

ZIRGAN[®]

MATERIAL SAFETY DATA SHEET

Effective Date: 11/11/10 Supersedes: 11/10/10

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Section 1: CHEMICAL PRODUCT AND COMPANY IDENTIFICATION**PRODUCT:**

Product Name: ZIRGAN[®] (ganciclovir ophthalmic gel 0.15%)
Product Code(s):
NDC No(s): NDC No. 42826-605-96 (1 gram tube)
NDC No. 42826-605-50 (5 gram tube)
NDC No. 24208-535-35 (5 gram tube)
NDC No. 24208-535-32 (1 gram tube)

Intended Use: Anti-viral
Chemical Name: NA
Chemical Family: NA

COMPANY IDENTIFICATION:

Bausch & Lomb, Incorporated
1400 N. Goodman Street
Rochester, New York 14609

For Information: 1-800-553-5340

EMERGENCY TELEPHONE NUMBER:

24-Hour Emergency: 1-800-535-5053

Section 2: HAZARDS IDENTIFICATION

CLASSIFICATION: Acute toxicity; Category 5 (GHS)

LABELING:

Pictograms: (None required)

Signal Word: Warning

Hazard Statements: May be harmful if swallowed
May cause eye irritation
May cause skin irritation
May be irritating if inhaled
Avoid inhalation of mists
Do not use if there exists hypersensitivity to any ingredient in this product

Precautionary Statements: Use only in accordance with label instructions and supplied prescribing information.
Avoid release to the environment.
Store product at room temperature: 15-25°C (59-77°F). Protect from freezing.
KEEP OUT OF REACH OF CHILDREN

Section 2: HAZARDS IDENTIFICATION (cont.)**PRECAUTIONS:****FOR OPHTHALMIC USE ONLY****Caution! Pharmacologically Active**

Do Not Use: if there exists hypersensitivity to any ingredient in this product.

Use only in accordance with product prescribing information.

WARNING: KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.

ZIRGAN® is a clear colorless gel containing 0.15% of ganciclovir in a polycoated aluminum tube with a white polyethylene tip and cap. ZIRGAN® ophthalmic gel presents little or no hazards if spilled and no unusual hazard if involved in fire.

IN ANIMAL AND IN VITRO STUDIES GANCICLOVIR (THE ACTIVE COMPONENT OF THE PRODUCT) CAUSED ASPERMATOGENESIS, MUTAGENICITY, TERATOGENICITY, AND CARCINOGENICITY; THEREFORE, IT SHOULD BE CONSIDERED A POTENTIAL TERATOGEN AND CARCINOGEN IN HUMANS. IT MAY CAUSE BIRTH DEFECTS AND/OR DEATH TO THE EXPOSED FETUS. ALL WORK PRACTICES MUST BE DESIGNED TO REDUCE HUMAN EXPOSURE TO THE LOWEST LEVEL. AS WITH ALL PRESCRIPTION MEDICATIONS, PATIENTS MUST FOLLOW THE INSTRUCTIONS AS DIRECTED BY THEIR PHYSICIAN IN ORDER TO SAFELY ADMINISTER THE MEDICATION.

POTENTIAL HEALTH EFFECTS**EYE:**

ZIRGAN® is not anticipated to be a significant route of occupational over-exposure via eye contact. However, it may cause reddening of the eye.

SKIN:

May cause irritation.

INGESTION:

May cause irritation.

INHALATION:

May cause irritation.

CHRONIC HEALTH EFFECTS

Clinical studies involving animals exposed to ganciclovir, the active component of this product, indicate carcinogenic effects and adverse effects on the reproductive system.

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Section 2: HAZARDS IDENTIFICATION (cont.)
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CARCINOGENICITY:

NTP: No ingredients listed.

IARC: No ingredients listed.

OSHA: No ingredients listed.

TARGET ORGANS:

Hematopoietic/blood system, bone marrow, male reproductive system/prostate, female reproductive system and central nervous system.

MEDICAL CONDITIONS AGGRAVATED BY OVER EXPOSURE:

This medicine is not to be taken by mouth. This medicine is not recommended for use in children less than two (2) years in age. If you are using any other eye drops or ointments at the same time as this eye gel, you should leave a five minute interval between the applications of each product into the eye. This eye gel should be applied to the eye last.

If you have any visual disturbances while using this medicine, either from the medicine itself or the condition being treated, you should not drive or operate machinery. May cause blurred vision.

Ganciclovir has the potential to cause cancer and birth defects. It may also inhibit sperm production in men, which may be temporary or permanent, and may suppress fertility in women. These effects are unlikely following instillation of the medicine into the eye due to the low systemic exposure following administration into the eye. However, for these reasons, this medicine should only used when the benefits of treatment outweigh the risks. Follow your physicians orders when using this medication and inform your physician of any other prescription medication and over the counter medications you are taking.

