

SAFETY DATA SHEET (SDS)

Date Prepared: 26.09.2022

Revision date: -

Revision: 0

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Product Name: VINCRISTINE-KOÇAK 1 mg/ 1 ml I.V Solution for Injection

Manufacturer Name and Address KOÇAK FARMA İlaç ve Kimya Sanayi A.Ş.
Mahmutbey Mah. 2477. Sok. No: 23 Bağcılar/İstanbul/TURKEY

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Ingredient Name Vincristine sulfate

Synonyms Leurocristine sulfate;
22-oxo-vincalkebustine sulfate

2. HAZARDS IDENTIFICATION

Note: This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the active substance or its intermediates regardless of the potential risk. The precautionary statements and warnings included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace

Emergency Overview

Appearance: clear, colorless solution**Statement of Hazard:** Non-hazardous in accordance with international standards for workplace safety.

Additional Hazard Information:

Long Term: Repeat-dose studies in animals have shown a potential to cause adverse effects on the developing fetus.**Known Clinical Effects:** Central nervous system effects such as dizziness, headache, insomnia, irritability and weakness have also been reported. Effects on blood and blood-forming organs have also occurred.

Clinically, this product is used to treat some types of cancers. It is cytotoxic. In the workplace, this product should be considered very irritating to the skin, eyes, and respiratory tract, a potential occupational reproductive hazard, harmful to the fetus, and a potential human carcinogen. Following an accidental over-exposure, possible target organs may include the bone marrow, gastrointestinal system, central nervous system, peripheral nervous system, kidneys, skin, gonads, and the fetus.

Occupational Exposure Potential

There are scientific studies that suggest that personnel (e.g. nurses, pharmacists, etc.) who prepare and administer parenteral antineoplastics (e.g. in hospitals) may be at some risk due to potential mutagenicity, teratogenicity, and/or carcinogenicity

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Signs and Symptoms

of these materials if workplace exposures are not properly controlled.
The actual risk in the workplace is not known.

Vincristine sulfate is irritating to the skin and mucous membranes and extravasation may cause necrosis, cellulitis, and sloughing. This material should also be considered very irritating to the eyes and respiratory tract. In clinical use, adverse effects may include bone-marrow depression, anorexia, nausea and vomiting, and central and peripheral neurotoxicity. Other adverse effects include headache, malaise, dizziness, skin reactions, alopecia, dyspnea and bronchospasm, and infertility. Aspermia in men and amenorrhea in women have been reported following treatment.

Medical Conditions Aggravated by Exposure

Pre-existing hypersensitivity to vincristine sulfate or other vinca alkaloids. Pre-existing bone marrow, gastrointestinal, central nervous system, peripheral nervous system, neuromuscular, renal, gonadal, or skin ailments; or pregnancy.

Carcinogen Lists:

IARC: Group 3-not classifiable as to its carcinogenicity to humans
NTP: Not listed
OSHA: Not listed

Classification

EU classification

EU Indication of danger:

Not classified

Australian Hazard Classification (NOHSC):

Non-Hazardous Substance. Non-Dangerous Goods.

3. COMPOSITION / INFORMATION ON INGREDIENTS

Active Ingredient Name Vincristine sulfate
Chemical Formula $C_{46}H_{56}N_4O_{10} \cdot H_2O_4S$ or $C_{46}H_{58}N_4O_{14}S$

Component	CAS Number	EU EINECS/ELINCS List	RTECS Number
Vincristine sulfate	2068-78-2	218-190-0	OH6340000
Mannitol	69-65-8	200-711-8	OP2050000

Non-hazardous ingredients include Water for Injection.

4. FIRST AID MEASURES

Eye contact

Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.

Skin contact

Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.

Inhalation

Remove to fresh air and keep patient at rest. Seek medical attention immediately.

Ingestion

Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.

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Symptoms and Effects of Exposure:

For information on potential signs and symptoms of exposure, See Section 2 – Hazards Identification and/or Section 11 - Toxicological Information.

5. FIRE FIGHTING MEASURES

Extinguishing Media:

Use carbon dioxide, dry chemical, or water spray.

Hazardous Combustion Products:

Formation of toxic gases is possible during heating or fire.

Fire Fighting Procedures:

During all firefighting activities, wear appropriate protective equipment, including selfcontained breathing apparatus.

