

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

1.1. Product identifier Meldonium dihydrate, CAS no. 86426-17-7
anhydrous form, CAS no. 76144-81-5

REACH registration number - no necessary according REACH regulation p.2, article 5 a)

1.2. Relevant identified uses of the substance or mixture and uses advised against - pharmaceutical industry and research. Drug.

1.3. Details of the supplier of the safety data sheet:

Manufacturer: JSC "OlainFarm"

Address: Rupnicu Street 5, Olaine, Olaines novads, LV -2114, Latvia

Telephone number: Phone: +371 67013700 Fax: +371 67013777 (from 8.30 till 16.30)

e-mail address for a competent person

responsible for the safety data sheet: olainfarm@olainfarm.lv

1.4. Emergency telephone Number:

Centre of Toxicology (Latvia): +371 67042468, +371 67042472

Centre of emergency and disaster medicine (Latvia): +371 29002626

JSC "OlainFarm"(during office hours): +371 67013808, +371 27890055, +371 67962125

2. HAZARDS IDENTIFICATION

2.1. Classification of the substance or mixture

Classification of the substance according to Regulation No. 1272/2008:

Skin irritation (Category 2)

Eye Irritation (Category 2)

Specific target organ toxicity – single exposure (Category 3)

Classification of the substance according to European Directive 67/548/EEC:

Irritant Xi.

Irritating to skin, eyes and respiratory system.

2.2. Label elements

Pictogram: GHS07



Signal word: Warning

Hazard statements

H315 Causes skin irritation

H319 Causes serious eye irritation

H335 May cause respiratory irritation

Precautionary statements

P261 Avoid breathing dust.

P305+P351+P338 IF IN EYES: Rinse

cautiously with water for several minutes.

Remove contact lenses, if present and easy to do. Continue rinsing.

2.3. Other hazards – Hygroscopic.

Hazards symbols



R-phrases

R36/37/38 Irritating to eyes, respiratory system and skin.

S-phrases

S22 Do not breathe dust

S26 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

3. COMPOSITION/INFORMATION ON INGREDIENTS

3.1. Substances

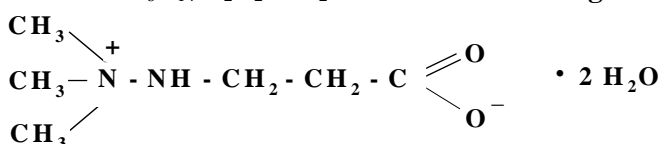
IUPAC name: 3-(2,2,2-Trimethylhydrazinium) propionate dihydrate

Synonyms: Hydrazinium,2-(2-carboxyethyl)-1,1,1-trimethyl-, inner salt, dihydrate (9CI);

1,1,1-Trimethyl-2-(2-carboxyethyl)hydrazine zwitterion dihydrate;

Meldonium; Quaterin; Mildronate; MET 88.

Formula: C₆H₁₄ N₂O₂ · 2H₂O **Molecular weight:** 182.22 g/mol



Chemical name	Index No.	*CAS No.	EC No.	Concentration, %	Classification
Meldonium dihydrate	-	86426-17-7	-	> 98.0	Eye Irrit 2; Skin Irrit 2; STOT SE 3 H315, H319, H335 Xi: R36/37/38

*Meldonium anhydrous, CAS no. 76144-81-5

4. FIRST AID MEASURES

4.1. Description of first aid measures

General advice: Consult a physician. Show this safety data sheet to the doctor.

If inhaled: where Medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise: For advice, contact a Poisons Information Centre or a doctor. Urgent hospital treatment is likely to be needed. If conscious, give water to drink.

In case of skin contact: immediately flush with plenty of soap and water for at least 15 minutes. Remove contaminated clothes and shoes. Seek medical attention in event of irritation.

In case of eye contact: Immediately flush eyes with plenty of water for at least 15 minutes, occasionally lifting the upper and lower eyelids. Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids. If pain persists or recurs seek medical attention. Skilled personnel should only undertake removal of contact lenses after an eye injury. Get medical aid immediately.