Section 3: COMPOSITION / INFORMATION ON INGREDIENTS
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CAS #	Chemical Identity	Concentration, % W/W	EINECS / ELINCS #
82410-32-0	Ganciclovir	0.15	NA
69-65-8	Mannitol, NF	> 1	200-711-8
9003-01-4	Carbopol 974P	< 1	NA
8001-54-5	Benzalkonium Chloride	< 1	NA

Note: May also contain Sodium Hydroxide to adjust pH.

Section 4: FIRST AID MEASURES

EYES:

If discomfort or irritation develops, immediately discontinue product use and contact your eye care professional. For accidental and non-therapeutic applications, flush eyes with copious amounts of water for at least 20 minutes. Get medical attention.

SKIN:

Remove all contaminated clothing and wash skin with copious amounts of water for at least 20 minutes. Get medical attention if irritation develops.

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Section 4: FIRST AID MEASURES (cont.)**INGESTION:**

Wash out mouth and give plenty of water and bland fluids. **Never give anything by mouth to an unconscious person.** Contact a physician immediately. Provide product prescribing information.

INHALATION:

No inhalation exposure expected with this formulation under normal conditions of use. If inhaled, remove to fresh air. If breathing is difficult, give oxygen. If not breathing, give artificial respiration. Contact a physician immediately.

ADDITIONAL NOTES TO PHYSICIAN:

Always inform your doctor if you are pregnant or planning a pregnancy, before using any medicine. This product should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is not known whether topical ophthalmic ganciclovir administration could result in sufficient systemic absorption to produce detectable quantities in breast milk. Caution should be exercised when ZIRGAN® is administered to nursing mothers.

Ganciclovir is rated as Pregnancy Category C. Adequate and well-controlled studies have not been carried out in pregnant women. Refer to section 11 for more information.

Additional details are available on the package insert or in the Physicians Desk Reference.

Section 5: FIRE FIGHTING MEASURES**FLAMMABLE PROPERTIES:**

Flash Point: Not Applicable

Method: NA

EXTINGUISHING MEDIA:

Water spray/fog, carbon dioxide, dry chemical powder, halon or appropriate foam for surrounding fire.

HAZARDOUS COMBUSTION PRODUCTS:

Emits hazardous products of combustion.

SPECIAL FIRE FIGHTING INSTRUCTIONS:

As in any fire, wear self-contained breathing apparatus and full protective gear. Use water spray to keep fire-exposed containers cool. **Do not** spray water into burning material.

Section 6: ACCIDENTAL RELEASE MEASURES**PERSONAL PRECAUTIONS:**

Wear suitable protective eyewear, clothing, respiratory protection, rubber boots and rubber gloves. Evacuate immediate area. Ensure adequate ventilation. Refer to Section 8.

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Section 6: ACCIDENTAL RELEASE MEASURES (cont.)

ENVIRONMENTAL PRECAUTIONS:

Prevent spilled material from entering storm sewers or drains, waterways, and contact with soil.

METHODS AND MATERIALS FOR CONTAINMENT AND CLEANING UP:

Ventilate area. Contain spilled product. For small spills, add suitable absorbent material. Scoop up and place in an appropriate liquid-tight container equipped with a tight cover for disposal. For large spills, dike spilled material or otherwise contain material to ensure runoff does not reach a waterway. Place spilled material in an appropriate, liquid-tight container equipped with a tight cover for disposal. Minimize contact of spilled material with soils to prevent runoff to surface waterways.

Dispose of in accordance with Section 13.

Section 7: HANDLING AND STORAGE

HANDLING:

Use only in accordance with product literature. Avoid contact with product. Wash thoroughly with warm water and soap after handling. Use caution to prevent puncturing containers. No special protective equipment or procedures are required in the clinical or home environment.

STORAGE:

Store product in original container, with cap tightly closed, at a controlled room temperature: 15-25°C (59-77°F). Do not freeze.

Shelf Life: Expiration date is listed on each package.

KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.

Section 8: EXPOSURE CONTROLS / PERSONAL PROTECTION

CONTROL PARAMETERS:

OCCUPATIONAL EXPOSURE LIMITS / GUIDELINES

CAS #	COMPONENT NAME	OSHA PEL TWA /STEL	ACGIH TLV TWA /STEL	NIOSH REL TWA /STEL	IRELAND TWA /STEL	HSE TWA /STEL	UNITS
82410-32-0	Ganciclovir	NE NE	NE NE	NE NE	NE NE	NE NE	NA
69-65-8	Mannitol, NF	NE NE	NE NE	NE NE	NE NE	NE NE	NA
9003-01-4	Carbopol 974P	NE NE	NE NE	NE NE	NE NE	NE NE	NA
8001-54-5	Benzalkonium Chloride	NE NE	NE NE	NE NE	NE NE	NE NE	NA

NOTE: Limits/standards shown for guidance only. Follow applicable regulations.