Fire / Explosion Hazards:

Not applicable

6. ACCIDENTAL RELEASE MEASURES

Health and Safety Precautions:

Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

Measures for Cleaning / Collecting:

Contain the source of spill if it is safe to do so. Collect spill with absorbent material. Clean spill area thoroughly.

Measures for Environmental Protections:

Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release

Additional Consideration for Large Spills:

Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

General Handling:

Vincristine sulfate is a cytotoxic agent. Appropriate procedures should be implemented during the handling and disposal of cytotoxic antineoplastics agents to minimize potential exposures. Several guidelines on handling cytotoxic antineoplastic agents have been published. Consult your hygienist or safety professional for your site requirements.

Avoid ingestion, inhalation, skin contact, and eye contact. When handling, precautions may include the use of a containment cabinet. The use of disposable gloves and respiratory protection is recommended. Proper disposal of contaminated vials, syringes, or other materials is required when working with this product.

Storage Conditions:

No special storage is required for hazard control. However, employees should be trained on the proper storage procedures for antineoplastic agents. For product protection, follow USP controlled room temperature storage recommendations noted on the product case label, the primary container label, or the product insert.

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Special

Precautions:

Persons with known hypersensitivities to vincristine sulfate or other vinca alkaloids, women who are pregnant, or women who want to become pregnant, should consult a health and/or safety professional prior to handling this Product.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

**Respiratory
protection:**

Respiratory protection is normally not needed during intended product use. However, if the generation of aerosols is likely, and engineering controls are not considered adequate to control potential airborne exposures, the use of an approved air-purifying respirator with a HEPA cartridge (N99 or equivalent) is recommended under conditions where airborne aerosol concentrations are not expected to be excessive. For uncontrolled release events, or if exposure levels are not known, provide respirators that offer a high protection factor such as a powered air purifying respirator or supplied air. A respiratory protection program that meets OSHA's 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions require respirator use. Personnel who wear respirators should be fit tested and approved for respirator use as required.

Eye protection:

As a minimum, the use of chemical safety goggles is recommended when handling this product.

Skin protection

When handling this product, disposable gloves should be worn at all times. Further, the use of double gloves is recommended. Disposable gloves made from nitrile, neoprene, polyurethane or natural latex generally have low permeability to this material. Persons known to be allergic to latex rubber should select a non-latex glove. Gloves should be changed regularly, and removed immediately after known contamination. Care should be taken to minimize inadvertent contamination when removing and/or disposing of gloves.

**Engineering
Controls**

Good local exhaust ventilation is recommended to minimize employee exposure. The use of an enclosure, such as an approved ventilated cabinet designed to minimize airborne exposures, is also recommended.

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9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance/Physical State	Colorless, clear solution
Odor	Odorless
Odor Threshold	NA
pH	3,5-5,5
Melting point/Freezing Point	NA
Initial Boiling Point/Boiling Point Range	100 °C
Flash Point	NA
Evaporation Rate	NA
Flammability (solid, gas)	NA
Upper/Lower Flammability or Explosive Limits	NA
Vapor Pressure	NA
Vapor Density (Air =1)	NA
Relative Density	NA
Solubility	Soluble in methanol, freely soluble in water, but only slightly soluble in 95% ethanol
Partition Coefficient: n-octanol/water	NA
Auto-ignition Temperature	NA
Decomposition Temperature	NA
Viscosity	NA

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10. STABILITY AND REACTIVITY

Reactivity

Not determined.

Chemical Stability

Stable under normal conditions of use.

Possibility of Hazardous Reactions

Not determined

Conditions to Avoid

Not determined

Incompatible Materials

Sensitive to hydrolysis, oxidation and heat. Incompatible with strong oxidizing agents.

Hazardous Polymerisation:

Not anticipated to occur with this product.

Hazardous Decomposition Products:

Not determined. During thermal decomposition, it may be possible to generate irritating vapors and/or toxic fumes of carbon oxides (COx), nitrogen oxides (NOx), and sulfur oxides (SOx).