If swallowed: rinse mouth with water. Rinse mouth with water. Never give anything by mouth to an unconscious person. INDUCE vomiting with fingers down the back of the throat, ONLY IF CONSCIOUS. Lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration. NOTE: Wear a protective glove when inducing vomiting by mechanical means.

4.2. Most important symptoms and effects, both acute and delayed.

If ingestion: in some cases can be allergy of skin (nettle - rash, itch, dyspepsia), tachycardia, dermatitis, fluster, change of blood pressure

4.3. Indication of any immediate medical attention and special treatment needed

In the meantime, qualified first-aid personnel should treat the patient following observation and employing supportive measures as indicated by the patient's condition. If the services of a medical officer or medical doctor are readily available, the patient should be placed in his/her care and a copy of the SDS should be provided. Further action will be the responsibility of the medical specialist. If medical attention is not available on the worksite or surroundings send the patient to a hospital together with a copy of the SDS.

5. FIREFIGHTING MEASURES

5.1. Extinguishing media:

Suitable extinguishing media: Use water spray, dry chemical, carbon dioxide or appropriate foam.

Unsuitable extinguishing media:

None

5.2. Special hazards arising from the substance or mixture:

Emits toxic fumes under fire conditions: carbon monoxide CO, carbon dioxide CO₂, nitrogen oxides NO_x, and other pyrolysis products typical of burning organic material. May emit corrosive fumes.

5.3. Advice for firefighters:

Wear breathing apparatus plus protective gloves. Use water delivered as a fine spray to control fire and cool adjacent area. DO NOT approach containers suspected to be hot. Cool fire exposed containers with water spray from a protected location. If safe to do so, remove containers from path of fire. Equipment should be thoroughly decontaminated after use.

6. ACCIDENTAL RELEASE MEASURES

6.1. Personal precautions, protective equipment and emergency procedures

Use personal protective equipment: wear self - contained breathing apparatus, rubber boots and heavy rubber gloves. Avoid dust formation. Avoid breathing dust. Ensure adequate ventilation.

For non-emergency personnel

Use personal protective equipment. Avoid dust formation. Avoid breathing dust. Ensure adequate ventilation.

For emergency responders

Wear self - contained breathing apparatus and protective clothing to prevent contact with skin and eyes.

6.2. Environmental precautions - do not let product enter drains.

6.3. Methods and material for containment and cleaning up

MINOR SPILLS: Remove all ignition sources. Clean up all spills immediately. Avoid contact with skin and eyes. Control personal contact by using protective equipment. Use dry clean up procedures and avoid generating dust. Place in a suitable, labelled container for waste disposal.

MAJOR SPILLS: Moderate hazard. **CAUTION:** Advise personnel in area. Alert Emergency Responders and tell them location and nature of hazard. Control personal contact by wearing protective clothing. Prevent, by any means available, spillage from entering drains or watercourses. Recover product wherever possible.

IF DRY: Use dry clean up procedures and avoid generating dust. Collect residues and place in sealed plastic bags or other containers for disposal. **IF WET:** Vacuum/shovel up and place in labelled containers for disposal.

ALWAYS: Wash area down with large amounts of water and prevent runoff into drains. If contamination of drains or waterways occurs, advise emergency services.

6.4. Reference to other sections: No.

7. HANDLING AND STORAGE

7.1. Precautions for safe handling

Avoid all personal contact, including inhalation. Wear protective clothing when risk of exposure occurs. Use in a well-ventilated area. Prevent concentration in hollows and sumps. **DO NOT** enter confined spaces until atmosphere has been checked. **DO NOT** allow material to contact humans, exposed food. Avoid contact with incompatible materials.

Keep containers securely sealed when not in use. Avoid physical damage to containers. Always wash hands with soap and water after handling. Work clothes should be laundered separately. Launder contaminated clothing before re-use. Use good occupational work practice. Observe manufacturer's storing and handling recommendations.

