

Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCTOP017.0625	TOPICAL PRODUCTS See Table 1 for covered Medications
Effective Date: 8/1/2025	Review/Revised Date: 09/10, 10/10, 12/10, 10/11, 04/12, 12/12, 04/14, 12/14, 03/16, 03/17, 03/18, 03/19, 10/19, 12/20, 04/21, 05/22, 04/23, 05/24, 04/25 (JH)
Original Effective Date: 10/08	P&T Committee Meeting Date: 10/08, 12/09, 10/10, 12/10, 10/11, 04/12, 04/14, 12/14, 04/16, 04/17, 04/18, 04/19, 12/19, 10/20 (off-cycle), 12/20, 06/21, 06/22, 06/23, 06/24, 06/25
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:

Providence Health Plan and Providence Health Assurance as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:

Commercial
Medicaid

POLICY CRITERIA:

COVERED USES:

All Food and Drug Administration (FDA)-approved indications not otherwise excluded in the benefit.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

REQUIRED MEDICAL INFORMATION:

For herpes labialis (cold sores):

1. Documented trial and failure, intolerance or contraindication to a generic oral antiviral medication
AND
2. Documented trial and failure, contraindication or intolerance to acyclovir 5% ointment. Trial and failure is defined as no improvement in lesions 10 days after starting treatment.
AND
3. For Medicaid members only, must meet one of the following criteria:
 - a. Documentation that the patient is immunocompromised (e.g. diagnosis of cancer **AND** currently undergoing chemotherapy or radiation, solid organ transplant, HIV/AIDS). Must provide corresponding ICD-10 code.
OR
 - b. Documentation that the patient is currently taking an immunosuppressive drug (e.g. methotrexate, hydroxychloroquine, tacrolimus, infliximab, adalimumab)

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ORPTCTOP017**

TOPICAL PRODUCTS
See [Table 1](#) for covered Medications

EXCLUSION CRITERIA:

1. Genital or mucocutaneous herpes simplex
2. Suppressive therapy (greater than 10 days course)

AGE RESTRICTIONS: N/A

PRESCRIBER RESTRICTIONS: N/A

COVERAGE DURATION:

Authorization will be approved until no longer eligible with the plan, subject to formulary or benefit changes

QUANTITY LIMIT:

The following quantities will be approved per rolling 365-day period

1. Xerese® - 10 grams
2. Denavir® - 10 grams
3. Acyclovir 5% cream (Zovirax®) - 10 grams

Additional quantities may be approved based on medical necessity. Medications being used as suppressive therapy is not considered medically necessary.

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:

Topical acyclovir (Zovirax®, Xerese®), and topical penciclovir (Denavir®) are medications used to treat herpes labialis (cold sores) caused by herpes simplex virus. These medications do not cure the disease but rather help the sores heal faster.

FDA APPROVED INDICATIONS:

- Zovirax® (acyclovir) Cream 5%: the treatment of recurrent herpes labialis (cold sores) in immunocompetent adults and adolescents 12 years of age and older.
- Xerese®(acyclovir/hydrocortisone) Cream: the early treatment of recurrent herpes labialis (cold sores) to reduce the likelihood of ulcerative cold sores and to shorten the lesion healing time in adults and children (six years of age and older).
- Denavir® (penciclovir) Cream: the treatment of recurrent herpes labialis (cold sores) in adults and children 12 years of age and older.

POSITION STATEMENT:

Herpes labialis (cold sores) are caused by herpes simplex virus (HSV-1). The herpes lesions typically last a week to 10 days (without treatment) and most often occur around the lips. Treatment options include oral antiviral therapies (e.g., acyclovir, famciclovir, or valacyclovir) and topical antiviral therapies (see [Appendix 1](#)). Topical antiviral treatments generally require frequent application of creams and produce only a modest clinical benefit.

- Acyclovir cream (Zovirax®) was evaluated based on two double-blind, randomized, placebo-control trials for the treatment of recurrent herpes labialis. Study participants started treatment within one hour of noticing signs or symptoms. Treatment consisted of application of study medication 5 times per day for 4 days. In both studies, acyclovir cream showed a modest improvement in the mean duration of lesion by one-half day (4.5 days for acyclovir vs. 5 days for placebo). No significant difference was found in prevention of progression of cold sore lesions.
- Acyclovir/hydrocortisone cream (Xerese®) was studied in a double-blind, randomized trial comparing acyclovir/hydrocortisone (Xerese®), 5% acyclovir in Xerese® vehicle and vehicle alone. Study drugs were applied five times per day for 5 days. The mean time to skin normalization was 1.6 days shorter in acyclovir/hydrocortisone treatment group compared to vehicle alone.
- The evidence of penciclovir (Denavir®) cream was demonstrated based on two studies similarly designed as the acyclovir cream trial. Study participants applied the study drugs every 2 hours while awake for 4 days. Results showed that a modest improvement in the mean duration of lesion by one-half day (4.5 days for penciclovir vs. 5 days for placebo).

