SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE
Zotrin 5 % (Topical Cream)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each gram topical cream contains 50 mg aciclovir
For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM
Topical cream. Smooth, white cream, with a characteristic odour, free from clumps, clots or foreign particles.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications
Zotrin 5 % is indicated for the treatment of herpes simplex virus infections of the skin, lips or genitalia in the initial and recurrent situation.

4.2. Posology and method of administration
Posology
Adults and Children: Zotrin 5 % should be applied five times daily at approximately four hourly intervals. Zotrin 5 % should be applied to the lesions or impending lesions as soon as possible, preferably during the earliest stages (prodroma or erythema). Treatment can also be started during the later (papule or blister) stages. Treatment should be continued for at least four days for *herpes labialis* and for 5 days for genital herpes. If healing has not occurred then treatment may be continued for up to 10 days.

Method of administration:
Zotrin 5 % is for topical use only.

4.3. Contraindications
Zotrin 5 % is contraindicated in:
- Hypersensitivity to aciclovir, valacyclovir or propylene glycol or to any of the excipients (see section 6.1).

4.4. Special warnings and precautions for use
Immunocompromised patients: The use of Zotrin 5 % in severely immunocompromised patients (e.g. bone marrow transplant recipients or AIDS patients) may not be appropriate. Such patients should be encouraged to consult a healthcare professional concerning the treatment of any infection.

Application to mucous membranes: Zotrin 5 % is not recommended for application to mucous membranes such as the mouth, eye or vagina, as it may be irritant. Particular care should be taken to avoid accidental introduction into the eye.

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

4.5. Interaction with other medicines and other forms of interaction
No clinically significant interactions have been identified. Probenecid increases aciclovir area under the plasma concentration curve as well as mean half-life. Medicine affecting renal physiology could potentially influence the pharmacokinetics of aciclovir.
Dilution: Zotrin 5 % contains a specifically formulated base and should not be diluted or used as a base for the incorporation of other medicines.

Paediatric population: No information is available with regards to interactions of acyclovir with other medicines in paediatrics.

4.6. Fertility, pregnancy and lactation
Pregnancy: Safety in pregnancy has not been established.

Breastfeeding: Safety in lactation has not been established. Limited human data show that aciclovir does pass into breast milk.

Fertility: The effect of Zotrin 5 % on human female fertility has not been established. No clinically significant effect on sperm count, motility or morphology has been identified.

4.7. Effects on ability to drive and use machines
No influence on these activities is foreseen.

4.8. Undesirable effects
a. Summary of the safety profile
The most common adverse reactions at the site of topical application were dry lips, desquamation, dryness of skin, cracked lips, burning skin, pruritus, flakiness of skin, and stinging on skin.

b. Tabulated list of adverse reactions

System Organ Class	Frequency	Undesirable effect
Immune system disorders	*Less frequent*	Immediate hypersensitivity reactions including angioedema.
Skin and subcutaneous tissue disorders	*Less frequent*	Transient burning or stinging following application; mild drying or flaking of the skin; itching erythema; contact dermatitis following application

c. Description of selected adverse reactions
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 medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9. Overdose
No untoward effects would be expected if the entire contents of a 10 g Zotrin 5 % tube containing 500 mg aciclovir were ingested orally.
Aciclovir is dialysable.

5. PHARMACOLOGICAL PROPERTIES
Category and class: A 20.2.8 Antiviral agents

5.1. Pharmacodynamic properties
Aciclovir is an antiviral medicine which is highly active in vitro against Herpes simplex virus (HSV) types I and II.
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.

5.2. Pharmacokinetic properties
Absorption: Percutaneous absorption of aciclovir after topical administration is low.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients
Cetostearyl alcohol, Liquid paraffin, Propylene glycol, Sodium laurilsulfate
Polaxamer 407, White soft paraffin, Purified water.

6.2. Incompatibilities
None known.

6.3. Shelf life
3 years

6.4. Special precautions for storage
Store below 25 °C. Do not refrigerate.

6.5. Nature and contents of container
Packed in an aluminium tube with white screw cap. Each tube contains 10 g topical cream packed in an outer cardboard carton.