7.2. Conditions for safe storage, including any incompatibilities

Store in a dry, dark place at temperature not more than 25 °C. Recommended storage with desiccant. Store in a well-ventilated area away from incompatible substances. Keep container tightly closed. Recommended polyethylene or polypropylene container. Check all containers are clearly labelled and free from leaks. Store in original containers. Keep containers securely sealed. Protect containers against physical damage.

7.3. Specific end use(s) – anti-ischemic drug, cardio protector.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control parameters. This product has not occupational exposure limits established by the region specific regulatory bodies in European Union.

TWA = 5 mg/m³ for all Active Pharmaceutical Ingredients (USA).

8.2. Exposure controls

Appropriate engineering controls - Local exhaust ventilation is required where solids are handled as powders or crystals; even when particulates are relatively large, a certain proportion will be powered by mutual friction. Exhaust ventilation should be designed to prevent accumulation and recirculation of particulates in the workplace.

Individual protection measures, such as personal protective equipment

Eye / face protection - safety glasses with side-shields conforming to EN166. Contact lenses pose a special hazard; soft lenses may absorb irritants and all lenses concentrate them. **DO NOT** wear contact lenses.

Skin and body protection - Choose body protection according to the amount and concentration of the dangerous substance at the work place.

Hand protection - The selected protective gloves have to satisfy the specifications of EU Directive 89/686/EEC and the standard EN 374 and US F739. Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include such as: frequency and duration of contact, chemical resistance of glove material, glove thickness and dexterity.

When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374) is recommended.

When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374) is recommended. Contaminated gloves should be replaced.

Other - barrier cream, skin-cleansing cream, eye wash unit.

Respiratory protection - where risk assessment shows air-purifying respirators are appropriate use a dust mask type N95 (US) or type P1 (EN 143) respirator. Use respirators and components tested and approved under appropriate government standards such as NIOSH (US) or CEN (EU). Respirators may be necessary when engineering and administrative controls do not adequately prevent exposures. The decision to use respiratory protection should be based on professional judgment that takes into account toxicity information, exposure measurement data, and frequency and likelihood of the worker's exposure - ensure users are not subject to high thermal loads which may result in heat stress or distress due to personal protective equipment (powered, positive flow, full face apparatus may be an option). Certified respirators will be useful for protecting workers from inhalation of particulates when properly selected and fit tested as part of a complete respiratory protection program. Use approved positive flow mask if significant quantities of dust becomes airborne.

Thermal hazards - none

Hygiene measures - handle in accordance with good industrial hygiene and safety practice. Wash hands before breaks and at the end of workday. Wash contaminated clothing before reuse. Discard contaminated shoes. When handling, DO NOT eat, drink or smoke.

Environmental exposure controls

Contact a licensed professional waste disposal service to dispose of this material. Do not let product enter drains.

9. PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on basic physical and chemical properties

Appearance:	Physical state: crystalline powder	Odour: odourless
	Colour: white or slightly yellow	Odour threshold: no
	pH	7.5 – 9.0 (10 % in water)
		5.0 – 7.0 (1.5 %)
	Melting point/freezing point:	84 - 90 °C
	Initial boiling point and boiling range:	No information available
	Flash point:	109 °C
	Evaporation rate:	No information available
	Flammability (solid, gas):	No information available
	Upper/lower flammability or explosive limits:	No information available
	Vapour pressure:	No information available
	Vapour density:	No information available
	Relative density:	0.65 g/ml (bulk density)
	Solubility:	Soluble in ethanol, <i>methanol, glacial acetic acid</i> Practically insoluble in chloroform, acetone, diethylether, <i>hexane</i>
	Water solubility:	Soluble - 1 g/1.5 ml
	Partition coefficient n-octanol/water:	Log Pow = 0,45
	Auto-ignition temperature:	483 °C
	Decomposition temperature:	> 250 °C (<i>with decomposition</i>)
	Viscosity:	No information available
	Explosive properties:	No information available
	Oxidising properties:	No information available
9.2. Other information		Hygroscopic

10. STABILITY AND REACTIVITY

10.1. Reactivity - No dangerous reactions known.

10.2. Chemical stability - Stable under recommended storage conditions.

10.3. Possibility of hazardous reactions - Avoid contamination with oxidizing agents i.e. nitrates, oxidizing acids, chlorine bleaches, pool chlorine etc. as ignition may result.