N/E: Not Established

OSHA: Occupational Safety & Health Administration

TWA: 8-Hour Time-Weighted Average

STEL: Short-Term Exposure Limit

ACGIH: American Conference of Governmental Industrial Hygienists

IOEL: Internal Occupational Exposure Limit

N/A: Not Applicable

PPM: Parts Per Million

C: Ceiling Limit

REL: Recommended Exposure Limit

NIOSH: National Institute for Occupational Safety & Health

I: Measured as inhalable fraction of the aerosol

Section 8: EXPOSURE CONTROLS / PERSONAL PROTECTION (cont.)**ENGINEERING CONTROLS:**

Not required during normal clinical use.

In the manufacturing plant, provide adequate ventilation for the raw material handling and compounding process which will maintain the dust and vapor levels below established occupation exposure limits for the ingredients. Ventilation fans should be explosion-proof.

RESPIRATORY PROTECTION:

Not required during normal clinical use.

In the event of a spill, or during material handling and compounding, a NIOSH-certified air-purifying respirator equipped with the appropriate cartridges may be permissible under certain circumstances where airborne concentrations are expected to exceed exposure limits and when adequate oxygen is present. Use a positive pressure air-supplied respirator if there is any potential for an uncontrolled release or any other circumstances where air purifying respirators may not provide adequate protection.

SKIN PROTECTION:

Not required during normal clinical use.

Wash thoroughly with warm water and soap after handling. Impervious chemical resistant gloves and appropriate protective clothing are recommended during material handling and compounding, or when handling bulk product.

EYE PROTECTION:

Not required during normal clinical use.

Use safety glasses (equipped with side-shields) or safety goggles when handling bulk product.

ADDITIONAL PROTECTIVE CLOTHING & EQUIPMENT:

No special recommendations during normal clinical use.

In the manufacturing plant, ensure the availability of safety eyewash/shower stations.

CONTAMINATED EQUIPMENT:

Wash contaminated clothing separately. Wash equipment with soap and water. Release rinse water into an approved wastewater treatment system, or containerize and dispose of in accordance with Section 13. Prevent material from entering storm sewers or drains, waterways, and contact with soil.

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Section 9: PHYSICAL AND CHEMICAL PROPERTIES

Physical State:	Gel
Color:	Clear to opaque
Odor:	No Odor
Odor Threshold:	Not determined
pH-Value:	Not applicable
Melting Point:	Not applicable
Freezing Point:	Not determined
Initial Boiling Point:	Not determined
Flash Point:	Not applicable
Evaporation Rate:	Not determined
Flammability:	Not applicable
Explosion Limits:	Not determined
Vapor Pressure:	Not determined
Vapor Density:	Not determined
Specific Gravity (H₂O=1):	1.0
Solubility:	Miscible in water
Partition Coefficient:	Not applicable
Auto-Ignition Temperature:	Not determined
Decomposition Temperature:	Not determined
Osmolality:	Not determined
Viscosity:	Not determined
Percent Volatile by Volume:	< 1

Section 10: STABILITY AND REACTIVITY**GENERAL:**

Stable

CONDITIONS TO AVOID:

Extreme heat or cold. Do not freeze.

INCOMPATIBLE MATERIALS:

Strong acids, bases, alkali metals, alkali hydrides and silver preparations, as well as strong oxidizing agents.

HAZARDOUS POLYMERIZATION:

Should not occur.

HAZARDOUS DECOMPOSITION PRODUCTS:

Emits toxic fumes, carbon dioxide (CO₂), and carbon monoxide (CO)

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Section 11: TOXICOLOGICAL INFORMATION**Summary of Risks:**

Toxicological information refers to raw materials only. Concentrations and toxicological effects are substantially reduced in the product. For more detailed information, refer to the component MSDS.

Ganciclovir (CAS# 82410-32-0)

IN ANIMAL AND IN VITRO STUDIES, GANCICLOVIR CAUSED ASPERMATOGENESIS, MUTAGENICITY, TERATOGENICITY, AND CARCINOGENICITY; THEREFORE, IT SHOULD BE CONSIDERED A POTENTIAL TERATOGEN AND CARCINOGEN IN HUMANS. IT MAY CAUSE BIRTH DEFECTS AND/OR DEATH TO THE EXPOSED FETUS.

