

SAFETY DATA SHEET

LONSURF TABLET 15 MG, 20 MG



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

1.1 Product identifier

Product name : LONSURF TABLET 15 MG, 20 MG
EC number : Mixture.
Chemical name : Not available.
Product description : Medicine
Product type : Solid.

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

Not applicable.

1.3 Details of the supplier of the safety data sheet

Manufacturer / Distributor : LES LABORATOIRES SERVIER INDUSTRIE
 905 route de Saran
 45520 GIDY
 FRANCE
 Tel.:+(33) (0)2 38 23 87 00
e-mail address of person responsible for this SDS : mail.reachoril@servier.com

1.4 Emergency telephone number

National advisory body/Poison Centre

Telephone number : +(33) (0)1 40 05 48 48

Supplier

Emergency telephone number (with hours of operation) : Permanence téléphonique DRD: +(33) (0)1 55 72 60 00
 Numéro ORFILA: 01 45 42 59 59
 (working days and hours)

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture

Product definition : Mixture

Classification according to Regulation (EC) No. 1272/2008 [CLP/GHS]

Acute Tox. 4, H302
 Skin Irrit. 2, H315
 Eye Irrit. 2, H319
 Muta. 2, H341
 Repr. 1B, H360D (Unborn child)
 STOT RE 1, H372 (gastrointestinal tract, haematopoietic system and lymphatic system)
 See Section 16 for the full text of the H statements declared above.
 See Section 11 for more detailed information on health effects and symptoms.

2.2 Label elements

Hazard pictograms :



Signal word : Danger

SECTION 2: Hazards identification

| | |
|--|---|
| Hazard statements | : Harmful if swallowed. Causes serious eye irritation. Causes skin irritation. May damage the unborn child. Suspected of causing genetic defects. Causes damage to organs through prolonged or repeated exposure. (gastrointestinal tract, haematopoietic system, lymphatic system) |
| Additional warning phrases | : Not available. |
| <u>Precautionary statements</u> | |
| Prevention | : Obtain special instructions before use. Wear protective gloves. Wear eye or face protection. Do not breathe dust. |
| Response | : Get medical attention if you feel unwell. IF SWALLOWED: Call a POISON CENTER or physician if you feel unwell. |
| Storage | : Store locked up. |
| Disposal | : Dispose of contents and container in accordance with all local, regional, national and international regulations. |
| Supplemental label elements | : Safety data sheet available for professional user on request. |

2.3 Other hazards

| | |
|--|---------------|
| Other hazards which do not result in classification | : None known. |
|--|---------------|

SECTION 3: Composition/information on ingredients

Substance/mixture : Mixture

| Product/ingredient name | Identifiers | % | Classification Regulation (EC) No. 1272/2008 [CLP] | Type |
|----------------------------|-------------------------------|----|--|---------|
| TRIFLURIDINE | EC: 200-722-8 CAS: 70-00-8 | 12 | Acute Tox. 4, H302 Skin Irrit. 2, H315 Eye Irrit. 2, H319 Muta. 2, H341 STOT RE 1, H372 (gastrointestinal tract, haematopoietic system and lymphatic system) | [1] [2] |
| TIPIRACIL HYDROCHLORIDE | CAS: 183204-74-2 | 6 | Skin Irrit. 2, H315 Eye Irrit. 2, H319 See Section 16 for the full text of the H statements declared above. | [1] [2] |

There are no additional ingredients present which, within the current knowledge of the supplier, are classified and contribute to the classification of the substance and hence require reporting in this section.

Type

[1] Substance classified with a health or environmental hazard

[2] Substance with a workplace exposure limit

[3] Substance meets the criteria for PBT according to Regulation (EC) No. 1907/2006, Annex XIII

[4] Substance meets the criteria for vPvB according to Regulation (EC) No. 1907/2006, Annex XIII

[5] Substance of equivalent concern

SECTION 4: First aid measures

4.1 Description of first aid measures

| | |
|-------------------|--|
| Inhalation | : Move exposed person to fresh air. Keep person warm and at rest. If not breathing, if breathing is irregular or if respiratory arrest occurs, provide artificial respiration or oxygen by trained personnel. Get medical attention if symptoms occur. |
| Ingestion | : Wash out mouth with water. Keep person warm and at rest. Get medical attention if symptoms occur. |

SECTION 4: First aid measures

- Skin contact** : Flush contaminated skin with plenty of water. Remove contaminated clothing and shoes. Get medical attention if symptoms occur.
- Eye contact** : Immediately flush eyes with plenty of water, occasionally lifting the upper and lower eyelids. Check for and remove any contact lenses. Get medical attention if irritation occurs.
- Protection of first-aiders** : Put on appropriate personal protective equipment (see Section 8). No action shall be taken involving any personal risk or without suitable training.

