SECTION 1: Identification of the substance/mixture and the company/business.

1.1. Product identifier

Chemical name: Lomustine
CAS number: 13010-47-4
EC number: 235-859-2
REACH registration number: N/A

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

Relevant identified uses: active pharmaceutical ingredient of a medicine. It is an anticancer cytotoxic compound.

1.3. Details of the supplier of the safety data sheet

Firm: Corden Pharma Latina S.P.A.
Contact address: Via del Murillo km 2,800 Sermoneta (LT)
Country: Italy
Telephone number: 07733101
Email address: she.latina@cordenpharma.com

1.4. Emergency telephone number

Poison control centre, Gemelli Hospital of Rome
Telephone: 06/3054343
Poison control centre, "La Sapienza" Rome
Telephone: 06/49970698

NextSource Biotechnology, Miami, FL
Telephone: 1-855-672-2468 opt #3
American Association of Poison Control Centers:
Telephone: 1-800-222-1222

SECTION 2: Hazards identification

2.1. Classification of the substance or mixture

Classification in accordance with the Regulation 1272/2008/EC (CLP)

Acute Tox.3 H301
Carc. 1B H350
Muta. 1B H340
STOT RE 1 H372
Repr. 1A H360FD
For the complete text of the hazard identifications (H) reported in this section, refer to section 16.

Classification according to the directive 67/548/EEC

T Toxic R45, R25
For the complete text of the R phrases reported in this section, refer to section 16.

Supplementary information

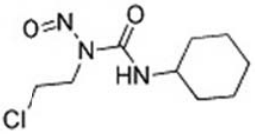
N/D

2.2. Label elements

Hazard indications
H301 Toxic if swallowed.
H350 May cause cancer.
H340: May cause genetic defects <state the route of exposure if it is confirmed that no other route of exposure method carries the same hazard>.
H372: Causes damage to organs <or state all the organs concerned, if known> through prolonged or repeated exposure <state the route of exposure if confirmed that no other route of exposure carried the same hazard>.
H360FD: May damage fertility or the unborn child.
Precautionary statements
P260 – Do not breathe dust/fumes/gas/mist/vapours/spray.
P280 - Wear protective gloves/protective clothing/eye protection/face protection.
P285 – In case of inadequate ventilation, wear respiratory protection.
P314 – Get medical advice/attention if you feel unwell.
P101 – If medical advice is needed, have product container or label at hand.
P201 – Obtain special instructions before use.

2.3. Other hazards
N/D

SECTION 3: Composition/information on ingredients

3.1. Substances
Synonyms: 1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea
CAS number: 13010-47-4
EC number: 235-859-2
Molecular formula: C9H16ClN3O2
Molecular weight: 233.70 g/mol
Molecular structure: 

Index number in attachment IV of the CLP: N/A
CAS number in attachment VI of the CLP: N/A
Identification of impurities, additives, stabilisers: there are no impurities that contribute to the classification of this substance

3.2 Mixtures
N/A

SECTION 4: First aid measures

4.1 Description of the first aid measures

General information
Consult a doctor. Show this safety sheet to the doctor.
Inhalation
If inhaled, take the person into the fresh air. If not breathing, administer artificial respiration. Consult a doctor.
Contact with the skin
Wash with soap and a lot of water. Immediately take the casualty to hospital. Consult a doctor.
Contact with the eyes
As a precaution, rinse the eyes with water.
Ingestion
Do not administer anything to an unconscious person. Rinse the mouth with water. Consult a doctor.

4.2. Main symptoms and effects, both acute and delayed

Acute effects
Nausea, vomiting, diarrhoea, loss of appetite, inflammation of the stomach, death, burning, pain, redness and swelling of the skin, bruising, dehydration, allergic reactions, anaphylaxis and depression of the central nervous system.
Chronic effects
Bleeding, loss of hair, infection, fever, chills, sore throat, jaundice, shortness of breath, coughing, swelling, neurological effects, confusion, ocular effects, changes to dermal pigments and changes in the blood vessels.
Aggravated Medical Conditions include: bone marrow suppression.

4.3. Indication of any need to immediately consult a doctor and for special treatments

It is recommended to carry out a preliminary preventive test with medical records for employees potentially exposed to this compound. A base line for the test includes: a complete blood count with differential, a blood test for kidney function, a blood test for liver function, a pulmonary function test, urine analysis. The need for subsequent periodic control tests should be considered depending on the duration and times of exposure to the substance. These tests should be supervised by a doctor furnished with complete knowledge of both the toxicity of the compound and the gravity of exposure in the workplace. It is recommended that the contents are similar to the preliminary tests.
Pregnant or breastfeeding employees or those who are involved in other reproductive activities must be encouraged to consult the company doctor responsible for monitoring the health of the workers.

