch correctly.
- ✓ Patients on long-term therapy should be assessed for continued need and aim to have treatment discontinued or alternatively, try to have a longer plaster-free period between treatments.

10. Expenditure on lidocaine 5% plaster

10.1 Primary Care expenditure

Figure 1 below illustrates the current expenditure on lidocaine 5% plasters under the GMS and DP schemes from January 2012 to December 2015. Expenditure on lidocaine 5% plaster in primary care as of December 2015 was €2.7 million per month with 18,802 patients receiving treatment.³ As discussed in section 1, total expenditure on lidocaine 5% plasters on the community drug schemes in 2015 totalled €28 million (Table 3).⁴

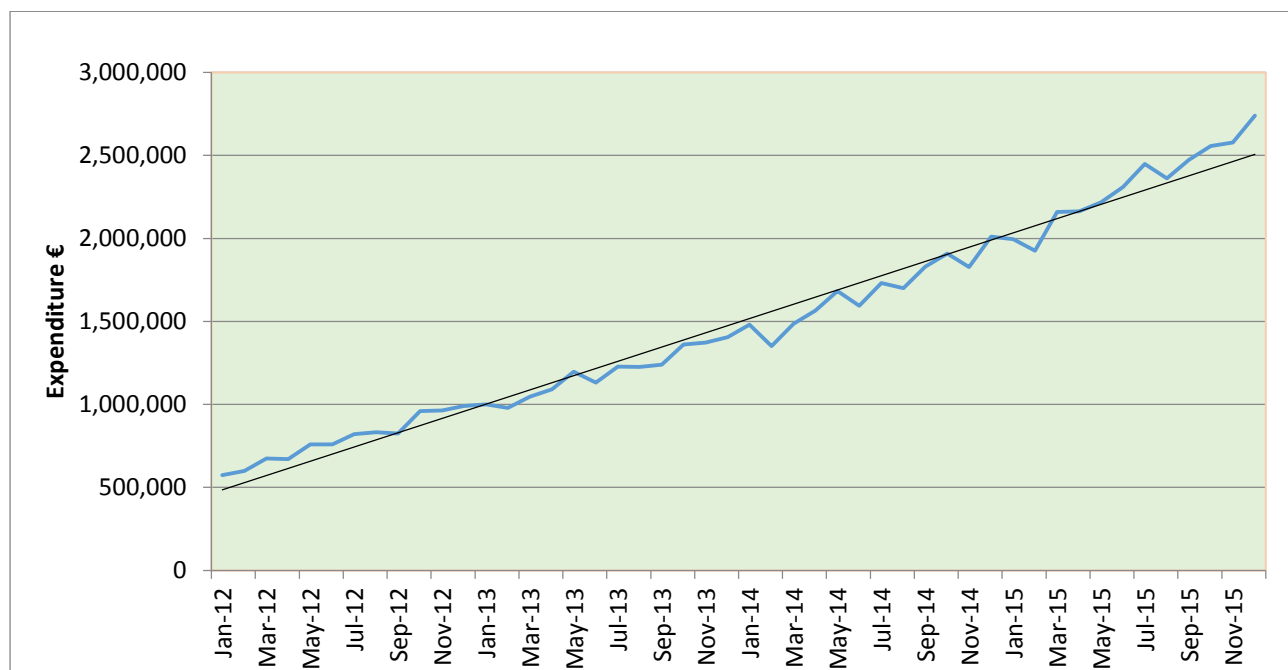


Figure 1: Total expenditure for lidocaine 5% plaster (Versatis®) under the GMS and DPS schemes from January 2012 to December 2015.

Preliminary figures from the first six months of 2016 show utilisation has continued to increase with over 20,500 patients in receipt of lidocaine 5% plaster in June 2016. Total expenditure in 2016 is therefore estimated to be in excess of €30million.³

Table 3: Overview of the utilisation of lidocaine 5% plaster

Reimbursement price per pack (30 plasters)	€77.52*
Total expenditure (GMS and DP schemes) 2014 ³	€20.17 million
Total expenditure (GMS and DP schemes) 2015 ³	€27.93 million
Total expenditure (GMS and DP schemes) January to June 2016 ³	€15.6 million†
Total number of patients receiving treatment as of December 2015 ³	18,802
Total number of patients receiving treatment as of June 2016 ³	20,569

*€93.96 prior to March 2016; † Figures from first six months of 2016 only

10.2 Hospital expenditure

Hospital expenditure is difficult to fully estimate due to a lack of complete information. The available figures for the four large Dublin teaching hospitals namely the Mater University Hospital, St. James's Hospital, St Vincent's University Hospital and the Adelaide and Meath Hospital Tallaght showed a combined total expenditure in 2015 of €485,025. Expenditure for University Hospital Galway and University Hospital Limerick for 2015 totalled €85,042 and €39,732 respectively.¹⁴

11. National Centre for Pharmacoeconomics evaluation of lidocaine 5% plaster

As previously outlined in Section 1, in accordance with the Health Act 2013, the HSE-CPU requested the NCPE to evaluate the cost-effectiveness of lidocaine 5% plaster in 2015.