4.2 Most important symptoms and effects, both acute and delayed

See section 11 for details.

4.3 Indication of any immediate medical attention and special treatment needed

- Notes to physician** : Treat symptomatically.

SECTION 5: Firefighting measures

5.1 Extinguishing media

- Suitable extinguishing media** : Use dry chemical or CO₂.

- Unsuitable extinguishing media** : None known.

5.2 Special hazards arising from the substance or mixture

- Hazards from the substance or mixture** : No specific fire or explosion hazard.

- Hazardous combustion products** : Decomposition products may include the following materials:
carbon dioxide
carbon monoxide
nitrogen oxides
halogenated compounds

5.3 Advice for firefighters

- Special precautions for fire-fighters** : Promptly isolate the scene by removing all persons from the vicinity of the incident if there is a fire.
- Special protective equipment for fire-fighters** : Fire-fighters should wear appropriate protective equipment and self-contained breathing apparatus (SCBA) with a full face-piece operated in positive pressure mode.

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

- Protection of fire-fighters** : Keep unnecessary and unprotected personnel from entering. Do not touch or walk through spilt material. Put on appropriate personal protective equipment (see Section 8).

6.2 Environmental precautions

Inform the relevant authorities if the product has caused environmental pollution (sewers, waterways, soil or air).

6.3 Methods and material for containment and cleaning up

- Spill** : Prevent entry into sewers, water courses, basements or confined areas. Use a tool to scoop up solid or absorbed material and place into appropriate labelled waste container.

SECTION 6: Accidental release measures

- 6.4 Reference to other sections** :
- See Section 1 for emergency contact information.
 - See Section 8 for information on appropriate personal protective equipment.
 - See Section 13 for additional waste treatment information.

SECTION 7: Handling and storage

7.1 Precautions for safe handling

- Protective measures** :
- Put on appropriate personal protective equipment (see Section 8). Workers should wash hands and face before eating, drinking and smoking. Avoid contact with eyes, skin and clothing.
- Advice on general occupational hygiene** :
- Remove contaminated clothing and protective equipment before entering eating areas. Workers should wash hands and face before eating, drinking and smoking.

7.2 Conditions for safe storage, including any incompatibilities

- :
- Store in accordance with local regulations. Store in original container protected from direct sunlight in a dry, cool and well-ventilated area, away from incompatible materials (see Section 10) and food and drink. Keep container tightly closed and sealed until ready for use. Use appropriate containment to avoid environmental contamination.

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

Occupational exposure limits

| Product/ingredient name | Exposure limit values |
|-------------------------|---|
| TRIFLURIDINE | EU OEL (Europe, 2/2017). OEL SERVIER: 0.02 µg/m ³ 8 hours. |
| TIPIRACIL HYDROCHLORIDE | EU OEL (Europe, 2/2017). OEL SERVIER: 34 µg/m ³ 8 hours. |

8.2 Exposure controls

- Appropriate engineering controls** :
- If this product contains ingredients with exposure limits, use process enclosures, local exhaust ventilation or other engineering controls to keep worker exposure below any recommended or statutory limits.

Individual protection measures

- Hygiene measures** :
- Wash hands, forearms and face thoroughly after handling chemical products, before eating, smoking and using the lavatory and at the end of the working period.
- Respiratory protection** :
- Use a type 2 dust mask.
- Eye/face protection** :
- Goggles should be worn.
- Hand protection** :
- Wear suitable gloves. If used in a solvent, choose gloves appropriated to solvent.
- Body protection** :
- Wear clothes dedicated to handling of chemical products. Suitable protective footwear.
- Environmental exposure controls** :
- In some cases, fume scrubbers, filters or engineering modifications to the process equipment will be necessary to reduce emissions to acceptable levels.

