SAFETY DATA SHEET

Levothyroxine Formulation

Version: 3.2
Revision Date: 23.03.2020
SDS Number: 1130720-00009
Date of last issue: 13.09.2019
Date of first issue: 30.11.2016

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Levothyroxine Formulation

Manufacturer or supplier’s details
Company: MSD
Address: Talcahuano 750, 6th floor, Ciudad Autonoma Buenos Aires, Argentina C1013AAP
Telephone: 908-740-4000
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATASTEWARD@msd.com
Telefax: 908-735-1496

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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
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
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.
P202 Do not handle until all safety precautions have been read and understood.
P210 Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking.
P260 Do not breathe mist or vapors.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P303 + P361 + P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water.
P308 + P313 IF exposed or concerned: Get medical advice/ attention.

Storage:
P405 Store locked up.

Disposal:
P501 Dispose of contents/ container to an approved waste disposal plant.

Other hazards which do not result in classification
Vapors may form explosive mixture with air.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Mixture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Components</td>
<td></td>
</tr>
<tr>
<td>Chemical name</td>
<td>CAS-No.</td>
</tr>
<tr>
<td>Ethanol</td>
<td>64-17-5</td>
</tr>
<tr>
<td>levothyroxine sodium</td>
<td>55-03-8</td>
</tr>
</tbody>
</table>

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 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 attention. Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and : Suspected of damaging fertility or the unborn child. Causes damage to organs through prolonged or repeated
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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 firefighting : 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 and personal protective equipment recommendations.

Environmental precautions : Discharge into the environment must be avoided.
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.
If advised by assessment of the local exposure potential, use only in an area equipped with explosion-proof exhaust ventilation.

Advice on safe handling: Avoid inhalation of vapor or mist.
Do not swallow.
Avoid contact with eyes.
Avoid prolonged or repeated contact with skin.
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 and sources of ignition.
Take precautionary measures against static discharges.
Take care to prevent spills, waste and minimize release to the environment.

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</th>
<th>Control parame-</th>
<th>Basis</th>
</tr>
</thead>
</table>

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<table>
<thead>
<tr>
<th>Ethanol</th>
<th>64-17-5</th>
<th>CMP</th>
<th>1.000 ppm</th>
<th>AR OEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Further information: A4 - Not classifiable as a human carcinogen, Irritation</td>
<td></td>
<td></td>
<td></td>
<td></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>Wipe limit</td>
<td>1 µg/100 cm²</td>
<td>Internal</td>
<td></td>
<td></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.

**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.

<table>
<thead>
<tr>
<th>Filter type</th>
<th>Combined particulates and organic vapor type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand protection</td>
<td>Chemical-resistant gloves</td>
</tr>
</tbody>
</table>

**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.
Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

**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.

**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.

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 : Flammable liquid and vapor. 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
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.

**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**
- Argentina. Carcinogenic Substances and Agents Registry: Not applicable
- Control of precursors and essential chemicals for the preparation of drugs: Ethanol

**International Regulations**
The ingredients of this product are reported in the following inventories:
- AICS: not determined
- DSL: not determined
- IECSC: not determined

**SECTION 16. OTHER INFORMATION**

**Further information**

**Full text of other abbreviations**
- ACGIH: USA. ACGIH Threshold Limit Values (TLV)
- AR OEL: Argentina. Occupational Exposure Limits
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ACGIH / STEL : Short-term exposure limit
AR OEL / CMP : TLV (Threshold Limit Value)

AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

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.

AR / Z8