

Safety Data Sheet (US)

Federal Hazard Communication Standard (29 CFR 1910.1200)

Date of issue: 23-MAR-2018

Replaces version of:

LEVOTHYROXINE SODIUM



Section 1: Identification

| | |
|-------------------------------|---|
| Product name | LEVOTHYROXINE SODIUM |
| Chemical Name | O-(4-hydroxy-3,5-diiodophenyl)-3,5-diiodo-L-Tyrosine, monosodium salt, hydrate |
| Synonyms | LEVOTHYROXINE SODIUM |
| CAS Number | 25416-65-3 |
| Usage | Pharmaceutical active ingredient |
| Company name | Novartis Pharma AG 4002 Basel Switzerland Tel: +41 61 324 11 11, email: sds.support@novartis.com |
| Emergency phone number | CHEMTEL (International) +1 813 676 1670 (365/24/7) |

Section 2: Hazards identification

GHS hazard category

Acute Toxicity (oral): not classified

Germ cell mutation: not classified

Specific organ toxicity (repeated exposure): Cat. 1; Evaluation: Target organ: Multiple organs

Explosives, oxidizing, self-reactive or self-heating, pyrophoric substances, substances which in contact with water emit flammable gases, organic peroxides: not classified

Flammable solid: not classified

Signal Word: Self assessment according REGULATION (EC) No 1272/2008



Danger

Hazard statements H372: Causes damage to organs through prolonged or repeated exposure.

Precautionary statements P314: Get medical advice/attention if you feel unwell.
P260: Do not breathe dust/fume/gas/mist/vapours/spray.

Other hazards

Specific hazards This substance is pharmacologically extremely active; any contact should be avoided.

Section 3: Composition / information on ingredients

Chemical characterisation of the substance / preparation:

| | |
|-----------------------|--|
| Type | Substance |
| Chemical Class | Hormon of the thyroid gland |
| Chemical Name | O-(4-hydroxy-3,5-diiodophenyl)-3,5-diiodo-L-Tyrosine, monosodium salt, hydrate |
| CAS Number | 25416-65-3 |
| Content: | > 99 % |

For TLV values of declared components, see Section 8, Exposure controls / Personal

Full text of H-Phrases see under Section 16

Section 4: First aid measures

| | |
|---------------------|--|
| Inhalation | Take patient immediately to factory medical centre or call for an ambulance. |
| Skin Contact | Remove contaminated clothing. Rinse contaminated skin immediately with plenty of water and |

Safety Data Sheet (US)

Federal Hazard Communication Standard (29 CFR 1910.1200)

Date of issue: 23-MAR-2018

Replaces version of:

LEVOTHYROXINE SODIUM



| | |
|--------------------|--|
| | soap and seek medical advice. |
| Eye Contact | Immediately rinse eyes thoroughly with running water as long as possible (approx. 15 min). Take injured quickly to factory medical center or call an ambulance (code word: eye accident). |
| Ingestion | If feeling sick, immediately call for a physician or take patient to factory medical centre (if necessary, call for an ambulance). If swallowed, seek medical advice immediately and show this container or label. |

Self-protection of the first aider

For personal protection see Section 8

Notes to Physician Apply general supportive and symptomatic treatment.

Section 5: Fire fighting measures

| | |
|--|---|
| Suitable Extinguishing Media | Water spray or fog, foam, dry chemical powder, CO2, dry sand |
| Unsuitable Extinguishing Media | High volume water jet |
| Dangerous Combustion Products | nitrogen oxides carbon monoxide hydrogen iodide Carbon dioxide Iodine |
| Protective equipment for firefighters | Wear self-contained breathing apparatus and fire protective suite. |

Section 6: Accidental release measures

| | |
|----------------------------------|---|
| Personal precautions | Wear chemical resistant protective suite. Minimize number of personnel in risk area. Keep away unprotected persons. Wear chemical-proof clothes and masks while undressing contaminated persons or cleaning contaminated equipment. |
| Environmental precautions | Firefighting water may not spill into open rivers and ponds. Collect spilled material by all available means. Do not release into the environment. |
| Methods for cleaning | Moisten spilled material with water (in order to avoid dust formation), cover with wet sand or wetted binder, then take up. Wash away remains with plenty of water. Put into lead-sealable and labelled drums. |

