Safety Data Sheet

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Section 1: Identification

Product identifier

Product Name
- **Dorzolamide Hydrochloride / Timolol Maleate Ophthalmic Solution**

Product Code
- AB48609; Core No. 486; NDC 24208-0486-10

Relevant identified uses of the substance or mixture and uses advised against

Recommended use
- Finshed Pharmaceutical Product; Dorzolamide HCl/Timolol Maleate Ophthalmic Solution is indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension who are insufficiently responsive to beta-blockers.

Restrictions on use
- Refer to the product insert and/or prescribing information for restrictions on use and contraindications.

Details of the supplier of the safety data sheet

Manufacturer
- Bausch & Lomb

  1400 North Goodman Street
  Rochester, NY 14609
  United States
  bausch.com

Telephone (General)
- 1-800-553-5340

Emergency telephone number

Manufacturer
- 1-800-535-5053 - Infotrac

This safety data sheet is written to provide health, safety and environmental information for people handling this formulated product in the workplace. It is not intended to provide information relevant to consumer use of the product.

Section 2: Hazard Identification

UN GHS

According to: UN Globally Harmonized System of Classification and Labelling of Chemicals (GHS)

Classification of the substance or mixture

UN GHS
- Reproductive Toxicity 2
  Skin Mild Irritation 3
  Eye Mild Irritation 2B

Label elements

UN GHS

WARNING



Hazard statements

- Causes mild skin irritation
  Causes eye irritation
  Suspected of damaging fertility or the unborn child.

Precautionary statements

Prevention

- Do not handle until all safety precautions have been read and understood.
  Wash thoroughly after handling.
  Use personal protective equipment as required.

Response

- IF ON SKIN: Wash with plenty of soap and water.
  If skin irritation or rash occurs: Get medical advice/attention.
  IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
  If eye irritation persists: Get medical advice/attention.

Storage/Disposal

- Keep tightly closed. Store at room temperature 20-25ºC (68-77ºF), to maintain product integrity. Use before date marked on carton and/or container.
  Protect from light.
  Dispose of content and/or container in accordance with local, regional, national, and/or international regulations.

Other hazards

UN GHS

- No data available

Section 3 - Composition/Information on Ingredients

Substances

- Material does not meet the criteria of a substance according to United Nations Globally Harmonized System of Classification and Labelling of Chemicals (GHS)

Mixtures

Composition			
Chemical Name	**Identifiers**	**%**	**Classifications According to Regulation/Directive**
1 N Sodium Hydroxide	**CAS:**1310-73-2 **EINECS:**215-185-5	< 1%	**UN GHS:** Skin Corr. 1A
Benzalkonium Chloride	**CAS:**63449-41-2 **EINECS:**264-151-6	0.0075%	**UN GHS:** Skin Corr. 1B; Acute Tox. Oral 4; Acute Tox. Dermal 4; Aquatic Acute 1
Dorzolamide Hydrochloride	**CAS:**130693-82-2	2% TO 3%	**UN GHS:** NDA
Hydroxyethyl Cellulose	**CAS:**9004-62-0	< 1%	**UN GHS:** Skin Irrit. 2; Eye Irrit. 2A
Mannitol	**CAS:**69-65-8 **EINECS:**200-711-8	1% TO 5%	**UN GHS:** NDA
Sodium Citrate Dihydrate	**CAS:**68-04-2 **EINECS:**200-675-3	< 1%	**UN GHS:** Eye Irrit. 2A

Timolol Maleate	**CAS:**26921-17-5 **EINECS:**248-111-5	0.5% TO 1%	**UN GHS:** NDA
Water	**CAS:**7732-18-5 **EINECS:**231-791-2	Balance	**UN GHS:** Classification criteria not met

The exact percentage of composition has been withheld as a trade secret.

Section 4: First-Aid Measures

Description of first aid measures

Inhalation
- No inhalation exposure expected with this formulation under normal conditions of use. If signs/symptoms develop, get medical attention.

Skin
- Flush with fresh water if contact with skin or eyes. If skin irritation occurs: Get medical advice/attention.

Eye
- For accidental and non-therapeutic applications, flush eyes with copious amounts of water for at least 15 minutes. Get medical attention. If eye irritation persists: Get medical advice/attention.

Ingestion
- No specific treatment is necessary since this material is not likely to be hazardous by ingestion. If large quantities are accidentally ingested (greater than a tablespoon), get medical attention immediately.