11.1 Outcome of Health Technology Assessment on lidocaine 5% plaster

The NCPE completed the HTA in September 2015 and concluded that the cost-effectiveness of lidocaine 5% plaster was not demonstrated for the following reasons:¹⁵

- The vast majority of prescribing of lidocaine 5% plaster under the state schemes was for indications other than PHN. The company did not submit a cost-effectiveness evaluation for other potential indications due to lack of relevant clinical evidence.
- As the cost-effectiveness analysis relates only to the indication of PHN it only represents a small percentage of overall use and does not give a clear indication of real world utilisation.
- The information submitted for HTA had limitations regarding the quality of the clinical efficacy data presented. This resulted in significant uncertainty with the reported outcomes associated with lidocaine 5% plaster.
- In the economic model submitted, the base case incremental cost-effectiveness ratios (ICERs) which are represented in quality adjusted life years (QALYs) were €9,871/QALY for lidocaine 5% plaster compared to pregabalin, €7,771/QALY for lidocaine 5% compared to gabapentin and €6,216/QALY for lidocaine 5% compared to amitriptyline. However, the NCPE did not consider these estimates to be robust and, as mentioned above, no ICERs were presented for non-PHN indications.
- In the budget impact analysis, the number of patients receiving the product and the duration of treatment differed substantially from the figures submitted by the company and the figures obtained by the NCPE from the national reimbursement database for 2014. The NCPE estimated that 5-10% of patients receive the product for its licensed indication of PHN.

Following the HTA assessment, the HSE agreed a price reduction in March 2016 reducing the price per 30 plasters from €93.96 to €77.52. In line with this development, the MMP has issued guidance on the use of Versatis® by means of prescribing tips and tools to highlight appropriate use and the prescribing of Versatis® off-license. The prescribing tips and tools are available on www.hse.ie/yourmedicines.

11.2 Health Technology Assessments in other jurisdictions

National Institute of Health and Care Excellence (NICE)

NICE Clinical Guideline 173 for 'Pharmacological treatment of neuropathic pain in adults in non-specialist setting' does not recommend the use of lidocaine 5% plaster as a treatment option for neuropathic pain due to limited clinical evidence to support its use. Initial treatment options, with the exception of trigeminal neuralgia, include a choice of amitriptyline, duloxetine, gabapentin or pregabalin. For patients who wish to avoid or are unable to take oral medication or where other treatment options are contraindicated in the treatment of PHN and painful DPN, topical capsaicin 0.075% cream is recommended as an alternative option.¹⁶

Scottish Medicines Consortium (SMC)

Lidocaine 5% medicated plaster is accepted for restricted use within the NHS Scotland for the treatment of neuropathic pain associated with previous herpes zoster infection, PHN. The SMC state that there is only limited comparative data available for lidocaine 5% plasters and the comparative clinical effectiveness remains unclear. It is restricted to use in patients who are intolerant to first-line systemic therapies for PHN or where other therapies have been ineffective.⁶

Pharmaceutical Benefits Advisory Committee (PBAC)

The PBAC of Australia rejected the request to list lidocaine 5% plaster for the treatment of patients with PHN on the basis of uncertain cost-effectiveness compared with pregabalin. The PBAC considered that there was a mismatch between the restriction, the clinical treatment algorithm, the model, and the clinical trial data.¹⁷

12. Alternative topical treatment options and associated costs

12.1 Topical treatment options for the treatment of post-herpetic neuralgia

As previously discussed in section 8.1 above, there is limited clinical evidence to support the use of topical lidocaine 5% plaster for PHN. There is also a lack of evidence comparing other topical therapies with lidocaine 5% plaster. For patients receiving treatment for PHN and who are unable to

tolerate or wish to avoid oral medication, NICE guidance 173 recommends the use of topical capsaicin 0.075% cream as a suitable alternative.¹⁶ Capsaicin 0.075% cream is licensed for the symptomatic relief of neuralgia associated with and following Herpes Zoster infections i.e. PHN after the open skin lesions have healed and also for the management of painful diabetic peripheral polyneuropathy under the supervision of a hospital specialist.¹⁸ Table 4 below details the approximate cost of lidocaine 5% plaster versus capsaicin 0.075% cream for topical treatment of PHN.

