HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all of the information needed to use ZIRGAN® safely and effectively. See full prescribing information for ZIRGAN.

ZIRGAN (ganciclovir ophthalmic gel) 0.15%,
for topical ophthalmic use
Initial U.S. approval: 1989

---------- INDICATIONS AND USAGE ----------

ZIRGAN is a nucleoside analog antiviral indicated for the treatment of acute herpetic keratitis (dendritic ulcers) in adults and pediatric patients aged 2 years and older. (1)

---------- DOSAGE AND ADMINISTRATION ----------

Apply 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. (2)

---------- DOSAGE FORMS AND STRENGTHS ----------

Ophthalmic gel: 0.15% ganciclovir. (3)

---------- CONTRAINDICATIONS ----------

None.

---------- WARNINGS AND PRECAUTIONS ----------

- ZIRGAN is indicated for topical ophthalmic use only. (5.1)
- Patients should not wear contact lenses if they have signs or symptoms of herpetic keratitis or during the course of therapy with ZIRGAN. (5.2)

---------- ADVERSE REACTIONS ----------

Most common adverse reactions were blurred vision (60%), eye irritation (20%), punctate keratitis (5%), and conjunctival hyperemia (5%). (6)

To report SUSPECTED ADVERSE REACTIONS, contact Bausch + Lomb Incorporated, at 1-800-553-5340 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 1/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

ZIRGAN is indicated for the treatment of acute herpetic keratitis (dendritic ulcers) in adults and pediatric patients aged 2 years and older.

2 DOSAGE AND ADMINISTRATION

The recommended dosage 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

Ophthalmic gel: 0.15% ganciclovir.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Topical Ophthalmic Use Only

ZIRGAN is indicated for topical ophthalmic use only.

5.2 Avoidance of Contact Lenses

Patients should not wear contact lenses if they have signs or symptoms of herpetic keratitis or during the course of therapy with ZIRGAN.

5.3 Risk of Contamination

Do not allow the tip of the container to touch any surface, as this may contaminate the ointment. If pain develops, or if redness, itching, or inflammation becomes aggravated, the patient should be advised to consult a physician.

6 ADVERSE REACTIONS

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available human data on use of ZIRGAN or ganciclovir during pregnancy to inform any drug-associated risk. Intravenous administration of ganciclovir to pregnant mice or rabbits during organogenesis or during the pre/postnatal period did not produce adverse embryofetal or offspring effects at clinically relevant doses *(see Data)*.

The background risk in the U.S. general population of major birth defects is 2 to 4% and the risk of miscarriage is 15 to 20% of clinically recognized pregnancies.

Data

Animal Data

Daily intravenous doses of ganciclovir were administered to pregnant mice [up to 108 mg/kg/day, approximately 1400 times the maximum recommended human ocular dose (RHOD) of 0.375 mg] and rabbits [up to 60 mg/kg/day, approximately 2400 times the maximum RHOD], and also to female mice [up to 90 mg/kg, approximately 1174 times the maximum RHOD] prior to mating, during gestation, and during lactation. Fetal resorptions were present in at least 85% of rabbits and mice. Additional effects observed in rabbits included fetal growth retardation, embryolethality, teratogenicity, and/or maternal toxicity. Teratogenic changes included cleft palate, anophthalmia/microphthalmia, aplastic organs (kidney and pancreas), hydrocephaly and brachygnathia. A maternal no observed adverse effect level (NOAEL) was observed at 36 mg/kg/day (approximately 470 times higher than the maximum RHOD, based on body surface area) in mice and at 6 mg/kg/day (approximately 240 times higher than the maximum RHOD, based on body surface area) in rabbits.

In pre/postnatal development studies in mice, there were maternal/fetal toxicity and embryolethality which included fetal effects of hypoplasia of the testes and seminal vesicles in the male offspring, as well as pathologic changes in the nonglandular region of the stomach. A maternal no observed adverse effect level (NOAEL) was observed at 20 mg/kg/day (approximately 261 times higher than the maximum RHOD, based on body surface area).

