ValgaMax™ 450

Valganciclovir Hydrochloride 450 mg Tablets

Maximize Viral Protection

Product Description:

ValgaMax 450: Each film coated tablet contains Valganciclovir hydrochloride tablet U.S.P. 450 mg

General Information

Valganciclovir is an antiviral agent,that is used for the prevention of Cytomegalovirus infections in organ transplant recipients & to treat cytomegalovirusretinitis in patients with AIDS.

As the L-valyl ester of ganciclovir, it is actually a prodrug for ganciclovir. After oral administration, it is rapidly converted to ganciclovir by intestinal and hepatic esterases.

Indication & Usage

Valganciclovir is an antiviral medication used for the treatment of cytomegalovirus infections.

Dosage and Administration

CMV prevention in Solid Organ Transplant

Indicated for the prevention of CMV disease in kidney, heart, and kidney-pancreas transplant patients

Kidney transplantation

- 900 mg per day
- Begin within 10 days of transplant until 200 days post-transplant

Kidney-pancreas transplantation

- 900 mg per day
- Begin within 10 days of transplant until 100 days post-transplant

Heart transplantation

- 900 mg per day

- Begin within 10 days of transplant until 100 days post-transplant

Valganciclovir dose for adult and adolescent patients greater than 16 years of age in renal compromised patients		
CreatinineClearance (mL/min)	**Valganciclovir dosage in Treatment of CMV Infection**	**Valganciclovir dosage in prevention of CMV Infection**
Greater and equal to 60	900 mg twice a day	900 mg daily
40 to 59	450 mg twice a day	450 mgdaily
25 to 39	450 mg daily	450 mg every 2 days
10 to 24	450 mg every 2 days	450 mgtwice weekly

Mechanism of action

Valganciclovir is an L-valyl ester (prodrug) of ganciclovir that exists as a mixture of two diastereomers. After oral administration, both diastereomers are rapidly converted to ganciclovir by intestinal and hepatic esterases. Ganciclovir is a synthetic analogue of 2'-deoxyguanosine, which inhibits replication of human cytomegalovirus.

In CMV-infected cells ganciclovir is initially phosphorylated to ganciclovir monophosphate by theviral protein kinase then phosphorylation occurs by cellular kinases to produceganciclovir triphosphate, which is then slowly metabolized intracellularly (half-life 18 hours). Asthe phosphorylation is largely dependent on the viral kinase, phosphorylation of ganciclovir occurspreferentially in virus-infected cells. The virustatic activity of ganciclovir is due to inhibition ofviral DNA synthesis by ganciclovir triphosphate.

Ganciclovir triphosphate is incorporated into the DNA strand replacing many of the adenosine bases. This results in the prevention of DNA synthesis, as phosphodiester bridges can longer to be built, destabilizing the strand. Ganciclovir inhibits viral DNA polymerases more effectively than it does cellular polymerase, and chain elongation resumes when ganciclovir is removed.

Pharmacokinetic

Absorption:

Following oral administration, valganciclovir is rapidly hydrolyzed to ganciclovir by esterases in the intestinal and hepatic cells. After administration of valganciclovir, ganciclovir bioavailability was 60% when taken with food. When taken with food steady state ganciclovir AUC increased by 30% and the Cmax increased by 14%, without any change in the time to peak plasma concentrations (Tmax).

Distribution:

Due to the rapid conversion of valganciclovir to ganciclovir, plasma protein binding of valganciclovir was not determined. Plasma protein binding of ganciclovir is 1% to 2% over concentrations of 0.5 and 51 µg/ml. When ganciclovir was administered intravenously, the steady state volume of distribution of ganciclovir was 0.703 ± 0.134 l/kg

Metabolism:

Valganciclovir is rapidly hydrolyzed to ganciclovir; no other metabolites have been detected. No metabolite of orally-administered radiolabelled ganciclovir (1000 mg single dose) accounted for more than 1% to 2% of the radioactivity recovered in the feces or urine.

Excretion:

The major route of elimination of valganciclovir is by renal excretion as ganciclovir through glomerular filtration and active tubular secretion. The renal clearance of ganciclovir was 2.99± 0.67 mL/min/kg

Use in Specific Population

Pregnancy: Ganciclovir causes birth defects and should not be used during pregnancy

Nursing Mother: Because of the potential for serious adverse events in nursing infants, mothers should be instructed not to breastfeed if they are receiving Valganciclovir tablets.

Pediatric Use: Valganciclovir tablets have not been studied in pediatric patients; the pharmacokinetic characteristics of valganciclovir in these patients have not been established.

Geriatic Use: No studies of valganciclovir tablets have been conducted in adults older than 65 years of age.

Contraindication:Valganciclovir tablets are contraindicated in patients with hypersensitivity to valganciclovir or ganciclovir.

Warning & Precaution:

Hematologic:
Valganciclovir should not be administered if the absolute neutrophil count is less than 500 cells/μL, the platelet count is less than 25,000/μL, or the haemoglobin is less than 8 g/dL.
Severe leukopenia, neutropenia, anaemia, thrombocytopenia, pancytopenia, bone marrow depression and aplastic anaemia have been observed in patients treated with valganciclovir.

Impairment of Fertility: It is consideredprobable that in humans, valganciclovir at the recommended doses may cause temporary orpermanent inhibition of spermatogenesis.

Teratogenesis, Carcinogenesis and Mutagenesis:
Because of the mutagenic and teratogenic potential of ganciclovir, women of childbearing potential should be advised to use effective contraception during treatment. Similarly, men should be advised to practice barrier contraception during, and for at least 90 days following, treatment with Valganciclovir

Drug Interaction:

Valganciclovir is a prodrug of ganciclovir, which is rapidly converted to ganciclovir after oral administration. The drug interaction associated with ganciclovir use can therefore be expected to occur with valganciclovir.

- Probenicid and other medications secreted by renal organic anion transport system are likely to reduce ganciclovir clearance, causing ganciclovir accumulation, increasing the risk of ganciclovir toxicity.
- Co-administration with other myelosuppressive agents (mycophenolic acids, azathioprine) increases the risk of toxicity.

- Seizures have been reported in patients taking ganciclovir and imipenem-cilastain concomitantly. This combination should be avoided.

Adverse Reactions:

Most common valganciclovir adverse drug reaction

Area of Effect	Adverse Effect
Gastrointestinal	Diarrhoea, nausea,vomiting, abdominal pain, oral candidiasis
Hematologic	Neutropenia, anemia, thrombocytopenia
Body	Fever, headache, fatigue
CNS	Insomnia,paresthesia, peripheral,neuropathy, dizziness
Eye	Retinal detachment
Other	Sinusitis