10.4. Conditions to avoid - avoid moisture and light.

10.5. Incompatible materials - strong oxidizing agents.

10.6. Hazardous decomposition products. Hazardous decomposition products formed under fire conditions - carbon monoxide CO, carbon dioxide CO₂, nitrogen oxides NO_x and other pyrolysis products typical of burning organic material.

11. TOXICOLOGICAL INFORMATION.

11.1. Information on toxicological effects**Acute toxicity**

LD50 **mice** intraperitoneal – 7850 mg/kg.

LD50 **mice** orally – 18500 mg/kg.

LD50 **rat** intraperitoneal – 12000 mg/kg.

Toxic effects: behavioural – somnolence (general depressed activity)

Lungs, Thorax, or Respiration – respiratory stimulation.

LD **rat** orally – 20000 mg/kg.

LD50 **mouse** intravenous – 4430 mg/kg.

LD **mammal-cat** intraperitoneal - > 4 gm/kg.

LDLo **rabbit** intravenous – 8 gm/kg.

Toxic effects: behavioural – somnolence (general depressed activity)

Lungs, Thorax, or Respiration – respiratory stimulation.

Lungs, Thorax, or Respiration – other changes.

Acute toxicity in experiments on white mice after intravenous application of 40 % solution of mildronate varied from 3164 to 6200 mg/kg.

Skin corrosion/irritation - can cause inflammation of the skin (*pH*: 7,5 – 9). The material may accentuate any pre-existing dermatitis condition. Entry into the blood stream, though, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects. Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

Eye damage/eye irritation - cause eye irritation (*pH*: 7,5 – 9).

Respiratory or skin sensitization - no data available.

Germ cell mutagenicity – not mutagen.

Carcinogenicity - IARC: No component of this product presents at levels greater than or equal to 0,1% is identified as probable, possible or confirmed human carcinogen by IARC.

Reproductive toxicity - *doses up to 10,000 mg/kg/day administered orally to white rats caused neither embryotoxic nor teratogenic effects.*

Specific target organ toxicity - single exposure.

Inhalation - May cause respiratory irritation.

Specific target organ toxicity - repeated exposure - no data available.

Aspiration hazard - no data available.

Potential health effects

ACUTE HEALTH EFFECTS

SWALLOWED - Accidental ingestion of the material may be harmful, see point 4.2.

EYE - can cause eye irritation and damage.

SKIN - can cause skin irritation.

INHALED The material can cause respiratory irritation. The body's response to such irritation can cause further lung damage. Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled.

CHRONIC HEALTH EFFECTS

Long-term exposure to respiratory irritants may result in disease of the airways involving difficult breathing and related systemic problems.

Skin contact with the material is more likely to cause a sensitization reaction in some persons compared to the general population.

Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.

Signs and Symptoms of Exposure – see 4.2.

Additional Information RTECS: MW0333620

12. ECOLOGICAL INFORMATION

12.1. Toxicity - not available

12.2. Persistence and degradability - log P = 0.45, substance is not stable in the environment, if log P < 1.

12.3. Bioaccumulative potential - BCF (pH 5.5) = 1,00 (predicted), substance is not bioaccumulative.

12.4. Mobility in soil - K_{OC} = 3.76 (predicted), mobility in soil is high, if K_{OC} < 100.

12.5. Results of PBT and vPvB assessment - not available

12.6. Other adverse effects - not available

13. DISPOSAL CONSIDERATIONS

13.1. Waste treatment methods - Observe all federal, state, and local environmental regulations. Contact a licensed professional waste disposal service to dispose of this material. All waste must be handled in accordance with local, state and federal regulations. Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area.

This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate.

