XERESE® (acyclovir and hydrocortisone) cream for topical use

Indications and Usage

XERESE, a combination of acyclovir, a herpes simplex virus nucleoside analog DNA polymerase inhibitor, and hydrocortisone, a corticosteroid, is indicated for the early treatment of recurrent herpes labialis (cold sores) to reduce the likelihood of ulcerative cold sores and to shorten the lesion healing time in adults and children (6 years of age and older).

Dosage and Administration

Topically apply XERESE 5 times per day for 5 days. Therapy should be initiated as early as possible after the first signs and symptoms (i.e., during the prodrome or when lesions appear).

Dosage Forms and Strengths

Topical cream containing 5% acyclovir and 1% hydrocortisone.

Warnings and Precautions

None.

Adverse Reactions

Common adverse reactions (<1%) were local skin reactions:
- Drying or flaking of the skin; burning or tingling, erythema; pigmentation changes; application site reactions including signs and symptoms of inflammation.

Drug Interactions

No drug interaction studies have been performed with XERESE.

Use in Specific Populations

Immunocompromised Patients: Benefit has not been adequately assessed.

See 17 for Patient Counseling Information and FDA-approved patient labeling.

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Acyclovir, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]-6H-purin-6-one, is a synthetic purine nucleoside analogue with inhibitory activity against herpes simplex viruses type 1 (HSV-1) and type 2 (HSV-2) in cell culture and in vivo. The inhibitory activity of acyclovir is highly selective due to its affinity for the enzyme thymidine kinase (TK) encoded by HSV. This viral enzyme converts acyclovir into acyclovir monophosphate, a nucleotide analogue. The monophosphate is further converted into diphosphate by cellular guanylate kinase and into triphosphate by a number of cellular enzymes. In cell culture, acyclovir triphosphate blocks replication of herpes viral DNA. This inhibition is accomplished in 3 ways: 1) competitive inhibition of viral DNA polymerase, 2) incorporation into and termination of the growing viral DNA chain, and 3) inactivation of the viral DNA polymerase.

Hydrocortisone is the main glucocorticoid secreted by the adrenal cortex. It is used topically for its anti-inflammatory effects which suppress the clinical manifestations of the disease in a wide range of disorders where inflammation is a prominent feature.

Antiviral Activity

The quantitative relationship between the cell culture susceptibility of herpes viruses to antivirals and the clinical response to therapy has not been established in humans, and virus sensitivity testing has not been standardized. Sensitivity testing results, expressed as the concentration of drug required to inhibit by 50% the growth of virus in cell culture (EC_{50}), vary greatly depending upon a number of factors. Using plaque-reduction assay on Vero cells, the median EC_{50} value of acyclovir against clinical herpes virus isolates (subjects receiving placebo) was 1.3 μM (range: <0.56 to 3.3 μM).

Resistance

Resistance of HSV to acyclovir can result from qualitative and quantitative changes in the viral TK and/or DNA polymerase. Clinical isolates of HSV with reduced susceptibility to acyclovir have been recovered from immunocompromised subjects, especially with advanced HIV infection. While most of the acyclovir-resistant mutants isolated from immunocompromised subjects thus far have been found to be TK-deficient mutants, other mutants involving the viral TK gene (TK partial and TK altered) and DNA polymerase have been isolated. TK-negative mutants may cause severe disease in infants and immunocompromised adults.

The possibility of viral resistance to acyclovir should be considered in patients who show poor clinical response during therapy.
13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Systemic exposure following topical administration of acyclovir is minimal. Results from previous studies of carcinogenicity, mutagenesis and fertility for acyclovir and hydrocortisone are not included in the full prescribing information for XERESE due to the minimal exposures that result from dermal application. Information on these studies following systemic exposure is available in the full prescribing information for acyclovir and hydrocortisone products approved for oral or parenteral administration. Dermal carcinogenicity studies have not been conducted.

14 CLINICAL STUDIES

14.1 Clinical Trial Experience in Adults
In a double-blind, clinical trial, 1443 subjects with recurrent labial herpes were randomized to receive XERESE, 5% acyclovir in XERESE vehicle or vehicle alone. Subjects had, on average, 5.6 episodes of herpes labialis in the previous 12 months. The median age was 44 years (range 18 to 80 years), 72% were female, and 91% were Caucasian. Subjects were instructed to initiate treatment within 1 hour of noticing signs or symptoms and continue treatment for 5 days, with application of study medication 5 times per day. Ulcerative cold sores occurred in 58% of the subjects treated with XERESE compared to 74% in subjects treated with vehicle and 65% in subjects treated with 5% acyclovir in XERESE vehicle. The mean time to skin normalization was approximately 1.6 days shorter in the subjects treated with XERESE compared to vehicle. Clinical signs in terms of size of the cold sore and symptoms such as tenderness were reduced with XERESE as compared to vehicle.

14.2 Clinical Trial Experience in Pediatric Subjects
An open label safety trial in adolescents with recurrent herpes labialis was conducted in 134 subjects. Subjects had, on average, 4 episodes of herpes labialis in the previous 12 months. The median age was 14 years (range 12 to 17 years); 50% were female and all were Caucasian. XERESE was applied using the same dosing regimen as in adults and subjects were monitored for adverse events and selected efficacy parameters. The safety profile of XERESE appeared similar to that observed in adults.

PATIENT INFORMATION

XERESE® (sér-e-eze)
(acyclovir and hydrocortisone) Cream 5%/1% Important information: XERESE is for use on cold sores on the lips and around the mouth only. XERESE should not be used in eyes, mouth, nose or on your genitals.

What is XERESE?
• XERESE is a prescription medicine used in people 6 years of age and older to shorten the healing time of cold sores (herpes labialis) and lower the chance of a cold sore becoming worse (ulcerating).
• XERESE is not a cure for cold sores.
• It is not known if XERESE is safe and effective in children less than 6 years of age.

What should I tell my healthcare provider before using XERESE?
Before using XERESE, tell your healthcare provider about all of your medical conditions, including if you:
• become sick very easily (have a weak immune system)
• are pregnant or plan to become pregnant. It is not known if XERESE will harm your unborn baby.
• are breastfeeding or plan to breastfeed. It is not known if XERESE passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I use XERESE?
• Use XERESE exactly as your healthcare provider tells you to use it.
• Use XERESE as soon as you have the first symptom of a cold sore such as itching, redness, burning or tingling. Do not use XERESE if the cold sore is very painful or not getting better.
• Avoid unnecessary rubbing of the affected area to avoid aggravating or transferring the infection.

What are the possible side effects of XERESE?
The most common side effects of XERESE are skin reactions at the treatment site and may include:
• dry skin or flaking, itching or burning after you apply XERESE, redness, changes in skin color where the cream is applied, and swelling.

How should I store XERESE?
• Store XERESE at room temperature between 68°F to 77°F (20°C to 25°C). Do not freeze XERESE.

Keep XERESE and all medicines out of the reach of children.

General information about the safe and effective use of XERESE
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use XERESE for a condition for which it was not prescribed. Do not give XERESE to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about XERESE that is written for health professionals.

What are the ingredients in XERESE?
Active ingredients: acyclovir and hydrocortisone
Inactive ingredients: cetostearyl alcohol, mineral oil, Poloxamer 188, propylene glycol, isopropyl myristate, sodium lauryl sulfate, white petrolatum, citric acid, sodium hydroxide and water. May also contain hydrochloric acid.

Manufactured for:
Valeant Pharmaceuticals North America LLC
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Manufactured by:
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For more information call 1-800-321-4576.
This Patient Information has been approved by the U.S. Food and Drug Administration. Rev. 02/2014
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