

## Real-World Benefits of Acyclovir Buccal Adhesive Tablets

A review of case reports.



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Large, randomized, double-blinded, placebo-controlled trials are critically important for us to evaluate the safety and efficacy of new medications under clinical development. However, clinical experience and case studies in the real world are also of vital importance to understand how a medicine actually works in patients outside of clinical trials.

Because of the pain and stigma associated with “cold sores” or “fever blisters,” stopping progression from prodrome to the blister stage and ensuring fewer future recurrences are of particular interest to our patients. To date, available interventions have not proven particularly effective in the latter regard. However, Phase 3 data have demonstrated clinical benefit of a novel formulation of acyclovir buccal tablet 50mg, or ABT-50mg (Sitavig, Cipher Pharmaceuticals), for recurrent herpes simplex labialis in immunocompetent adults,<sup>1</sup> making ABT-50mg the first antiviral drug that has demonstrated a reduction in the number of cold sore outbreaks with episodic treatment. And, importantly, results of recently published case studies show real-world patient experiences with acyclovir buccal adhesive tablets also demonstrate a reduction in cold sore outbreaks.<sup>2</sup>

### CASE REPORTS

In both reported cases,<sup>2</sup> patients with a history of recurrent cold sores (with viral cultures confirming HSV-1 as the causative agent of labial herpes) reported less frequent outbreaks with episodic treatment with ABT-50mg.

In the first case, a 23-year-old female reported a 10-year history of painful labial herpes on her lateral upper lip with recurrences on an average of every 60.4 days over five years. Previous treatments included docosanol 10% cream or penciclovir 1%. This patient was prescribed acyclovir buccal adhesive tablet monotherapy—she applied ABT-50mg as a single dose upon prodrome (See Figure 1) and reported that no vesicles appeared after she started treatment. At this point, she was instructed to treat again upon any recurrence. Her first recurrence occurred 142 days later, more than twice as long as her average time between previous outbreaks. With continued use of ABT-50mg as needed, the patient reported a



Figure 1



Figure 2

recurrence about once every nine months.

In the second case, a 66-year-old male patient reported recurrent bouts of labial herpes approximately every three months. Prior to trying ABT-50mg therapy, the patient treated outbreaks with valacyclovir 2000mg and reported that topical antiviral creams had not worked. The patient was prescribed ABT-50mg—81 days after initial presentation, the patient used his first ABT-50mg upon prodrome. (See Figure 2) With his first treatment, the patient said he still developed vesicles, but reported less pain and tenderness. He was instructed to treat with ABT-50mg upon recurrence. He reported not needing his second dose until 146 days later, and a third dose 213 days after the second. Nine months later he had not had a recurrence.

Both patients reported satisfaction with treatment and noted that treatment did not interfere with eating or drinking.

### DISCUSSION

ABT-50mg is indicated for the treatment of recurrent herpes labialis in immunocompetent adults. Rapid relief of symptoms associated with recurrences and prompt resolution of visible lesions are important in this most stigmatizing skin disorder. There are many ways to accomplish these goals, both through the application of prescription and over-the-counter topical antiviral preparations and via the administration of oral acyclovir and its various analogues. While immediate alleviation of signs and symptoms as well as interfering with progression from prodrome to overt vesiculation are desirable, to the labial herpes sufferer, primary prevention of recurrence is even more attractive. Results of the Phase 3 LIP trial indicate that usage, especially

## HSV-1 FACTS

- Herpes simplex virus-1 (HSV-1) infection is estimated to affect 85 percent of the world's population
- About 40 percent of these patients manifest clinical infections as many carry the virus asymptomatically
- Patients with frequent herpes labialis infections experience at least four episodes per year
- HSV outbreaks are highly stigmatized and affect quality of life, making early, effective treatments essential

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when starting within one hour of prodrome onset, can hasten episode resolution, reduce time to healing of the primary lesion, reduce the number of blistering episodes and increase the time between subsequent outbreaks.<sup>1</sup> However, the real allure of this medication lies in the latter two properties. By achieving extremely high acyclovir concentrations at the site of labial herpes infection, this agent is uniquely able to actually change the course of the disease. The ABT-50mg group had a mean improvement of 105 days free from cold sores compared to placebo.<sup>1</sup> Reliance on this simple, single-dose acyclovir therapy should enhance

compliance while also obviating worries about potentially serious systemic ramifications (such as nephrotoxicity<sup>3</sup>) since plasma levels of drug are quite low.<sup>4</sup> It is reasonable to speculate that this particular acyclovir dosage form achieves clinical benefit due to a locally-targeted antiviral assault. Despite low acyclovir plasma concentration, the buccal adhesive tablet provides extremely high concentrations in saliva and both oral and labial tissue.<sup>4</sup> In this manner, the overall viral load may be reduced by addressing the likely HSV-1 reservoirs—not only in the trigeminal ganglia—but in both the peripheral nerves and soft tissues.

A reduction of recurrences has previously required once- or twice-daily ingestion of an oral antiviral medication over a protracted time period. We are all aware that adherence falls off significantly over time for virtually all skin diseases, especially when the patient is expected to take (or apply) medication every single day. ABT-50mg is the first antiviral drug that has demonstrated a reduction in the number of fever blister episodes following episodic treatment. As these two case histories illustrate, patient satisfaction is excellent. Use of the drug was considered to be convenient and simple by members of both sexes and of different age groups. Although we do not yet have a “cure” for labial HSV-1 infection, we do have a way to mitigate against the disorder's adverse effect on an individual's life by reducing the number of lesions progressing from prodrome to the blister stage and increasing the time to recurrence of the next herpes labialis episode. ■

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## ABT-50mg: An Innovative Delivery System

Sitavig (Cipher Pharmaceuticals) is a 50mg acyclovir mucoadhesive buccal tablet that uses Lauriad technology to provide a sustained release of active drug within the oral cavity and labial mucosa. The drug is designed to be applied to the gum in the canine fossa

above the incisor tooth, where it stays in place and slowly dissolves over 12-14 hours releasing the drug directly into the oral cavity. In this way, drug levels are rapidly detectable in the saliva and labial mucosa within minutes and sustained for greater than 24 hours.