Recycle wherever possible. Consult Waste Management Authority for disposal if no suitable treatment or disposal facility can be identified. Dispose in a licensed landfill or Incineration in a licensed apparatus (after admixture with suitable combustible material). Decontaminate empty containers. Observe all label safeguards until containers are cleaned and destroyed.

14. TRANSPORT INFORMATION - not regulated for transport of dangerous goods

14.1. UN Number	ADR/RID – IMDG – IATA – no
14.2. UN proper shipping name	ADR/RID: Not dangerous goods IMDG: Not dangerous goods IATA: Not dangerous goods
14.3. Transport hazard class(es)	ADR/RID – IMDG – IATA – no
14.4. Packing group	ADR/RID – IMDG – IATA – no
14.5. Environmental hazards	ADR/RID: no; IMDG Marine pollutant: no; IATA: no
14.6. Special precautions for user	None

15. REGULATORY INFORMATION

This safety data sheet complies with the requirements of Regulation (EC) No. 1907/2006, No. 453/2010 and No. 1272/2008.

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

Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency.

Commission regulation (EU) No 453/2010 of 20 May 2010 amending Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

Council Directive (1967th on June 27) regulations and administrative provisions relating to the classification, packaging and labelling (67/548/EEC).

Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.

15.2. Chemical safety assessment – none

16. OTHER INFORMATION

Version 3 **Version 3** – additional information in p. 2.3., 7.2., 9.1., 10.1., 11.1., 12.

Version 4 – additional information in p.1.4., 9.1., 11.1., 12.6.

Abbreviations and acronyms:

Text of H-code(s) and R-phrases mentioned in Section 3.

Eye Irrit. 2 - Eye irritation (Category 2)

Skin Irrit. 2 - Skin irritation (Category 2)

STOT SE 3 - Specific target organ toxicity, single exposure (Category 3)

H315 Causes skin irritation.

H319 Causes serious eye irritation.

H335 May cause respiratory irritation.

Xi - Irritant

R36/37/38 Irritating to eyes, respiratory system and skin.

ADR/RID – The European agreements concerning the international carriage of dangerous goods by Rail (RID) and by Road (ADR).

BCF - Bioaccumulative potential is the concentration of a substance in a biological tissue per concentration of that chemical in water surrounding that tissue. Tissues with BCF > 1000 are considered high, and < 250 - low, with those between - classified as moderate.

CAS No. - CAS Registry Number is unique numerical identifier assigned by the "Chemical Abstracts Service" to every chemical described in the open scientific literature.

CEN (EU) - the European Committee for Standardization.

EC No. - Seven-digit code that is assigned to chemical substances that are commercially available within the European Union, assigned by the Commission of the European Communities.

IATA – International Air Transport Association guideline to the safe transportation of dangerous goods by air.

IMDG – International Maritime Dangerous Goods code is accepted as an international guideline to the safe transportation or shipment of dangerous goods or hazardous materials by water on vessel.

JSC - joint-stock company.

Koc – Soil absorption potential with values >10000 indicate that substance is very strongly attached to soil. If Koc = 100 to 10 000 indicate that substance less likely to move unless soil erosion occurs. Koc = 1-100 indicate that substance tend to move with water and have the potential to leach or move with surface runoff.

LD50 - Lethal dose, 50 percent kill. **LD** – lethal dose.

LDLo – Lowest published lethal dose.

NIOSH (US) - the National Institute for Occupational Safety and Health.

OSHA - Occupational Safety and Health Administration, part of the United States Department of Labour.

PBT and **vPvB** refer to substances with "Persistent, Bioaccumulative and Toxic" or "very Persistent and very Bioaccumulative" properties (Regulation (EC) No 1907/2006).

RTECS – Registry of Toxic Effects of Chemical Substances.

TWA - Time Weighted Averages - are an average value of exposure over the course of an 8-hour work shift.

The data and information presented here correspond to the present state of our knowledge and experience and can be used only as a guide. JSC "Olainfarm" shall not be held liable for any damage resulting from handling or from contact with the product.

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