

# Valacyclovir

**Class:**

Valacyclovir is a prodrug of acyclovir.

**Antiviral Activity:**

Valacyclovir has activity against herpesviruses.

**Mechanism of Action:**

Valacyclovir is converted to acyclovir, which is converted to its triphosphate form, acyclovir triphosphate (ACV-TP). ACV-TP competitively inhibits viral DNA polymerase, incorporates into and terminates the growing viral DNA chain, and inactivates of the viral DNA polymerase.

**Mechanism of Resistance:**

The primary mechanism of resistance to valacyclovir is related to viral thymidine kinase and DNA polymerase mutations.

**Pharmacodynamics:**

No relationship has been established between the effective *in vitro* and *in vivo* concentrations of valacyclovir.

**Pharmacokinetics:**

Valacyclovir is well absorbed via intestinal brush border membranes and undergoes rapid and extensive first-pass intestinal/hepatic metabolism by the enzyme valacyclovir hydrolase to acyclovir and L-valine.

Table 2

**Adverse Effects:**

Adverse effects include nausea, headache, vomiting, dizziness and abdominal pain.

**Dosage:**

Oral: 500mg and 1g caplet

HSV infections of skin and mucous membranes including initial and recurrent genital herpes

Adult: Initial genital: 1 g po bid for 7 – 10 days

Recurrent genital: 500 mg bid for 3 – 5 days or 1 g po qd x 5 days

Pediatric: Safety and efficacy in pre-pubertal pediatric patients not established.

Episodic HSV treatment in HIV-infected patients

Adult: 1 g po bid x 5 – 10 days

Pediatric: No data

Suppression of recurrent HSV in immunocompetent patients

Adult: 1 g qd or

500 mg qd if = 9 recurrences per year

Pediatric: No data

Prophylaxis of HSV in immunocompromised patients

Adult: 500 mg bid

Pediatric: No data

Herpes labialis (cold sores)

Adult: 2 g bid for 1 day taken 12 hours apart (initiate at earliest symptom of cold sore i.e. tingling, itching, burning)

Recurrent orolabial infection in HIV-infected patients: 500 mg bid

Pediatric: No data

VZV infections including varicella (chicken pox) and herpes zoster (shingles)

Adult: 1 g po q8h x 7 days

Pediatric: No data

Disease state based dosing:

Renal Impairment: Herpes Zoster: CrCl 30 to 49ml/min give 1000mg PO q12h

CrCl 10 to 29ml/min give 1000mg PO q24h

CrCl <10ml/min give 500mg PO q24h

Genital herpes: CrCl 10 to 29ml/min give 1000mg PO q24h

CrCl <10ml/min give 500mg PO q24h

Suppressive therapy: CrCl <29ml/min give 500mg PO q24h

Cold sores: CrCl 30 to 49ml/min give 1000mg PO q12h x 2 doses

CrCl 10 to 29ml/min give 500mg PO q12h x 2 doses

CrCl <10ml/min give 500mg PO x 1 dose

Hepatic Impairment: No dosage adjustment necessary in hepatic insufficiency

**Contraindications/Warnings/ Precautions:**

Thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS), in some cases resulting in death, has occurred in patients with advanced HIV disease and also in allogeneic bone marrow transplant and renal transplant recipients participating in clinical trials of valacyclovir at doses of 8 grams per day.

**Drug Interactions:**

Use caution when combining valacyclovir with potentially nephrotoxic agents.

**Pregnancy:**

Category B: No evidence of risk in humans but studies inadequate.

**Monitoring Requirements:**

Baseline serum creatinine/BUN

**Brand names/Manufacturer:**

Valtrex®/Glaxo Smithkline