

SECTION 1: Identification of the substance/mixture and of the company/undertaking

- 1.1 Product identifier

- **Trade name:** Levothyroxine sodium (BP, USAN, USP)

- **Article number:**

9106700

9108800

9109400

9109300

- **Synonyms:**

Levothyroxine sodium x hydrate

Thyroxine sodium (P.Cx.)

Sodium salt of L-3[4-(4-Hydroxy-3,5-diiodophenoxy)-3,5-diiodophenyl]alanine (WHO)

L-Thyroxine sodium salt -x- hydrate

Sodium levothyroxine

Sodium O-(4-hydroxy-3,5-diiodophenyl)-3,5-diiodo-L-tyrosinehydrate

3,3',5,5'-Tetraiodo-L-thyroninemonosodium salthydrate

- **CAS Number:**

25416-65-3

- **Registration number**

A registration number is not available for this substance

as the substance or its use are exempted from registration according to Article 2 REACH Regulation (EC) No. 1907/2006,

the annual tonnage does not require a registration

or the registration is envisaged for a later registration deadline.

- **1.2 Relevant identified uses of the substance or mixture and uses advised against**

No further relevant information available.

- **Application of the substance / the mixture** Active pharmaceutical ingredients

- **1.3 Details of the supplier of the safety data sheet**

- **Manufacturer/Supplier:**

EXCELLA GmbH

Nürnberg Str. 12

D-90537 Feucht

Tel.: +49 (0) 9128/404 0

Germany

Fax +49(0)9128 404581

E-mail: info.excella@fareva.com

- **Informing department:** Abteilung Chemische Produktion

- **1.4 Emergency telephone number:**

EXCELLA GmbH

Nürnberg Str. 12

D-90537 Feucht

Tel. +49(0)9128/404 0

Germany

(Inside normal business hours)

e-mail: info.excella@fareva.com

SECTION 2: Hazards identification

- **2.1 Classification of the substance or mixture**

- **Classification according to Regulation (EC) No 1272/2008**



GHS08 health hazard

Repr. 2 H361 Suspected of damaging fertility or the unborn child.

STOT RE 1 H372 Causes damage to organs through prolonged or repeated exposure.

- **Classification according to Directive 67/548/EEC or Directive 1999/45/EC**



T; Toxic

(Contd. on page 2)

Trade name: Levothyroxine sodium (BP, USAN, USP)

(Contd. of page 1)

Repr. Cat. 2

R61-48/23/24/25: May cause harm to the unborn child. Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed.



Xn; Harmful

R62: Possible risk of impaired fertility.

- 2.2 Label elements
- Labelling according to Regulation (EC) No 1272/2008

The substance is classified and labelled according to the CLP regulation.

- Hazard pictograms


GHS08

- Signal word Danger
- Hazard statements

H361 Suspected of damaging fertility or the unborn child.

H372 Causes damage to organs through prolonged or repeated exposure.

- Precautionary statements

P201 Obtain special instructions before use.

P260 Do not breathe dust/fume/gas/mist/vapours/spray.

P301+P310 IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician.

P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

P361 Remove/Take off immediately all contaminated clothing.

P405 Store locked up.

- 2.3 Other hazards
- Results of PBT and vPvB assessment
- PBT: Not applicable.

- vPvB: Not applicable.

SECTION 3: Composition/information on ingredients
- 3.1 Chemical characterisation: Substances
- CAS No. Designation:

25416-65-3 L-Thyroxine sodium salt -x- hydrate

SECTION 4: First aid measures
- 4.1 Description of first aid measures
- General information

Instantly remove any clothing soiled by the product.

Symptoms of poisoning may even occur after several hours; therefore medical observation for at least 48 hours after the accident.

- After inhalation

Supply fresh air or oxygen; call for doctor.

In case of unconsciousness bring patient into stable side position for transport.

- After skin contact

Instantly wash with water and soap and rinse thoroughly.

If skin irritation continues, consult a doctor.

- After eye contact

Rinse opened eye for several minutes (10 - 15) under running water. Then consult doctor.

Use eye protection.

