ALLERGAN

SAFETY DATA SHEET

Issuing Date 22-Dec-2014 **Revision Date** 22-Dec-2014 **Revision Number** 0

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND THE COMPANY/UNDERTAKING

GHS product identifier

Product Name **COMBIGAN® (Brimonidine Tartrate, 0.2%/Timolol, 0.5%) Ophthalmic Solution**

Other means of identification

Synonyms None

Recommended use of the chemical and restrictions on use

Recommended Use No information available

Uses advised against No information available

Supplier's details

Supplier Address
Allergan, Inc.
2525 Dupont
Irvine, CA
TEL: 1-714-246-4500

Emergency telephone number

Emergency Telephone Number Chemtrec 1-800-424-9300

2. HAZARDS IDENTIFICATION

Classification

Specific Target Organ Toxicity (Repeated Exposure)	Category 2

GHS Label elements, including precautionary statements

Emergency Overview

Signal Word **Warning**

Hazard Statements

• May cause damage to the cardiovascular system through prolonged or repeated exposure.

Appearance Clear, Light yellow, Liquid **Physical State** Liquid. **Odor** Slight

Precautionary Statements

Prevention
• Do not breathe dust/fume/gas/mist/vapors/spray.

General Advice
• Get medical attention/advice if you feel unwell

Storage
• None

Disposal
• Dispose of contents/container to an approved waste disposal plant.

Hazard Not Otherwise Classified (HNOC)

Not applicable

Other information
Overdose or overexposure may result in symptoms associated with beta-adrenergic blocking agents including headache, dizziness, fatigue, chest pain, nausea, breathing difficulty and cardiac abnormalities. Repeated ocular use has been shown to produce oral dryness, eye irritation, ocular allergic reactions, headache or fatigue or drowsiness when used as directed. Ocular allergies have also been shown in sensitive individuals (fewer than 10% of all clinical subjects).

3. COMPOSITION/INFORMATION ON INGREDIENTS

Chemical Name	CAS-No	Weight %	Trade secret
Timolol maleate	26921-17-5	0.68	*
Brimonidine tartrate	70359-46-5	0.2	*

** Where range is displayed, the exact percentage (concentration) of composition has been withheld as a trade secret.*

4. FIRST AID MEASURES

Description of necessary first-aid measures

Eye Contact Rinse thoroughly with plenty of water, also under the eyelids. Get medical attention if irritation persists.

Skin Contact Wash skin with soap and water. Get medical attention if symptoms occur.

Inhalation IF INHALED: If breathing is difficult, remove to fresh air and keep at rest in a position comfortable for breathing. Get medical attention.

Ingestion Clean mouth with water and afterwards drink plenty of water. Do NOT induce vomiting. Get medical attention.

Most important symptoms/effects, acute and delayed

Most Important Symptoms/Effects Irregular cardiac activity. Central nervous system depression. Headache. Eye irritation/reactions. Difficulty in breathing.

Indication of immediate medical attention and special treatment needed, if necessary

Notes to Physician Treat symptomatically.

5. FIRE-FIGHTING MEASURES

Suitable Extinguishing Media
Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Unsuitable Extinguishing Media No information available.

Specific Hazards Arising from the Chemical
No information available.

Explosion Data

Sensitivity to Mechanical Impact	None.
Sensitivity to Static Discharge	None.

Protective Equipment and Precautions for Firefighters
As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures

Personal Precautions Avoid contact with skin, eyes and clothing. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing. Refer to Section 8 for personal protective equipment.

Environmental Precautions

Environmental Precautions See Section 12 for additional Ecological Information.

Methods and materials for containment and cleaning up

Methods for Containment Small spills: Wipe up with absorbent material (e.g. cloth, fleece). Large spills: Prevent further leakage or spillage if safe to do so. Contain and collect spillage with non-combustible absorbent material, (e.g. sand, earth, diatomaceous earth, vermiculite) and place in container for disposal according to local / national regulations (see Section 13).

Methods for Cleaning Up Clean contaminated surface thoroughly.

7. HANDLING AND STORAGE

Precautions for safe handling

Handling Handle in accordance with good industrial hygiene and safety practice. Avoid contact with skin, eyes and clothing. Wear personal protective equipment. Refer to Section 8.

Conditions for safe storage, including any incompatibilities

Storage Keep containers tightly closed in a dry, cool and well-ventilated place.

