

# Penciclovir for the treatment of herpes simplex labialis: A review

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Recurrent herpes labialis is of significant morbidity in a small segment of the population with up to twelve or more episodes occurring per year and the clinical lesions lasting up to fifteen days.<sup>1-4</sup> Palliative treatment, such as keeping the lesions moist, application of topical anesthetics, use of systemic analgesics, and administration of antiviral medication, has been advocated. Acyclovir, marketed under the trade name Zovirax (Glaxo Wellcome), has been one such medication used in topical form. It has been thought that application of topical acyclovir in the early stages of the prodrome syndrome, may shorten the clinical course of the infection.<sup>5-8</sup> Topical acyclovir treatment is an option but has the disadvantage of having to be applied very early when symptoms appear and its overall effectiveness in an immunocompetent patient in abating the course of the disease is minimal. Recently, penciclovir (trade name Denavir, SmithKline Beecham Consumer Healthcare) has been made available, formulated as a topical cream for use in herpes labialis. Penciclovir is a relatively new antiviral medication and is similar in chemical structure and pharmacologic function to acyclovir.

Penciclovir is poorly absorbed through the gastrointestinal wall.<sup>9-11</sup> Famciclovir is an oral prodrug of penciclovir and is converted to penciclovir inside the gastrointestinal wall. The conversion from famciclovir to penciclovir enables 77 percent of penciclovir to be-

come available systemically.<sup>12</sup> Oral famciclovir has been shown to decrease healing time by approximately one day when used for recurrent genital herpes, if treatment is initiated within six hours of prodrome symptoms.<sup>13</sup>

Topically applied 1 percent penciclovir cream has been shown to decrease the healing time from 5.5 days to 4.8 days or 0.7 days more quickly than with a placebo. One percent penciclovir cream has also been shown to decrease the duration of pain from 4.1 days to 3.5 days or 0.6 days. These two effects occurred when penciclovir treatment was initiated within one hour of the first sign or symptom of cold-sore recurrence and then every two hours while awake for four consecutive days. The study participants were immunocompetent men and women over the age of eighteen with a history of recurrent herpes labialis. Healing and pain resolution occurred even if therapy was initiated later than the prodrome or erythema stage of lesion development. Although statistically significant, the clinical benefit of topical penciclovir treatment in this study was minimal. Healing time was decreased by 13 percent and the duration of pain was decreased by 15 percent, when penciclovir was applied at the first sign or symptom and every two hours thereafter for four days.<sup>14</sup> In another similar study recurrent herpes labialis lesions were induced by ultraviolet radiation. When topical 1 percent penciclovir cream was applied within one hour of prodrome symptoms and every two hours thereafter while awake, for four days, there was a small but significant decrease in healing time from eight days to seven days or 12.5 percent. This same study also reported

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a minimal decrease in pain, itching, burning and tenderness of the lesions.<sup>15</sup>

The mechanism of action for penciclovir is similar to acyclovir in that it is activated only in virus infected cells to the triphosphate form by way of virally encoded thymidine kinase and cellular enzymes.<sup>9-11,16</sup> Penciclovir inhibits viral DNA synthesis through competitive inhibition of DNA polymerase. Acyclovir becomes incorporated into the viral DNA causing immediate chain termination. Penciclovir is converted to the triphosphate form more quickly and to a greater extent than is acyclovir; acyclovir has, however, a much greater affinity for DNA polymerase. Penciclovir has a much longer intracellular half-life than acyclovir.<sup>11,17,18</sup> It is not known what the significance of these differences are clinically.

Topical application of penciclovir offers slightly quicker resolution of the disease process, if a strict regimen is followed and may have some advantage over topical application of acyclovir. Topical acyclovir is available in a 5 percent ointment. The official Food and Drug Administration (FDA) approval for use of acyclovir is initial and recurrent mucocutaneous herpes simplex. Topical penciclovir is available in a 1 percent cream and the official FDA use approval is for herpes simplex labialis. Acyclovir has a FDA pregnancy risk category of C and penciclovir is rated at B. Pregnancy risk category B is defined as: Animal studies have not demonstrated a risk to the fetus, but there are no adequate studies in pregnant women or animal studies that have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus during the first trimester of pregnancy, and there is no evidence of risk in later trimesters. Category C is: Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; the benefits of the drug in pregnant women may be acceptable despite its potential risks or there are no animal reproduction studies and no adequate studies in humans. Topical acyclovir has poor skin penetration.<sup>19</sup>

In summary, there is currently no ideal topical treatment for herpes labialis. Topical acyclovir and penciclovir may be used with limited benefit. Topical penciclovir probably has some advantages over topical acyclovir due to the following data. Penciclovir has been shown to increase slightly the healing rate and minimally decrease associated lesion pain when treatment is started within one hour of symptoms and applied every two hours while awake. Penciclovir has a longer intracellular half-life, is placed in pregnancy risk category B and has FDA approval for herpes simplex labialis. Acyclovir is FDA approved for muco-

cutaneous herpes simplex, is placed in pregnancy risk category C and has poor skin penetration.

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