

Therapeutic Class Overview Topical Antivirals

Therapeutic Class

- Overview/Summary:** Both acyclovir (Zovirax®) and penciclovir (Denavir®) are synthetic nucleoside analogs derived from guanine that are approved for the management of initial herpes genitalis, recurrent herpes labialis and/or non-life-threatening mucocutaneous herpes simplex virus infections in immunocompromised patients. In addition, a combination of acyclovir and hydrocortisone (Xerese®) is approved to reduce the likelihood of ulcerative cold sores and to shorten the lesion healing time in recurrent herpes labialis. These agents are active against various herpes simplex virus including types 1 and 2 (HSV-1 and HSV-2).¹⁻⁵ The two most common cutaneous manifestations of the herpes simplex virus infection are orolabial and genital herpes. Orolabial herpes presents most commonly as cold sores and is the most prevalent form of mucocutaneous herpes infection. Approximately 35 to 60% of Caucasians in the United States have serologic evidence of having been infected by HSV-1.⁶ Genital herpes, is one of the most common viral sexually transmitted diseases in the world, but has demonstrated a decreased prevalence over the past few years. A majority of patients infected with HSV-2 have not been diagnosed, as symptoms may be mild in many cases and the presentation is highly variable between patients. Although infections may be mild or unrecognized, the virus continues to be shed intermittently in the genital tract. After resolution of primary infection, the virus persists in the nerve roots of the sacral plexus, causing recurrent (often less severe) outbreaks.

Prior to the introduction of acyclovir as an antiviral drug in the early 1980s, cutaneous HSV infection was managed with drying agents and other local care. Today, treatment options include multiple oral, intravenous and topical antiviral agents. Oral antiviral treatments are effective in reducing symptoms, while intravenous administration may be required in immunocompromised patients and those with severe disseminated infection.⁶ Topical antivirals reduce the duration of viral shedding and the length of time before all lesions become crusted; however, the topical treatment is much less effective compared to oral or intravenous therapies. No antiviral agent currently available will eradicate HSV, and treatment is aimed at managing symptoms and reducing disease duration rather than curing the disease. Currently, acyclovir ointment is available generically.

Table 1. Current Medications Available in the Therapeutic Class²⁻⁵

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Single-Entity Agents			
Acyclovir (Zovirax®*)	Management of initial herpes genitalis [†] , treatment of recurrent herpes labialis [‡] , management of non-life-threatening mucocutaneous herpes simplex virus infections in immunocompromised patients [‡]	Cream: 5% (2, 5 g tubes) Ointment: 5% (5, 15, 30 g tube)	✓
Penciclovir (Denavir®)	Treatment of recurrent herpes labialis	Cream: 1% (1.5 g tube)	-
Combination Products			
Acyclovir/hydrocortisone (Xerese®)	Treatment of recurrent herpes labialis [#]	Cream: 5%/1% (5 g tube)	-

*Generic available in at least one dosage form or strength.

† Acyclovir 5% ointment only.

‡ Acyclovir 5% cream only.

#To reduce the likelihood of ulcerative cold sores and to shorten the lesion healing time.

Evidence-based Medicine

- When the efficacy of acyclovir 5% cream was evaluated compared to placebo for the treatment of genital herpes, there was only a significant decrease in the duration of itching with acyclovir treatment compared to placebo.⁷ When penciclovir 1% cream was compared to acyclovir 3% cream for the treatment of genital herpes, the only significant difference seen between the two treatment groups was time to crusting of lesions, which favored penciclovir treatment.⁸
- In the treatment of recurrent herpes labialis, acyclovir 5% cream significantly shortens the mean clinician-assessed duration of herpes labialis episodes and mean patient-assessed duration of pain when compared to placebo. The lesion healing time and the number of episodes per month was not found to be significant between treatments.⁹⁻¹³
- The combination formulation of acyclovir/hydrocortisone 5%/1% cream was evaluated in a double-blind, active and placebo controlled study of more than 2,400 patients ≥ 18 years of age with a history of herpes simplex labialis who had experienced at least three recurrent episodes in the past year. The primary endpoint, prevention of ulcerative herpes simplex labialis lesions (frequency of patients with nonulcerative recurrences) was significantly greater in patients treated with acyclovir/hydrocortisone compared to patients treated with acyclovir or placebo (42 vs 35 and 26%, respectively; $P < 0.05$ for both).¹⁴
- Compared to placebo, patients treated with penciclovir 1% cream experienced significant decreases in the overall lesion healing time, healing in early, late and vesicle stages, resolution of lesion pain and resolution of symptoms including itching, tingling, burning, numbness and tenderness.¹⁵⁻¹⁷ Patients treated with penciclovir also were shown to have a significantly higher percent of cases healed at six and eight days. When penciclovir 1% cream was compared to acyclovir 5% cream, there was a significantly shorter time to crusting with penciclovir treatment compared to acyclovir. The percent of patients cured at seven days was not significantly different.^{18,19}

Key Points within the Medication Class

- According to Current Clinical Guidelines:
 - National and international guidelines including those published by the Centers for Disease Control and Prevention, state that the topical antiviral agents offer minimal clinical benefit and should not be recommended over other options in general use, such as the oral antivirals.^{20,21}
- Other Key Facts
 - Acyclovir 5% ointment is the only topical antiviral agent available generically; however, several oral antiviral formulations are available generically in various formulations.

References

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