11. TOXICOLOGICAL INFORMATION

General Information The information included in this section describes the potential hazards of the individual ingredient

Acute Toxicity:

(Species, Route, End Point, Dose)

Vincristine Sulfate	Rat	Para-periosteal	LD ₅₀ 1.9 mg/kg
	Rat	Para-periosteal	LD ₅₀ 1 mg/kg
	Rat	Oral	LD ₅₀ > 5 mg/kg
	Mouse	Intraperitoneal	LD ₅₀ 3 mg/kg
	Mouse	Intravenous	LD ₅₀ 1,7 mg/kg
Mannitol	Rat	Oral	LD ₅₀ 13500 mg/kg
	Mouse	Oral	LD ₅₀ 22 g/kg

Acute Toxicity Comments:

A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

Irritation / Sensitization: (Study Type, Species, Severity)

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Vincristine Sulfate Skin Irritation , Rabbit, Mild

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

Vincristine Sulfate 6 Week(s) Dog Intravenous 0.02 mg/kg/week LOAEL Central nervous system

Reproduction & Developmental Toxicity: (Study Type, Species, Route, Dose, End Point, Effect(s))

Vincristine Sulfate	Embryo / Fetal Development	Rat	Intraperitoneal	0,05 mg/kg	LOAEL	Teratogenic
	Embryo / Fetal Development	Hamster	Intravenous	0,1 mg/kg	LOAEL	Teratogenic
	Embryo / Fetal Development	Mouse	Intraperitoneal	0,2 mg/kg	LOAEL	Teratogenic

Genetic Toxicity:
(Study Type, Cell Type/Organism, Result)

Vincristine Sulfate Bacterial Mutagenicity (Ames) Negative
In Vivo Micronucleus Mouse Positive
In Vitro Cytogenetics Human Lymphocytes Equivocal
 Chromosome Aberration Rodent Negative
 Mammalian Cell Mutagenicity Mouse Lymphoma Positive

Carcinogen Status: None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA. See below

Vincristine Sulfate IARC: Group 3 (Not Classifiable)

12. ECOLOGICAL INFORMATION

Environmental Overview:

Environmental properties have not been investigated. Releases to the environment should be avoided.

13. DISPOSAL CONSIDERATIONS

Waste Disposal

All waste materials must be properly characterized by the waste generator. Disposal should be performed in accordance with the federal, state or local regulatory requirements.

Container Handling and Disposal

Dispose of containers and unused contents in accordance with federal, state and local regulations.

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14. TRANSPORT INFORMATION

The following refers to all modes of transportation unless specified below.
Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

15. REGULATORY INFORMATION

Classification(s):

Harmful

Irritant

Toxic to
Reproduction
Category 2

Carcinogen
Category 3



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Xi

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Xn

Risk Phrases:

R22- Harmful if swallowed
R36/37/38 - Irritating to eyes, respiratory system, and skin
R40 - Limited evidence of a carcinogenic effect
R41 - Risk of serious damage to eyes
R60 - May impair fertility
R61 - May cause harm to the unborn child
R64 - May cause harm to breastfed babies

Safety Phrases:

S24: Avoid contact with the skin
S25: Avoid contact with eyes
S35: This material and its container must be disposed of in a safe way.
S36/37/39: Wear suitable protective clothing, gloves and eye/face protection

EU Indication of danger:

Not classified

OSHA Label:

Non-hazardous in accordance with international standards for workplace safety.

Canada - WHMIS: Classifications

WHMIS hazard class:

Class D, Division 2, Subdivision A



Mannitol

- | | |
|---|-----------|
| - Inventory - United States TSCA - Sect. 8(b) | Present |
| - Australia (AICS): | Present |
| - REACH - Annex IV - Exemptions from the obligations of Register: | Present |
| - EU EINECS/ELINCS List | 200-711-8 |

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Water

- | | |
|---|-----------|
| - Inventory - United States TSCA - Sect. 8(b) | Present |
| - Australia (AICS): | Present |
| - REACH - Annex IV - Exemptions from the obligations of Register: | Present |
| - EU EINECS/ELINCS List | 200-791-2 |

Vincristine sulfate

- | | |
|-----------------------------|--|
| - California Proposition 65 | Developmental toxicity initial date 7/1/90 |
| - Australia (AICS): | Present |
| - EU EINECS/ELINCS List | 218-190-0 |

16. OTHER INFORMATION

Notes:

ACGIH TLV American Conference of Governmental Industrial Hygienists – Threshold Limit Value
CAS Chemical Abstracts Service Number
CERCLA US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act
DOT US Department of Transportation Regulations
EEL Employee Exposure Limit
IATA International Air Transport Association
LD₅₀ Dosage producing 50% mortality
NA Not applicable/Not available
NE Not established
NIOSH National Institute for Occupational Safety and Health
OSHA PEL US Occupational Safety and Health Administration – Permissible Exposure Limit
RTECS Registry of Toxic Effects of Chemical Substances
TSCA Toxic Substance Control Act

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End of Safety Data Sheet