Genital herpes are also caused by a herpes simplex virus (HSV-2). According to the Centers for Disease Control and Prevention (CDC) recommendation, oral antiviral therapy is considered the mainstay of management to treat first clinical and recurrent episodes (See [Appendix 2](#) for recommended regimens).

- Randomized control studies for the treatment of mucocutaneous herpes simplex are limited and show that topical acyclovir or penciclovir is either of no benefit

over the vehicle itself or up to ½ day to 1 day improvement in duration. Further, in severely immunocompromised patients, acyclovir 5% or 10% ointment has proved ineffective for the treatment of recurrent orofacial herpes.

- Consequently, the CDC discourages the use of topical therapy with antiviral drugs for the treatment of genital or mucocutaneous herpes due to minimal clinical benefit.
- There is no evidence for the use of topical acyclovir as suppressive therapy.

REFERENCE/RESOURCES:

1. Relevant package inserts
2. Bieber T, Chosidow O, Bodsworth N et al. Efficacy and Safety of Aciclovir Mucoadhesive Buccal Tablet in Immunocompetent Patients With Labial Herpes (LIP Trial): A Double-Blind, Placebo-Controlled, Self-Initiated Trial. *Drugs Dermatol.* 2014;13(7):791-798.
3. Famciclovir, valacyclovir, acyclovir, penciclovir. In: DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc. Updated periodically.
4. Niimura M, Honda M, Nishikawa T, et al: The optimal concentration of aciclovir ointment for the treatment of cutaneous herpes simplex virus infections. A controlled clinical trial. *Rinsho Iyaku* 1992; 8:289-297.
5. Shaw M, King M, Best JM, et al. Failure of acyclovir cream in treatment of recurrent herpes labialis. *Br Med J* 1985; 291:7-9.
6. Spruance SL, Crumpacker CS, Schnipper LE, et al. Early, patient-initiated treatment of herpes labialis with topical 10% acyclovir. *Antimicrob Agents Chemother* 1984; 25:553-555.
7. Centers for Disease Control and Prevention. Sexually Transmitted Infections Treatment Guidelines, 2021. Available at: <https://www.cdc.gov/std/treatment-guidelines/herpes.htm> (Accessed April 22, 2025)
8. Cernik C, Gallina K, Brodell RT. The treatment of herpes simplex infections: an evidence-based review. *Arch Intern Med.* 2008 Jun 9;168(11):1137-44. Review.

Table 1

Brand Name	Generic Name
Denavir®	penciclovir cream
Xerese®	acyclovir/hydrocortisone cream
Zovirax®	acyclovir cream

Appendix 1 – Recommended Regimens for herpes labialis

Product	Recommended Dosing Regimen
acyclovir tablets	200 mg five times daily for 10 days <ul style="list-style-type: none"> • HIV-infected: 400 mg orally 3 times daily for 5 to 10 days
acyclovir ointment	Apply ointment topically (using a finger cot or glove) every 3 hours (6 times per day) for 7 days in sufficient quantities to adequately cover lesions
valacyclovir tablets	2 g twice daily for 1 day; separate doses by 12 hours <ul style="list-style-type: none"> • HIV-infected: 1 g twice daily for 5 to 10 days
famciclovir tablets	Herpes labialis, Initial episode (HIV infection): 500 mg twice daily for 5 to 10 days Recurrent herpes simplex labialis: 1500 mg as a single dose; initiate at earliest sign or symptom of a cold sore <ul style="list-style-type: none"> • HIV-infected: 500 mg ORALLY twice daily for 5 to 10 days

Appendix 2 – Recommended Regimens for Genital Herpes

First Clinical Episode*
<ul style="list-style-type: none"> • Acyclovir 400 mg orally three times a day for 7-10 days • Famciclovir 250 mg orally three times a day for 7-10 days • Valacyclovir 1 g orally twice a day for 7-10 days <p>* Treatment can be extended if healing is incomplete after 10 days of therapy.</p>
Episodic Therapy for Recurrent Disease
<ul style="list-style-type: none"> • Acyclovir 800 mg orally twice a day for 5 days • Acyclovir 800 mg orally three times a day for 2 days • Famciclovir 125 mg orally twice daily for 5 days • Famciclovir 1 g orally twice daily for 1 day • Famciclovir 500 mg once, followed by 250 mg twice daily for 2 days • Valacyclovir 500 mg orally twice a day for 3 days • Valacyclovir 1 g orally once a day for 5 days
Suppressive Therapy
<ul style="list-style-type: none"> • Acyclovir 400 mg orally twice a day • Famciclovir 250 mg orally twice a day • Valacyclovir 500 mg orally once a day • Valacyclovir 1 g orally once a day