Most important symptoms and effects, both acute and delayed

- The following adverse events have occurred either at low incidence (<1%) during clinical trials or have been reported during the use of Dorzolamide HCl Ophthalmic Solution in clinical practice where these events were reported voluntarily from a population of unknown size and frequency of occurrence cannot be determined precisely. They have been chosen for inclusion based on factors such as seriousness, frequency of reporting, possible causal connection to Dorzolamide HCl Ophthalmic Solution, or a combination of these factors: signs and symptoms of systemic allergic reactions including angioedema, bronchospasm, pruritus, and urticaria; Stevens-Johnson syndrome and toxic epidermal necrolysis; dizziness, paresthesia; ocular pain, transient myopia, choroidal detachment following filtration surgery, eyelid crusting; dyspnea; contact dermatitis, epistaxis, dry mouth and throat irritation.

Indication of any immediate medical attention and special treatment needed

Notes to Physician
- Symptoms consistent with systemic administration of beta-blockers or carbonic anhydrase inhibitors may occur, including electrolyte imbalance, development of an acidotic state, dizziness, headache, shortness of breath, bradycardia, bronchospasm, cardiac arrest and possible central nervous system effects. Serum electrolyte levels (particularly potassium) and blood pH levels should be monitored.

Other information

- Have the product container or label with you when calling a poison control center or doctor, or going for treatment.

Section 5: Fire-Fighting Measures

Extinguishing media

Suitable Extinguishing Media
- SMALL FIRES: Dry chemical, CO2, water spray or regular foam.
  LARGE FIRE: Water spray, fog or regular foam.

Unsuitable Extinguishing Media
- No data available

Special hazards arising from the substance or mixture

Unusual Fire and Explosion Hazards
- None known.

Hazardous Combustion Products
- None known.

Advice for firefighters

- Structural firefighters' protective clothing will only provide limited protection. Wear positive pressure self-contained breathing apparatus (SCBA).

Section 6 - Accidental Release Measures

Personal precautions, protective equipment and emergency procedures

Personal Precautions
- No special controls or personal protection required under conditions of intended use. In the event of bulk spills, wear suitable protective eyewear, clothing, protective boots and protective gloves. Evacuate immediate area. Ensure adequate ventilation. Refer to Section 8.

Emergency Procedures
- Keep unauthorized personnel away. Ventilate closed spaces before entering. Stop leak if you can do it without risk.

Environmental precautions

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

Methods and material for containment and cleaning up

Containment/Clean-up Measures
- 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.
Dispose of in accordance with Section 13.

Section 7 - Handling and Storage

Precautions for safe handling

Handling
- No special handling is required. Refer to Section 8. Use only in accordance with product literature. Use only in accordance with product literature.

Conditions for safe storage, including any incompatibilities

Storage
- Keep tightly closed. Store at room temperature 20-25ºC (68-77ºF), to maintain product integrity. Use before date marked on carton and/or container. Protect from light.

Incompatible Materials or Ignition Sources
- None specified.

Section 8 - Exposure Controls/Personal Protection

Control parameters

Exposure Limits/Guidelines
- Refer to the occupational exposure limits / guidelines for the individual product components.

Exposure Limits/Guidelines					
	Result	**ACGIH**	**Canada Quebec**	**NIOSH**	**OSHA**
1 N Sodium Hydroxide (1310-73-2)	Ceilings	2 mg/m3 Ceiling	2 mg/m3 Ceiling	2 mg/m3 Ceiling	Not established
	TWAs	Not established	Not established	Not established	2 mg/m3 TWA

Exposure controls

Engineering Measures/Controls
- Good general ventilation should be used. Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits.

If exposure limits have not been established, maintain airborne levels to an acceptable level.

Personal Protective Equipment

Respiratory
- In the event of a bulk spill, and where risk assessment shows that air-purifying respirators are appropriate, a NIOSH (US) or CEN (EU) -certified air-purifying respirator equipped with HEPA cartridges may be permissible under certain circumstances where airborne concentrations are expected to exceed exposure limits, when adequate oxygen is present and as a backup to engineering controls. 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.

Eye/Face
- Wear protective eyewear (goggles, face shield, or safety glasses) when handling bulk product before closed in final packaging. In the event of a spill, appropriate eye protection should be worn.

Hands
- Wear appropriate gloves.

Skin/Body
- No special personal protection required under conditions of intended use. In the event of a bulk spill, wear appropriate protective clothing.

General Industrial Hygiene Considerations
- Wash thoroughly after handling.

