נובמבר 2021

רופא/ה נכבד/ה
רוקח/ת נכבד/ה,

הנדון:

Zovirax suspension זובירקס תרחיף

Aciclovir 200 mg / 5 mL

חברת גלקסוסמיתקליין ישראל בע"מ (GSK) מבקשת להודיע על עדכון העלון לרופא של התכשיר שבנדון.

בהודעה זו כלולים העדכונים המהותיים בלבד. קיימים עדכונים נוספים.

תוספת מידע מסומנת בקו תחתון, מחיקת מידע מסומנת ~~בקו חוצה~~.

ההתוויות הרשומות לתכשיר:

Zovirax suspension is indicated for the treatment of herpes simplex virus infections of the skin and mucous membranes including initial and recurrent genital herpes (excluding neonatal HSV and severe HSV infections in immunocompromised children).
Zovirax suspension is indicated for the suppression (prevention of recurrences) of recurrent herpes simplex infections in immune-competent patients.
Zovirax suspension is indicated for the prophylaxis of herpes simplex infections in immune-compromised patients.
Zovirax suspension is indicated for the treatment of varicella (chickenpox) and herpes zoster (shingles) infections.

העדכונים בעלון לרופא

5 PHARMACOLOGICAL PROPERTIES

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5.2 Pharmacokinetic properties

Absorption
Aciclovir is only partially absorbed from the gut. The average oral bioavailability varies between 10 and 20%. Under fasting conditions, mean peak concentrations (Cmax) of 0.4 microgram/ml are achieved at approximately 1.6 hours after a 200 mg dose administered as oral suspension or capsule. Mean peak plasma concentrations (Cssmax) increase to 0.7 microgram/ml (3.1 micromoles) at steady state following doses of 200 mg administered every four hours. A less than proportional increase is observed for Cssmax concentrations following doses of 400 mg and 800 mg administered four-hourly, with values reaching 1.2 and 1.8 microgram/ml (5.3 and 8 micromoles), respectively.

~~Aciclovir is only partially absorbed from the gut. Mean steady state peak plasma concentrations (CSSmax) following doses of 200mg aciclovir administered four-hourly were 3.1 microMol (0.7 microgram/ml) and the equivalent trough plasma levels (CSSmin) were 1.8 microMol (0.4 microgram/ml). Corresponding steady-state~~

plasma concentrations following doses of 400mg and 800mg aciclovir administered four-hourly were 5.3 microMol (1.2 microgram/ml) and 8 microMol (1.8 microgram/ml) respectively, and equivalent trough plasma levels were 2.7 microMol (0.6 microgram/ml) and 4 microMol (0.9 microgram/ml).

Distribution

In adults the terminal plasma half-life after administration of intravenous aciclovir is about 2.9 hours. Most of the drug is excreted unchanged by the kidney. Renal clearance of aciclovir is substantially greater than creatinine clearance, indicating that tubular secretion, in addition to glomerular filtration, contributes to the renal elimination of the drug.

The mean volume of distribution of 26 L indicates that aciclovir is distributed within total body water. Apparent values after oral administration (Vd/F) ranged from 2.3 to 17.8 L/kg. As plasma protein binding is relatively low (9 to 33%), drug interactions involving binding site displacement are not anticipated. Cerebrospinal fluid concentrations are approximately 50% of corresponding plasma concentrations at steady-state.

9-carboxymethoxymethylguanine is the only significant metabolite of aciclovir, and accounts for 10-15% of the dose excreted in the urine. When aciclovir is given one hour after 1 gram of probenecid the terminal half-life and the area under the plasma concentration time curve is extended by 18% and 40% respectively.

Metobolism

In adults, mean steady state peak plasma concentrations (CSSmax) following a one hour infusion of 2.5mg/kg, 5mg/kg and 10mg/kg were 22.7 microMol (5.1 microgram/ml), 43.6 microMol (9.8 microgram/ml) and 92 microMol (20.7 microgram/ml), respectively. The corresponding trough levels (CSSmin) 7 hours later were 2.2 microMol (0.5 microgram/ml), 3.1 microMol (0.7 microgram/ml) and 10.2 microMol (2.3 microgram/ml), respectively.

Aciclovir is predominantly excreted unchanged by the kidney. The only known urinary metabolite is 9-[(carboxymethoxy) methyl]guanine, and accounts for 10-15% of the dose excreted in the urine.

Elimination

In adults mean systemic exposure (AUC0-∞) to aciclovir ranges between 1.9 and 2.2 microgram*h/mL after a 200 mg dose. At this dose, the mean terminal plasma half-life after oral administration has been shown to vary between 2.8 and 4.1 hours.

Renal clearance of aciclovir (CLr= 14.3 L/h) is substantially greater than creatinine clearance, indicating that tubular secretion, in addition to glomerular filtration, contributes to the renal elimination of the drug. The half-life and total clearance of aciclovir are dependent on renal function. Therefore, dosage adjustment is recommended for renally impaired patients.

In children over 1 year of age similar mean peak (CSSmax) and trough (CSSmin) levels were observed when a dose of 250mg/m2 was substituted for 5mg/kg and a dose of 500mg/m2 was substituted for 10mg/kg. In neonates (0 to 3 months of age) treated with doses of 10mg/kg administered by infusion over a one-hour period every 8 hours the CSSmax was found to be 61.2 microMol (13.8 microgram/ml) and CSSmin to be 10.1 microMol (2.3 microgram/ml). The terminal plasma half-life in

~~these patients was 3.8 hours. A separate group of neonates treated with 15 mg/kg every 8 hours showed approximate dose proportional increases, with a Cmax of 83.5 micromolar (18.8 microgram/ml) and Cmin of 14.1 micromolar (3.2 microgram/ml).~~

There is no pharmacokinetic data for oral formulation in neonates. Only pharmacokinetic data available is for the IV formulation in this age group.

Special Patient Populations
Elderly

In the elderly patients with normal renal function total clearance falls with increasing age due to decreases in creatinine clearance. However, the possibility of renal impairment in the elderly must be considered and the dosage should be adjusted accordingly.

~~In the elderly total body clearance falls with increasing age associated with decreases in creatinine clearance although there is little change in the terminal plasma half-life.~~

Renal impairment

In patients with chronic renal failure the mean terminal half-life was found to be 19.5 hours. The mean aciclovir half-life during haemodialysis was 5.7 hours. Plasma aciclovir ~~levels~~ concentrations dropped approximately 60% during dialysis.

~~Cerebrospinal fluid levels are approximately 50% of corresponding plasma levels. Plasma protein binding is relatively low (9 to 33%) and drug interactions involving binding site displacement are not anticipated.~~

העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות:
https://israeldrugs.health.gov.il/#!/byDrug
וניתן לקבל מודפס על-ידי פניה לחברת גלקסוסמיתקליין רח' בזל 25 פתח תקוה בטלפון: 03-9297100.

בברכה,

שני לוי
רוקחת ממונה