Vectatone 1 % cream

05-03-2014, Versio 7.3

Public Summary of Risk Management Plan

8.2 VI.2. Elements for a Public Summary

8.2.1 VI.2.1 Overview of disease epidemiology

Herpes labialis, also known as cold sores, is a very common worldwide skin disease caused by the Herpes Simplex Virus (HSV) types 1 and 2. The symptoms associated with this condition include pain, tenderness, and burning, which are of particular concern to patients, not only due to discomfort, but also because they may interfere with everyday activities such as eating and drinking. HSV infections may already occur in children, usually at preschool or kindergarten age; adolescents and young adults are normally infected through non-sexual contact. The incidence of infection increases steadily with age, reaching 80-90% among those 50 years or older. Among the adult population, 30-45% have a history of symptomatic herpes labialis (Harmenberg et al., 2010; Usatine and Tinitigan, 2010; Piret and Boivin, 2011), while antibodies to HSV (indicating the virus presence in the body) are found in 60-80% of the general population (Schmid-Wendtner and Korting, 2004). The frequency of viral attacks can vary from rare episodes to 12 or more attacks per year. The lesions require between 5 to 15 days to resolve (on average 7 to 8 days), depending on the immune system of the affected subjects (Spruance et al., 1997; Arduino and Porter, 2008).

8.2.2 VI.2.2 Summary of treatment benefits

Clinical studies with penciclovir 1% have been performed either with healthy persons or patients with repeated facial cold sores. Healthy persons (adult men and women) were part of the initial studies with the product to evaluate the safety of the product; later, patients with repeated cold sores participated in studies to evaluate the clinical efficacy and safety.

Small studies were performed initially to evaluate the safety and effectiveness of the treatment with penciclovir cream. Depending on the study, the number of participants was 12 to 288. In addition to the smaller studies, the results from 2 large placebo-controlled studies involving a total of more than 4,500 patients, formed the basis to obtain permission to market the medication in 44 countries worldwide.

In addition, two large evaluations were also performed. These involved prescription and adverse event records from more than 5 thousand of patients, using large national prescription and health databases in the United Kingdom.

Furthermore, 4 studies were performed by doctors who, through their own initiative in their usual clinical setting, used penciclovir 1% cream to investigate its effectiveness and safety in patients with repeated cold sores. The number of patients included in those studies was between 40 and 541; the countries involved in these studies were China, Italy, and United Kingdom.

Overall, the results of all studies indicate that penciclovir 1% cream is an effective and well tolerated treatment for recurrent cold sores. The cream shortens healing time, reduces pain and inactivates the virus causing the cold sores. The cream is effective even when applied at a late stage of the infection, i.e. when the full cold sore has developed.

8.2.3 VI.2.3 Unknowns relating to treatment benefits

The following items have been identified as unknowns, because no work has been carried out in the indicated groups of subjects related to treatment benefits:

- Children below 12 years of age
- Use during pregnancy or in nursing mothers; excretion in human milk

Warnings about use in these populations are provided in the SmPC. Moreover, use during pregnancy and lactation and in children <12 years of age are discussed as missing information in this RMP.

8.2.4 VI.2.4 Summary of safety concerns

Table 8-3 Important identified risks

Risk	What is known	Preventability
Hypersensitivity	Some patients have reported hypersensitivity reactions following the use of penciclovir cream. These include local skin irritation, rash, hives, itching and swelling. The vast majority of reactions are not serious and resolve after penciclovir cream is discontinued.	Patients with known allergies to penciclovir, its pro-drug famciclovir, or any of the ingredients (e.g. propylene glycol, cetostearyl alcohol) should not use the product. The PIL clearly provides this information. In general, however, allergic reactions cannot be prevented. Patients should seek medical advice if such reactions get serious.

Table 8-4 Missing information

Risk	What is known
Use during pregnancy and lactation	A human volunteer study has shown that the absorption of penciclovir cream into the bloodstream is negligible. As a result, adverse effects on the foetus or breastfed child are unlikely. Nonetheless, penciclovir cream has not been specifically studied in pregnant or breastfeeding women and therefore should only been used upon doctor's advice.
Use in children <12 years of age	There are no data about the efficacy and safety of penciclovir cream in children below the age of 12. Therefore, the use in this population is not recommended.

8.3 VI.2.5 Summary of risk minimization measures by safety concern

Not applicable as no additional risk minimization measures are proposed.

8.4 VI.2.6 Planned post authorization development plan

A planned post-authorisation development plan is not required for this product.

8.4.1 Studies which are a condition of the marketing authorization

No studies have been established as conditions of the marketing authorization.

8.5 VI.2.7 Summary of changes to the Risk Management Plan over time

There were no changes that concerned important risks or missing information discussed in the RMP.