# Zovirax Genital

## PRODUCT SUMMARY

## 1. NAME OF THE MEDICINAL PRODUCT

Zovirax Genital

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Aciclovir 5.0% w/w
For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Topical Cream

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Zovirax Genital is indicated for local treatment of genital Herpes Simplex virus infections.

Route of administration: topical.

Do not use in eyes.

### 4.2 Posology and method of administration

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

Zovirax Genital 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 5 days. 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

Zovirax Genital is contraindicated in patients known to be hypersensitive to aciclovir, valaciclovir, propylene glycol or any of the excipients of Zovirax Genital listed in section 6.1.

## 4.4 Special warnings and precautions for use

Zovirax Genital 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 (e.g. AIDS patients or bone marrow transplant recipients) oral Zovirax 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).

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

## 4.5 Interactions with other medicinal products and other forms of interaction

No clinically significant interactions have been identified.

## 4.6. Fertility, pregnancy and breast-feeding

*Pregnancy:*
A post-marketing aciclovir pregnancy registry has documented pregnancy outcomes in women exposed to any formulation of Zovirax. 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 Zovirax Genital should be considered only when the potential benefits outweigh the possibility of unknown risks however the systemic exposure to aciclovir from topical application of Zovirax Genital 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 Zovirax Genital 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.

See Clinical Studies in section 5.2

## 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 Zovirax Genital
- 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 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 (http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.health.gov.il).
Additionally, you should also report to GSK Israel (il.safety@gsk.com).

## 4.9 Overdose

No untoward effects would be expected if the entire contents of a 10 gram tube of Zovirax Genital 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, Zovirax Cream 5% was compared to vehicle cream. In these studies, time from start of treatment to healing was 4.6 days using Zovirax Cream and 5.0 days using vehicle cream ($p<0.001$). Duration of pain was 3.0 days after start of treatment in the Zovirax 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 Zovirax Genital.

## 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

Propylene glycol
White soft paraffin
Cetostearyl alcohol
Liquid paraffin
Arlacel 165 (containing glycerol monostearate and macrogol stearate 100)
Poloxamer 407
Dimeticone 20
Sodium laurylsulfate
Purified water

### 6.2 Incompatibilities

None known.

### 6.3 Shelf life

The expiry date of the product is indicated on the label and packaging.
Use within 10 days after opening.

### 6.4 Special precautions for storage

Store below 25ºC. Do not refrigerate.

### 6.5 Nature and contents of container

Aluminium tube with plastic screw cap
Pack size: 10g tube

### 6.6 Special precautions for disposal

No special requirements.

## 7. MANUFACTURER

Glaxo Operations (UK) Limited, Barnard Castle, UK

## 8. LICENSE HOLDER AND IMPORTER

GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva

## 9. LICENSE NUMBER

046-50-23031



*ZovGen Dr v4.1*