

ACYCLOVIR (Topical)

INN: Aciclovir 12

Commonly used brand name(s):Zovirax.

A commonly used name is acycloguanosine 6.

Category

Antiviral (topical).

Indications

Note: Bracketed information in the Indications section refers to uses that are not included in U.S. product labeling.

Accepted

Herpes simplex (treatment)³⁴Topical acyclovir is indicated in the treatment of limited non-life-threatening mucocutaneous herpes simplex virus (HSV-1 and HSV-2) infections in immunocompromised patients; 1, 4, 25, 56, 57 however, systemic acyclovir is more effective and may be preferred. 33, 47

[Herpes zoster (treatment adjunct)] * 46³⁴Topical acyclovir is used as adjunctive therapy 33, 47 to improve cutaneous healing of localized herpes zoster 33, 47 in immunosuppressed persons being treated systemically with other treatment regimens 33, 47 for herpes zoster. 26, 27, 28, 29, 33, 34

Resistance to acyclovir, although currently of minor clinical significance, has been reported to develop with prolonged treatment 7 in immunocompromised patients. 33 Resistance does not appear to be significant in patients with normal immune function. 33

Unaccepted

Herpes genitalis (treatment)³⁴Although topical acyclovir is FDA-approved for the treatment of initial herpes genitalis infections caused by herpes simplex virus (HSV), 1, 4, 25, 47, 48, 56, 57 the Centers for Disease Control (CDC) and USP medical experts do not recommend it for use, because oral acyclovir is considerably more effective. 33, 45, 47

Topical acyclovir 33 is not effective in the treatment of recurrent herpes genitalis or herpes febrilis 35 (labialis) infections in nonimmunocompromised patients, 25, 56 although topical acyclovir may cause some reduction in the duration of viral shedding. 25, 56 Also, there is no evidence that topical acyclovir will prevent the transmission of herpes infection to others or that it will prevent recurrent infections in the absence of signs and symptoms of infection. 1, 4, 25, 56, 57, 58

Mechanism of action/Effect:

Acyclovir is converted to acyclovir monophosphate, a nucleotide, by herpes simplex virus (HSV)-coded thymidine kinase. 56, 57, 58 Acyclovir monophosphate is converted to the diphosphate 57 by cellular guanylate kinase 56 and to the triphosphate 56, 57, 58 by a number of cellular enzymes. 56 Acyclovir triphosphate interferes with HSV DNA polymerase and inhibits viral DNA replication. 56, 57, 58 The triphosphate can be incorporated into growing chains of DNA by viral DNA polymerase, resulting in termination of the DNA chain. 56 Since acyclovir is preferentially taken up and selectively converted to the active triphosphate form by HSV-infected cells, it is much less toxic to normal uninfected cells. 1, 4, 56, 57, 58

Precautions to Consider

Carcinogenicity

Lifetime bioassays in rats and mice given daily doses of 50, 150, and 450 mg per kg of body weight (mg/kg) by gavage 56 have not shown any evidence of carcinogenicity. 25 However, in vitro cell transformation assays have given conflicting results, being positive at the highest dose used in one system. 25, 56 The resulting morphologically transformed cells induced tumors when inoculated into immunosuppressed, syngeneic, weanling mice, although results were negative in another animal 33 system. 1, 25, 56

Pregnancy/Reproduction

Fertility³⁴Studies in mice given oral doses of up to 450 mg/kg or in rats given subcutaneous doses of up to 25 mg/kg per day 56 have not shown that acyclovir impairs fertility or reproduction. 56 Female rabbits given acyclovir subcutaneously at a dose of 50 mg/kg per day displayed a significant decrease in implantation efficiency. 56

Pregnancy³⁴Adequate and well-controlled studies in humans have not been done. 25, 56

Studies done in rats (given subcutaneous doses) and rabbits (given subcutaneous or intravenous doses) of up to 50 mg/kg daily and in mice given oral doses of up to 450 mg/kg daily have not shown that acyclovir causes adverse effects on the fetus. 1, 25, 56 In a nonstandard test in rats, fetal abnormalities, such as head and tail anomalies, were observed following subcutaneous administration of acyclovir at a very high dose, which was associated with toxicity in the maternal rat. 56, 57

FDA Pregnancy Category C. 55, 56

Breast-feeding

It is not known whether topical acyclovir is distributed into breast milk. 25, 56 After oral administration of acyclovir, concentrations that ranged from 0.6 to 4.1 times the corresponding plasma levels have been documented in the breast milk of two women. 56 However, acyclovir is unlikely to be distributed into breast milk in significant amounts following topical administration, since the total daily dose is small, even though absorption through diseased skin is moderate. 1, 4

Pediatrics

Appropriate studies on the relationship of age to the effects of topical acyclovir have not been performed in the pediatric population. Safety and efficacy have not been established. 56, 57 However, limited data are available about the use of oral acyclovir in the pediatric population, and no unusual toxicity or pediatrics-specific problems have been observed in studies done in children using doses of up to 3000 mg per square meter of body surface per day and 80 mg/kg per day. 39, 40, 41, 42, 43, 44

Geriatrics

Appropriate studies on the relationship of age to the effects of topical acyclovir have not been performed in the geriatric population. However, no geriatrics-specific problems have been documented to date.