SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

VIRLESS (Acyclovir 200 mg tablet)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 200 mg acyclovir.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

4. CLINICAL PARTICULARS

4.1 Therapeutic indication:

a) Infections caused by Varicella-Zoster Virus.

b) Skin and mucous membrane infections due to Herpes Simplex Virus.

c) Prophylaxis of Herpes Simplex infection in patients who are immunocompromised including those with bone marrow transplant and leukemia.

d) Suppression of recurrent Herpes Simplex Virus infections.

4.2 Posology and method of administration:

i) Adult dose:

a) Treatment of Herpes Simplex Infection:

200mg (400mg in the immunocompromised patient) 5 times daily, usually for 5 days.

b) Prevention of recurrent Herpes Simplex Infection:

200mg to be taken 4 times daily, or 400mg twice daily, possibly reduced to 200mg 2 or 3 times daily.

Therapy should be interrupted periodically at interval 6-12 months in order to observe possible changes in the nature history of the disease.

c) Prophylaxis of Herpes Simplex Infection in immunocompromised patients:

200mg to be taken 4 times daily at approximately 6 hours interval. In situation of severe immunocompromised, eg., after bone marrow transplantation, or in patients with impaired gastrointestinal absorption, the dose may be doubled to 400mg.

d) Treatment of Varicella and Herpes Zoster infection:

800mg, 5 times daily for 7 days.

ii) Pediatric Dose:

a) For treatment of *Herpes Simplex Infection* and for *Prophylaxis* of *Herpes Simplex Infection* in immunocompromised, children 2 years and over should be given adult dosage, and children < 2 years should be given half the adult dose.

b) For treatment of *Varicella Infection,*

children > 6 years : 800mg 4 times a day.

2 – 6 years : 400mg 4 times a day.

below 2 years : 200mg 4 times a day

c) Dosing may be calculated as 20mg/kg body weight (not to exceed 800mg), 4 times daily. Treatment should be continued for 5 days.

No specific data are available on the treatment of *Herpes Simplex Infection* in immune-competent children.

iii) Dosage in Elderly

Elderly patients are more likely to have an age-related decreased in renal function, which may required an adjustment of dosage or dosing interval.

iv) Dosage in Renal Impairment

For patient with renal impairment (creatinine clearance < 10ml/min), the dosage should be decreased to 200mg every 12 hours for treatment of *Herpes Simplex Infection*, and 800mg twice daily for treatment of *Varicella* and *Zoster Infection.*

Method of administration: Oral

4.3 Contraindication:

Contraindicated in patients who develop hypersensitivity or intolerance to any of the components of the formulation.

4.4 Special warnings and special precautions for use:

Acyclovir should be administered with caution to patients with renal impairment and doses should be adjusted according to creatinine clearance. The risk of renal impairment is increased by dehydration and by the concomitant use of other nephrotoxic drugs.

4.5 Interaction with other FPPs and other forms of interaction:

Probenecid is reported to block the renal clearance of Acyclovir.

4.6 Pregnancy and lactation:

Acyclovir crosses placenta, caution should be exercised by balancing the potential benefits of treatment against any possible hazard. Acyclovir passes into breast milk at concentration from 0.2 - 4.1 times the corresponding plasma levels. Therefore, caution is advised if it is to be administered to a nursing woman.

4.7 Effects on ability to drive and use machines:

No information available.

4.8 Undesirable effects:

a) Skin rashes, only a few cases reported. The rashes have resolved on withdrawal of drug.
b) Gastrointestinal effect: nausea, vomiting, abdominal pains.
c) Neurological: occasionally dizziness and hallucination, somnolence.
d) Rises in bilirubin and liver-related enzyme.
e) Increase in blood urea and creatinine.
f) Decrease in haematological indices.

4.9 Overdose:

Since there is no specific antidote, treatment of adverse effects and/or overdose should be symptomatic and supportive with possible utilization of the following:

- Adequate hydration to prevention precipitation of Acyclovir in the renal tubules.

- Hemodialysis to aid in the removal of Acyclovir from the blood, especially in patients with acute renal failure and anuria.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties:

a) Acyclovir is a synthetic purine nucleoside analogue with *in vitro* and *in vivo* inhibitory activity against human herpes viruses including Herpes Simplex Types 1 (HSV–1) and 2 (HSV–2), Varicella-Zoster Virus (VZV), Epstein-Barr virus (EBV), and Cytomegalovirus (CMV). In cell culture, Acyclovir has the highest antiviral activity against HSV-1, followed in decreasing order of potency against HSV-2, VZV. EBV and CMV.

b) Acyclovir is preferentially taken up and selectively converted to the active triphosphate form by Herpes Virus- infected cells. Thus, Acyclovir is much less toxic *in vitro* for normal unaffected cells because: (1) less is taken up; (2) less in converted to the active form; (3) cellular α- DNA polymerase is less sensitive to the effects of the active form.

5.2 Pharmacokinetic properties:

a) Acyclovir is slowly and poorly absorbed from the gastrointestinal tract and the time to reach peak concentration is 1.5 to 2 hours. With multiple administration, steady-state plasma concentrations are achieved by the second day. The estimated bioavailability is 13-21% and appears to decrease with decreasing dosage. Following oral administration in adult patients with normal renal function the plasma half-life is 3.3 hours.

b) It is widely distributed in tissue and body fluids including brain, kidney, lung, liver, muscle, spleen, uterus, vaginal mucosa, vaginal secretions, cerebrospinal fluid and herpetic vesicular fluid. Concentration in kidney and lung were 10-13 times plasma concentrations after multiple dose therapy and 25-75% of the plasma level was found in brain, spinal cord and cerebrospinal fluid. Limited human data shows that Acyclovir passes into breast milk and levels can be 3-4 times higher than in serum.

c) Renal excretion is the major route of elimination in individuals with normal renal function. The renal clearance for Acyclovir, which is approximately three-fold

greater than the creatinine clearance, indicates that the drug removed by tubular secretion as well as glomerular filtration. Acyclovir persist in the plasma of patients with renal insufficiency and the mean terminal plasma half-life recorded in patients with end stage renal disease is 19.5 hours. Acyclovir is readily removed by hemodialysis. As renal function decreases, a greater percentage of the drug is eliminated by metabolic conversion to carboxymethoxymethyl guanine.

5.3 Preclinical safety data:

No information available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients:

Potato Starch
Microcrystalline Cellulose
Sodium Starch Glycolate
Food Color Blue No. 1
Magnesium Stearate

6.2 Incompabilities:

No information available.

6.3 Shelf life:

3 years.

6.4 Special precautions for storage:

Keep in a container. Store at temperature below 30°C. Protect from light and moisture.

6.5 Nature and contents of container:

Strip Pack of 10’s x 5

6.6 Instructions for use and handling <and disposal>:

None has been mentioned.

7. MARKETING AUTHORIZATION HOLDER

Y. S. P. INDUSTRIES (M) SDN. BHD.
Lot 3, 5 & 7, Jalan P/7, Section 13,
Kawasan Perindustrian Bandar Baru Bangi,
43000 Kajang, Selangor Darul Ehsan,
Malaysia.

8. MARKETING AUTHORIZATION NUMBER

YSP / MAA / 005

9. DATE OF ~~FIRST AUTHORIZATION /~~ RENEWAL OF THE AUTHORIZATION

07 Dec 2020

10. DATE OF REVISION OF THE TEXT

28 Jul 2023