Incompatible Products Oxidizing agents.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Control parameters

Exposure Guidelines Allergan OEL: Brimonidine Tartrate: 12.5 ug/m^3 (8 hr. TWA)

Appropriate engineering controls

Engineering Measures Showers
Eyewash stations
Ventilation systems

Individual protection measures, such as personal protective equipment

Eye/Face Protection No special protective equipment required. If splashes are likely to occur, wear: Safety glasses with side-shields.

Skin and Body Protection	No protective equipment is needed under normal use conditions. Risk of contact: Lightweight protective clothing. Protective gloves.
Respiratory Protection	None required under normal usage.
Hygiene Measures	Handle in accordance with good industrial hygiene and safety practice. Do not eat, drink or smoke when using this product. Keep away from food, drink and animal feeding stuffs. Provide regular cleaning of equipment, work area and clothing. Remove and wash contaminated clothing and gloves, including the inside, before re-use. Wash hands before breaks and immediately after handling the product.

9. PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Physical State	Liquid	**Appearance**	Clear, Light yellow Liquid
Odor	Slight	**Odor Threshold**	No information available

Property	**Values**	**Remarks/ - Method**
pH	6.8-7	None known
Melting Point/Range	No data available	None known
Boiling Point/Boiling Range	>100 °C / >212 °F	None known
Flash Point	> 93.3 °C / > 200 °F	Seta closed cup
Evaporation rate	No data available	None known
Flammability (solid, gas)	No data available	None known
Flammability Limits in Air		
upper flammability limit	No data available	
lower flammability limit	No data available	
Vapor Pressure	No data available	None known
Vapor Density	No data available	None known
Specific Gravity	1.0	None known
Water Solubility	Soluble in water.	None known
Solubility in other solvents	No data available	None known
Partition coefficient: n-octanol/water	No data available	None known
Autoignition Temperature	No data available	None known
Decomposition Temperature	No data available	None known
Viscosity	No data available	None known

Flammable Properties	Not flammable
Explosive Properties	No data available
Oxidizing Properties	No data available

Other information

VOC Content (%)	No data available

10. STABILITY AND REACTIVITY

Reactivity

Not reactive under normal conditions.

Chemical stability

Stable under recommended storage conditions.

Possibility of hazardous reactions

None under normal processing.

Hazardous Polymerization

Hazardous polymerization does not occur.

Conditions to avoid

Heat.

Incompatible materials

Oxidizing agents.

Hazardous decomposition products

None known.

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure

Product Information

Inhalation Not an expected route of exposure. Inhalation of mist may cause irritation to the respiratory system.

Eye Contact May cause eye irritation with susceptible persons. Repeated ocular use has been shown to produce oral dryness, eye irritation, ocular allergic reactions, headache or fatigue or drowsiness when used as directed. Ocular allergies have also been shown in sensitive individuals (fewer than 10% of all clinical subjects). Systemic symptoms including headache, dizziness, bradycardia after timolol maleate administration at the therapeutic doses have also been reported after ocular administration.

Skin Contact Prolonged skin contact may cause skin irritation.

Ingestion May cause irritation to the gastrointestinal tract. Ingestion of large quantities may cause central nervous system effects.

Component Information Brimonidine Tartrate (active ingredient): Oral LD50 = 50 mg/kg (mouse); 100 mg/kg (rat). Clinical signs included sedation, ataxia, prostration, ptosis, reduced blink reflex, hypotension, hypothermia, respiratory depression/arrest, and circulatory collapse. At 10 mg/kg, transient decreased motor activity, ataxia and/or prostration were observed in both species.

Chemical Name	LD50 Oral	LD50 Dermal	LC50 Inhalation
Timolol maleate	= 1028 mg/kg (Rat)	-	-
Brimonidine tartrate	100 mg/kg (Rat) 50 mg/kg (Mouse)	-	-

Symptoms related to the physical, chemical and toxicological characteristics

Symptoms Symptoms of overexposure or overdose may include dizziness, headache, shortness of breath, bronchospasm, heart rhythm abnormalities, or cardiac arrest.

Delayed and immediate effects and also chronic effects from short and long term exposure

Sensitization No information available.

Mutagenic Effects No specific testing was done on this product. Mutagenic testing of the hazardous ingredients in this product has resulted in negative results.

