1. NAME OF THE MEDICINALPRODUCT

ANNIE ACYCLOVIR OINTMENT (Acyclovir USP..50 mg)

2. QUALITATIVE AND QUANTITATIVECOMPOSITION

Acyclovir USP…..50 mg

3. PHARMACEUTICALFORM

Topical

A white soft and smooth textured ointment.

4. CLINICAL PARTICULARS

4.1 Therapeuticindications

For External Use Only

Annie Acyclovir is an antiviral ointment used to treat infections caused by certain types of viruses. It decreases the severity and length of outbreaks. It can speed up healing of thesores and decrease symptoms (such as tingling, pain, burning, itching). Annie acyclovir ointment is available on prescription for the treatment of cold sores and genital herpes infections.

4.2 Posology and method of administration

Route of administration: topical use.

Adults

Acyclovir ointment should be applied five times daily at approximately four hourly intervals, omitting the night time application.

Acyclovir ointment 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.

Older people

Clinical studies of ZOVIRAX Ointment did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. Systemic absorption of acyclovir after topical administration is minimal.

Paediatric population

Safety and efficacy of Acyclovir ointment in pediatric patients below the age of two years has not been established.

4.3 Contraindications

Acyclovir Ointment 50 mg is contraindicated in patients who develop hypersensitivity to the components of the formulation.

4.4 Special warnings and precautions for use

Annie Acyclovir Ointment 50 mg is intended for cutaneous use only and should not be used inthe eye.

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: The use of acyclovir cream should be considered only when the potential benefits outweigh the possibility of unknown risks. However, the systemic exposure to acyclovir from topical application of acyclovir cream is very low. A post-marketing acyclovir pregnancy registry has documented pregnancy outcomes in women exposed to any formulation of acyclovir. The registry findings have not shown an increase in the number of birth defects amongst acyclovir exposed subjects compared with the general population, and any birth defects showed no uniqueness or consistent pattern to suggest a common cause. Systemic exposure to acyclovir from topical application of acyclovir cream is very low. Systemic administration of acyclovir 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.

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 acyclovir cream would be insignificant.

4.7 Effects on ability to drive and use machines

Not Applicable

4.8 Undesirable effects

Uncommon

- Transient burning or stinging following application of Acyclovir Ointment
- 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 acyclovir.

Very Rare

- Immediate hypersensitivity reactions including angioedema and urticaria.

4.9 Overdose

Overdosage by topical application of ointment is unlikely because of limited transcutaneous absorption

5. PHARMACOLOGICALPROPERTIES

5.1 Pharmacodynamic properties

Antibiotics and chemotherapeutics for dermatological use.

Acyclovir 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. Acyclovir is phosphorylated after entry into herpes infected cells to the active compound acyclovir triphosphate. The first step in this process is dependent on the presence of the HSV-coded thymidine kinase.

5.2 Pharmacokinetic properties

Limited pharmacology studies have shown only minimal systemic absorption of acyclovir following repeated topical administration of acyclovir cream.

5.3 Preclinical safety data

Limited pharmacology studies have shown only minimal systemic absorption of acyclovir following repeated topical administration of acyclovir cream.

6. PHARMACEUTICALPARTICULARS

6.1 List of excipients

Polyethylene Glycol 4000

Polyethylene Glycol 400

Propylene Glycol

6.2 Incompatibilities

Not Applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 30 ºC in a dry place.

Keep all medicines out of the reach of children.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

20 gm lacquered aluminium tube

6.6 Special precautions for disposal <and otherhandling>

Not Applicable

7. <APPLICANT/MANUFACTURER>

Annie Pharma Ltd.

Plot 6 Abimbola Way,

Isolo Industrial Estate,

Isolo, Lagos, Nigeria

Manufacturer:

JAWA INTERNATIONAL LTD.

Jawa House Compound,

Plot 6 Abimbola Way,

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E-mail: contactus@jawasil.com

8. <APPLICANT/MANUFACTURER>

Annie Pharma Ltd.

Plot 6 Abimbola Way,

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JAWA INTERNATIONAL LTD.

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Isolo, Lagos, Nigeria

E-mail: contactus@jawasil.com

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Acyclovir Ointment is indicated in the management of initial genital herpes and in limited non-life-threatening mucocutaneous Herpes simplex virus infections in immunocompromised patients.

4.2 Posology and method of administration

Acyclovir Ointment should be applied five times a day. Use every four hours during the day. Dab the ointment onto the area rather than rubbing it in and continue the use for five days. Wash your hands before and after using Acyclovir Ointment to prevent spreading any infection. Acyclovir Ointment is NOT RECCOMENDED FOR CHILDREN BELOW 12YEARS.

4.3 Contraindications:

Acyclovir Ointment is contraindicated in patients who develop hypersensitivity to the components of the formulation

4.4 Special warnings and precautions for use:

Acyclovir Ointment is intended for cutaneous use only and should not be used in the eye. The recommended dosage, frequency of applications, and length of treatment should not be exceeded (see DOSAGE AND ADMINISTRATION). There are no data to support the use of acyclovir ointment to prevent transmission of infection to other persons or prevent recurrent infections when applied in the absence of signs and symptoms. Acyclovir ointment 5% should not be used for the prevention of recurrent HSV infections. Although clinically significant viral resistance associated with the use of acyclovir ointment has not been observed, this possibility exists.

4.5 Interaction with other medicinal products and other forms of interaction

Clinical experience has identified no interactions resulting from topical or systemic administration of other drugs concomitantly with acyclovir ointment.