6.6. Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product
No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
TRINITY PHARMA (PTY) LTD.
106 16th Road, Building 2, Midrand, 1686, South Africa

8. REGISTRATION NUMBER(S)
Zotrin 5 %: 50/20.2.8/0414

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
16 March 2021

10. DATE OF REVISION OF TEXT
N.A.

TRINITY PHARMA

Tel: 010 594 5610. Email: PV@kahmagroup.co.za

SKEDULERINGSTATUS: S4

1. NAAM VAN DIE GENEESMIDDEL
Zotrin 5 % (Topikale Room)

2. KWALITATIEWE EN KWANTITATIEWE SAMESTELLING
Elke gram topikale room bevat 50 mg asiklovir.
Vir 'n volledige lys van bymiddels, sien afdeling 6.1.

3. DOSEERVORM
Topikale room. 'n Gladde wit room, met 'n kenmerkende reuk, sonder stollings, klonte of vreemde deeltjies.

4. KLINIENSE INLIGTING

4.1. Terapeutiese indikasies
Zotrin 5 % is aangedui vir die behandeling van herpes simplex virale infeksies van die vel, lippe of genitalieë in die aanvanklike en herhalende situasies.

4.2. Posologie en metode van toediening
Posologie
Volwassenes en kinders: Zotrin 5 % moet 5 keer daagliks teen ongeveer vier uurlikse tussenposes aangewend word. Zotrin 5 % moet so spoedig moontlik op die letsel of die dreigende letsels aangewend word, verkieslik gedurende die vroegste stadiums (prodromale of eriteem). Behandeling kan ook begin word gedurende die latere (papule- of blaasvormige) stadiums. Behandeling van *herpes labialis* moet aanhou vir ten minste vier dae en 5 dae vir genitale herpes. Indien genesing nie plaasgevind het nie, kan die behandeling tot en met 10 dae voortgesit word.

Metode van toediening:
Zotrin 5 % is alleenlik vir topikale gebruik.

4.3. Kontraïndikasies
Zotrin 5 % is teenaangedui vir:
- Hipersensitiwiteit vir asiklovir, valasiklovir of propileenglikol of vir enige van die ander hulpmiddels (sien afdeling 6.1).

4.4. Spesiale waarskuwings en voorsorg vir gebruik
Pasiënte met gekomprimeerde immuniteit: Die gebruik van Zotrin 5 % erg gekomprimeerde pasiënte (bv. beenmurgoorplanting ontvangers of VIGS pasiënte) mag nie geskik wees nie. Sulke pasiënte moet aangemoedig word om 'n gesondheidswerker te raadpleeg oor die behandeling van enige infeksie.

Aanwending aan slymvliese: Zotrin 5 % word nie aanbeveel vir die aanwending aan slymvliese soos by die mond, oog of vagina nie, aangesien dit tot irritasie kan lei. Wees versigtig en vermy aanwending per ongeluk in die oog.

Propileenglikol en setostearielalkohol: Die bymiddel propileenglikol kan lokale velirritasies veroorsaak, en die bymiddel setostearielalkohol kan lokale velreaksies (bv. kontakdermatitis) veroorsaak.

4.5. Interaksie met ander geneesmiddels en ander vorme van interaksies
Geen klinies beduidende interaksies is geïdentifiseer nie. Probenesied verhoog die asiklovir area onder die plasma konsentrasie kurwe sowel die gemiddelde half-leeftyd. Geneesmiddels wat die renale fisiologie beïnvloed kan potensieel die farmakokinetika van asiklovir beïnvloed.
Verdunning: Zotrin 5 % bevat 'n spesifiek-geformuleerde basis en moet nie verdun of gebruik word as 'n basis vir die inkorporering van ander medisyne nie.
Pediatriese bevolkingsgroep: Geen inligting is beskikbaar rakende die interaksies van asiklovir met ander geneesmiddels in pediatrie nie.

4.6. Fertiliteit, swangerskap en laktasie
Swangerskap: Die veiligheid vir die gebruik tydens swangerskap is nie vasgestel nie.

Borsvoeding: Die veiligheid vir gebruik tydens laktasie is nie bepaal nie. Beperkte menslike data wys dat asiklovir in borsmelk uitgeskei word.

Fertiliteit: Die effek van Zotrin 5 % op vroulike fertiliteit by die mens is nog nie vasgestel nie. Geen klinies beduidend effekte op spermtelling, beweeglikheid en morfologie is geïdentifiseer nie.

