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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

ZIRGAN (ganciclovir ophthalmic gel) 0.15% is indicated for the treatment of acute herpetic keratitis (dendritic ulcers).

2 DOSAGE AND ADMINISTRATION

The recommended dosing regimen for ZIRGAN is 1 drop in the affected eye 5 times per day (approximately every 3 hours while awake) until the corneal ulcer heals, and then 1 drop 3 times per day for 7 days.

3 DOSAGE FORMS AND STRENGTHS

ZIRGAN contains 0.15% of ganciclovir in a sterile preserved topical ophthalmic gel.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

• ZIRGAN is indicated for topical ophthalmic use only.
• Patients should not wear contact lenses if they have signs or symptoms of herpetic keratitis or during the course of therapy with ZIRGAN.

6 ADVERSE REACTIONS

Most common adverse reactions reported in patients were blurred vision (60%), eye irritation (20%), punctate keratitis (5%), and conjunctival hyperemia (5%).

7 CLINICAL PHARMACOLOGY

ZIRGAN (ganciclovir ophthalmic gel) 0.15% contains the active ingredient, ganciclovir, which is a guanosine derivative that, upon phosphorylation, inhibits DNA polymerase by inhibiting the synthesis of viral DNA in 2 ways: competitive inhibition of viral DNA-polymerase and direct incorporation into viral primer strand replication by herpes simplex viruses (HSV). Ganciclovir is transformed by viral and cellular thymidine kinases (TK) to ganciclovir monophosphate, which is then converted to ganciclovir triphosphate (GTP) by cellular thymidine kinases (TK). GTP acts as an antiviral agent by inhibiting the synthesis of viral DNA in 2 ways: competitive inhibition of viral DNA-polymerase and direct incorporation into viral primer strand DNA, resulting in DNA chain termination and prevention of replication.

11 DESCRIPTION

The estimated maximum daily dose of ganciclovir administered as 1 drop, 5 times per day is 0.375 mg. Compared to maintenance doses of systemically administered ganciclovir (900 mg [oral valganciclovir]) and 5 mg [for ganciclovir], the ophthalmically administered daily dose is approximately 0.04% and 0.1% of the oral dose and 9 doses, respectively, thus minimal systemic exposure is expected.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertility

Carcinogenicity: Ganciclovir was not mutagenic in the Ames Salmonella assay at concentrations of 500 mg/liter. Ganciclovir caused decreased mating behavior, decreased fertility, and an increased incidence of infertility in female mice following intravenous doses of 90 mg/kg/day, approximately 14,000 times the human ocular dose.

14 CLINICAL STUDIES

14.1 HOW SUPPLIED/STORAGE AND HANDLING

ZIRGAN is supplied in 5 grams of a sterile, preserved, clear, colorless, topical ophthalmic gel containing 0.15% of ganciclovir in a polyethylene oxide gel.

17 PATIENT COUNSELING INFORMATION

This product is sterile when packaged. Patients should be advised not to allow the dropper tip to touch any surface, as this may contaminate the gel.

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