For personal protection see Section 8, for disposal considerations see Section 13

Section 7: Handling and storage

| | |
|---|---|
| Storage and Handling Precautions | Plant and processes should be designed to provide the highest possible degree of security against any hazardous exposure. Open handling without suitable personal protective equipment must be avoided. Keep container tightly closed. Keep dry. Avoid formation of dust. Store in a dark place |
|---|---|

For Industrial Hygiene Measures see Section 8, Exposure controls / Personal protection

Technical measures/ Precautions Handle in closed system.

Preventive Precautions (fire/explosion) No particular measures required.

Section 8: Exposure controls / Personal protection

Control parameters

| List type | Value | Unit | |
|-----------------------------------|-------|-------|--------------|
| Occupational Exposure Limit (OEL) | 0.4 | µg/m3 | HHA Database |

Safety Data Sheet (US)

Federal Hazard Communication Standard (29 CFR 1910.1200)

Date of issue: 23-MAR-2018

Replaces version of:

LEVOTHYROXINE SODIUM



Exposure Controls

Industrial Hygiene

The personal protective measure may be adapted appropriately when working in closed systems or under laboratory conditions.

Regular cleaning of equipment, work area and clothing.

No open handling without using reliable equipment. Double barrier principle has to be applied between substance and employee resp. environment.

Restricted and controlled access for trained personnel only.

Designated washing, changing and shower facilities must be available.

Internal working procedures available to personnel covering personal hygiene, decontamination /cleaning, consideration of worst case incidents, spills, emergency, alarms, waste disposal and maintenance.

Personnel comprehensively instructed, highly trained and experienced. Regular refresher training established including appropriate record keeping.

Equipment and protective garments must either be decontaminated or properly contained for disposal before leaving the area.

Disposable protective equipment is to be decontaminated before removal (decontamination shower) followed by hygiene shower.

Open Handling

Respiration : If the Breathing Zone sampling results exceed the established occupational exposure limit (OEL) or the minimum concentration defined by the occupational hazard band, use respiratory protection with sufficient protection factor to ensure exposure is below the exposure limit. Unless the exposure results indicate the requirement for an air supplied device, use HEPA filters for powders or aerosols and cartridge or canister filters for vapors and gases.

Eye : Yes, by face mask

Hand : Double gloves (chemical resistant), worn with long-sleeved or taped outer gloves (EN374/EN388)

Glove Material : Nitrile
Breakthrough time: 240 min
Thickness: 0.4 mm

Additional protection : Disposable dust-proof protective suit, fresh-air supplied (EN465, type 4) worn over long underwear

These values are derived from experiments, literature and information from the glove manufacturer.

They can also be derived from similar materials. In daily work please be aware that the using time depends on several factors and can be shorter than the officially tested permeation time.

Section 9: Physical and chemical properties

Formulation powder

Physical state solid

Particle Size 4 µm (Concentration: ≤ 50 %)
Method: Median value

Colour white slightly creme

Odour odourless

Odour threshold no data available

pH 8.4 - 9.4 (Concentration: 0.1 g/l, Temperature: 20 °C)

Melting point/range 207 - 210 °C (decomposing)

Boiling Point no data available

Flash Point not applicable

Evaporation Rate (Ref: Ether) not applicable

Combustibility Test Standard conditions: 2 = after ignition the fire dies out rapidly (Temperature: 20 °C)

Standard conditions: 2 = after ignition the fire dies out rapidly (Temperature: 100 °C)

Explosion Limits not applicable

Safety Data Sheet (US)

Federal Hazard Communication Standard (29 CFR 1910.1200)

Date of issue: 23-MAR-2018

Replaces version of:

LEVOTHYROXINE SODIUM



| | |
|--|--|
| Vapour Pressure [hPa] | not applicable |
| Vapour Density | not applicable |
| Density | no data available |
| Solubility (Aqueous Solvents) | Water: 0.15 g/l (Temperature: 25 °C) |
| Solubility (Solvents) | mineral acids dil.: soluble (Temperature: 20 °C) ethyl alcohol abs.: soluble (Temperature: 20 °C) |
| Partition Coefficient | no data available |
| Autoignition/MIT | Temperature: > 500 °C Method: BAM (fluidized dust) |
| Dynamic Decomposition | Exotherm: 170 °C (Air open cup) Method: Lütolf, open cup, as is (Temp.progr. 2.5°C/min, examined up to 500°C) Exotherm: 120 °C Method: Grever test method, air stream, as is (temp.progr. 1,2°C/min, examined up to 350°C) Reaction spontaneous exothermic Exotherm: 155 °C Decomposition energy: 208 J/g Method: Radex dynamic decomposition test (temp.progr. 0.75°C/min, examined up to 360°C) |
| Isoperibolic Decomposition (>8h) | Stable up to: 100 °C (Air open cup) Method: Radex isoperibolic (long duration decomposition test open cup 8h) |
| Viscosity | not applicable |
| Explosivity/Reactivity | Deflagration: No suspect of deflagration based on thermal data Drop-Weight Test: Negative Method: Lütolf test method |
| Test for self-heating | no data available |
| Fire-promoting properties | no data available |
| Other information | |
| Bulk Density | 350 kg/m ³ |
| Dust Explosion | Negative Minimum Ignition Energy: > 1 J Method: modified Hartmann tube |
| Specific Resistivity | 8.6 - 10 * 10 ⁸ Ohm m (humidity: 43 %, Temperature: 23 °C) |

Section 10: Stability and reactivity

| | |
|-------------------------------------|---------------------|
| Reaction products with water | None known |
| Hydrolysis | : no data available |

Possibility of hazardous reactions

| | |
|---------------------------|------------------------------|
| Materials to avoid | strong acids strong bases |
|---------------------------|------------------------------|

Conditions to avoid

| | |
|----------------------------|-----------------------------|
| Conditions to avoid | Stable at normal conditions |
|----------------------------|-----------------------------|

Hazardous Decomposition Products

| | |
|---|--|
| Hazardous Decomposition Products | None, when used and handled as intended. |
|---|--|

Section 11: Toxicological information

Safety Data Sheet (US)

Federal Hazard Communication Standard (29 CFR 1910.1200)

Date of issue: 23-MAR-2018

Replaces version of:

LEVOTHYROXINE SODIUM



| | |
|------------------------------|--|
| Acute Toxicity | LD50: > 10000 mg/kg Route: oral Species: rat |
| Irritation, Corrosion | no data available |
| Sensitisation | no data available |
| Mutagenicity | Positive without metabolic activation (Sister Chromatid Exchange) in vitroCell: Cultured peripheral human lymphocytes Negative (Micronucleus Test) in vivo, Species: mouse Negative (Chromosome Aberration Study) in vivo, Species: mouse Negative without activation (Chromosome Aberration Study) in vitroCell: Cultured peripheral human lymphocytes Positive without metabolic activation (Micronucleus Test) in vitroCell: Cultured peripheral human lymphocytes |
| Chronic Effects | Pharmacological effects (Repeated Dose Toxicity) LOAEL: 60 µg/kg Route: oral Species: rat, Organ: Multiple organs Dosage: 0.16 µg/kg, Duration: 1 months Pharmacological effects (Repeated Dose Toxicity) LOAEL: 850 µg/kg Route: oral Species: rat, Organ: Multiple organs Dosage: 850 µg/kg, Duration: 410 days Pharmacological effects (Repeated Dose Toxicity) LOAEL: 1440 µg/kg Route: oral Species: rat, Organ: Multiple organs Dosage: <= 1440 µg/kg, Duration: <= 30 days Pharmacological effects (Repeated Dose Toxicity) LOAEL: 200 µg/kg Route: intraperitoneal Species: rat, Organ: Multiple organs Dosage: <= 300 µg/kg, Duration: <= 30 days Pharmacological effects (Repeated Dose Toxicity) NOAEL: 50 µg/kg Route: oral Species: dog, Organ: Multiple organs Dosage: <= 50 µg/kg, Duration: <= 6 weeks Pharmacological effects (Repeated Dose Toxicity) LOAEL: 10 µg/kg Route: oral Species: dog, Organ: Multiple organs Dosage: <= 30 µg/kg, Duration: <= 22 weeks |
| Reproduction Toxicity | Fertility effects (Fertility and early Embryonic Development) TDLo: 8000 µg/kg Route: subcutaneous Species: mouse Effect on embryo-fetal development (Fertility and early Embryonic Development) LOAEL: 2000 µg/kg Route: subcutaneous Species: mouse Fertility effects (Fertility and early Embryonic Development) LOAEL: 6750 µg/kg Route: subcutaneous |