Table 4: Topical products and price comparison of treatments for PHN

Product	Cost* per 30 days	Directions	Licensed indications
Lidocaine 5% plasters (Versatis®) ^{1,5}	€77.52 - €232.56	Apply one to three patches for 12 hours in a 24 hour period.	-Licensed for post-herpetic neuralgia (PHN) only.
Capsaicin cream 0.075% (Axsain®) 45g ^{5,18}	€17.52	Apply sparingly 3-4 times daily.	-Licensed for PHN & -Painful diabetic peripheral polyneuropathy (DPN) under specialist supervision.

PHN= Post-herpetic neuralgia
DPN= Diabetic polyneuropathy

Similar to lidocaine 5% plaster, capsaicin 0.075% cream should be used after open skin lesions have healed. Both also have a similar safety and adverse-effect profile. It is important to be aware that transient burning may occur on application of capsaicin 0.075% cream. This burning is observed more frequently when applications greater than four times daily are used and hands should be washed immediately after application. Patients and carers should avoid inhalation of the vapours of the cream as transient irritation of the mucous membranes of the eyes and the respiratory tract may occur.¹⁸

12.2 Topical treatment options for the treatment of muscular/rheumatic pain

Topical analgesics are commonly used for the treatment of muscular and rheumatic pain e.g. non-steroidal anti-inflammatory (NSAID) gels. While lidocaine 5% plaster is not licensed for these types of pain, due to the high volume of dispensing of this product in Ireland, there is potential that prescribing is occurring for other forms of pain. As previously discussed, the evidence has failed to demonstrate efficacy in other forms of pain other than PHN and so the treatment of lidocaine 5% plaster in these patients should be reviewed and therapy discontinued. Table 5 below, outlines the different costs associated with licensed topical therapies for muscular and rheumatic pain compared to the cost of lidocaine 5% plaster if used in this patient cohort. The list is not exhaustive. A full list of topical NSAID preparations and associated reimbursed cost can be found on www.PCRS.ie.⁵

The recommendations of this report should be applied in conjunction with clinical judgement and decision-making appropriate to the individual patient. Prescribers should refer to the drug's SmPC and the BNF to inform decisions made with individual patients.

Table 5: Topical products and price comparisons of treatments for non-PHN indications

Product	Cost* per original pack	Directions for use	Licensed indications
Difene® Gel 1% 50g (Diclofenac)¹⁹	€1.18	Apply 2-4 times daily for a recommended 14 days. Treatment should not exceed 6 weeks.	Licensed for trauma of the tendons, ligaments, muscles and joints & localised forms of soft tissue rheumatism
Phorpain 5% Gel 100g (Ibuprofen)²⁰	€4.07	Apply a thin layer up to 3 times daily. Review after 2 weeks.	-Licensed as a topical analgesic and anti-inflammatory for backache, rheumatic and muscular pain, sprains, strains and neuralgia.
Fastum Gel 2.5% 100g (Ketoprofen)²¹	€6.69	Apply 2-3 times daily. Maximum duration should not exceed 10 days.	-Licensed for local relief of pain and inflammation associated with rheumatic, muscular disorders and soft tissue injuries.
Lidocaine 5% plasters (Versatis®)¹	€77.52 - €232.56	Apply one to three patches for 12 hours in a 24 hour period.	-Licensed for post-herpetic neuralgia (PHN) only.

*Cost = reimbursed price as listed on www.PCRS.ie. Costs are correct as of December 2016.

PHN= Post-herpetic neuralgia

12.3 Cochrane review on 'Topical NSAIDs for acute musculoskeletal pain in adults'

The Cochrane Library published a review in 2010 titled "Topical NSAIDs for acute pain in adults" and this updated review in 2015 was titled "Topical NSAIDs for acute musculoskeletal pain in adults" to better reflect the content of the report. The inclusion criteria for the 2015 review remained the same as the original analysis and were randomised, double-blind trials comparing topical NSAIDs to placebo or another active treatment and outcomes close to seven days (minimum 3 days). There were 61 studies and included 8,386 participants. The results showed that gel formulations of topical diclofenac, ibuprofen, ketoprofen, piroxicam and indomethacin (not licensed in Ireland) demonstrated significant higher rates of clinical success (more participants with at least 50% pain relief) than matching topical placebo. However, benzydamine cream did not. Three drug formulation combinations had numbers needed to treat (NNT) for clinical success below 4. For diclofenac, the Emulgel® formulation had the lowest NNT of 3.2. Ketoprofen gel had an NNT of 2.5 and Ibuprofen gel had a NNT of 3.9. All of the other drugs and formulation had a NNT above 4, indicating lower

efficacy. Local skin reactions were generally mild and transient and did not differ from placebo. There were also very few systemic adverse reactions or withdrawals due to adverse effects. In conclusion, gel formulations of diclofenac (as Emulgel®), ketoprofen and ibuprofen provided the best clinical efficacy based on NNT. Benzydamine was not significantly better to placebo (based on pooled analysis from 3 studies).²²