Environmental Exposure Controls
- No data available

Section 9 - Physical and Chemical Properties

Information on Physical and Chemical Properties

Material Description			
Physical Form	Liquid	Appearance/Description	Not relevant
Color	Not relevant	Odor	Not relevant
Odor Threshold	Not relevant	Physical and Chemical Properties	Not relevant
General Properties			
Boiling Point	No data available	Melting Point	Not relevant
Decomposition Temperature	No data available	pH	5.65
Specific Gravity/Relative Density	= 1.016	Water Solubility	Soluble
Viscosity	No data available		
Volatility			
Vapor Pressure	Not relevant	Vapor Density	Not relevant
Evaporation Rate	Not relevant		
Flammability			
Flash Point	Not relevant	UEL	Not relevant
LEL	Not relevant	Autoignition	Not relevant
Environmental			
Octanol/Water Partition coefficient	0.292 log Kow		

Section 10: Stability and Reactivity

Reactivity

- No dangerous reaction known under conditions of normal use.

Chemical stability

- Stable under normal temperatures and pressures.

Possibility of hazardous reactions

- No data available

Conditions to avoid

- Extreme heat or cold. Do not freeze.

Incompatible materials

- No data available

Hazardous decomposition products

- No data available

Section 11 - Toxicological Information

Information on toxicological effects

Components		
Dorzolamide Hydrochloride (2% TO 3%)	130693-82-2	**Acute Toxicity:** Ingestion/Oral-Rat LD50 • 1927 mg/kg; *Sense Organs and Special Senses:Eye*:**Ptosis**; *Behavioral*:**Somnolence (general depressed activity)**; *Behavioral*:**Ataxia**; **Reproductive:** Ingestion/Oral-Rat TDLo • 12 mg/kg (6-17D preg); *Reproductive Effects:Effects on Embryo or Fetus*:**Fetotoxicity (except death, e.g., stunted fetus)**; *Reproductive Effects:Specific Developmental Abnormalities*:**Musculoskeletal system**
Timolol Maleate (0.5% TO 1%)	26921-17-5	**Acute Toxicity:** Ingestion/Oral-Rat LD50 • 1028 mg/kg
Benzalkonium Chloride (0.0075%)	63449-41-2	**Acute Toxicity:** Ingestion/Oral-Mouse LD50 • 150 mg/kg; *Behavioral*:**Somnolence (general depressed activity)**; *Blood*:**Hemorrhage**
Sodium Citrate Dihydrate (< 1%)	68-04-2	**Acute Toxicity:** Intravenous-Mouse LD50 • 170 mg/kg; *Behavioral*:**Convulsions or effect on seizure threshold**; *Lungs, Thorax, or Respiration*:**Cyanosis**; *Gastrointestinal*:**Changes in structure or function of salivary glands**
Mannitol (1% TO 5%)	69-65-8	**Acute Toxicity:** Ingestion/Oral-Rat LD50 • 13500 mg/kg
1 N Sodium Hydroxide (< 1%)	1310-73-2	**Acute Toxicity:** Ingestion/Oral-Rabbit LDLo • 500 mg/kg

GHS Properties	Classification
Acute toxicity	**UN GHS** • Classification criteria not met
Aspiration Hazard	**UN GHS** • Classification criteria not met
Carcinogenicity	**UN GHS** • Classification criteria not met
Germ Cell Mutagenicity	**UN GHS** • Classification criteria not met
Skin corrosion/Irritation	**UN GHS** • Skin Mild Irritation 3
Skin sensitization	**UN GHS** • Classification criteria not met
STOT-RE	**UN GHS** • Classification criteria not met
STOT-SE	**UN GHS** • Classification criteria not met
Toxicity for Reproduction	**UN GHS** • Toxic to Reproduction 2
Respiratory sensitization	**UN GHS** • Classification criteria not met
Serious eye damage/Irritation	**UN GHS** • Eye Mild Irritation 2B

Potential Health Effects

Inhalation

Acute (Immediate)

- Under normal conditions of use, no health effects are expected.

Chronic (Delayed)
- No data available.

Skin

Acute (Immediate)
- May cause mild irritation.

Chronic (Delayed)
- No data available.

Eye

Acute (Immediate)
- May cause irritation.

Chronic (Delayed)
- Refer to the product insert and/or product prescribing information for comprehensive information regarding adverse reactions and other important symptoms and effects. Under normal conditions of use, no health effects are expected.

Ingestion

Acute (Immediate)
- Not expected to be an exposure route. However, may cause gastric and intestinal irritation if ingested.

Chronic (Delayed)
- No data available.

Carcinogenic Effects		
	CAS	NTP
Mannitol	69-65-8	Evidence of Carcinogenicity

Reproductive Effects
- Developmental toxicity studies with dorzolamide hydrochloride in rabbits at oral doses of × 2.5 mg/kg/day (31 times the recommended human ophthalmic dose) revealed malformations of the vertebral bodies. These malformations occurred at doses that caused metabolic acidosis with decreased body weight gain in dams and decreased fetal weights. No treatment-related malformations were seen at 1.0 mg/kg/day (13 times the recommended human ophthalmic dose). There are no adequate and wellcontrolled studies in pregnant women.