8.2 Lactation

Risk Summary

No data are available regarding the presence of ganciclovir in human milk, the effects on the breastfed infant, or the effects on milk production. It is not known whether topical ophthalmic ganciclovir administration could result in sufficient systemic absorption to produce detectable quantities in breast milk. Animal data indicate that ganciclovir is excreted in the milk of lactating rats. Caution should be exercised when ZIRGAN is administered to nursing mothers.

8.3 Females and Males of Reproductive Potential

Infertility

It is not known whether topical ophthalmic ganciclovir administration could result in sufficient absorption to impair fertility in humans. Animal data indicate decreased fertility in female mice following intravenous doses at 90 mg/kg/day, approximately 1174 times the maximum RHOD (based on body surface area), and decreased fertility and hypospermatogenesis in male mice and dogs following intravenous doses at 10 mg/kg/day for mice, approximately 130 times the maximum RHOD (based on body surface area), and 3.6 mg/kg/day for dogs, approximately 240 times the maximum RHOD (based on body surface area).

8.4 Pediatric Use

The safety and effectiveness of ZIRGAN for the treatment of acute herpetic keratitis (dendritic ulcers) have been established in pediatric patients aged 2 years and older. Use of ZIRGAN for this indication is supported by evidence from adequate and well-controlled studies.

The safety and effectiveness of ZIRGAN have not been established in pediatric patients below the age of 2 years.

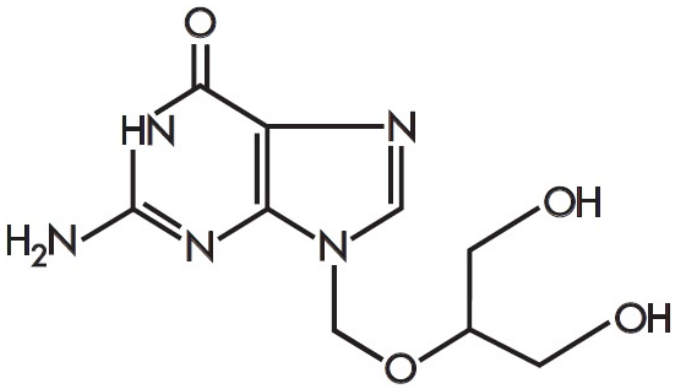
8.5 Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and younger patients.

11 DESCRIPTION

ZIRGAN (ganciclovir ophthalmic gel) 0.15% contains ganciclovir, a nucleoside analog antiviral. ZIRGAN is a sterile, preserved, clear, colorless, ophthalmic gel for topical ophthalmic use.

The chemical name is 9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]guanine (CAS number 82410-32-0). Ganciclovir is represented by the following structural formula:



Ganciclovir has a molecular weight of 255.23, and the empirical formula is $C_9H_{13}N_5O_4$.

Each gram of gel contains: ACTIVE: ganciclovir 1.5 mg (0.15%). INACTIVES: carbomer homopolymer, water for injection, sodium hydroxide (to adjust the pH to 7.2–7.6), mannitol. PRESERVATIVE: benzalkonium chloride 0.075 mg (0.0075%).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

ZIRGAN is an antiviral drug *[see Microbiology (12.4)]*.

12.3 Pharmacokinetics

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 of 900 mg (oral valganciclovir) and 5 mg/kg (IV ganciclovir), the ophthalmically administered daily dose is approximately 0.04% and 0.1% of the oral dose and IV doses, respectively, thus minimal systemic exposure is expected.

