



SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Aciclovir Cream BP 5% w/w

2. Qualitative and quantitative composition

Composition:

Aciclovir BP5% w/w

In a Cream base.....q.s

S.no	Name of Ingredients	Function of ingredients	Quantity required per gm.	Overage (%)	Quantity required per gm.	Water/LO D content (%)	Total quantity required per gm.
Active							
1.	Aciclovir BP	Active Ingredient	50.0 mg	Nil	50.0 mg	Nil	50.0 mg
Inactive							
2.	White soft paraffin BP	Emollient	93.750 mg	Nil	93.750 mg	Nil	93.750 mg
3.	Cetostearyl alcohol BP	Emulsifying agent	72.0 mg	Nil	72.0 mg	Nil	72.0 mg
4.	Cetomacrogol -1000 IHS	Emulsifying agent	22.500 mg	Nil	22.500 mg	Nil	22.500 mg
5.	Light liquid paraffin BP	Emollient	60.00 mg	Nil	60.00 mg	Nil	60.00 mg
6.	Propylene Glycol USP	Plasticizer	100.00 mg	Nil	100.00 mg	Nil	100.00 mg
7.	Chlorocresol BP	Preservative	1.00 mg	Nil	1.00 mg	Nil	1.00 mg
8.	Anhydrous disodium hydrogen phosphate BP	Buffering agent	3.00 mg	Nil	3.00 mg	Nil	3.00 mg
9.	Purified Water BP	Solvent	597.750 mg	Nil	597.750 mg	Nil	597.750 mg

Total Weight: 1.0 gm.



3. Pharmaceutical form

Topical cream

Off White colored cream.

4. Clinical particulars

4.1 Therapeutic indications

Aciclovir Cream is indicated for the treatment of Herpes Simplex virus infections of the skin including initial and recurrent genital herpes and herpes labialis.

Route of administration: topical. Do not use in eyes.

4.2 Posology and method of administration

Adults and Children: Aciclovir Cream should be applied five times daily at approximately four hourly intervals, omitting the night time application.

Aciclovir Cream should be applied to the lesions or impending lesions as soon as possible, preferably during the early stages (prodrome or erythema). Treatment can also be started during the later (papule or blister) stages.

Treatment should be continued for at least 4 days for herpes labialis and for 5 days for genital herpes. If healing has not occurred then treatment may be continued for up to an additional 5 days.

Use in the elderly: No special comment

4.3 Contraindications

Hypersensitivity to terbinafine or any of the excipients contained in the cream.



4.4 Special warnings and precautions for use

Aciclovir Cream is not recommended for application to mucous membranes such as in the mouth, eye or vagina, as it may be irritant.

Particular care should be taken to avoid accidental introduction into the eye.

In severely immunocompromised patients (eg AIDS patients or bone marrow transplant recipients) oral Aciclovir dosing should be considered. Such patients should be encouraged to consult a physician concerning the treatment of any infection.

The excipient propylene glycol can cause skin irritations and the excipient cetyl alcohol can cause local skin reactions (e.g. contact dermatitis).

Aciclovir Cream contains a specially formulated base and should not be diluted or used as a base for the incorporation of other medicaments.

4.5 Interaction with other medicinal products and other forms of interaction

No clinically significant interactions have been identified.

4.6 Fertility, pregnancy and lactation

Pregnancy:

A post-marketing aciclovir pregnancy registry has documented pregnancy outcomes in women exposed to any formulation of Aciclovir. The registry findings have not shown an increase in the number of birth defects amongst aciclovir exposed subjects compared with the general population, and any birth defects showed no uniqueness or consistent pattern to suggest a common cause. Systemic administration of aciclovir in internationally accepted standard tests did not produce embryotoxic or teratogenic effects in rabbits, rats or mice.



In a non-standard test in rats, foetal abnormalities were observed but only following such high subcutaneous doses that maternal toxicity was produced. The clinical relevance of these findings is uncertain.

The use of Aciclovir Cream should be considered only when the potential benefits outweigh the possibility of unknown risks however the systemic exposure to aciclovir from topical application of Aciclovir Cream is very low.

Teratogenicity:

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure to indicate little relevance to clinical use (see section 5.3).

Breast-feeding:

Limited human data show that the drug does pass into breast milk following systemic administration. However, the dosage received by a nursing infant following maternal use of Aciclovir Cream would be insignificant.