12.4 Cochrane review on ‘Topical NSAIDs for chronic musculoskeletal pain in adults’

The Cochrane Library also updated its 2012 review titled “Topical NSAIDs for chronic musculoskeletal pain in adults” in 2016. The inclusion criteria for this review differed from that of the review of topical NSAIDs for ‘acute’ musculoskeletal pain in adults. For inclusion, studies needed to be randomised, controlled, double-blind trials comparing topical NSAIDs with placebo or other active treatment for chronic musculoskeletal pain, with at least 10 participants per treatment arm and duration of at least two weeks, but ideally 6 weeks or longer. There were 33 studies included in this review involving 10,873 participants comparing topical NSAIDs to each other, placebo, another oral NSAID or alternative topical remedy. All studies examined topical NSAIDs for use in osteoarthritis. In studies lasting 6 to 12 weeks, topical diclofenac and topical ketoprofen were significantly more effective at reducing pain. With regards to diclofenac, the NNT for clinical success based on 6 trials was 9.8. With regards to topical ketoprofen, the NNT based on 4 trials was 6.9. There was too little information for analysis of the other individual topical NSAIDs. These efficacy results were almost completely derived from patients with knee osteoarthritis. In conclusion, topical diclofenac and ketoprofen provide good levels of pain relief in osteoarthritis but there is little evidence for other chronic painful conditions.²³

13. Potential savings

There is potential to make significant cost savings by both discontinuing lidocaine 5% plaster that are inappropriately prescribed or by switching patients to a more appropriately licensed alternative. Any savings will depend on each individual patient diagnosis and the cost of the alternative treatment that is prescribed. Figure 2 below gives two scenarios of potential cost savings that can be made by reviewing treatment. Firstly, switching patients on one lidocaine 5% plaster per 12 hours to one tube (45g) of capsaicin 0.075% cream for PHN will save €720 per patient per year. Secondly, switching patients from one lidocaine 5% plaster per 12 hours to a NSAID gel e.g. one tube (50g) of Difene® 1% gel for rheumatic or muscular pain will save €912 per patient per year.

For topical treatment of pain in PHN

Switching patients from 30 lidocaine 5% plasters to 45g capsaicin 0.075% cream per month will save **€720** per patient per year.

For topical treatment of pain for non-PHN indications

Switching patients from 30 lidocaine 5% plasters (unlicensed use) to 50g Difene[®] 1% gel per month will save **€912** per patient per year.

Figure 2: The potential for cost savings by switching in different scenarios

14. Conclusion

The place in therapy for lidocaine 5% plaster is unclear as evidence supporting its use in PHN and other unlicensed indications is limited. The potential benefit of treatment in PHN patients needs to be balanced against the high cost of treatment compared to other options available. Significant savings can be made by reviewing all patients on treatment and assessing their need for lidocaine 5% plaster.¹³ Most recent figures available show there are over 20,500 patients receiving treatment with lidocaine 5% plaster, therefore significant savings can be made by reducing the amount of inappropriate prescribing. A summary of MMP recommendations are detailed below and tips and tools to support the prescribing of lidocaine 5% plaster is detailed in Appendix A of this report.

MMP recommendations on the use of lidocaine 5% plaster

- ✓ Prescribing of lidocaine 5% plaster should be restricted to patients diagnosed with post-herpetic neuralgia (PHN).
- ✓ Treatment should be reviewed after 2-4 weeks and stopped if ineffective or if the relieving effect is solely due to protection of the area by the plaster.
- ✓ Prescribers should ensure all patients are using the patch correctly and have at least a 12 hour free period every 24 hours.
- ✓ Patients on long-term therapy should be assessed for continued need and aim to have treatment discontinued or alternatively, try to have a longer plaster-free period between treatments.
- ✓ Patients prescribed lidocaine 5% plaster for unlicensed indications must be reviewed and treatment should be discontinued.
- ✓ NICE clinical guidance 173 does not recommend the use of topical lidocaine 5% plaster in its guidance.
Patients who wish to avoid or who are unable to tolerate oral medication for PHN, capsaicin 0.075% cream is recommended.
- ✓ MMP does not recommend the use of topical lidocaine 5% plaster for unlicensed indications due to lack of clinical evidence.
Patients receiving treatment for unlicensed indications should be switched to a suitable alternative e.g. for muscular/rheumatic pain a topical NSAID gel should be considered.

15. References

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