4.6 Fertility, Pregnancy and lactation

Pregnancy

Pregnancy Category B. Acyclovir was not teratogenic in the mouse, rabbit, or rat at exposures greatly in excess of human exposure. There are no adequate and well-controlled studies of systemic acyclovir in pregnant women. A prospective epidemiologic registry of acyclovir use during pregnancy was established in 1984 and completed in April 1999. There were 749 pregnancies followed in women exposed to systemic acyclovir during the first trimester of pregnancy resulting in 756 outcomes. The occurrence rate of birth defects approximates that found in the general population. However, the small size of the registry is insufficient to evaluate the risk for less common defects or to permit reliable or definitive conclusions regarding the safety of acyclovir in pregnant women and their developing fetuses. Systemic acyclovir should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Breast-feeding

It is not known whether topically applied acyclovir is excreted in breast milk. Systemic exposure following topical administration is minimal. After oral administration of acyclovir, acyclovir concentrations have been documented in breast milk in 2 women and ranged from 0.6 to 4.1 times the corresponding plasma levels. These concentrations would potentially expose the nursing infant to a dose of acyclovir up to 0.3 mg/kg per day. Nursing mothers who have active herpetic lesions near or on the breast should avoid nursing.

Fertility

There is no information on the effects of acyclovir on human fertility. There were no adverse effects on fertility in animals (see section 5.3).

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

In the controlled clinical trials, mild pain (including transient burning and stinging) was reported by about 30% of patients in both the active and placebo arms; treatment was discontinued in 2 of these patients. Local pruritus occurred in 4% of these patients. In all studies, there was no significant difference between the drug and placebo group in the rate

or type of reported adverse reactions nor were there any differences in abnormal clinical laboratory findings.

Observed During Clinical Practice: Based on clinical practice experience in patients treated with acyclovir ointment 5% in the US, spontaneously reported adverse events are uncommon. Data are insufficient to support an estimate of their incidence or to establish causation. These events may also occur as part of the underlying disease process. Voluntary reports of adverse events that have been received since market introduction include:
General: Edema and/or pain at the application site.
Skin: Pruritus, rash.

4.9 Overdose

Overdosage by topical application of acyclovir ointment is unlikely because of limited transcutaneous absorption (see CLINICAL PHARMACOLOGY).

5. Pharmacological properties

5.1 Pharmacodynamic properties

Mechanism of Antiviral Action:

Acyclovir is a synthetic purine nucleoside analogue with in vitro and in vivo inhibitory activity against herpes simplex virus types 1 (HSV-1), 2 (HSV-2), and varicella-zoster virus (VZV).

The inhibitory activity of acyclovir is highly selective due to its affinity for the enzyme thymidine kinase (TK) encoded by HSV and VZV. This viral enzyme converts acyclovir into acyclovir monophosphate, a nucleotide analogue. The monophosphate is further converted into diphosphate by cellular guanylate kinase and into triphosphate by a number of cellular enzymes. In vitro, acyclovir triphosphate stops replication of herpes viral DNA. This is accomplished in 3 ways: 1) competitive inhibition of viral DNA polymerase, 2) incorporation into and termination of the growing viral DNA chain, and 3) inactivation of the viral DNA polymerase. The greater antiviral activity of acyclovir against HSV compared to VZV is due to its more efficient phosphorylation by the viral TK.

5.2 Pharmacokinetic properties

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5.3 Preclinical safety data

In common with other potent selective β2-agonists, salbutamol has been shown to be teratogenic in mice when given subcutaneously. In a reproductive study, 9.3% of fetuses were found to have cleft palate at 2.5mg/kg dose, 4 times the maximum human oral dose. In rats, treatment at the levels of 0.5, 2.32, 10.75 and 50mg/kg/day orally throughout pregnancy resulted in no significant fetal abnormalities. The only toxic effect was an increase in neonatal mortality at the highest dose level as the result of lack of maternal care. Reproductive studies in the rabbit at doses of 50mg/kg/day orally (i.e. much higher than the normal human dose) have shown fetuses with treatment related changes; these included open eyelids (ablepharia), secondary palate clefts (palatoschisis), changes in ossification of the frontal bones of the cranium (cranioschisis) and limb flexure.

In an oral fertility and general reproductive performance study in rats at doses of 2 and 50 mg/kg/day, with the exception of a reduction in number of weanlings surviving to day 21 post partum at 50 mg/kg/day, there were no adverse effects on fertility, embryofetal development, litter size, birth weight or growth rate.

6. Pharmaceutical particulars

6.1 List of excipients

Polyethylene glycol 4000

Polyethylene glycol 400

Propylene Glycol

6.2 Incompatibilities

None

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store below 30oc. Do not refrigerate.
Keep this medicine out of sight and reach of children

6.5 Nature and contents of container

20 gm lacquered aluminium tubes

7. MARKETING AUTHORISATION HOLDER

ANNIE PHARMACEUTICAL LIMITED
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Isolo Industrial Estate, Isolo,
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Phone: +2347011305714
E- mail; sptanniepharma@gmail.com

8. MANUFACTURED BY:

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Lagos, Nigeria
Phone: +2348073894283. E-mail: contactus@jawasil.com

9. MARKETING AUTHORISATION NUMBER(S)

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10. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

- - - - - -.

11. DATE OF REVISION OF THE TEXT

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1.3.2 Labelling (outer & inner labels)

Enclosed