SAFETY DATA SHEET

Levothyroxine Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Levothyroxine Formulation

Manufacturer or supplier's details
Company : MSD
Address : Rua Coronel Bento Soares, 530 Cruzeiro - Sao Paulo - Brazil CEP 12730-340
Telephone : 908-740-4000
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASTEWARD@msd.com

Recommended use of the chemical and restrictions on use
Recommended use : Veterinary product

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification in accordance with ABNT NBR 14725 Standard
Flammable liquids : Category 3
Reproductive toxicity : Category 2
Specific target organ toxicity - repeated exposure : Category 1 (Thyroid, Cardio-vascular system, Central nervous system)

GHS label elements in accordance with ABNT NBR 14725 Standard
Hazard pictograms :

Signal Word : Danger
Hazard Statements : H226 Flammable liquid and vapor.
H361 Suspected of damaging fertility or the unborn child.
H372 Causes damage to organs (Thyroid, Cardio-vascular system, Central nervous system) through prolonged or repeated exposure.

Precautionary Statements : Prevention:
P201 Obtain special instructions before use.
P210 Keep away from heat/ sparks/ open flames/ hot surfaces. No smoking.
P233 Keep container tightly closed.
P264 Wash skin thoroughly after handling.
P280 Wear protective gloves/ protective clothing/ eye protec-
SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol#</td>
<td>64-17-5</td>
<td>Flammable liquids, Category 2 Eye irritation, Category 2A</td>
<td>&gt;= 10 &lt;- 20</td>
</tr>
<tr>
<td>levothyroxine sodium</td>
<td>55-03-8</td>
<td>Acute toxicity (Oral), Category 2 Reproductive toxicity, Category 2 Specific target organ toxicity - repeated exposure (Thyroid, Cardio-vascular system, Central nervous system), Category 1</td>
<td>&gt;= 0,1 &lt;- 1</td>
</tr>
</tbody>
</table>

# Voluntarily-disclosed non-hazardous substance

SECTION 4. FIRST AID MEASURES

General advice : In the case of accident or if you feel unwell, seek medical advice immediately. When symptoms persist or in all cases of doubt seek medical advice.

If inhaled : If inhaled, remove to fresh air. Get medical attention.
In case of skin contact : In case of contact, immediately flush skin with soap and plenty of water. Remove contaminated clothing and shoes. Get medical attention. Wash clothing before reuse. Thoroughly clean shoes before reuse.
In case of eye contact : Flush eyes with water as a precaution. Get medical attention if irritation develops and persists.
If swallowed : If swallowed, DO NOT induce vomiting. Get medical advice. Rinse mouth thoroughly with water.
Most important symptoms : Suspected of damaging fertility or the unborn child.
and effects, both acute and delayed
Protection of first-aiders: First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

Notes to physician: Treat symptomatically and supportively.

SECTION 5. FIRE-FIGHTING MEASURES

Suitable extinguishing media:
- Water spray
- Alcohol-resistant foam
- Carbon dioxide (CO2)
- Dry chemical

Unsuitable extinguishing media:
- High volume water jet

Specific hazards during fire fighting:
- Do not use a solid water stream as it may scatter and spread fire.
- Flash back possible over considerable distance.
- Vapors may form explosive mixtures with air.
- Exposure to combustion products may be a hazard to health.

Hazardous combustion products:
- Carbon oxides

Specific extinguishing methods:
- Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
- Use water spray to cool unopened containers.
- Remove undamaged containers from fire area if it is safe to do so.
- Evacuate area.

Special protective equipment for fire-fighters:
- In the event of fire, wear self-contained breathing apparatus.
- Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures:
- Remove all sources of ignition.
- Use personal protective equipment.
- Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

Environmental precautions:
- Avoid release to the environment.
- Prevent further leakage or spillage if safe to do so.
- Prevent spreading over a wide area (e.g., by containment or oil barriers).
- Retain and dispose of contaminated wash water.
- Local authorities should be advised if significant spillages cannot be contained.

Methods and materials for containment and cleaning up:
- Non-sparking tools should be used.
- Soak up with inert absorbent material.
- Suppress (knock down) gases/vapors/mists with a water spray jet.
- For large spills, provide diking or other appropriate containment to keep material from spreading. If diked material can be pumped, store recovered material in appropriate...
container.
Clean up remaining materials from spill with suitable absorbent.
Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable.
Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

SECTION 7. HANDLING AND STORAGE

Technical measures : See Engineering measures under EXPOSURE CONTROLS/PERSONAL PROTECTION section.
Local/Total ventilation : If sufficient ventilation is unavailable, use with local exhaust ventilation.
Use explosion-proof electrical, ventilating and lighting equipment.
Advice on safe handling : Do not breathe mist or vapors.
Do not swallow.
Avoid contact with eyes.
Avoid prolonged or repeated contact with skin.
Wash skin thoroughly after handling.
Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment
Non-sparking tools should be used.
Keep container tightly closed.
Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking.
Take precautionary measures against static discharges.
Do not eat, drink or smoke when using this product.
Take care to prevent spills, waste and minimize release to the environment.

