Acyclovir

Product Availability

Solid	• Tablet: 400 mg, 800 mg (Zovirax® [Mylan]; others) • Capsule: 200 mg (Zovirax® [Mylan]; others)
Liquid	• Oral suspension: 200 mg/5 mL (Zovirax® [Mylan]; others)

Physicochemical (drug)

Molecular weight: • 225.21	**Permeability**: • LogP –1.56 • LogD –1.76 (pH 7.4)	**Water solubility**: • Base 2.5 mg/mL (37°C) • Na-salt 100 mg/mL
pKa: • 2.27, 9.25	**Classification**: • BCS Class 3 or 4; BDDCS Class 4	

Pharmaceutical (product)

Solid	• Tablets disperse in water (20 mL) within 2 minutes
Liquid	• Suspension: ○ pH 6.2 ○ Osmolality: 874 mOsm/kg (measured 1:4 dilution with sterile water); 4205 mOsm/kg (calculated based on measurement of 1:5 dilution with sterile water)[1] ○ Viscosity 282 mPa·s ○ May contain glycerin and sorbitol ○ Maintain at controlled room temperature (do not refrigerate).
Note	• Capsules and oral suspension are considered bioequivalent.

Pharmacokinetic (patient)

Absorption	• Specific site not known; t_{max} within 2 hours after oral dose • Bioavailability ~10%–30% (variable, incomplete).
Transport	• Substrate for MATE1 efflux; OAT1 and OCT1 uptake • Plasma protein binding ~9%–33% • V_d ~0.69 L/kg
Metabolism	• Minimal hepatic metabolism to 9-CMMG and 8-hydroxy-acyclovir • Most is eliminated unchanged in urine. • Cl ~327 mL/min/1.73 m^2

Enteral Administration and Nutrition Considerations

Compatibility, Stability, and Bioavailability Considerations

- Tablet contents are absorbed when administered into duodenum.[2]
- Specific excipients (sodium lauryl sulfate and/or sodium caprate) can act as permeability enhancers for acyclovir, when included.[3]
- Acyclovir is unstable (HPLC analysis) in sucrose/maltitol or fructose/glucose solutions.[4]

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- Commercial suspension combined (1:1) with Osmolite 1.2, under simulated clinical conditions, would result in clogging an 8 Fr, but not a 20 Fr, feeding tube.[1]
- Solid dispersions of acyclovir with multiple hydrophilic carriers resulted in enhanced dissolution and permeability.[5]
- Several amino acid ester prodrugs of acyclovir (eg, valine → valacyclovir) improve bioavailability by enhancing transport.[6]

Drug-Nutrition Interactions

- Drug may influence nutrition status directly or indirectly:
  - CNS: headache, encephalopathy, confusion, ataxia, paresthesia
  - GI: nausea, vomiting, diarrhea, elevated LFTs
  - Metabolic: hemolysis, anemia, transient elevation of BUN
  - Other: peripheral edema, myalgia
- Influence of malnutrition or obesity on drug disposition:
  - The body weight–normalized volume of distribution (L/kg) is much smaller in obesity and suggests that the drug is best dosed based on a lean body weight.[7]
- No known influence of food on oral absorption or bioavailability.

Recommendations

Gastric	• Disperse tablet in water (20 mL) prior to administration. • Avoid using the suspension for enteral access device administration. • No need to hold EN beyond the time required to flush-administer-flush.
Postpyloric	• As above. • Monitor for any unexpected change in effect.
Other	• As with all antimicrobials, consider parenteral alternative for acutely ill patients to ensure therapeutic concentrations.

References

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