SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
PENSIVIR 1% cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 1 g cream contains,

Active substance:

Penciclovir	10 mg

Excipients:

Propylene glycol	397.0 mg
Cetostearyl alcohol	55.0 mg

For a full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM
Cream

White or almost white, homogenous looking cream

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
It is indicated for the treatment of cold sores (herpes labialis).

4.2 Posology and method of administration
Posology/frequency and duration of administration:
Adults (including the elderly) and children over the age of 12:
PENSIVIR should be applied at approximately two-hour intervals throughout the day (approximately 8 times a day). Treatment should be continued for 4 days.
Treatment should be started as early as possible from the first sign of the infection. However, PENSIVIR has been shown to accelerate lesion healing, reduce pain, and shorten the duration of viral transmission, even in those who begin treatment after the onset of the disease (e.g. after blistering).

Method of administration:
It is used externally.

Additional information on special populations:
Renal/Hepatic failure: The use of PENSIVIR in patients with renal and hepatic failure has not been investigated.

Pediatric population:
PENSIVIR has not been investigated in children under 12 years of age.

Geriatric population:
PENSIVIR can be used in the recommended dosage for adults in the elderly.

4.3. Contraindications
PENSIVIR is contraindicated in patients with hypersensitivity to penciclovir, famciclovir, or any of the ingredients in the composition.

4.4. Special warnings and precautions for use
The cream should only be used on cold sores on lips and around mouth. Administration to mucous membranes (e.g., eye, mouth or nose or genital area) is not recommended. The administration to the eye and eye area should be avoided.

In severe cold sores, it should be consulted to a doctor.

Patients with severe immunosuppression (e.g. AIDS patients or bone marrow transplant patients) should seek medical advice if oral therapy is needed.

Caution should be exercised for virus transmission when there is an active lesion.

PENSİVİR contains propylene glycol and cetostearyl alcohol. Setostearyl alcohol may cause local skin reactions (e.g. contact dermatitis). Propylene glycol may cause skin irritation.

4.5. Interaction with other medicinal products and other forms of interaction
Clinical trials with penciclovir have not reported any interaction resulting from the administration of concurrent topical or systemic drugs.

Additional information on special populations
No interaction studies have been conducted on the use in special populations.

Pediatric population:
No interaction study has been conducted on the use in pediatric populations.

4.6 Pregnancy and lactation
General recommendation
Pregnancy category: C

Women with childbearing capacity / Birth control (Contraception)
The potential risk for humans is unknown. There is insufficient data on the use of penciclovir in pregnant women (see section 5.3).

Since penciclovir systemic absorption is shown to be minimal after topical application of penciclovir-containing cream, it is unlikely that the cream will cause any concern about the adverse effects when used in pregnant women (see section 5.2).

Pregnancy
There is no adequate data on the use of penciclovir in pregnant women.
Animal studies are inadequate in terms of the effects on pregnancy / and-or / embryonal / fetal development / and-or / birth / and / or postnatal development (see section 5.3). The potential risk for humans is unknown.

Since penciclovir systemic absorption is shown to be minimal after topical application of penciclovir-containing cream, it is unlikely that the cream will cause any concern about the adverse effects when used in pregnant women (see section 5.2).

Since penciclovir is not shown to be safe for use in pregnancy, PENSIVIR should only be used in gestation with doctor's advice when the benefit to the patient are superior to the potential risks associated with treatment

Lactation
Since penciclovir systemic absorption is shown to be minimal after topical application of penciclovir-containing cream, it is unlikely that the cream will cause any concern about the adverse effects when used in nursing women (see section 5.2)

It is not known whether penciclovir is excreted in human milk. When deciding whether or not to stop breastfeeding or treatment with penciclovir, the benefit of breastfeeding for the child and the benefit of treatment with penciclovir for the nursing mothers should be considered.

Reproduction ability / Fertility
No effect on male and female fertility was observed in animal studies.

4.7. Effects on ability to drive and use of machines
No adverse effects on driving and using machines were observed.

4.8. Undesirable effects
Penciclovir has been well tolerated in studies on humans. Clinical trials have shown that there is no difference between penciclovir and placebo in terms of the proportion or type of adverse reactions reported. The most common events are administration site reactions.