Hygiene measures : If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place.
When using do not eat, drink or smoke.
Wash contaminated clothing before re-use.
The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

Conditions for safe storage : Keep in properly labeled containers.
Store locked up.
Keep tightly closed.
Keep in a cool, well-ventilated place.
Store in accordance with the particular national regulations.
Keep away from heat and sources of ignition.

Materials to avoid : Do not store with the following product types:
Strong oxidizing agents
Organic peroxides
Flammable solids
Pyrophoric liquids
Pyrophoric solids
Self-heating substances and mixtures
Substances and mixtures which in contact with water emit flammable gases
Explosives
Gases

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol</td>
<td>64-17-5</td>
<td>LT</td>
<td>780 ppm</td>
<td>1.480 mg/m³</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>STEL</td>
<td>1.000 ppm</td>
</tr>
<tr>
<td>levothyroxine sodium</td>
<td>55-03-8</td>
<td>TWA</td>
<td>0.1 µg/m³ (OEB 5)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>1 µg/100 cm²</td>
</tr>
</tbody>
</table>

Engineering measures:
- Use closed processing systems or containment technologies to control at source (e.g., glove boxes/isolators) and to prevent leakage of compounds into the workplace.
- All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
- No open handling permitted.
- Totally enclosed processes and materials transport systems are required.
- Operations require the use of appropriate containment technology designed to prevent leakage of compounds into the workplace.
- Use explosion-proof electrical, ventilating and lighting equipment.

Personal protective equipment

Respiratory protection:
- If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.
- Filter type: Combined particulates and organic vapor type

Hand protection:
- Material: Chemical-resistant gloves

Remarks:
- Consider double gloving. Take note that the product is flammable, which may impact the selection of hand protection.

Eye protection:
- Wear safety glasses with side shields or goggles.
- If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles.
Skin and body protection:
- Work uniform or laboratory coat.
- Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces.
- Use appropriate degowning techniques to remove potentially contaminated clothing.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: liquid
Color: colorless
Odor: slight
Odor Threshold: No data available
pH: 9.7 - 10.7
Melting point/freezing point: No data available
Initial boiling point and boiling range: No data available
Flash point: 44 °C
Evaporation rate: No data available
Flammability (solid, gas): Not applicable
Flammability (liquids): Not applicable
Upper explosion limit / Upper flammability limit: No data available
Lower explosion limit / Lower flammability limit: No data available
Vapor pressure: No data available
Relative vapor density: No data available
Relative density: No data available
Density: 1.05 g/cm³
Solubility(ies)
- Water solubility: soluble

Partition coefficient: n-octanol/water: Not applicable
Autoignition temperature: No data available
Decomposition temperature: No data available
Viscosity
  Viscosity, kinematic: No data available
Explosive properties: Not explosive
Oxidizing properties: The substance or mixture is not classified as oxidizing.
Particle size: Not applicable

SECTION 10. STABILITY AND REACTIVITY

Reactivity: Not classified as a reactivity hazard.
Chemical stability: Stable under normal conditions.
Possibility of hazardous reactions:
  Vapors may form explosive mixture with air.
  Can react with strong oxidizing agents.

Conditions to avoid: Heat, flames and sparks.
Incompatible materials:
  Oxidizing agents
  Acids
Hazardous decomposition products: No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure:
  Inhalation
  Skin contact
  Ingestion
  Eye contact

Acute toxicity
Not classified based on available information.

Product:
  Acute oral toxicity: Acute toxicity estimate: > 5.000 mg/kg
  Method: Calculation method

Components:
Ethanol:
  Acute oral toxicity: LD50 (Rat): > 5.000 mg/kg
  Method: OECD Test Guideline 401
  Acute inhalation toxicity: LC50 (Rat): 124,7 mg/l
  Exposure time: 4 h
  Test atmosphere: vapor

levothyroxine sodium:
  Acute oral toxicity: TDLo (Humans): 10 mg/kg
TDLo (Dog): 10 mg/kg
LD50 (Rat): > 1.000 mg/kg

Acute dermal toxicity: LD50 (Rat): > 50 mg/kg

Acute toxicity (other routes of administration): LD50 (Rat): 20 mg/kg
Application Route: Intraperitoneal
LD50 (Rat): 50 mg/kg
Application Route: Subcutaneous

**Skin corrosion/irritation**
Not classified based on available information.

**Components:**

**Ethanol:**
Species: Rabbit
Method: OECD Test Guideline 404
Result: No skin irritation

**Serious eye damage/eye irritation**
Not classified based on available information.

**Components:**

**Ethanol:**
Species: Rabbit
Result: Irritation to eyes, reversing within 21 days
Method: OECD Test Guideline 405

**Respiratory or skin sensitization**

**Skin sensitization**
Not classified based on available information.

**Respiratory sensitization**
Not classified based on available information.

**Components:**

**Ethanol:**
Test Type: Local lymph node assay (LLNA)
Routes of exposure: Skin contact
Species: Mouse
Result: negative

**Germ cell mutagenicity**
Not classified based on available information.
Components:

Ethanol:
Genotoxicity in vitro: Test Type: In vitro mammalian cell gene mutation test
Result: negative

Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Genotoxicity in vivo: Test Type: Rodent dominant lethal test (germ cell) (in vivo)
Species: Mouse
Application Route: Ingestion
Result: equivocal

Carcinogenicity
Not classified based on available information.

