SUMMARY OF PRODUCT CHARACTERISTIC

1. Name of the medicinal product
Novirax Cream

2. Qualitative and quantitative composition
Aciclovir BP 5.0% w/w

3. Pharmaceutical form
Topical Cream
Smooth uniform, white to off-white semi-solid cream. Clear free from foreign particles.

4. Clinical particulars

4.1 Therapeutic indications
Novirax 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: Novirax Cream should be applied five times daily at approximately four hourly intervals, omitting the night time application.
Novirax 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
Novirax Cream is contraindicated in patients known to be hypersensitive to aciclovir, valaciclovir, propylene glycol or any of the excipients of Novirax Cream.

4.4 Special warnings and precautions for use
Novirax 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 Novirax 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).
Novirax 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. Pregnancy and lactation
Pregnancy:
A post-marketing aciclovir pregnancy registry has documented pregnancy outcomes in women exposed to any formulation of Novirax. The birth defects described amongst Novirax exposed subjects have not shown any uniqueness or consistent pattern to suggest a common cause.
The use of Novirax 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 Novirax 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)

Lactation:
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 Novirax 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 1g per day for up to six months has been shown to have no clinically significant effect on sperm count, motility or morphology.

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 ≥1/10, common ≥1/100 and <1/10, uncommon ≥1/1000 and <1/100, rare ≥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 Novirax 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 authorization of the medicinal product is important as it allows continued monitoring of the benefit–risk balance of the medicinal product. Healthcare professionals are requested to report any suspected adverse reactions to the marketing authorization holder or, where applicable, via the national reporting system https://pv.pharmacyboardkenya.org/

4.9 Overdose

No untoward effects would be expected if the entire contents of a 10 gram tube of Novirax Cream containing 500 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, Novirax Cream 5% was compared to vehicle cream. In these studies, time from start of treatment to healing was 4.6 days using Novirax Cream and 5.0 days using vehicle cream ($p<0.001$). Duration of pain was 3.0 days after start of treatment in the Novirax 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 Novirax 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
Anhydrous Disodium hydrogen Phosphate
Sodium Dihydrogen Phosphate Anhydrous
Methyl hydroxybenzoate
Propyl Hydroxybenzoate
White soft Paraffin

Light Liquid Parafin
Cetostearyl Alcohol
Cetomacrogol Emulsifying Wax
Propylene Glycol.

6.2 Incompatibilities
None known

6.3 Shelf life
24 Months

6.4 Special precautions for storage
Store below 30°C.
Keep out of the Reach of Children

6.5 Nature and contents of container
Aluminium Collapsible tubes 15g

6.6 Special precautions for disposal and other handling
No special instructions.

7. Marketing Authorization Holder
Zynova/Oman Pharmaceutical Product Co. L.L.C.
P.O Box No 1885, Seeb, Postal
code 111, Sultanate of Oman.

8. Marketing Authorization Number(S)
H2022/CTD8101/16836

9. Date of First Authorization/Renewal of the Authorization
19/04/2023

10. Date of Revision of the Text
19/04/2023