Ganciclovir was carcinogenic in the mouse at oral doses of 20 and 1,000 mg/kg/day (approximately 3,000x and 160,000x 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 (160x 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. 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) (24,000x to 80,000x the human ocular dose) but not 50 mg/kg (8,000x the human dose). Ganciclovir was not mutagenic in the Ames Salmonella assay at concentrations of 500 to 5,000 mcg/mL. Ganciclovir caused decreased mating behavior, decreased fertility, and an increased incidence of embryo lethality in female mice following intravenous doses of 90 mg/kg/day (approximately 14,000x 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 (30x to 1,600x the human ocular dose).

RTECS No.: MF8407000

LD50 Oral (Mouse): > 2000 mg/kg
LD50 Intraperitoneal (Mouse): 1000 mg/kg
LD50 Intravenous (Mouse): 900 mg/kg

Mannitol, NF (CAS# 69-65-8)

Mannitol, NF is non-hazardous as defined in the Federal Hazardous Substance Act. It is also not toxic as defined in OSHA Regulations 29 CFR 1900.1200, Appendix A – health hazard. Dusts, such as finely milled Mannitol, NF can irritate the upper respiratory tract in large quantities, resulting in cough. Excessive ingestion of Mannitol, NF can cause irritation of the stomach, as well as nausea and diarrhea. In extreme cases, vomiting, chills, dizziness, chest pain, cardiac failure and pulmonary edema. Dermal exposure can irritate and discolor the skin, particularly in sensitive areas.

RTECS No.: OP2060000

LD50 Oral (Rat): 13,500 mg/kg
LD50 Oral (Mouse): 22,000 mg/kg

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Section 12: ECOLOGICAL INFORMATION

Chemical Fate Information:

Product administered to patients present a negligible impact on the environment. No additional data is available on the environmental impact of this product. Prevent material from entering storm sewers or drains, waterways, and contact with soil.

Section 13: DISPOSAL CONSIDERATIONS
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All disposal methods must be in compliance with all Federal, State/Provincial and local laws and regulations. Regulations may vary in different locations. Waste characterizations and compliance with applicable laws are the responsibility solely of the waste generator.

Section 14: TRANSPORT INFORMATION
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	US DOT	IATA	IMO	RID/ADR	Canadian DG
Shipping Name:	Not Regulated	Not Regulated	No Information Available	No Information Available	No Information Available
Hazard Class:	NA	NA			
UN Number:	NA	NA			
Package Group:	NA	NA			

There are no unreasonable risks (health, safety, or property), that this product would pose when transported in commerce.

Section 15: REGULATORY INFORMATION

OSHA HAZARD COMMUNICATION STANDARD (29 CFR 1910.1200):

ZIRGAN® is considered hazardous under the Occupational Safety & Health Administration's Hazard Communication Standard.

OSHA DESIGNATIONS:

Not Listed (29 CFR 1910.1000, Table Z)

REACH:

CAS# 82410-32-0 Not Registered
 CAS# 69-65-8 Pre-Registered
 CAS# 9003-01-4 Pre-Registered
 CAS# 8001-54-5 Pre-Registered

TOXIC SUBSTANCE CONTROL ACT (TSCA):

All components of this product are listed on the TSCA inventory list, or are exempt from listing requirements.

RCRA Hazardous Waste (40 CFR 261.33): Not Listed

SARA TITLE III (Superfund Amendments and Reauthorization Act):

- **SECTION 302 (Extremely Hazardous Substances):** Not listed
- **SECTION 311/312 (HAZARD CATEGORIES):** Acute, Chronic
- **SECTION 313 (Toxic Chemicals):** Not Listed

Section 15: REGULATORY INFORMATION (cont.)**FDA DESIGNATIONS:**

Prescription only medication.

NDC No. 42826-605-96 (1 gram tube)

NDC No. 42826-605-50 (5 gram tube)

NDC No. 24208-535-35 (5 gram tube)

NDC No. 24208-535-32 (1 gram tube)

CALIFORNIA PROPOSITION 65:

Ganciclovir (CAS# 82410-32-0): Cancer, Developmental Toxicity, Male Reproductive Toxicity

Section 16: OTHER INFORMATION

To the best of our knowledge, the information contained herein is accurate. However, neither Bausch & Lomb Incorporated nor any of its subsidiaries assumes any liability whatsoever for the accuracy or completeness of the information contained herein. Final determination of suitability of any material is the sole responsibility of the user. All materials may present unknown hazards and should be used with caution. Although certain hazards are described herein, we cannot guarantee that these are the only hazards which exist. NO WARRANTY, EXPRESS OR IMPLIED, OF MERCHANTABILITY, FITNESS OR OTHERWISE IS MADE. In no event shall Bausch & Lomb Incorporated nor any of its subsidiaries be liable for any special, incidental or consequential damages.