Valacyclovir Therapeutic Cheat Sheet

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TRADE NAME

- Valtrex

MECHANISM OF ACTION

- Valacyclovir is the prodrug L-valyl ester of acyclovir, a purine nucleoside analogue with activity against human herpesvirus. Once ingested, valacyclovir is rapidly converted in vivo to acyclovir by plasma and hepatic esterase.[1] Acyclovir is further converted to acyclovir triphosphate, a nucleotide analogue, by viral thymidine kinase and other cellular enzymes. Acyclovir triphosphate competitively inhibits viral DNA polymerase by incorporating itself into the growing DNA chain, leading to its termination. The bioavailability of acyclovir is 3-5-fold higher when given as valacyclovir than when given as acyclovir.

FDA INDICATIONS

ADULTS:[2]
- Herpes labialis/orofacial herpes
- Genital herpes
  - Treatment for recurrent or initial or episode in immunocompetent individuals
  - Suppression in immunocompetent or HIV-infected individuals
  - Reduction of transmission
- Herpes Zoster/varicella zoster virus (VZV)

PEDIATRIC PATIENTS:[2]
- Herpes labialis/orofacial herpes
- Chickenpox

OFF-LABEL USES IN DERMATOLOGY

- Other cutaneous herpes simplex virus infections such as eczema herpeticum, herpetic whitlow, herpes gladiatorum
- HSV-associated erythema multiforme (EM)[3]
- Orofacial herpes prophylaxis following cosmetic treatments such as resurfacing lasers, chemical peels and injectable fillers

DOSING[2]

- Herpes labialis/orofacial herpes (adults and pediatric patients): 2g twice daily for 1 day
- Genital herpes:
  - Initial episode: 1g twice daily for 10 days
  - Recurrence: 500 mg twice daily for 3 days
  - Suppressive therapy
    - Immunocompetent: 1g daily or 500mg daily in patients with ≤ recurrences per year
    - HIV-infected patients: 500mg twice daily
  - Reduction of transmission: 500mg once daily
- Herpes zoster: 1g three times daily for 7 days
- Chickenpox (pediatric patients ages 2-18): 20mg/kg 3 times daily for 5 days. Dose should not exceed 1g three times daily.
- Orofacial herpes prophylaxis following facial cosmetic procedures: 500mg twice daily starting 1-2 days prior to procedure and continuing for 5-10 days post-procedure.[4]
- Valacyclovir has also been used to help prevent recurrent HSV-associated EM. Treatment can be initiated at a dose of 500mg twice daily for 5-10 days, followed by a prophylactic dose of 500mg daily for several months, until patients have been free of recurrence for at least 3-4 months.[3,5]

Of note, dosing should be reduced in patients with significant renal insufficiency (creatinine clearance < 50). Dosing will vary based on intended dosing regimen and creatinine clearance.

ADVERSE EFFECTS

- Headaches
- Nausea
- Abdominal pain
- Vomiting
- Transaminitis and increased alkaline phosphatase (especially in HIV-infected patients)
- Neutropenia (mostly reported in immunosuppressed patients with HIV or transplant recipients)[6]
- Nasopharyngitis
- Rash. Some reported cutaneous adverse reactions include: urticaria[7], fixed drug eruption[8], drug induced hypersensitivity syndrome (DIHS)[9], exanthematous drug eruptions[10] and photosensitivity.
- Hypersensitivity reaction
- Nephrotoxicity
- Less commonly reported adverse effects include diarrhea, dysmenorrhea, leukopenia, thrombocytopenia, arthralgia, dizziness, fatigue, depression, aggressive behavior, psychosis, confusion, seizures (may lower seizures threshold), rhinorrhea, fever, decreased hemoglobin

PRECAUTIONS/CONTRAINDICATIONS

- Precautions:
  - Thrombotic thrombocytopenic purpura (TTP)/hemolytic uremic syndrome (HUS). Use of valacyclovir in higher doses (2g four times daily) has been associated with the development of TTP/HUS in patients with advanced HIV/AIDS[11], renal transplant patients and allogeneic bone marrow transplant patients.[2]
  - Acute renal failure may occur in patients with underlying renal dysfunction, those taking other nephrotoxic medications, or patients inadequately hydrated. Patients with renal dysfunction may require dose adjustments and closer monitoring.[2]
  - Use with caution in immunosuppressed and elderly patients, as these patients are more likely to experience some of the more serious adverse effects. Additionally, development of drug resistance to valacyclovir is most commonly seen in immunosuppressed patients, such as those with HIV and transplant recipients.
- Contraindication:
  - Hypersensitivity to valacyclovir, acyclovir or any component of the formulation[2]

DRUG INTERACTIONS

- Valacyclovir is a weak CYPA2 inhibitor and may increase drug levels of medications metabolized by this enzyme, such as: clozapine, tizanidine and theophylline derivatives
- May decrease therapeutic effects of the varicella and zoster virus vaccines[12,13]
- May decrease efficacy of talimogene laherparepvec[14]

PREGNANCY

- Valacyclovir may be used during pregnancy and breastfeeding. There is no known risk of teratogenicity or infant harm based on limited human data.[15]

SAFETY MONITORING

- A baseline creatinine may be warranted in certain patient populations