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Systemic antiviral agents

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Name	Mechanism of action	Indication	Comments
Acyclovir	Phosphorylated by viral thymidine kinase to acyclovir monophosphate, which blocks viral DNA polymerase → stops viral DNA synthesis	Herpes simplex virus (HSV) Varicella – zoster virus (VZV)	Side effects: IV infusion is associated with reversible obstructive nephropathy, seizures (rare) Resistance noted when there is mutated viral thymidine kinase
Valacyclovir	Prodrug of acyclovir Viral thymidine kinase dependent activity, blocks viral DNA polymerase and blocks DNA synthesis	HSV, VZV Cytomegalvirus (CMV)	Better bioavailability than acyclovir Side effects: TTP/HUS seen in advanced HIV and transplant patients taking high doses for CMV
Penciclovir	Phosphorylated by viral thymidine kinase	HSV, VZV	Low bioavailability Used in topical form
Famciclovir	Phosphorylated by viral thymidine kinase. Prodrug of penciclovir	HSV, VZV Used for VZV in immunocompetent patients and recurrent HSV genital infections	Better bioavailability than acyclovir Side effects: pruritus, paresthesias, headache, fatigue, GI upset
Ganciclovir	Phosphorylated by viral thymidine kinase (similar mechanism to acyclovir)	CMV (retinitis) in	Better activity against CMV; administered intravenous (IV) or oral (PO), but PO has lower bioavailability Side effects: neutropenia, bone marrow suppression, mucositis, thrombocytopenia, nephrotoxicity; worsened by concomitant administration of Zidovudine (AZT)
Foscarnet	Inhibits viral DNA polymerase at the pyrophosphate binding site Does not require phosphorylation for antiviral activity	CMV retinitis in AIDS patients HSV, VZV resistant to acyclovir Ganciclovir resistant CMV	Only IV form; active against infections resistant to acyclovir, famciclovir, ganciclovir Side effect: Penile erosions are known to occur when using foscarnet
Cidofovir	Nucleotide analog Does not require phosphorylation for antiviral activity	CMV resistant to ganciclovir and foscarnet	IV use only. Used in CMV retinitis in AIDS patients who have failed ganciclovir, foscarnet Side effects: iritis, nephrotoxicity, gastrointestinal disturbances

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ANTIRETROVIRAL AGENTS

Name	Mechanism of action	Important side effects
NUCLEOSIDE/NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS		
Zidovudine (AZT)	Inhibits HIV reverse transcriptase	Melanonychia, bone marrow suppression, lipodystrophy
Didanosine (ddI)	Inhibits HIV reverse transcriptase	Pancreatitis, optic neuritis, peripheral neuropathy.
Abacavir (ABC)	Inhibits transcriptase inhibitor	Abacavir hypersensitivity reaction (AHR); fatal on rechallenge Pretreatment screening for HLAB57-01 to reduce risk of AHR
Tenofovir	Inhibits reverse transcriptase	Cushingoid appearance
PROTEASE INHIBITORS		
Indinavir, Ritonavir, Lopinavir	Blocks enzymes responsible for assembly of viral proteins	Lipodystrophy, periungual pyogenic granulomas

References:

1. Wolverson, S. *Comprehensive Dermatologic Drug Therapy*. Saunders Elsevier; 2013.
2. Bologna J, Jorizzo J, Schaffer I. *Dermatology*. Philadelphia: Elsevier; 2017