4.7. Effek op die vermoë om te bestuur en masjinerie te gebruik
Geen invloed op hierdie aktiwiteite word voorsien nie.

4.8. Ongewenste effekte
a. Opsomming van die veiligheidsprofiel
Die algemeenste newe effekte by die plek van toediening was droë lippe, afskilfering, droogheid van die vel, gebarste lippe, branderigheid, pruritis, vlokking, en steek-sensasie op die vel.

b. Opsomming van ongewenste effekte in tabelvorm

Orgaanstelsel Klas	Frekwensie	Ongewenste effek
Immuunstelsel afwykings	*Minder gereeld*	Onmiddellike hipersensitiwiteitsreaksie insluitend angio-edeem.
Versteurings van die vel en subkutane weefsel	*Minder gereeld*	Verbygaande branderige of steek sensasie na aanwending; matige droogheid of vlokking, eriteem jeuk, kontakdermatitis na aanwending.

c. Beskrywing van spesifieke nadelige reaksies
Kontakdermatitis na aanwending. Ten tye van sensitiwiteitstoetse, was die reaktiewe substanse meestal bymiddels van die room, eerder as asiklovir.

Rapportering van vermoedelik nadelige reaksies: Dit is belangrik om vermoedelike newe-effekte wat waargeneem word nadat die medisyne goedgekeur is, te rapporteer. Dit laat volgehoue monitering van voordeel/risiko-balans van die medisyne toe. Gesondheidsorgverskaffers word versoek om enige vermoedelike newe-effekte aan SAHPRA te rapporteer via die "**6.04 Adverse Drug Reaction Reporting Form**", aanlyn by SAHPRA se publikasies gevind kan word: https://www.sahpra.org.za/Publications/Index/8

4.9. Oordosering
Geen nadelige effekte word verwag indien die hele inhoud van 'n 10 g Zotrin 5 % buisie wat 500 mg asiklovir bevat, oraal ingeneem word nie.
Asiklovir is dialiseerbaar.

5. FARMAKOLOGIESE EIENSKAPPE
Kategorie en klas: A 20.2.8 Antivirale middels

5.1. Farmakodinamiese eienskappe
Asiklovir is 'n antivirale geneesmiddel wat *in vitro* baie aktief is teen Herpes simplex (HSV) tipes I en II. Asiklovir word gefosforileer nadat dit herpes-geïnfekteerde selle binnegedring het na die aktiewe verbinding asiklovirtrifosfaat. Die eerste stap in hierdie proses is afhanklik van die teenwoordigheid van die HSV-gekodeerde timidienkinase. Asiklovirtrifosfaat dien as remmer, en substraat vir die herpes-gespesifiseerde DNA-polimerase, wat verdere virale DNA sintese verhoed, sonder om normale sellulêre prosesse te beïnvloed.

5.2. Farmakokinetiese eienskappe
Absorpsie
Perkutane absorpsie van asiklovir na topikale toediening is laag.

6. FARMASEUTIESE BESONDERHEDE/INLIGTING

6.1. Lys van bymiddels
Setostearielalkohol, Vloeibare paraffien, Propileenglikol, Natriumlaurielsulfaat, Polaxamer 407, Wit sagteparaffien, Gesuiwerde water.

6.2. Onverenigbaarheid
Geen bekend.

6.3. Rakleeftyd
3 jaar

6.4. Spesiale voorsorgmaatreëls tydens berging
Bewaar teen of benede 25 °C. Moenie in die yskas hou nie.

6.5. Aard en inhoud van die houer
Verpak in 'n aluminium buis met 'n wit skroefdop. Elke buis bevat 10 g topikale room verpak in 'n buitenste karton boksie.

6.6. Spesiale voorsorg vir die wegdoening van 'n gebruikte medisyne of afvalmateriaal van die medisyne en ander hantering
Geen spesiale voorsorgmaatreëls.

7. HOUER VAN DIE REGISTRASIESERTIFIKAAT
TRINITY PHARMA (PTY) LTD.
106 16de Weg, Gebou 2, Midrand, 1686, Suid-Afrika

8. REGISTRASIENOMMER(S)
Zotrin 5 %: 50/20.2.8/0414

9. DATUM VAN DIE EERSTE GOEDKEURING / HERNUWING VAN DIE GOEDKEURING
16 Maart 2021

10. DATUM VAN DIE HERSIENING VAN DIE TEKS
N.A.