(Contd. on page 3)

Trade name: Levothyroxine sodium (BP, USAN, USP)

(Contd. of page 2)

- **After swallowing**
 Instantly call for doctor.
 Rinse out mouth and then drink plenty of water (200 - 300 ml).
- **4.2 Most important symptoms and effects, both acute and delayed**
 Headache
 Diarrhea
 Vomiting
 Fever
 Profuse sweating
 hot flashes
 Muscular symptoms
 Spasms, convulsions
 Tremor
 Tachycardia
 Palpitation
 Anxiety
 Sleep disturbances
- **Information for doctor** Pharmacological group:
- **Danger** Danger of disturbed cardiac rhythm.
- **4.3 Indication of any immediate medical attention and special treatment needed**
 If swallowed, gastric irrigation with added, activated carbon.
 No specific antidote available. Treat symptomatically and supportively.
 Medical supervision for at least 48 hours

*

SECTION 5: Firefighting measures

- **5.1 Extinguishing media**
- **Suitable extinguishing agents**
 CO₂, extinguishing powder or water jet. Fight larger fires with water jet or alcohol-resistant foam.
- **For safety reasons unsuitable extinguishing agents** Do not use a heavy water stream.
- **5.2 Special hazards arising from the substance or mixture**
 Formation of toxic gases is possible during heating or in case of fire.
 Can be released in case of fire
 metal fumes
 Carbon monoxide (CO), carbon dioxide (CO₂)
 Nitrogen oxides (NO_x)
 Hydrogen iodide (HI)
 Iodide
- **5.3 Advice for firefighters**
- **Protective equipment:**
 Wear self-contained breathing apparatus.
 Do not inhale explosion gases or combustion gases.
 Wear full protective suit.
- **Additional information**
 Dispose of fire debris and contaminated fire fighting water in accordance with official regulations.

SECTION 6: Accidental release measures

- **6.1 Personal precautions, protective equipment and emergency procedures**
 Wear protective equipment (described in section 8). Keep unprotected persons away.
 Avoid causing dust.
 Do not inhale dust.
 Avoid contact with substance.
- **6.2 Environmental precautions:** Do not allow to enter drainage system, surface or ground water.
- **6.3 Methods and material for containment and cleaning up:**
 Dispose of contaminated material as waste according to item 13.
 Collect mechanically.

(Contd. on page 4)

GB

Trade name: Levothyroxine sodium (BP, USAN, USP)

(Contd. of page 3)

- Ensure adequate ventilation.
 Send for recovery or disposal in suitable containers.
- 6.4 Reference to other sections
 See Section 8 for information on personal protection equipment.

SECTION 7: Handling and storage

- **7.1 Precautions for safe handling**
 Thorough dedusting.
 Ensure good ventilation/exhaustion at the workplace.
 Prevent formation of dust.
 Work only in fume cupboard.
 Waste air is to be released into the atmosphere only via suitable separators.
- **Information about protection against explosions and fires:** No special measures required.
- **7.2 Conditions for safe storage, including any incompatibilities**
- **Storage**
- **Requirements to be met by storerooms and containers:** No special requirements.
- **Information about storage in one common storage facility:** Not required.
- **Further information about storage conditions:**
 Protect from the effects of light.
 Protect from humidity and keep away from water.
 Keep container tightly closed.
- **Recommended storage temperature:** Store at 2-8 °C.
- **7.3 Specific end use(s)** No further relevant information available.

SECTION 8: Exposure controls/personal protection

- **Additional information about design of technical systems:** No further data; see item 7.
- **8.1 Control parameters**
- **Components with limit values that require monitoring at the workplace:** Not required.
- **DNELs** No information available
- **PNECs** No information available
- **Additional information:**
 The lists that were valid during the compilation were used as basis.
 OEL (Pfizer): 0.6 µg/m³ (Levothyroxin)
 OEL (SANDOZ): 1 µg/m³ (Levothyroxin Natrium)
 MSDS BEDFORD LABORATORIES: 2 µg/m³
- **8.2 Exposure controls**
- **Personal protective equipment**
- **General protective and hygienic measures**
 The usual precautionary measures should be adhered to general rules for handling chemicals.
 Keep away from foodstuffs, beverages and food.
 Wash hands during breaks and at the end of the work.
 Avoid contact with the eyes and skin.
 Do not inhale dust
- **Breathing equipment:** Use breathing protection only if dust is formed.
- **Recommended filter device for short term use:**



Filter P3

(Contd. on page 5)

GB

Trade name: Levothyroxine sodium (BP, USAN, USP)

(Contd. of page 4)

- Protection of hands:


Protective gloves (EN 374).

The glove material has to be impermeable and resistant to the product/ the substance/ the preparation.
 Due to missing tests no recommendation to the glove material can be given for the product/ the preparation/ the chemical mixture.

To avoid skin problems reduce the wearing of gloves to the required minimum.

Selection of the glove material on consideration of the penetration times, rates of diffusion and the degradation

- Material of gloves

The selection of the suitable gloves does not only depend on the material, but also on further marks of quality and varies from manufacturer to manufacturer.

- Penetration time of glove material

The exact break through time has to be found out by the manufacturer of the protective gloves and has to be observed.