Section 12 - Ecological Information

Toxicity

- This material has not been tested for environmental effects.

Persistence and degradability

- No data available.

Bioaccumulative potential

- No data available

Mobility in Soil

- No data available

Other adverse effects

Section 13 - Disposal Considerations

Waste treatment methods

Product waste
- Waste characterizations and compliance with applicable laws are the responsibility solely of the waste generator.

Packaging waste
- Dispose of content and/or container in accordance with local, regional, national, and/or international regulations.

Section 14 - Transport Information

	UN number	UN proper shipping name	Transport hazard class (es)	Packing group	Environmental hazards
DOT	NDA	Not regulated	NDA	NDA	NDA
TDG	NDA	Not regulated	NDA	NDA	NDA
IMO/IMDG	NDA	Not regulated	NDA	NDA	NDA
IATA/ICAO	NDA	Not regulated	NDA	NDA	NDA

Special precautions for user • No data available

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code • No data available

Section 15 - Regulatory Information

Safety, health and environmental regulations/legislation specific for the substance or mixture

SARA Hazard Classifications • No data available

Inventory				
Component	**CAS**	**Canada DSL**	**EU EINECS**	**TSCA**
Timolol Maleate	26921-17-5	Yes	Yes	No
Dorzolamide Hydrochloride	130693-82-2	No	No	No
Benzalkonium Chloride	63449-41-2	Yes	Yes	Yes
Hydroxyethyl Cellulose	9004-62-0	Yes	No	Yes
Mannitol	69-65-8	Yes	Yes	Yes
1 N Sodium Hydroxide	1310-73-2	Yes	Yes	Yes
Sodium Citrate Dihydrate	68-04-2	Yes	Yes	Yes
Water	7732-18-5	Yes	Yes	Yes

Canada

Labor

Canada - WHMIS - Classifications of Substances

• Sodium Citrate Dihydrate	68-04-2	Uncontrolled product according to WHMIS classification criteria
• Mannitol	69-65-8	Uncontrolled product according to WHMIS classification criteria
• Benzalkonium Chloride	63449-41-2	Not Listed
• 1 N Sodium Hydroxide	1310-73-2	E (including 0.04% in aqueous solution, 0.08%, 0.4% in aqueous solution, 2%, 2.5%, 4% in aqueous solution, 5%, 10%, 16%, 20%, 40%, 50% in aqueous solution, 8.7N)
• Hydroxyethyl Cellulose	9004-62-0	Uncontrolled product according to WHMIS classification criteria

• Water	7732-18-5	Uncontrolled product according to WHMIS classification criteria
• Timolol Maleate	26921-17-5	Not Listed
• Dorzolamide Hydrochloride	130693-82-2	Not Listed

Canada - WHMIS - Ingredient Disclosure List

• Sodium Citrate Dihydrate	68-04-2	Not Listed
• Mannitol	69-65-8	Not Listed
• Benzalkonium Chloride	63449-41-2	Not Listed
• 1 N Sodium Hydroxide	1310-73-2	1 %
• Hydroxyethyl Cellulose	9004-62-0	Not Listed
• Water	7732-18-5	Not Listed
• Timolol Maleate	26921-17-5	Not Listed
• Dorzolamide Hydrochloride	130693-82-2	Not Listed

Europe

Other

EU - CLP (1272/2008) - Annex VI - Table 3.2 - Classification

• Sodium Citrate Dihydrate	68-04-2	Not Listed
• Mannitol	69-65-8	Not Listed
• Benzalkonium Chloride	63449-41-2	Xn; R21/22 C; R34 N; R50
• 1 N Sodium Hydroxide	1310-73-2	C; R35
• Hydroxyethyl Cellulose	9004-62-0	Not Listed
• Water	7732-18-5	Not Listed
• Timolol Maleate	26921-17-5	Not Listed
• Dorzolamide Hydrochloride	130693-82-2	Not Listed

EU - CLP (1272/2008) - Annex VI - Table 3.2 - Concentration Limits

• Sodium Citrate Dihydrate	68-04-2	Not Listed
• Mannitol	69-65-8	Not Listed
• Benzalkonium Chloride	63449-41-2	Not Listed
• 1 N Sodium Hydroxide	1310-73-2	5%<=C: C; R:35 2%<=C<5%: C; R:34 0.5%<=C<2%: Xi; R:36/38
• Hydroxyethyl Cellulose	9004-62-0	Not Listed
• Water	7732-18-5	Not Listed
• Timolol Maleate	26921-17-5	Not Listed
• Dorzolamide Hydrochloride	130693-82-2	Not Listed

