Indiana Medicaid Therapeutics Committee
Therapeutic Class Review Summary

Therapeutic Class:
Topical Antivirals

Overview:
The topical antiviral agents in this review primarily offer antiviral activity against infections caused by herpes simplex viruses (HSV), both HSV-1 and HSV-2. HSV-1 is normally associated with orofacial infections and encephalitis; HSV-2 is usually the cause for genital herpes. In the United States, approximately 130 million people over the age of 12 are infected with HSV-1. The first episode of HSV-1 infection generally occurs in children and young adults and is asymptomatic. HSV-1 infections are one of the most common infections in the world.

Herpes labialis (cold sores) can be caused by either HSV-1 or HSV-2. It is the most frequent clinical sign of reactivation of HSV infection. Once latency is established, about 20%-40% of people will have symptomatic recurrences. Certain factors such as UV light, febrile illnesses, stress, premenstrual tension, and surgical procedures can trigger a recurrence.

Acyclovir, penciclovir, and docosanol are the available topical antiviral agents in the U.S. While acyclovir and penciclovir's mechanisms target inhibition of the herpes viral DNA synthesis, docosanol modulates the host cell to prevent entry of the virion.

All three agents have indications for treatment of recurrent herpes labialis infections in adults and adolescents 12 years of age and older. Acyclovir is the only topical agent with additional indications. Acyclovir ointment is indicated for management of initial genital herpes and in non-life-threatening mucocutaneous herpes simplex virus infections in immunocompromised patients. While acyclovir ointment has the indication, use of topical antiviral agents in the treatment of genital herpes infections is not recommended by the Centers for Disease Control (CDC).

Currently, no head-to-head studies exist comparing the three topical antiviral agents in this review. All of the agents have supporting data from randomized, placebo-controlled studies, favoring herpes labialis lesion healing and reduction of pain. The dosing regimens and adverse event profiles are comparable for each agent. None of the topical antiviral agents have a generic alternative.

Generic Name	Brand Name	Manufacturer	Generic Available
Acyclovir	Zovirax®	Biovail	No
Penciclovir	Denavir®	Novartis	No
Docosanol	Abreva®	GlaxoSmithKline	No

Summary:

The primary place in therapy for the topical antiviral agents is in the treatment of herpes simplex labialis infections (cold sores). Topical acyclovir (cream), penciclovir, and docosanol have been proven more effective than placebo for the treatment of herpes simplex labialis infections. At this time, no head-to-head studies fitting our search criteria have documented comparative efficacy between these agents for this condition. The evidence suggests all three agents improve lesion healing time and pain compared with placebo. Each topical antiviral must be applied frequently (five times daily or every two hours) and initiated as early as possible once symptoms begin. Additionally, these agents are well-tolerated, with the most common adverse events being application site reactions such as burning and stinging.

Acyclovir ointment is the only topical antiviral indicated for initial genital herpes infections. However, the Centers for Disease Control and Prevention (CDC) do not recommend use of topical antiviral agents for the management of genital herpes due to minimal clinical benefit. Acyclovir ointment is also the only topical antiviral agent indicated for treatment of mucocutaneous herpes simplex virus infections in immunocompromised patients.

None of the topical antiviral agents reviewed in this class are available with generic alternatives; however, topical docosanol is available over-the-counter (OTC). Consideration of approved indications should drive selection of one or more agents for the preferred drug list.