- Eye protection:


Safety glasses

- Body protection: Protective work clothing.
SECTION 9: Physical and chemical properties
- 9.1 Information on basic physical and chemical properties
- General Information
- Appearance:

Form: Crystalline powder

Colour: Cream coloured

- Odour: Odourless

- Taste tasteless

- pH-value at 20 °C: 8.5 - 9.0 (Sat.aq. Solution)

- Change in condition

Melting point/Melting range: 207 - 210 °C

Boiling point/Boiling range: Not determined

- Flash point: Not applicable

- Inflammability (solid, gaseous) Product is not inflammable.

- Ignition temperature:

Decomposition temperature: > 100 °C

langsame Zersetzung

- Danger of explosion: Product is not explosive.

Fine particles (such as dust and mists) may fuel fires/explosions.

- Critical values for explosion:

Lower: Not determined.

Upper: Not determined.

- Vapour pressure: Not applicable.

- Density at 20 °C 2.381 g/cm³

- Solubility in / Miscibility with

Water at 25 °C: 0.15 g/l

- Organic solvents: Soluble in many organic solvents
 abs. Ethanol

- Partition coefficient (n-octanol/water): 4.099 log POW (Levothyroxin)

(Contd. on page 6)

Trade name: Levothyroxine sodium (BP, USAN, USP)

(Contd. of page 5)

- **Viscosity:**
 - dynamic:** Not applicable.
 - kinematic:** Not applicable.
- **9.2 Other information** No further relevant information available.

SECTION 10: Stability and reactivity

- **10.1 Reactivity**
- **10.2 Chemical stability**
- **Thermal decomposition / conditions to be avoided:** No decomposition if used according to specifications.
- **10.3 Possibility of hazardous reactions** No dangerous reactions known
- **10.4 Conditions to avoid** No further relevant information available.
- **10.5 Incompatible materials:** Strong oxidizing materials
- **10.6 Hazardous decomposition products:** No dangerous decomposition products known

SECTION 11: Toxicological information

- **11.1 Information on toxicological effects**
- **Acute toxicity:**

- LD/LC50 values that are relevant for classification:
55-03-8 Levothyroxin natrium (INN.L3.D, ASK)

Oral	LD50	10 000 mg/kg (Rat)
	TDLo	0.020 mg/kg (chd)
		0.117 mg/kg (Woman)

6106-07-6 Levothyroxine sodium salt pentahydrate

scu LD50	50 mg/kg (Rat)
----------	----------------

- **Primary irritant effect:**
- **on the skin:** No irritant effect known.
- **on the eye:** No irritant effect known.
- **Sensitisation:** No sensitizing effect known.
- **Subacute to chronic toxicity:**
- **Carcinogenicity** No information available
- **Genetic Toxicity** No information available
- **Reproductive Effects** No information available
- **Teratogenic effect** No information available
- **Mutagen effect** No information available
- **Additional toxicological information:**
- No data for acute toxicity available.
- Dangerous properties can not be excluded.
- **CMR effects (carcinogenity, mutagenicity and toxicity for reproduction)**
- Repr. 2

SECTION 12: Ecological information

- **12.1 Toxicity**
- **Aquatic toxicity:** No further relevant information available.
- **12.2 Persistence and degradability** No further relevant information available.
- **12.3 Bioaccumulative potential**
- High bioaccumulation potential.
- Bioaccumulation is to be expected (Segregation coefficient (n-octanol/water): 4.099 (Lecothyroxin))
- **12.4 Mobility in soil** No further relevant information available.
- **Additional ecological information:**
- Adverse ecological effects cannot be excluded in the event of improper handling or disposal.

(Contd. on page 7)

Trade name: Levothyroxine sodium (BP, USAN, USP)

(Contd. of page 6)

- General notes:
At present there are no ecotoxicological assessments.
Water danger class 3 (German Regulation) (Self-assessment): extremely hazardous for water.
Do not allow product to reach ground water, water bodies or sewage system, even in small quantities.
- 12.5 Results of PBT and vPvB assessment No information available.

- 12.6 Other adverse effects No further relevant information available.

SECTION 13: Disposal considerations
- 13.1 Waste treatment methods
- Recommendation
Hand over to disposers of hazardous waste.
Chemicals must be disposed of in compliance with restrictive national regulations.
- Uncleaned packagings:
- Recommendation:
Disposal must be made according to official regulations.
Packaging must be disposed of in compliance with country-specific regulations or must be passed to a packaging return system.
SECTION 14: Transport information
- 14.1 UN-Number
- ADR, ADN, IMDG, IATA Void

- 14.2 UN proper shipping name
- ADR Void

- ADN, IMDG, IATA Void

- 14.3 Transport hazard class(es)
- ADR, ADN, IMDG, IATA
- Class Void

- 14.4 Packing group
- ADR, IMDG, IATA Void

- 14.5 Environmental hazards: Not applicable.