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

- Physical state** :
- Solid. [Coated tablet]
- Colour** :
- White. Pink

SECTION 10: Stability and reactivity

- 10.1 Reactivity** : No specific test data related to reactivity available for this product or its ingredients.
- 10.2 Chemical stability** : The product is stable.
- 10.3 Possibility of hazardous reactions** : Under normal conditions of storage and use, hazardous reactions will not occur.
- 10.4 Conditions to avoid** : No specific data.
- 10.5 Incompatible materials** : No specific data.
- 10.6 Hazardous decomposition products** : Under normal conditions of storage and use, hazardous decomposition products should not be produced.

SECTION 11: Toxicological information

11.1 Information on toxicological effects

Acute toxicity

| Product/ingredient name | Result | Species | Dose | Exposure |
|-------------------------|-----------|---------|-------------|----------|
| TRIFLURIDINE | LD50 Oral | Rat | 2000 mg/kg | - |
| TIPIRACIL | LD50 Oral | Rat | >2000 mg/kg | - |
| HYDROCHLORIDE | | | | |

Irritation/Corrosion

- Conclusion/Summary** : Not available.
- Skin** : Irritating to skin.
- Eyes** : Irritating to eyes.

Sensitiser

- Conclusion/Summary** : Not available.

Mutagenicity

| Product/ingredient name | Test | Experiment | Result |
|-------------------------|---|---|----------|
| TRIFLURIDINE | OECD 471 Bacterial Reverse Mutation Test | Experiment: In vitro | Positive |
| | OECD 473 In vitro Mammalian Chromosomal Aberration Test | Subject: Bacteria Experiment: In vitro | Positive |
| | OECD 474 Mammalian Erythrocyte Micronucleus Test | Subject: Mammalian-Human Experiment: In vivo | Positive |
| | TIPIRACIL | Subject: Mammalian-Animal Experiment: In vitro | Negative |
| HYDROCHLORIDE | OECD 471 Bacterial Reverse Mutation Test | Subject: Bacteria Experiment: In vitro | Negative |
| | OECD 473 In vitro Mammalian Chromosomal Aberration Test | Subject: Mammalian-Human Experiment: In vivo | Negative |
| | OECD 474 Mammalian Erythrocyte Micronucleus Test | Subject: Mammalian-Animal | Negative |


- Conclusion/Summary** : Genotoxic potential suspected.

Carcinogenicity

- Conclusion/Summary** : Not available.

SECTION 11: Toxicological information

Reproductive toxicity

Conclusion/Summary :  Increases in the corpus luteum count, implanting site count and post-implantation loss were observed in pregnant rats with trifluridine:tipiracil combination (1:0.5) at 150 mg FTD/kg/day with embryo lethality occurring in a relatively early phase of implantation.
 ✖ Embryo-fetal developmental toxicity was observed in association with maternal toxicity with trifluridine:tipiracil (1:0.5) combination. These effects were cautiously considered to be evidence of developmental toxicity based on the mechanism of action of the product (trifluridine).

Teratogenicity

Conclusion/Summary : Not available.

Specific target organ toxicity (single exposure)

Not available.

Specific target organ toxicity (repeated exposure)

Not available.

Aspiration hazard

Not available.

Potential chronic health effects

| Product/ingredient name | Result | Species | Dose | Exposure |
|----------------------------|----------------------|---------|------------|----------|
| TRIFLURIDINE | Sub-acute NOAEL Oral | Rat | 50 mg/kg/j | 4 weeks |
| | Sub-acute NOAEL Oral | Monkey | 25 mg/kg/j | 4 weeks |
| TIPIRACIL HYDROCHLORIDE | Sub-acute NOAEL Oral | Rat | 400 mg/kg | 4 weeks |

SECTION 12: Ecological information

12.1 Toxicity

Conclusion/Summary : Not available.

12.2 Persistence and degradability

Conclusion/Summary : Not available.

12.3 Bioaccumulative potential

| Product/ingredient name | LogP _{ow} | BCF | Potential |
|-------------------------|--------------------|-----|-----------|
| TRIFLURIDINE | -0.46 | - | low |

12.4 Mobility in soil

Soil/water partition coefficient (K_{oc}) : Not available.

