Drug Quantity Management – Per Rx
Antivirals – Valacyclovir tablets (Valtrex®)

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Product Identifier(s)

Effective 1/1/23 to 2/6/23: 107340

Effective 2/7/23: 34115

INSTRUCTIONS FOR USE
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National Formulary Medical Necessity

This Drug Quantity Management program has been developed to promote dose consolidation of valacyclovir. If the Drug Quantity Management rule is not met for the requested medication at the point of service, coverage will be determined by the Criteria below. All approvals are provided for 1 year.

Drug Quantity Limits

Product	Strength and Form	Maximum Quantity per Rx
Valtrex® (valacyclovir tablets, generic)	500 mg tablets	30 tablets
	1 gram tablets	30 tablets

Criteria

Cigna covers quantities as medically necessary when the following criteria are met:

Valacyclovir 500 mg tablets

1. If the medication is being requested for the chronic suppression or prevention of mucocutaneous herpes (genital, perianal, oral) in immunocompromised patients, approve up to 60 tablets per dispensing.

2. If the medication is being requested for the prophylaxis of herpes gladiatorum, approve a one-time override of 60 tablets.

3. If the medication is being requested for an ophthalmic infection, approve the requested quantity for a 30-day supply per dispensing.

4. If the medication is being requested for the suppression of herpes simplex virus (HSV) in pregnancy from 36 weeks of gestation until delivery, approve the quantity requested for a 30-day supply per dispensing.

5. If the medication is being requested for the prophylaxis of herpes zoster/varicella zoster virus after solid organ transplantation, approve 60 tablets per dispensing.

6. Exceptions are not recommended for treatment of multiple sclerosis, chronic fatigue syndrome, or Epstein-Barr virus.

Valacyclovir 1 gram tablets

1. If the medication is being requested for the prevention of cytomegalovirus disease after solid organ transplantation (e.g., renal, renal-pancreas, heart), bone marrow transplantation, or stem cell transplantation, approve the quantity requested for a 30-day supply per dispensing.

2. If the medication is being requested for an ophthalmic infection, approve the quantity requested for a 30-day supply per dispensing.

3. If the medication is being requested for the treatment of mucocutaneous herpes infections in an immunocompromised patient, approve up to 60 tablets per dispensing.

4. If the medication is being requested for the treatment of acute local dermatomal herpes zoster in an immunocompromised patient, approve up to 90 tablets per dispensing.

5. Exceptions are not recommended for treatment of multiple sclerosis, chronic fatigue syndrome, or Epstein-Barr virus.

Conditions Not Covered

Any other exception is considered not medically necessary.

Background

Overview

Valacyclovir is a deoxynucleoside analogue DNA polymerase inhibitor indicated for:[1]

Adults

- **Cold Sores** (Herpes labialis)
- **Genital Herpes**
  - Treatment in immunocompetent patients (initial or recurrent episode)
  - Suppression in immunocompetent or patients with HIV-1
  - Reduction of transmission
- **Herpes Zoster**

Pediatric Patients

- Cold Sores (Herpes labialis)
- **Chickenpox**

The efficacy and safety of valacyclovir has not been established in immunocompromised patients other than for the suppression of genital herpes inpatients with HIV-1.[1]

Dosing

See Table 1 for the manufacturer recommended dosing.[1] The maximum number of tablets needed per course of treatment is 30 tablets.

Table 1. FDA-Approved Indications and Dosing.[1]

Indication	Normal Dosage Regimen (CrCl ≥ 50 mL/min)	Renal Dosing Adjustment†		
		CrCl ≥ 30 to ≤ 49 mL/min	CrCl ≥ 10 to ≤ 29 mL/min	CrCl < 10 mL/min
Adult				
Cold sores (Herpes labialis)	2 grams Q12H for 1 day	1 gram Q12H for 1 day	500 mg Q12H for 1 day	500 mg single dose
Genital herpes				
Initial episode	1 gram Q12H for 10 days		1 gram Q24H for 10 days	500 mg Q24H for 10 days
Recurrent episodes	500 Q12H for 3 days		500 mg Q24H for 3 days	
Suppressive therapy (immunocompetent patients)	1 gram Q24H OR 500 mg Q24H*		500 mg Q24H OR 500 mg Q48H*	
Suppressive therapy (HIV-infected patients)	500 mg Q12H		500 mg Q24H	
Reduction of transmission	500 mg Q24H	--	--	--

Table 1 (continued). FDA-Approved Indications and Dosing.[1]

Indication	Normal Dosage Regimen (CrCl ≥ 50 mL/min)	Renal Dosing Adjustment†		
		CrCl ≥ 30 to ≤ 49 mL/min	CrCl ≥ 10 to ≤ 29 mL/min	CrCl < 10 mL/min
Adult				
Herpes zoster (Shingles)	1 gram Q8H for 7 days	1 gram Q12H for 7 days	1 gram Q24H for 7 days	500 mg Q24H for 7 days
Pediatric				
Cold sores (Herpes labialis, age ≥ 12 years)	2 grams Q12H for 1 day	--	--	--
Chickenpox (age ≥ 2 to < 18 years)	20 mg/kg administered TID for 5 days; not to exceed 1 gram TID	--	--	--

CrCl – Creatinine clearance; † Patients requiring hemodialysis should receive the recommended dose of valacyclovir after hemodialysis. Q12H – Every 12 hours; Q24H – Every 24 hours; * Alternative regimen in patients with a history of ≤ 9 recurrences per year; Q48H – Every 48 hours; HIV – Human immunodeficiency virus; Q8H – Every 8 hours; TID – Three times daily.