- 14.6 Special precautions for user Not applicable.

- 14.7 Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code Not applicable.

- Transport/Additional information: Not dangerous according to the above specifications.

- UN "Model Regulation": -

SECTION 15: Regulatory information
- 15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture
- Labelling according to Regulation (EC) No 1272/2008
The substance is classified and labelled according to the CLP regulation.
- Hazard pictograms


GHS08

(Contd. on page 8)

Trade name: Levothyroxine sodium (BP, USAN, USP)

(Contd. of page 7)

- Signal word *Danger*
- Hazard statements
H361 Suspected of damaging fertility or the unborn child.
H372 Causes damage to organs through prolonged or repeated exposure.
- Precautionary statements
P201 Obtain special instructions before use.
P260 Do not breathe dust/fume/gas/mist/vapours/spray.
P301+P310 IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician.
P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P361 Remove/Take off immediately all contaminated clothing.
P405 Store locked up.
- National regulations
- Information about limitation of use:
Employment restrictions concerning young persons must be observed.
Employment restrictions concerning pregnant and lactating women must be observed.
- Water hazard class: *Water danger class 3 (Self-assessment): extremely hazardous for water.*
- 15.2 Chemical safety assessment: *A Chemical Safety Assessment has not been carried out.*
SECTION 16: Other information

These data are based on our present knowledge. However, they shall not constitute a guarantee for any specific product features and shall not establish a legally valid contractual relationship.

- Reson for alteration *Changing of labelling (Chapter 15).*
- Department issuing data specification sheet:
- Contact:
Mr. Madre
Dept. EHS
- Abbreviations and acronyms:
RID: Règlement international concernant le transport des marchandises dangereuses par chemin de fer (Regulations Concerning the International Transport of Dangerous Goods by Rail)
ICAO: International Civil Aviation Organisation
ims: intramuscular
ipr: intraperitoneal
ivn: intravenous
scu: subcutaneous
LCx: Lethal concentration, x percent kill
LDx: Lethal dose, x percent kill
LCLo: Lowest published lethal concentration
LDLo: Lowest published lethal dose
TCLo: Lowest published toxic concentration
TDLo: Lowest published toxic dose
NOEL: No effect level
NOEC: No observed Effect Concentration
NOAEL: No observed adverse effect level
LOAEL: Low adverse effect level
LOEL: Lowest Observed Effect Level
MTD: Maximum tolerated dose
MIC: Minimal inhibitory concentration is the lowest concentration of drug that inhibits more than 99% of the bacterial population
IC50: The IC50 (Inhibitory Concentration) is a measure of the effectiveness of a compound in inhibiting biological or biochemical function. This quantitative measure indicates how much of a particular drug or other substance is needed to inhibit a given biological by half.
Other percentage values (IC10, IC20, etc.) are sometimes used.
EC50: Concentration of a material in water, a single dose which is expected to cause a biological effect on 50% of a group of test animals.
Other percentage values (EC25, EC40, etc.) are sometimes used.
LOEC: Lowest Observed Effect Concentration
ADR: Accord européen sur le transport des marchandises dangereuses par Route (European Agreement concerning the International Carriage of Dangerous Goods by Road)
IMDG: International Maritime Code for Dangerous Goods
IATA: International Air Transport Association
GHS: Globally Harmonised System of Classification and Labelling of Chemicals
CAS: Chemical Abstracts Service (division of the American Chemical Society)
DNEL: Derived No-Effect Level (REACH)
PNEC: Predicted No-Effect Concentration (REACH)

(Contd. on page 9)

Trade name: Levothyroxine sodium (BP, USAN, USP)

(Contd. of page 8)

LC50: Lethal concentration, 50 percent

LD50 - Median Lethal Dose

vPvB: very Persistent and very Bioaccumulative

Repr. 2: Reproductive toxicity, Hazard Category 2

STOT RE 1: Specific target organ toxicity - Repeated exposure, Hazard Category 1

- Sources

Sax's Dangerous Properties of Industrial Materials; ninth Edititon

HAGERS Handbuch der pharmazeutischen Praxis 5. Aufl., Bd.: 8, Seite: 731 ff

The classification is According to Information about this substance from supplier companies and/or MSDS's of different producers.

Sorbe: Sicherheitstechnische Kenndaten chemischer Stoffe sicherheitsNet.de GmbH, Landsberg

(=> CAS 6106-07-6);

Fachinformation: L-Thyroxin Henning April 2006

- * Data compared to the previous version altered.

GB