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 (can not be estimated from the available data).

General disorders and administration site conditions
Common: Administration site reactions (e.g., burning sensation in the skin, skin pain, hypoesthesia)

Post-marketing experience has shown that the following adverse events (all reactions can be seen as localized or generalized) are occurred. The post-marketing adverse events are difficult to estimated, and therefore the frequency of the following events is considered as “unknown”.

Immune system diseases:
Unknown: Hypersensitivity, urticaria

Skin and subcutaneous tissue diseases:
Unknown: Allergic dermatitis (rash, urticaria, itching, blisters and edema)

4.9. Overdose
Even if all the contents of a PENSIVIR cream package are taken orally, no undesirable effects are expected, and absorption after penciclovir oral administration is very low. However, slight irritation may occur in the mouth. No special treatment is required if ingested accidentally by mouth

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Topical antiviral agents
ATC Code: D06BB06

Mode of action:
Penciclovir has proven *in vivo* and *in vitro* activity against herpes simplex viruses (type 1 and 2) and varicella zoster virus. In virus-infected cells, the penciclovir (via the virus-induced thymidine kinase) rapidly and efficiently transforms into a triphosphate. The residence time of penciclovir triphosphate in infected cells for which viral DNA replication is inhibited is over 12 hours and it has a half-life of 9, 10 and 20 hours respectively in the infected cells with varicella zoster virus, Type 1 and Type 2 herpes simplex virus. Penciclovir triphosphate is only in detectable concentrations in uninfected cells to which penciclovir is administered. Accordingly, it is unlikely that uninfected cells will be affected by therapeutic concentrations of penciclovir

In clinical trials, patients treated with penciclovir have recovered 30% faster than placebo; pain and transmission has terminated in a shorter time by 25-30% and 40%, respectively.

5.2. Pharmacokinetic properties

Penciclovir was not detected in the plasma or urine after administration of occlusion and application of a daily dose of 180 mg (approximately 67 times the clinical dose) over irritated skin for 4 days.

5.3. Preclinical safety data

Topical administration of 5% penciclovir cream in rats and rabbits for 4 weeks was well tolerated. No sensitization was observed at the administration site in guinea pigs.

The entire study program was completed using intravenous penciclovir. These studies have not revealed any results regarding the safety of topical penciclovir use. There is minimal systemic absorption with topical administration of penciclovir.

In animal studies, no effect on any embryotoxic or teratogenic effect (1200 times doses recommended for topical route in clinical use)or male and female fertility and general reproductive performance (1600 times doses recommended for topical route in clinical use) was observed with penciclovir administered intravenously (1200 times doses recommended for topical route in clinical use). The results of larger *in vitro* and *in vivo* mutagenicity studies have shown that penciclovir does not have a genotoxic risk in humans. Studies in rats have shown that famciclovir (the oral form of penciclovir, it is converted into penciclovir in vivo), when given orally, penciclovir is excreted by the milk of lactating females.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cetomacrogol 1000
Propylene glycol
Cetostearyl alcohol
Liquid paraffin
White paraffin
Deionized water

6.2 Incompatibilities
There are no known incompatibilities.

6.3. Shelf life
24 months

6.4. Special precautions for storage
Store at room temperature below 25 ºC.
Do not freeze.

6.5. Nature and contents of container
PENSIVIR is marketed in 2 g, 5 g and 10 g aluminum tubes closed with HDPE cap. Each cardboard box contains one tube.

6.6 Special precautions for disposal and other handling
Any unused product or waste material should be disposed of in accordance with "Directive on Control of Medical Waste" and "Directive on the Control of Packaging and Packaging Waste".

7. MARKETING AUTHORIZATION HOLDER
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8. MARKETING AUTHORIZATION NUMBER(S)
2014/801

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION
Date of the first authorization: 05.11.2014
Date of the renewal of the authorization: 14.01.2020

10. DATE OF REVISION OF THE TEXT

17.12.2019