EU - CLP (1272/2008) - Annex VI - Table 3.2 - Labelling

• Sodium Citrate Dihydrate	68-04-2	Not Listed
• Mannitol	69-65-8	Not Listed
• Benzalkonium Chloride	63449-41-2	C N R:21/22-34-50 S:(2)-36/37/39-45-61
• 1 N Sodium Hydroxide	1310-73-2	C R:35 S:(1/2)-26-37/39-45
• Hydroxyethyl Cellulose	9004-62-0	Not Listed
• Water	7732-18-5	Not Listed
• Timolol Maleate	26921-17-5	Not Listed
• Dorzolamide Hydrochloride	130693-82-2	Not Listed

EU - CLP (1272/2008) - Annex VI - Table 3.2 - Safety Phrases

• Sodium Citrate Dihydrate	68-04-2	Not Listed
• Mannitol	69-65-8	Not Listed

• Benzalkonium Chloride	63449-41-2	S:(2)-36/37/39-45-61
• 1 N Sodium Hydroxide	1310-73-2	S:(1/2)-26-37/39-45
• Hydroxyethyl Cellulose	9004-62-0	Not Listed
• Water	7732-18-5	Not Listed
• Timolol Maleate	26921-17-5	Not Listed
• Dorzolamide Hydrochloride	130693-82-2	Not Listed

United States

Environment

U.S. - CERCLA/SARA - Hazardous Substances and their Reportable Quantities

• Sodium Citrate Dihydrate	68-04-2	Not Listed
• Mannitol	69-65-8	Not Listed
• Benzalkonium Chloride	63449-41-2	Not Listed
• 1 N Sodium Hydroxide	1310-73-2	1000 lb final RQ; 454 kg final RQ
• Hydroxyethyl Cellulose	9004-62-0	Not Listed
• Water	7732-18-5	Not Listed
• Timolol Maleate	26921-17-5	Not Listed
• Dorzolamide Hydrochloride	130693-82-2	Not Listed

United States - California

Environment

U.S. - California - Proposition 65 - Carcinogens List

• Sodium Citrate Dihydrate	68-04-2	Not Listed
• Mannitol	69-65-8	Not Listed
• Benzalkonium Chloride	63449-41-2	Not Listed
• 1 N Sodium Hydroxide	1310-73-2	Not Listed
• Hydroxyethyl Cellulose	9004-62-0	Not Listed
• Water	7732-18-5	Not Listed
• Timolol Maleate	26921-17-5	Not Listed
• Dorzolamide Hydrochloride	130693-82-2	Not Listed

U.S. - California - Proposition 65 - Developmental Toxicity

• Sodium Citrate Dihydrate	68-04-2	Not Listed
• Mannitol	69-65-8	Not Listed
• Benzalkonium Chloride	63449-41-2	Not Listed
• 1 N Sodium Hydroxide	1310-73-2	Not Listed
• Hydroxyethyl Cellulose	9004-62-0	Not Listed
• Water	7732-18-5	Not Listed
• Timolol Maleate	26921-17-5	Not Listed
• Dorzolamide Hydrochloride	130693-82-2	Not Listed

U.S. - California - Proposition 65 - Reproductive Toxicity - Female

• Sodium Citrate Dihydrate	68-04-2	Not Listed
• Mannitol	69-65-8	Not Listed
• Benzalkonium Chloride	63449-41-2	Not Listed
• 1 N Sodium Hydroxide	1310-73-2	Not Listed
• Hydroxyethyl Cellulose	9004-62-0	Not Listed
• Water	7732-18-5	Not Listed
• Timolol Maleate	26921-17-5	Not Listed
• Dorzolamide Hydrochloride	130693-82-2	Not Listed

U.S. - California - Proposition 65 - Reproductive Toxicity - Male

• Sodium Citrate Dihydrate	68-04-2	Not Listed
• Mannitol	69-65-8	Not Listed
• Benzalkonium Chloride	63449-41-2	Not Listed
• 1 N Sodium Hydroxide	1310-73-2	Not Listed
• Hydroxyethyl Cellulose	9004-62-0	Not Listed
• Water	7732-18-5	Not Listed
• Timolol Maleate	26921-17-5	Not Listed
• Dorzolamide Hydrochloride	130693-82-2	Not Listed

Section 16 - Other Information

Last Revision Date
- 11/May/2015

Preparation Date
- 11/May/2015

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