

PJ PRACTICE CHECKLIST

ACICLOVIR CREAM FOR COLD SORES

A topical formulation of aciclovir (Zovirax cold sore cream) can now be sold over the counter for treatment of cold sores. This card outlines points to consider when counterprescribing the product. It also outlines the natural history of cold sores and reviews the clinical data on use of aciclovir

COUNTERPRESCRIBING POINTS

- **When to use** — Treatment should be started as soon as prodromal symptoms, such as tingling or burning, occur. Cream is licensed for use five times a day for five days, continued for another five days if cold sore is not healed after this time
- **Infants** — Refer for medical supervision. Herpes simplex infection is sometimes severe in the very young
- **Other drug therapy** — Refer patients taking immunosuppressant drugs (eg, oral steroids, cytotoxic drugs, cyclosporin and some antirheumatic drugs)
- **Severity** — Refer patients who present with spreading lesions, with abnormally severe infection or with symptoms of systemic disturbance (such as fever)
- **Time scale** — Refer if condition does not heal within three weeks
- **Eczema or skin sensitivity** — Patients with eczema or a history of sensitivity to topical formulations should exercise particular care. Should the cold sore appear to worsen significantly after application of the cream, the patient should be referred
- **Propylene glycol** — Avoid use of cream in patients with a history of sensitivity to propylene glycol
- **Pregnancy** — Despite negligible systemic absorption following topical application, good practice dictates that use in pregnancy should be avoided
- **Caution** — Aciclovir cream should not be used inside the mouth or in the eyes
- **Legal status** — Only the OTC product (Zovirax cold sore cream) should be sold without prescription. Zovirax cream remains POM

WHAT ARE COLD SORES?

Cold sores are lesions produced by the herpes simplex virus. Typically, the blisters appear in the lip area and, for this reason, the term herpes simplex labialis is used often in the medical literature to describe the condition. The lesions are sometimes also called fever blisters.

IS GENITAL HERPES CAUSED BY SAME VIRUS?

Both conditions are caused by the herpes simplex virus but different types are involved. Cold sore lesions

almost invariably involve the type 1 virus (HSV₁). Genital infection is associated more commonly with the type 2 virus (HSV₂), although HSV₁ is being isolated increasingly frequently in genital infection too.

SITES AFFECTED: The nose, the oropharynx, the cervix, the intestines and the cornea are all potential sites of infection by herpes simplex viruses. Infection of the nail bed produces lesions known as herpetic whitlow. The oro-pharynx and the lips are the most common sites of primary lesions.

WHY DO COLD SORES OFTEN RECUR?

As yet there is no cure for cold sores. Clearance of the lesions is not accompanied by eradication of the virus. Following the primary attack, the virus retreats into the nerve ganglia and lies dormant until reactivated by trigger factors. Variability in the efficiency of the immune system is the most likely explanation for why some individuals are more susceptible to recurrence of cold sores than others.

COMMON TRIGGER FACTORS:

Other infections, physical abrasions, sunlight, general ill-health, specific drugs such as 5-fluorouracil, and immunosuppressant drugs in general, are commonly cited as trigger factors for cold sores. All are plausible. Experimental exposure to ultraviolet radiation of patients with a history of sun-induced herpes labialis shows that some 20 per cent will develop lesions within seven days.



NATURAL HISTORY OF A COLD SORE:

It is said that primary infections with HSV₁ often go unnoticed. Recurrent episodes are characterised by a prodromal stage with itching, burning, tingling and pain. This lasts for anything between a few hours and three days. The prodromal stage is followed by erythema and vesicle formation, usually within 24 to 36 hours. Ulceration and crusting are seen typically within the next 24 hours. During the ulcerative stage virus shedding is at its highest and discomfort most intense. Lesions disappear within the next seven days or so after this active phase. Most cold sores will therefore have healed within about two weeks of initiation.

HOW INFECTIOUS AND DANGEROUS IS HERPES SIMPLEX?

Infected patients can transmit infection to individuals with no prior history of herpes simplex. This means that infants are at special risk. Immunocompromised patients may develop fulminant infections on re-exposure to the virus. Immunity to HSV₁ does not confer immunity to HSV₂. For this reason, genital herpes is often transmitted during sexual contact, even in individuals who are apparently immune to cold sores. Eczematous patients form a special at-risk group as herpes infections can be severe in such patients.

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ACICLOVIR AND HERPES SIMPLEX:

Oral therapy with aciclovir is effective in the management of genital herpes and ocular herpes simplex. For those indications, many authorities consider aciclovir to be an important advance and the drug of first choice, particularly if started sufficiently early. Aciclovir has an innovative mode of action. On entry into the virus-infected cells, the drug is converted to aciclovir triphosphate by the herpes-specific enzyme thymidine kinase and host cell enzymes. The triphosphate then competes with deoxyguanosine triphosphate for incorporation into viral DNA and as a result interrupts viral replication.

IS TOPICAL ACICLOVIR EFFECTIVE IN COLD SORES?

Three distinct types of activity can be distinguished when discussing cold sores: treatment of lesions, aborting a recurrent infection and prophylaxis. The published trials are difficult to interpret because it is not always clear what formulation was used. Of the two types of formulations (ointment and cream) evaluated, positive results were more reproducible with the cream although, with both formulations, inconsistency was observed. The available evidence suggests that the product's effectiveness is only modest.

TREATING ESTABLISHED LESIONS:

The evidence to date suggests that aciclovir cream is of little value in the treatment of formed lesions. No significant decrease in pain or itch can be expected nor is a shortening of the infection likely. Therefore, starting treatment once a cold sore is established would be inappropriate.

ABORTING A COLD SORE:

While some data support the claim that topical aciclovir, applied at the first onset of the prodromal symptoms, may prevent the development of the lesion, other data provide contradictory evidence. Thus, in one study, involving 24 patients receiving placebo cream and 25 patients receiving 5 per cent aciclovir cream, a significant increase in number of abortive lesions was reported. A second small study, using an ointment and including 13 patients, provided some further supportive data. However, a larger placebo-controlled study involving 352 patients who used 10 per cent aciclovir in polyethylene glycol ointment showed no decrease in the percentage of prodromal or erythematous lesions progressing to vesicle or ulcer. Two published studies with the cream formulation suggest that, if applied early, aciclovir shortens the total healing time of subsequent lesions by a day or so. A third, more recent study, failed to confirm this.

PROPHYLAXIS:

Ultraviolet radiation is a known trigger factor for recurrence of cold sores. A study of aciclovir cream, involving 196 patients with a history of sun-induced herpes simplex labialis, failed to show any protective effect against UV radiation-induced recurrence. In contrast, some recent work suggests that sunscreens with a high protection factor are effective for prophylaxis.

IS TOPICAL TREATMENT SAFE?

Aside from some concern about resistance (see below), topical aciclovir has not been associated with any serious adverse effects. Some patients may report transient stinging after first application and flaking of the skin after repeated applications but the frequencies are no higher than seen with placebos.

VIRAL RESISTANCE:

Viral resistance as a result of widespread use of aciclovir is a subject of some concern since such resistance can be induced in vitro. However, the available data do not indicate any substantial risk to immunocompetent individuals although resistant viruses have been recovered in some immunocompromised patients.

SUMMARY:

If aciclovir cream is applied at the first prodromal stage, cold sore lesions may be aborted in some people. In others, treatment may shorten the healing time by about a day. Prophylaxis against sun-induced recurrence is probably better achieved with a total block sunscreen.

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