Prescribing information

1. Name of the medicinal product

Fenlips®

2. Qualitative and quantitative composition

Each gram of the cream contains:

10 mg Penciclovir, 1% w/w.

Excipients with known effect: cetostearyl alcohol, propylene glycol.

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Cream

Smooth white cream of homogeneous appearance.

4. Clinical particulars

4.1 Therapeutic indications

Fenlips is indicated for the topical treatment of cold sores (oral herpes).

4.2 Posology and method of administration

Adults (including older people) and children over 12 years of age:

Fenlips should be applied at approximately two hourly intervals during waking hours (approximately 8 times a day). Treatment should be continued for 4 days. If the condition gets worse or does not improve after 4 days treatment, seek medical advice.

Treatment should be started as early as possible after the first sign of an infection; moreover, the product has been shown to be beneficial in accelerating lesion healing, reducing lesion pain and shortening the duration of viral shedding even in patients who begin treatment later in the disease (e.g. when the papule or vesicle has developed).

Paediatric population

Children (under 12 years):

The safety and efficacy in children below 12 years of age have not been established. No data are available.

4.3 Contraindications

Hypersensitivity to Penciclovir, famciclovir or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

The cream should only be used on cold sores on the lips and around the mouth. It is not recommended for application to mucous membranes (e.g. in the eyes, mouth, or nose or on the genitals). Particular care should be taken to avoid application in or near the eyes.

Patient with particularly severe cold sores should be encouraged to seek medical advice.

Patients should be advised to avoid transmitting the virus, particularly when active lesions are present.

Immunocompromised patients (e.g. AIDs patients or bone marrow transplant recipients) should be encouraged to consult a physician in case oral therapy is indicated.

The cream contains cetostearyl alcohol, which may cause local skin reactions (e.g. contact dermatitis). It also contains propylene glycol, which may cause skin irritation.

4.5 Interaction with other medicinal products and other forms of interaction

Clinical trial experience has not identified any interactions resulting from concomitant administration of topical or systemic drugs with Penciclovir.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is unlikely to be any cause for concern regarding adverse effects when the cream is used in pregnant women as systemic absorption of Penciclovir following topical administration of Penciclovir has been shown to be minimal (see Section 5.2).

Since the safety of Penciclovir in human pregnancy has not been established, Fenlips should only be used during pregnancy or in nursing mothers on the advice of a doctor, if the potential benefits are considered to outweigh the potential risks associated with treatment.

Lactation

There is unlikely to be any cause for concern regarding adverse effects when the cream is used in lactating women as systemic absorption of Penciclovir following topical administration of Penciclovir has been shown to be minimal (see Section 5.2).

There is no information on excretion of Penciclovir in human milk.

Fertility

No fertility data available.

4.7 Effects on ability to drive and use machines

Penciclovir has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

Penciclovir has been well-tolerated in human studies. Clinical trial experience has shown that there was no difference between Penciclovir and placebo in the rate or type of adverse reactions reported.

The most common events are application site adverse events.

Tabulated list of adverse reactions

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); unknown (cannot be estimated from available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

General disorders and administration site condition: Common	Application site reactions (including skin burning sensation, pain of skin, hypoaesthesia)

Post-marketing surveillance has revealed the following adverse events (all reactions were either localised or generalised). Adverse events from post-marketing experience are difficult to calculate a frequency and therefore the events are listed as unknown frequency.

Immune System disorders: Not known	hypersensitivity, urticarial
Skin and subcutaneous disorders: Not known	dermatitis allergic (including rash, pruritus, blisters and oedema)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il.
In addition, you can report to Padagis via the following address: Padagis.co.il

4.9 Overdose

No untoward effects would be expected even if the entire contents of a container of Penciclovir were ingested orally; Penciclovir is poorly absorbed following oral administration. However, some irritation in the mouth could occur. No specific treatment is necessary if accidental oral ingestion occurs.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Topical antiviral agent, ATC code: D06BB06

Mechanism of action

Penciclovir has demonstrated in vivo and in vitro activity against herpes simplex viruses (types 1 and 2) and varicella zoster virus. In virus-infected cells Penciclovir is rapidly and efficiently converted into a triphosphate (mediated via virus-induced thymidine kinase).Penciclovir triphosphate persists in infected cells for more than 12 hours where it inhibits replication of viral DNA and has a half-life of 9, 10 and 20 hours in cells infected with varicella zoster virus, herpes simplex virus type 1 and herpes simplex virus type 2 respectively. In uninfected cells treated with Penciclovir, concentrations of Penciclovir triphosphate are only barely detectable. Accordingly, uninfected cells are unlikely to be affected by therapeutic concentrations of Penciclovir.

Clinical efficacy and safety

In clinical studies, Penciclovir treated patients healed 30% faster than placebo (up to one day earlier), pain resolution was 25-30% faster (median improvement of up to one day) and infectivity resolved up to 40% faster (one day earlier) than placebo.

5.2 Pharmacokinetic properties

General characteristics

Following application of Penciclovir in a human volunteer study at a daily dose of 180mg Penciclovir (approximately 67 times the proposed daily clinical dose), to occluded and abraded skin for 4 days, Penciclovir was not quantifiable in plasma and urine.

5.3 Preclinical safety data

General toxicology

Topical application of 5% Penciclovir for 4 weeks to rats and rabbits was well tolerated. There was no evidence of contact sensitisation in guinea pigs.

A full programme of studies has been completed using intravenous Penciclovir. These studies did not raise any safety concerns regarding topical use of Penciclovir. There is a minimal systemic absorption of Penciclovir following topical administration.

Genotoxicity and Reproductive toxicity

Animal studies have not shown any embryotoxic or teratogenic effects with Penciclovir given intravenously (at doses greater than 1200 times those recommended for clinical use via topical application), nor were there any effects on male and female fertility and general reproductive performance (at doses greater than 1600 times those recommended for clinical use via topical application). Studies in rats show that Penciclovir is excreted in the breast milk of lactating females given oral famciclovir (famciclovir; the oral form of Penciclovir, is converted in vivo to Penciclovir).

The results of a wide range of mutagenicity studies in vitro and in vivo indicates that Penciclovir does not pose a genotoxic risk to man.

6. Pharmaceutical particulars

6.1 List of excipients

Fenlips:

Propylene glycol
Purified water
White soft paraffin
Cetostearyl alcohol
Liquid paraffin
Cetomacrogol 1000
Nitrogen

6.2 Incompatibilities

Not applicable

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Fenlips:
Store below 30°C. Do not freeze.

6.5 Nature and contents of container

2 g aluminium tube.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Registration Holder

Padagis Israel Agencies Ltd., 1 Rakefet St., Shoham.

8. Registration number

142-41-31798

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