12.4 Microbiology

Mechanism of Action

ZIRGAN contains ganciclovir, a guanosine derivative that upon phosphorylation inhibits DNA replication by herpes simplex viruses (HSV). Ganciclovir is transformed by viral and cellular thymidine kinases (TK) to ganciclovir triphosphate, which works 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.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Ganciclovir was carcinogenic in the mouse at oral doses of 20 and 1,000 mg/kg/day (approximately 3,000 and 160,000 times the human ocular dose of 6.25 mcg/kg/day, assuming complete absorption). At the dose of 1,000 mg/kg/day there was a significant increase in the incidence of tumors of the preputial gland in males, forestomach (nonglandular mucosa) in males and females, and reproductive tissues (ovaries, uterus, mammary gland, clitoral gland, and vagina) and liver in females. At the dose of 20 mg/kg/day, a slightly increased incidence of tumors was noted in the preputial and harderian glands in males, forestomach in males and females, and liver in females. No carcinogenic effect was observed in mice administered ganciclovir at 1 mg/kg/day (160 times the human ocular dose). Except for histocytic sarcoma of the liver, ganciclovir-induced tumors were generally of epithelial or vascular origin. Although

the preputial and clitoral glands, forestomach and harderian glands of mice do not have human counterparts, ganciclovir should be considered a potential carcinogen in humans.

Mutagenesis

Ganciclovir increased mutations in mouse lymphoma cells and DNA damage in human lymphocytes *in vitro* at concentrations between 50 to 500 and 250 to 2,000 mcg/mL, respectively.

In the mouse micronucleus assay, ganciclovir was clastogenic at doses of 150 and 500 mg/kg (IV) (24,000 to 80,000 times the human ocular dose) but not 50 mg/kg (8,000 times the human ocular dose). Ganciclovir was not mutagenic in the Ames Salmonella assay at concentrations of 500 to 5,000 mcg/mL.

Impairment of Fertility

Ganciclovir caused decreased mating behavior, decreased fertility, and an increased incidence of embryolethality in female mice following intravenous doses of 90 mg/kg/day (approximately 14,000 times the human ocular dose of 6.25 mcg/kg/day). Ganciclovir caused decreased fertility in male mice and hypospermatogenesis in mice and dogs following daily oral or intravenous administration of doses ranging from 0.2 to 10 mg/kg (30 to 1,600 times the human ocular dose).

14 CLINICAL STUDIES

In one open-label, randomized, controlled, multicenter clinical trial which enrolled 164 patients with herpetic keratitis, ZIRGAN was non-inferior to acyclovir ophthalmic ointment, 3% in patients with dendritic ulcers. Clinical resolution (healed ulcers) at Day 7 was achieved in 77% (55/71) for ZIRGAN versus 72% (48/67) for acyclovir, 3% (difference 5.8%, 95% CI - 9.6%-18.3%). In three randomized, single-masked, controlled, multicenter clinical trials which enrolled 213 total patients, ZIRGAN was non-inferior to acyclovir ophthalmic ointment, 3% in patients with dendritic ulcers. Clinical resolution at Day 7 was achieved in 72% (41/57) for ZIRGAN versus 69% (34/49) for acyclovir (difference 2.5%, 95% CI - 15.6%-20.9%).

16 HOW SUPPLIED/STORAGE AND HANDLING

ZIRGAN (ganciclovir ophthalmic gel) 0.15% is supplied as 5 grams of a sterile, preserved, clear, colorless, topical ophthalmic gel containing 0.15% of ganciclovir in a polycoated aluminum tube with a white polyethylene tip and cap and protective band (NDC 24208-535-35).

Storage

Store at 15°C to 25°C (59°F to 77°F). Do not freeze.

17 PATIENT COUNSELING INFORMATION

When to Consult a Physician

Advise patients to consult a physician if pain develops, or if redness, itching, or inflammation becomes aggravated.

Risk of Contamination

ZIRGAN is sterile when packaged. Advise patients to not allow the dropper tip to touch any surface, as this may contaminate the gel.

Avoidance of Contact Lenses

Advise patients to not wear contact lenses when using ZIRGAN.

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