Safety Data Sheet (US)

Federal Hazard Communication Standard (29 CFR 1910.1200)

Date of issue: 23-MAR-2018

Replaces version of:

LEVOTHYROXINE SODIUM



Species: rat
Effect on embryo-fetal development (Fertility and early Embryonic Development)
LOAEL: 30 µg/kg
Route: intravenous
Species: rabbit
Peri- & postnatal mortality at maternally toxic dose (Peri- and Postnatal Development)
LOAEL: 200 µg/kg
Route: subcutaneous
Species: rat
Peri- & postnatal mortality at maternally toxic dose (Peri- and Postnatal Development)
LOAEL: 250 µg/kg
Route: intramuscular
Species: rat

Toxicological Hazard Classification

Acute Toxicity (oral): not classified
Acute Toxicity (dermal): not classifiable
Acute Toxicity (inhalation): not classifiable
Eye Corrosion / Irritation: not classifiable
Skin Corrosion / Irritation: not classifiable
Respiratory sensitizer: not classifiable
Skin sensitizer: not classifiable
Germ cell mutation: not classified
Carcinogenicity: not classifiable
Reproductive toxicity: not classifiable
Specific organ toxicity (single dose), not lethal: not classifiable
Specific organ toxicity (repeated exposure): Cat.1
Aspiration Hazard: not applicable

Carcinogenicity listing

Public Lists (International) International Lists: Not Listed

Section 12: Ecological information

Ecotoxicity Summary No quantifiable data available.
Avoid release to the environment.
Fish acute toxicity no data available
Aquatic invertebrate acute toxicity no data available
Algae Toxicity no data available
Bacterial Respiration Inhibition no data available
Biological Elimination no data available
Partition Coefficient no data available
Biological accumulation no data available
Soil and Sludge no data available

Safety Data Sheet (US)

Federal Hazard Communication Standard (29 CFR 1910.1200)

Date of issue: 23-MAR-2018

Replaces version of:

LEVOTHYROXINE SODIUM



Sorption/Desorption

PBT assessment no data available

Other adverse effects no data available

Section 13: Disposal considerations

Disposal Requirements May be incinerated if local official regulations are observed.

Container Disposal For disposal local regulation is binding.

Section 14: Transport information

| Regulation | IMDG-Code: | ICAO/IATA-DGR: |
|----------------------------|----------------------------|----------------------------|
| UN Number | 0 | 0 |
| UN Proper Shipping Name | - | - |
| Transport Hazard Class(es) | | |
| Transport Label(s) | | |
| Packing group | | |
| Environmental Hazard | | |
| Additional Information | Comment: no dangerous good | Comment: no dangerous good |

Special Precaution for User

Transport within user's premises: always transport in closed containers that are upright and secure. Ensure that persons transporting the product know what to do in the event of an accident or spillage.

Temperature Transport condition: Transport: $\leq 30^{\circ}\text{C}$

Conditions for Transport

Section 15: Regulatory information

International Lists: Not Listed

Toxic Substances Not listed or exempted

Control Act

Section 16: Other information

Pharmacological Action Hormone replacement therapy

Abbreviations used

Recipient .

Product should be stored, handled and used in accordance with good industrial hygiene practices and in conformity with legal regulations. The information contained herein is based on the present state of our knowledge and is intended to describe our products from the point of view of safety requirements. It should therefore not be construed as guaranteeing specific properties.