Reproductive toxicity
Suspected of damaging fertility or the unborn child.

Components:

Ethanol:
Effects on fertility: Test Type: Two-generation reproduction toxicity study
Species: Mouse
Application Route: Ingestion
Result: negative

Levothyroxine sodium:
Effects on fetal development: Test Type: Development
Species: Rat
Application Route: Oral
Developmental Toxicity: LOAEL: 0,25 mg/kg body weight

Test Type: Development
Species: Mouse
Application Route: Oral
Developmental Toxicity: NOAEL: 3 mg/kg body weight

Test Type: Development
Species: Rabbit
Result: No teratogenic effects.

Test Type: Development
Species: Guinea pig
Result: No teratogenic effects.

Reproductive toxicity - Assessment
Suspected of damaging the unborn child.

STOT-single exposure
Not classified based on available information.
STOT-repeated exposure
Causes damage to organs (Thyroid, Cardio-vascular system, Central nervous system) through prolonged or repeated exposure.

Components:
levothyroxine sodium:
Target Organs : Thyroid, Cardio-vascular system, Central nervous system
Assessment : Causes damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:
Ethanol:
Species : Rat
NOAEL : 1.280 mg/kg
LOAEL : 3.156 mg/kg
Application Route : Ingestion
Exposure time : 90 Days

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:
levothyroxine sodium:
Ingestion :
Target Organs: Thyroid
Target Organs: Cardio-vascular system
Target Organs: Central nervous system
Symptoms: Palpitation, hypotension, Tremors, Headache, increase in appetite, Sweating, Vomiting, Diarrhea, Fever, nervousness, weight loss

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:
Ethanol:
Toxicity to fish :
LC50 (Pimephales promelas (fathead minnow)): > 1.000 mg/l
Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates :
EC50 (Ceriodaphnia (water flea)): > 1.000 mg/l
Exposure time: 48 h

Toxicity to algae/aquatic plants :
ErC50 (Chlorella vulgaris (Fresh water algae)): 275 mg/l
Exposure time: 72 h

EC10 (Chlorella vulgaris (Fresh water algae)): 11,5 mg/l
Exposure time: 72 h
Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):
NOEC (Daphnia magna (Water flea)): 9.6 mg/l
Exposure time: 9 d

Toxicity to microorganisms:
EC50 (Pseudomonas putida): 6.500 mg/l
Exposure time: 16 h

Persistence and degradability

Components:

Ethanol:
Biodegradability: Result: Readily biodegradable.
Biodegradation: 84 %
Exposure time: 20 d

Bioaccumulative potential

Components:

Ethanol:
Partition coefficient: n-octanol/water: log Pow: -0.35

Mobility in soil
No data available

Other adverse effects
No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues: Dispose of in accordance with local regulations.
Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal. Empty containers retain residue and can be dangerous. Do not pressurize, cut, weld, braze, solder, drill, grind, or expose such containers to heat, flame, sparks, or other sources of ignition. They may explode and cause injury and/or death. If not otherwise specified: Dispose of as unused product.

SECTION 14. TRANSPORT INFORMATION

International Regulations

UNRTDG
UN number: UN 1170
Proper shipping name: ETHANOL SOLUTION
Class: 3
Packing group: III
Labels: 3

IATA-DGR
SAFETY DATA SHEET
Levothyroxine Formulation

UN/ID No. : UN 1170
Proper shipping name : Ethanol solution
Class : 3
Packing group : III
Labels : Flammable Liquids
Packing instruction (cargo aircraft) : 366
Packing instruction (passenger aircraft) : 355

IMDG-Code
UN number : UN 1170
Proper shipping name : ETHANOL SOLUTION
Class : 3
Packing group : III
Labels : 3
EmS Code : F-E, S-D
Marine pollutant : no

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

Domestic regulation
ANTT
UN number : UN 1170
Proper shipping name : ETHANOL SOLUTION
Class : 3
Packing group : III
Labels : 3
Hazard Identification Number : 30

Special precautions for user
The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
National List of Carcinogenic Agents for Humans - (LINACH) : Not applicable
Brazil. List of chemicals controlled by the Federal Police : Ethanol

The ingredients of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
IECSC : not determined
Further information
Sources of key data used to compile the Material Safety Data Sheet:

Full text of other abbreviations:
- ACGIH: USA. ACGIH Threshold Limit Values (TLV)
- BR OEL: Brazil. NR 15 - Unhealthy activities and operations
- ACGIH / STEL: Short-term exposure limit
- BR OEL / LT: Up to 48 hours /week

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and shall not be considered a warranty or quality specification of any type. The information provided relates only to the specific material identified at the top of this SDS and may not be valid when the SDS material is used in combination with any other materials or in any process, unless specified in the text. Material users should review the information and recommendations in the specific...
context of their intended manner of handling, use, processing and storage, including an assessment of the appropriateness of the SDS material in the user’s end product, if applicable.

BR / Z8