Cost Effectiveness of the 5% lidocaine plaster (Versatis®) for the symptomatic relief of neuropathic pain associated with previous Herpes zoster infection (post-herpetic neuralgia, PHN).

The NCPE performed an evaluation of the use of the 5% lidocaine plaster for this indication. The NCPE concludes that the cost effectiveness of the 5% lidocaine plaster has not been demonstrated.

The HSE has asked the National Centre for Pharmacoeconomics (NCPE) to evaluate the applicant's (Grünenthal) economic dossier on the cost effectiveness of the 5% lidocaine plaster. The NCPE uses a decision framework to systematically assess whether a technology is cost effective. This includes clinical effectiveness and health related quality of life benefits that the new treatment may provide and whether the cost requested by the pharmaceutical company is justified.

Following the recommendation from the NCPE, the HSE examine all the evidence that may be relevant for the decision; the final decision on reimbursement is made by the HSE. In the case of cancer drugs, the NCPE recommendation is also considered by the National Cancer Control Programme (NCCP) Technology Review Group.

About the National Centre for Pharmacoeconomics

The NCPE are a team of clinicians, pharmacists, pharmacologists and statisticians who evaluate the benefit and costs of medical technologies and provide advice to the HSE. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. Our aim is to provide impartial advice to help decision makers provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has a responsibility for commissioning or providing healthcare, public health or social care services.

National Centre for Pharmacoeconomics ***September 2015***

Summary

The 5% lidocaine plaster (Versatis®) has been in use in Ireland since 2010. The product is licensed for the symptomatic relief of neuropathic pain associated with previous Herpes zoster infection (post-herpetic neuralgia, PHN) in adults. In accordance with the Health Act (Pricing and Supply of Medical Goods) 2013 (section 18(4)), the HSE has requested the NCPE to examine the cost effectiveness of the product.

Grünenthal submitted a dossier on the cost effectiveness of the 5% lidocaine plaster (Versatis®) in PHN in November 2014. However, as discussed below under 'Budget Impact Analysis', the vast majority of the prescribing of this product under the state schemes is for indications other than PHN. The applicant did not submit a cost effectiveness evaluation for indications other than PHN due to the lack of relevant clinical evidence.

1. Comparative Effectiveness and Safety

The relevant comparators to the 5% lidocaine plaster for the decision maker are the oral treatments pregabalin, gabapentin and amitriptyline. The evidence submitted by the applicant for the effectiveness of the 5% lidocaine plaster in the PHN indication was derived from an open-label non-inferiority trial of four weeks duration which compared pain response rates between the 5% lidocaine plaster and pregabalin in patients with PHN and diabetic polyneuropathy (DPN). In the overall mixed population of patients (PHN+DPN), the lidocaine plaster was found to be non-inferior to pregabalin in the full analysis set following statistical testing. The review group had concerns over a number of aspects of the trial including the unblinded trial design, the differing baseline demographic for the PHN group and the lack of adequate power for the PHN group which is the focus of this assessment. Clinical efficacy data was not available for the comparison of the 5% lidocaine plaster to gabapentin or amitriptyline; response rates for these comparators were assumed to equal those found in the above study which compared 5% lidocaine to pregabalin.

Regarding safety, there are fewer withdrawals from treatment due to adverse events for patients on 5% lidocaine plaster than pregabalin. Most adverse events associated with topical lidocaine relate to the tolerability of the plaster at the application site. Such adverse events are of mild intensity and due to the low absorption of lidocaine from the plaster, systemic effects are unlikely.

The lignocaine 5% patch was assessed by the MHRA through the decentralised procedure and they have concluded that there is some evidence of small clinical benefit, even though it is likely this product has an additional placebo effect in this condition.

2. Cost-Effectiveness analysis

The cost effectiveness analysis submitted relates only to the indication of PHN which represents a small percentage of overall usage of 5% lidocaine in Ireland. The cost utility analysis presented provided evidence for the cost effectiveness of the 5% lidocaine plaster versus the comparators (i) pregabalin; (ii) gabapentin; (iii) amitriptyline in PHN. The perspective of the HSE (payer) was presented. The submitted model was a Markov model constructed in TreeAge®. The time horizon was 6 months, with extrapolation of efficacy and safety data beyond the four weeks of trial data for the 5% lidocaine plaster versus pregabalin. Absolute costs and quality-adjusted life years (QALYs), and incremental costs and QALYs, associated with the 5% lidocaine plaster, and the comparators pregabalin, gabapentin, and amitriptyline were presented.

The NCPE review group had a number of concerns regarding the model, particularly regarding the sourcing and application of utilities, and the associated potential for bias. The utility values for treatment with 5% lidocaine and its comparators were derived from two main sources. The first was a published economic study which assigned the utility of adverse events according to results from a different patient cohort (patients with hypertension). The second source was from a Delphi panel study undertaken by the applicant with 9 GPs. The methodology of how this study was undertaken was not provided. In relation to adverse events specifically the applicant has assumed that everyone in the model receives adverse events; evidence to support this assumption was not provided. The review group are concerned that given the limitations of the data used to inform the utilities and the impact of utilities on the overall cost effectiveness that there may be undue bias introduced to the estimates.

Furthermore, as no clinical data was available for the comparators gabapentin and amitriptyline, transition probabilities and other model inputs for these comparators were assumed to equal those for pregabalin.

Results

Under the conditions of the submitted model, the base case ICERs were €9,871/QALY for the comparison of 5% lidocaine to pregabalin, €7,771/QALY for the comparison to gabapentin and €6,216/QALY for the comparison to amitriptyline. However the NCPE do not consider these estimates to be robust for PHN and no ICERs were presented for non PHN indications.

Sensitivity analysis

One way and probabilistic sensitivity analyses were included in the submission to explore the uncertainty in the model. The model was found to be particularly sensitive to the daily number of lidocaine plasters (varied from 1 to 2.47), though this did not greatly change the resultant ICERs. While the applicant estimated that the probability of the cost effectiveness of the 5% lidocaine plaster was high, the review group consider that this result is dependent on the parameters used and the model structure applied, and that substantial uncertainty exists around these.

3. Budget Impact Analysis

Budget impact estimates were submitted by the applicant based on the expected adult PHN population in Ireland who would be likely to receive the 5% lidocaine plaster. The number of patients receiving the product and the expected duration of use of the product differed substantially from the overall 5% lidocaine plaster usage figures observed by the NCPE upon examination of the national reimbursement data (2014) data. The review group considers that the applicant estimates represent 5-10% of the total number of patients receiving the product under the community drugs schemes in Ireland, i.e. that the vast majority of the prescribing of the product is for unlicensed indications.

NCPE analysis of the GMS, Drug Payment Scheme and LTI scheme for the months January-December 2014 inclusive found that ingredient cost expenditure on the 5% lidocaine plaster amounted to €15.7million and that expenditure has increased on a monthly basis in line with steadily increasing patient numbers.

4. Conclusion

The submitted evidence represents the cost effectiveness of the product in a minority of the population who receive the product. As such, the NCPE conclude that the cost effectiveness of the product has not been demonstrated.