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FAST TRACK

A number of oral and topical treatments will reduce the duration of herpes outbreaks by about a day

What are the best treatments for herpes labialis?

Evidence-based answer

There are 3: valacyclovir, acyclovir, and topical penciclovir. Valacyclovir, 2 g twice in 1 day taken during the prodromal stage of herpes labialis, reduces the episode duration and time to healing. Acyclovir, 400 mg, taken 5 times a day for 5 days, decreases the pain duration and healing time to loss of crust (strength of recommendation [SOR]: **A**, based on randomized controlled trials [RCTs]).

Topical penciclovir 1%, acyclovir 5%, or docosanol 10% also decrease the duration of pain and healing time (SOR: **A**, based on RCTs).

The best prophylaxis for herpes labialis is oral valacyclovir 500 mg daily; it reduces the frequency and severity of attacks (SOR: **B**, based on RCT). Sunscreen may be effective in sunlight-induced recurrence (SOR: **B**, based on 2 small crossover RCTs).

Clinical commentary

Let patients self-treat before breakouts

An effective management for the treatment of recurrent herpes labialis at the prodromal stage is a patient-initiated, self-treatment approach. In my experience, providing these patients with a prescription for valacyclovir prior to breakouts results in better overall outcomes. Patients are able to start self-treatment at the earliest signs of symptoms and feel more in control of their disease. With the lower pill burden and shorter treatment duration of valacyclovir, many patients report significantly shorter

healing times, reduction in duration of pain, better compliance, and overall satisfaction.

This approach is particularly useful for patients like medical personnel and daycare workers, for whom outbreaks can pose significant adverse outcomes, such as loss of work days and increased risk of infecting others. If breakouts are frequent and risk of infecting others is high, consider daily valacyclovir as prophylaxis for these patients.

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Evidence summary

Herpes labialis is the most common presentation of herpes simplex virus 1 (HSV-1) infection and generally represents reactivation. The disease progresses quickly; therefore, early treatment is required.

Patient-initiated treatment can be effective. **TABLE 1** shows the comparison of

oral (valacyclovir and acyclovir) and topical (penciclovir, acyclovir, and docosanol) antiviral agents for treatment of herpes labialis.¹⁻⁵

Oral treatments: Shortening episodes by a day

Two RCTs have shown that valacyclovir (the prodrug of acyclovir, which has

TABLE 1

Antiviral agents for herpes labialis: A comparison

	DRUG	REGIMEN (OR PLACEBO)	N	OUTCOME (VS PLACEBO)	
				HEALING TIME	PAIN DURATION
Oral	Valacyclovir*	2 g twice daily for 1 day	603	1.3 days ↓ (95% CI, -1.9 to -0.7) (4.8 vs 6.1 days) ¹	
			615	1.3 days ↓ (95% CI, -1.8 to -0.7) (5.1 vs 6.4 days) ¹	
	Acyclovir	400 mg 5 times a day for 5 days	174		1.3 days ↓ (2.5 vs 3.8 days) ²
Topical	Penciclovir*1%	Every 2 hours during waking hours for 4 days	3057	31% ↓ (HR=1.31; 95% CI, 1.20-1.42) ³	28% ↓ (HR=1.28; 95% CI, 1.17-1.39) ³
			1573	0.7 days ↓ (4.8 vs 5.5) ³	0.6 days ↓ (3.5 vs 4.1) ³
	Acyclovir 5%	5 times a day for 4 days	689	0.5 days ↓ (4.3 vs 4.8) (HR=1.23; 95% CI, 1.06-1.44) ⁴	0.3 days ↓ (2.9 vs 3.2 days, HR=1.20; 95% CI, 1.03-1.40) ⁴
	Docosanol* 10% (available OTC)	5 times daily	737	0.7 days ↓ (95% CI, 0.08-0.92 days) (4.1 vs 4.8 days) ⁵	0.56 days ↓ (95% CI, 0.125-0.69 days) (2.18 vs 2.74 days) ⁵

* FDA approved

CI, confidence interval; ↓, decrease; HR, hazard ratio.

3 to 5 times greater bioavailability) at a dosage of 2 g twice in 1 day significantly decreased the episode duration and time to lesion healing compared with placebo. In the first study (n=603), the mean episode duration was decreased by 1.1 days (5.0 vs 6.1 days; 95% confidence interval [CI], -1.6 to -0.6); in the second study (n=615) by 1.0 day (5.3 vs 6.3 days; 95% CI, -1.0 to -0.5).¹

Oral acyclovir has also been shown to be effective in a well-done RCT (TABLE 1). For a subgroup of patients who started acyclovir in the prodrome or erythema stage, the duration decreased (2.5 vs 3.9 days, $P=.02$), but in the papular stage, it did not decrease significantly (2.5 vs. 3.6 days, $P=.36$).²

Topical treatments speed healing, reduce pain

Topical penciclovir 1% cream decreases the duration of lesion healing and pain compared with a vehicle control, as shown by 2 RCTs (n=3057, 1573). Patients initiated self-treatment every 2 hours during waking hours for 4 days.

In one RCT, the treatment patients lost classic lesions 31% faster than the placebo group. In another trial, healing of classical lesions was faster by 0.7 days (4.8 vs 5.5). Benefits were achieved in both the early ($P=.001$) and later stages ($P=.0055$) of recurrence.³

Two RCTs of topical acyclovir 5% cream, 5 times a day for 4 days (n=689, 699) showed that topical acyclovir, compared with placebo, shortened the duration of an outbreak by 0.5 day (4.3 vs 4.8) and 0.6 day (4.6 vs 5.2), respectively.⁴ When it comes to prophylaxis, several studies have shown that oral valacyclovir and sunscreen may be effective for prophylaxis of herpes labialis (TABLE 2).⁶⁻⁸

Recommendations from others

The BMJ Clinical Evidence Guideline reiterates that oral agents (acyclovir or valacyclovir) and topical agents (acyclovir or penciclovir) slightly reduce healing time and duration of pain in treating recurrent attack. As prophylaxis, oral acyclovir or sunscreen are likely to be beneficial.⁹

FAST TRACK

Oral valacyclovir is the best prophylaxis for herpes, reducing severity and frequency of outbreaks

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TABLE 2

Valacyclovir and sunscreen: Helpful in preventing a herpes labialis outbreak

DRUG	REGIMEN	N	OUTCOME (VS PLACEBO)
Valacyclovir (oral)	500 mg daily	98	24%↓; attack rate, 38% vs 62%; NNT=4 ⁶
Sunscreen	Various	19	Attack rate, 0% vs 71%; NNT=1 ⁷
Sunscreen	Various	19	Attack rate, 5% vs 58%; NNT=2 ⁸

↓, decrease; NNT, number needed to treat

UpToDate reports that recurrent herpes labialis is usually not treated with antivirals unless a prodromal stage can be identified. In these cases, oral acyclovir or penciclovir cream can be prescribed for 4 days' duration. Chronic suppressive therapy can be useful in immunocompetent patients with more than 2 episodes in 4 months, and for recurrences associated with systemic complications or those that affect job performance. As prophylaxis, oral acyclovir (200 mg 3–5 times a day) is generally used, but valacyclovir (500 mg once daily) is also effective.¹⁰ ■

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