Carcinogenicity	Contains no ingredient listed as a carcinogen. In a two-year study of timolol maleate administered orally to rats, there was a statistically significant increase in the incidence of adrenal pheochromocytomas in male rats administered 300 mg/kg/day (approximately 42,000 times the systemic exposure following the maximum recommended human ophthalmic dose). Similar differences were not observed in rats administered oral doses equivalent to approximately 14,000 times the maximum recommended human ophthalmic dose. In a lifetime oral study in mice, there were statistically significant increases in the incidence of benign and malignant pulmonary tumors, benign uterine polyps and mammary adenocarcinomas in female mice at 500 mg/kg/day, (approximately 71,000 times the systemic exposure following the maximum recommended human ophthalmic dose), but not at 5 or 50 mg/kg/day (approximately 700 to 7,000, respectively, times the systemic exposure following the maximum recommended human ophthalmic dose). In a subsequent study in female mice, in which post-mortem examinations were limited t othe uterus and the lungs, a statistically significant increase in the incidence of pulmonary tumors was again observed at 500 mg/kg/day.
Reproductive Toxicity	Animal testing did not show any effects on fertility.
Developmental Toxicity	Animal testing did not show any effects on fetal development.
STOT - single exposure	Based on available data, the classification criteria are not met.
STOT - repeated exposure	May cause damage to organs through prolonged or repeated exposure. See listed target organs below.
Chronic Toxicity	Oral administration of Brimonidine Tartrate (active ingredient) for one year in rats resulted in toxicity only at the high dose (1.0 mg/kg/day). All changes were reversible within the 8 week recovery period. In monkeys, administration of Brimonidine Tartrate for one year resulted in sedation, slight hypotension, sinus bradycardia, and occasionally, sinus arrhythmia at a dose of 2.5 mg/kg/day. No observable effects were noted at a dose of 0.1 mg/kg/day. Brimonidine Tartrate at varying concentrations was administered in repeated doses (one drop into one eye twice per day) to rabbits for six months and monkeys for one year. Rabbits exhibited dose-dependent sedation at the 0.5 % concentration but not at the 0.2% concentration.
Target Organ Effects	Cardiovascular system.
Aspiration Hazard	No information available.

Numerical measures of toxicity - Product

LD50 Oral	>5000 mg/kg; Acute toxicity estimate

12. ECOLOGICAL INFORMATION

Ecotoxicity

The environmental impact of this product has not been fully investigated.

Persistence and Degradability	No information available.
Bioaccumulation	No information available.

Other Adverse Effects

No information available.

13. DISPOSAL CONSIDERATIONS

Waste Disposal Methods	Dispose of in accordance with local regulations.
Contaminated Packaging	Do not re-use empty containers.

14. TRANSPORT INFORMATION

DOT	Not regulated.
TDG	Not regulated.
MEX	Not regulated.
IATA	Not regulated.
IMDG/IMO	Not regulated.

15. REGULATORY INFORMATION

International Inventories

TSCA	Exempt
DSL	Exempt

Legend

TSCA - United States Toxic Substances Control Act Section 8(b) Inventory
DSL/NDSL - Canadian Domestic Substances List/Non-Domestic Substances List

U.S. Federal Regulations

Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product does not contain any chemicals which are subject to the reporting requirements of the Act and Title 40 of the Code of Federal Regulations, Part 372.

SARA 311/312 Hazard Categories

Acute Health Hazard	Yes
Chronic Health Hazard	Yes
Fire Hazard	No
Sudden Release of Pressure Hazard	No
Reactive Hazard	No

Clean Water Act
This product does not contain any substances regulated as pollutants pursuant to the Clean Water Act (40 CFR 122.21 and 40 CFR 122.42).

CERCLA
This material, as supplied, does not contain any substances regulated as hazardous substances under the Comprehensive Environmental Response Compensation and Liability Act (CERCLA) (40 CFR 302) or the Superfund Amendments and Reauthorization Act (SARA) (40 CFR 355). There may be specific reporting requirements at the local, regional, or state level pertaining to releases of this material.

U.S. State Regulations

California Proposition 65
This product does not contain any Proposition 65 chemicals.

U.S. State Right-to-Know Regulations

This product does not contain any substances above threshold limits that are regulated by state right-to-know.

U.S. EPA Label Information
EPA Pesticide Registration Number Not applicable

16. OTHER INFORMATION

NFPA	**Health Hazard** 1	**Flammability** 0	**Instability** 0	**Physical and Chemical Hazards** -
HMIS	**Health Hazard** 1*	**Flammability** 0	**Physical Hazard** 0	**Personal Protection** X

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General Disclaimer

The information provided on this SDS is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guide for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered as a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other material or in any process, unless specified in the text.

End of Safety Data Sheet