Fertility:

There is no information on the effect of aciclovir on human female fertility.

In a study of 20 male patients with normal sperm count, oral aciclovir administered at doses of up to 1 g per day for up to six months has been shown to have no clinically significant effect on sperm count, motility or morphology.

See Clinical Studies in section 5.1.

4.7 Effects on ability to drive and use machines

Not applicable



4.8 Undesirable effects

The following convention has been used for the classification of undesirable effects in terms of frequency: very common $\geq 1/10$, common $\geq 1/100$ and $< 1/10$, uncommon $\geq 1/1000$ and $< 1/100$, rare $\geq 1/10,000$ and $< 1/1000$, very rare $< 1/10,000$.

Immune system disorders:

Very rare

Immediate hypersensitivity reactions including angioedema and urticaria.

Skin and subcutaneous tissue disorders:

Uncommon

Transient burning or stinging following application of Aciclovir Cream

Mild drying or flaking of the skin

Itching

Rare

- Erythema
- Contact dermatitis following application. Where sensitivity tests have been conducted, the reactive substances have most often been shown to be components of the cream rather than aciclovir.

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.

4.9 Overdose

No untoward effects would be expected if the entire contents of a 15 gram tube of Aciclovir Cream containing 750 mg of aciclovir were ingested orally. However the accidental, repeated



overdose of oral aciclovir, over several days has resulted in gastrointestinal effects (nausea and vomiting) and neurological effects (headache and confusion). Aciclovir is dialysable by haemodialysis.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Aciclovir is an antiviral agent which is highly active in vitro against herpes simplex virus (HSV) types I and II and varicella zoster virus. Toxicity to mammalian host cells is low. Aciclovir is phosphorylated after entry into herpes infected cells to the active compound aciclovir triphosphate. The first step in this process is dependent on the presence of the HSV- coded thymidine kinase. Aciclovir triphosphate acts as an inhibitor of, and substrate for, the herpes-specified DNA polymerase, preventing further viral DNA synthesis without affecting normal cellular processes.

In two large, double blind, randomised clinical studies involving 1,385 subjects treated over 4 days for recurrent herpes labialis, Aciclovir Cream 5% was compared to vehicle cream. In these studies, time from start of treatment to healing was 4.6 days using Aciclovir Cream and 5.0 days using vehicle cream ($p < 0.001$). Duration of pain was 3.0 days after start of treatment in the Aciclovir Cream group and 3.4 days in the vehicle group ($p = 0.002$). Overall, approximately 60% of patients started treatment at an early lesion stage (prodrome or erythema) and 40% at a late stage (papule or blister). The results were similar in both groups of patients.

5.2 Pharmacokinetic properties

Pharmacology studies have shown only minimal systemic absorption of aciclovir following repeated topical administration of Aciclovir Cream.

5.3 Preclinical safety data

The results of a wide range of mutagenicity tests in vitro and in vivo indicate that aciclovir does



not pose a genetic risk to man.

Aciclovir was not found to be carcinogenic in long term studies in the rat and the mouse.

Largely reversible adverse effects on spermatogenesis in association with overall toxicity in rats and dogs have been reported only at doses of aciclovir greatly in excess of those employed therapeutically. Two generation studies in mice did not reveal any effect of orally administered aciclovir on fertility.

Systemic administration of aciclovir in internationally accepted standard tests did not produce embryotoxic or teratogenic effects in rats, rabbits or mice.

In a non-standard test in rats, foetal abnormalities were observed, but only following such high subcutaneous doses that maternal toxicity was produced. The clinical relevance of these findings is uncertain.

6. Pharmaceutical particulars

6.1 List of excipients

White soft paraffin BP
Cetostearyl alcohol BP
Cetomacrogol -1000 IHS
Light liquid paraffin BP
Propylene Glycol USP
Chlorocresol BP
Anhydrous disodium hydrogen phosphate BP
Purified Water BP



6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 30° C. Protect from light.

6.5 Nature and contents of container

15 gm printed lami tube & sealed with white colored plastic cap packed in a printed box with leaflet.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing authorisation holder

NA

8. Marketing authorisation number(s)

NA

9. Date of first authorisation/renewal of the authorization

NA

10. Date of revision of the text

NA

11. Manufactured by:

KWALITY PHARMACEUTICALS LTD.

Village Nag Kalan, Majitha Road,

Amritsar-143601 (INDIA)