HERPES SIMPLEX VIRUS (HSV) VARICELLA ZOSTER VIRUS (VZV) INFECTIONS

Acyclovir

Feature	Details
Class	Nucleoside analog (Guanosine analog)
Mechanism	Requires 3 phosphorylation steps (1st by viral thymidine kinase) → active form → Inhibits viral DNA polymerase → DNA chain termination
Spectrum	HSV-1, HSV-2, VZV (more potent against HSV)
Pharmacokinetics	Oral bioavailability: low (15–20%) - Available IV & topical - Half-life: 2.5–3 hours - Renal excretion
Clinical Uses	Herpes labialis (limited effect) - Genital herpes - Varicella (chickenpox)
Adverse Effects	Oral: nausea, vomiting, headache - Topical: local irritation - IV: nephrotoxicity (especially if dehydrated)
Resistance	↓ thymidine kinase - Mutated DNA polymerase
Notes	Requires frequent dosing (short half-life) - Selectively activated in infected cells

Valacyclovir

Feature	Details
Class	Prodrug of acyclovir
Mechanism	Converted to acyclovir after absorption
Key Advantage	Higher bioavailability (3–5x than acyclovir)
Clinical Uses	Genital herpes (first & recurrent) - Suppression of recurrent herpes - Orolabial herpes - Varicella & herpes zoster
Dosing Advantage	Less frequent dosing → better compliance
Special Note	Reduces transmission of genital herpes

Foscarnet

Feature	Details
Class	Non-nucleoside antiviral (pyrophosphate analog)
Mechanism	Directly inhibits viral DNA & RNA polymerase (no activation needed)
Spectrum	CMV, HSV, HIV
Clinical Uses	CMV retinitis (especially in immunocompromised) - Acyclovir-resistant HSV
Pharmacokinetics	Poor oral absorption → IV only - Deposits in bone - Renal excretion
Adverse Effects	Nephrotoxicity (most common) - Electrolyte imbalance (↓Ca, ↓Mg, ↓K) - Seizures, arrhythmias
Notes	Does NOT require phosphorylation (Works against TK-deficient strains)

Vidarabine

Feature	Details
Class	Nucleoside analog
Mechanism	Inhibits viral DNA polymerase + causes chain termination
Spectrum	HSV, VZV, Vaccinia
Clinical Uses	Topical treatment of severe HSV - Keratitis, keratoconjunctivitis - Previously used for HSV encephalitis
Notes	Use is now limited (mostly replaced by acyclovir due to safety/efficacy)

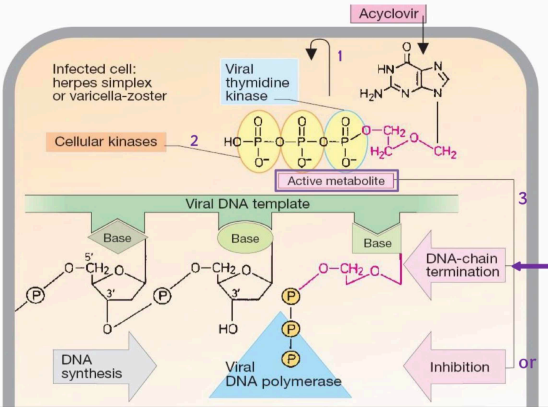
Ganciclovir

Feature	Details
Drug class	Nucleoside analog
Mechanism of Action	Same as acyclovir (requires phosphorylation → inhibits DNA polymerase → chain termination)
Spectrum	All herpes viruses (Very potent vs CMV)
Clinical Uses	Drug of choice for CMV infections (retinitis, pneumonia, colitis)
Pharmacokinetics	Low oral bioavailability → IV mainly - Gel available for keratitis
Adverse Effects	Bone marrow suppression (leukopenia, thrombocytopenia) - CNS effects (headache, seizures, coma)
Serious Risks	Teratogenic - Mutagenic - Carcinogenic
Important Note	⚠️ Black Box Warning

Famciclovir[1]	Oral	First episode genital herpes treatment
		Recurrent genital herpes treatment
		Genital herpes in the HIV-infected host treatment
		Genital herpes suppression
		Genital herpes suppression in the HIV-infected host
		Orolabial herpes treatment
		Orolabial or genital herpes suppression
		Zoster
Valacyclovir[1]	Oral	First episode genital herpes treatment
		Recurrent genital herpes treatment
		Genital herpes in the HIV-infected host treatment
		Genital herpes suppression
		Genital herpes suppression in the HIV-infected host
		Orolabial herpes
		Varicella (age ≥ 12 years)
		Zoster
Foscarnet[1]	Intravenous	Acyclovir-resistant HSV and VZV infections
Docosanol	Topical (10% cream)	Recurrent herpes labialis
Penciclovir	Topical (1% cream)	Herpes labialis or herpes genitalis
Trifluridine	Topical (1% solution)	Acyclovir-resistant HSV infection

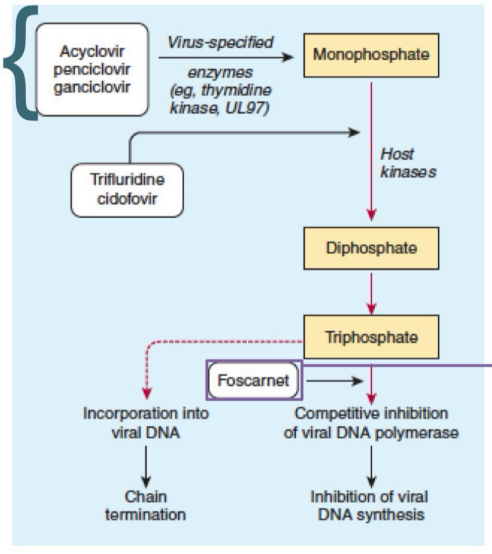
	Route of Administration	Use
Acyclovir[1]	Oral	* First episode genital herpes treatment
		* Recurrent genital herpes treatment
		* Genital herpes in the HIV-infected host treatment
	can lead to	* Genital herpes suppression in the HIV-infected host
		* Herpes proctitis treatment
		* Orolabial herpes treatment
		* Varicella treatment (age ≥ 2 years)
		* Zoster treatment
	Intravenous	* Severe HSV treatment
		* Mucocutaneous herpes in the immunocompromised host treatment
		* Herpes encephalitis treatment
		* Neonatal HSV infection treatment
		* Varicella or zoster in the immunosuppressed host treatment
	Topical (5% cream)	* Herpes labialis treatment

Acyclovir activation & action



Incorporating in the elongation of DNA chain leading to:

All are nucleoside analogs



- Foscarnet:
  - Unlike Acyclovir and Valacyclovir (which are nucleoside analogs) Foscarnet is a **non- nucleoside antiviral.**
  - It directly inhibits the viral DNA, it causes competitive inhibition of viral DNA polymerase (the enzyme responsible for DNA synthesis of the virus).
  - It does so by interfering with the enzyme function preventing the addition of new nucleosides to the growing DNA chain.