In addition to FDA-approved uses, literature and guidelines also support use of valacyclovir for several indications related to reactivation of latent varicella (chickenpox) virus.[10,15-19] For example, oral therapy can be required for up to 6 weeks for the eyes or up to 10 days for the ears/facial nerves (Ramsay Hunt).[5,6,8,9]

Valacyclovir has been used in acute retinal necrosis, a reactivation of herpes zoster virus.[8,9,15,16] In immunocompetent patients with acute retinal necrosis, the recommended treatment is acyclovir IV for 10 to 14

days, followed by oral valacyclovir 1 gram three times daily (TID) for approximately 6 weeks.[16] The major otologic complication of varicella zoster virus reactivation is the Ramsay Hunt syndrome, which includes ipsilateral facial paralysis, ear pain, and vesicles in the auditory canal and auricle.[15] For this indication, valacyclovir 1 gram TID for 7 to 10 days has been used.

Valacyclovir has been used for the management of herpes simplex keratitis at a dose of 500 mg TID for 2 weeks.[15] For patients with frequent or recurrent herpes simplex epithelial keratitis, suppressive oral antiviral therapy with valacyclovir 500 mg once daily for 12 months has been used.[17] Valacyclovir has been used or the treatment of localized herpes zoster (dermatonal) in solid organ transplant recipients at a dose of 1 gram TID for 7 days, or until lesions have crusted over which may be delayed in immunocompromised hosts.[18] Valacyclovir 500 mg twice daily (BID) can be used for short-term prophylaxis of herpes zoster virus/varicella zoster in patients with solid organ transplant who are herpes simplex virus seropositive and not receiving cytomegalovirus prophylaxis. It may also be considered in seronegative receipients.[18]

In human immunodeficiency virus (HIV)-infected adults and adolescents, valacyclovir has several uses for the prevention or treatment of opportunistic infections.[10] For the treatment of herpes simplex virus (HSV) orolabial lesions, valacyclovir 1 gram BID for 7 to 10 days is recommended. For initial or recurrent genital HSV valacyclovir 1 gram BID for 5 to 14 days is recommended. In severe mucocutaneous HSV, after initial intravenous (IV) therapy, oral therapy can be used as oral lesions begin to regress (valacyclovir 1 gram BID continued until lesions are completely healed). For chronic suppressive therapy of HSV, the recommended dose of valacyclovir is 500 mg BID. For the treatment of primary varicella infection (chickenpox), the dose of valacyclovir in uncomplicated cases is 1 gram TID for 5 to 7 days; for severe or complicated cases patients are treated with IV therapy then transitioned to oral therapy with valacyclovir after defervescence if no evidence of visceral improvement is noted. For the treatment of acute, localized, dermatonal herpes zoster (shingles), the recommended dose is valacyclovir 1 gram TID for 7 to 10 days, or longer if lesions are slow to resolve. For varicella zoster virus with extensive cutaneous lesions or visceral involvement after IV therapy, patients may switch to oral therapy with valacyclovir after clinical improvement and continue for 10 to 14 days. Similar dosing is also recommended in solid organ transplant recipients.[18]

For individuals with < 2 years history of herpes gladiatorum infection valacyclovir 1 gram daily has been used.[13] In those with history of disease for $\geq$ 2 years doses of 500 mg to 1 gram mg daily have been used in prophylaxis.

For the suppression of herpes simplex virus in pregnant women in the third trimester until delivery, valacyclovir 500 mg BID has been used.[14]

For the short-term prophylaxis of varicella zoster/herpes zoster in solid organ transplant recipients who are herpes simplex virus seropositive and not receiving cytomegalovirus (CMV) prophylaxis, valacyclovir 500 mg BID daily has been used.[18] It may also be considered in seronegative recipients. For the prevention of CMV after solid organ transplantation (e.g., renal, renal-pancreas, heart), bone marrow transplantation, or stem cell transplantation, valacyclovir 1 gram TID or 2 grams four times daily (QID) have been used.[2,19]

Availability
Valacyclovir is available in 500 mg and 1,000 mg (1 gram) tablets.[1] Valacyclovir oral suspension (25 mg/mL or 50 mg/mL) may be prepared extemporaneously from 500-mg valacyclovir tablets for use in pediatric patients for whom a solid dosage form is not appropriate. In situations where a 1 gram dose is indicated, the participant should be referred to the 1 gram strength (e.g., for the treatment of herpes zoster [shingles], the initial episode of genital herpes, or chronic suppression of recurrent genital herpes [≥ 9 episodes per year]).

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Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	**Valacyclovir 500 mg tablets.** Override criteria for the prophylaxis of herpes zoster/varicella zoster virus after solid organ transplantation were added to allow for 60 tablets per dispensing. **Valacyclovir 1 gram tablets.** For the treatment of acute local dermatonal herpes zoster in an immunocompromised patient, override criteria were updated to approve up to 90 tablets per dispensing (previously up to 42 tablets were approved). **Exclusions.** Chronic suppression of genital herpes in immunocompetent patients with frequent recurrence (≥ 6 episodes of genital herpes per year) was removed from exclusion criteria for valacyclovir 500 mg tablets (this condition is no longer addressed in the policy, current quantity limits cover appropriate dosing).	04/06/2022