12.6 Other adverse effects : No known significant effects or critical hazards.

SECTION 13: Disposal considerations

13.1 Waste treatment methods

Methods of disposal : Send to an appropriate hazardous waste incineration facility, in compliance with legislation. Disposal of this product, solutions and any by-products should at all times comply with the requirements of environmental protection and waste disposal legislation and any regional local authority requirements. Care should be taken when handling emptied containers that have not been cleaned or rinsed out. Empty containers or liners may retain some product residues. Avoid dispersal of spilt material and runoff and contact with soil, waterways, drains and sewers.

Hazardous waste : Within the present knowledge of the supplier, this product is not regarded as hazardous waste, as defined by EU Directive 91/689/EEC.

SECTION 14: Transport information

| | ADR/RID | IATA |
|-----------------------------------|--|--|
| 14.1 UN number | Not regulated. | Not regulated. |
| 14.2 UN proper shipping name | - | - |
| 14.3 Transport hazard class(es) | - | - |
| 14.4 Packing group | - | - |
| 14.5 Environmental hazards | No. | No. |
| 14.6 Special precautions 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. | 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. |
| Additional information | - | - |

SECTION 15: Regulatory information**15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture****EU Regulation (EC) No. 1907/2006 (REACH)****Annex XIV - List of substances subject to authorisation****Substances of very high concern**


None of the components are listed.

Annex XVII - Restrictions on the manufacture, placing on the market and use of certain dangerous substances, mixtures and articles

Restricted to professional users.

Other EU regulations**Europe inventory** : Not determined.**15.2 Chemical Safety Assessment** : This product contains substances for which Chemical Safety Assessments are still required.**SECTION 16: Other information**
 Indicates information that has changed from previously issued version.
Abbreviations and acronyms

: ATE = Acute Toxicity Estimate
 CLP = Classification, Labelling and Packaging Regulation [Regulation (EC) No. 1272/2008]
 DNEL = Derived No Effect Level
 EUH statement = CLP-specific Hazard statement
 PNEC = Predicted No Effect Concentration
 RRN = REACH Registration Number

Classification according to Regulation (EC) No. 1272/2008 [CLP/GHS] Acute Tox. 4, H302

Skin Irrit. 2, H315

Eye Irrit. 2, H319

Muta. 2, H341

Repr. 1B, H360D (Unborn child)

STOT RE 1, H372 (gastrointestinal tract, haematopoietic system and lymphatic system)

Procedure used to derive the classification according to Regulation (EC) No. 1272/2008 [CLP/GHS]

SECTION 16: Other information

| Classification | Justification |
|--|---|
| Acute Tox. 4, H302 Skin Irrit. 2, H315 Eye Irrit. 2, H319 Muta. 2, H341 Repr. 1B, H360D (Unborn child) STOT RE 1, H372 (gastrointestinal tract, haematopoietic system and lymphatic system) | On basis of test data Calculation method Calculation method Calculation method Expert judgment Expert judgment |

Full text of abbreviated H statements

| | |
|---|--|
| H302 | Harmful if swallowed. |
| H315 | Causes skin irritation. |
| H319 | Causes serious eye irritation. |
| H341 | Suspected of causing genetic defects. |
| H360D (Unborn child) | May damage the unborn child. |
| H372 (gastrointestinal tract, haematopoietic system and lymphatic system) | Causes damage to organs through prolonged or repeated exposure. (gastrointestinal tract, haematopoietic system and lymphatic system) |

Full text of classifications [CLP/GHS]

| | |
|--|--|
| Acute Tox. 4, H302 | ACUTE TOXICITY (oral) - Category 4 |
| Eye Irrit. 2, H319 | SERIOUS EYE DAMAGE/ EYE IRRITATION - Category 2 |
| Muta. 2, H341 | GERM CELL MUTAGENICITY - Category 2 |
| Repr. 1B, H360D (Unborn child) | TOXIC TO REPRODUCTION (Unborn child) - Category 1B |
| Skin Irrit. 2, H315 | SKIN CORROSION/IRRITATION - Category 2 |
| STOT RE 1, H372 (gastrointestinal tract, haematopoietic system and lymphatic system) | SPECIFIC TARGET ORGAN TOXICITY (REPEATED EXPOSURE) (gastrointestinal tract, haematopoietic system and lymphatic system) - Category 1 |

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Notice to reader

The information provided herein is derived from tests carried out by SERVIER or accredited laboratories.

To the best of our knowledge, the information contained herein is accurate.

All materials may present unknown hazards and should be used with caution. Although certain hazards are described herein, we cannot guarantee that these are the only hazards that exist.