SECTION 5: Fire prevention measures

5.1. Extinguishing media

Suitable extinguishing media
Use water spray, alcohol-resistant foam, dry chemical products or carbon dioxide.

Suitable extinguishing media
Water jets

5.2. Special hazards arising from the substance or the mixture

Hazardous combustion products: oxides of carbon, oxides of nitrogen (NOx), hydrochloric acid gas

5.3. Advice for fire-fighters

In case of fire, wear respiratory protection equipment, if necessary, with an independent air supply.

5.4 Further information
N/D

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures
Use respiratory protection. Avoid the formation of dust. Avoid breathing in steam/mist/gas.
Provide adequate ventilation. Evacuate the personnel to safe areas.
Do not inhale dust.
See Section 8 for the Personal Protective Equipment.

6.2. Environmental precautions
Avoid leakage or spillage, if this can be achieved safely. Do now allow the product to enter drains.

6.3. Methods and materials for containment and cleaning up
Collect and dispose of without creating dust. Sweep up and shovel. Store in suitable, sealed containers for disposal.

6.4. References to other sections
For disposal, refer to section 13.

SECTION 7: Handling and storage

7.1. Precautions for safe handling
Avoid contact with eyes and skin. Avoid the formation of dust and the dispersal of the product in the air.
Avoid exposure – obtain special instructions before use.
Arrange suitable ventilation in places where dust gathers.
For the precautions, see section 2.2.

7.2. Conditions for safe storage , including any incompatibilities
Store in a well-ventilated place. Keep the container hermetically sealed in a dry and well-ventilated environment.

Recommended storage temperature: -20 °C
Light sensitive.

7.3 Specific end uses
Apart from the uses described in section 1.2, other specific uses are not envisaged.

SECTION 8: Exposure control/personal protection

8.1 Control parameters
Components with exposure limits
TWA= 0.01 mg/m^3

8.2 Exposure controls

Suitable technical controls

Avoid contact with skin, eyes and clothing. Wash hands before breaks and immediately after handling the product.

Personal protection

Eye/face protection

Visor and protective goggles. Use eye protection equipment tested and approved in accordance with the requirements of the appropriate technical standards such as NIOSH (USA) or EN 166 (EU).

Skin protection

Handle with gloves. Gloves must be checked before use. Use an appropriate technique for the removal of gloves (without touching the external surfaces of the glove) in order to avoid skin contact with this product. Dispose of contaminated gloves after use in accordance with the current regulations and good laboratory practice.

Wash and dry hands. The selected protective gloves must satisfy the requirements of the EU directive 89/686/EEC and the EN 374 standards drawn from it.

Physical protection

Complete protective clothing resistant to chemical substances. The type of protective equipment must be selected on the basis of the concentration and quantity of hazardous substance in the workplace.

Respiratory protection

Should the risk assessment envisage the need for purified air respirators, use a filtering facemask with P3 (EN 143) type filter as a backup to the technical measures. If the respirator is the only means of protection, use a full-face ventilated system. Use respirators and components tested and approved by the competent regulatory bodies, such as NIOSH (USA) and CEN (EU).

Environmental exposure control

Avoid leakage or spillage, if this can be achieved safely. Do not allow the product to enter drains.

SECTION 9: Physical and chemical properties

9.1. Information on the basic physical and chemical properties

a) Appearance: Physical state: powder
Colour: light yellow

b) Odour: N/D

c) Olfactory threshold: N/D

d) pH: N/D

e) Melting point/freezing point: Melting point/range: 88 - 90 °C

f) Initial boiling point and boiling range: N/D

g) Flash point: N/D

h) Evaporation rate: N/D

i) Flammability: N/D

j) Upper/lower limits of flammability or explosiveness: N/D

k) Vapour pressure: N/D

l) Vapour density: N/D

m) Relative density: N/D

n) Water solubility: 0.111 g/l at 25°C

o) n-Octonal/water partition coefficient: log Pow: 2,365

p) Autoignition temperature: N/D

q) Decomposition temperature: N/D

r) Viscosity: N/D

s) Explosive properties: N/D

t) Oxidising properties: N/D

9.2 Other information

a) Solubility: alcohol: soluble
methylene chloride: soluble
chloroform: soluble
acetone: soluble
sodium hydroxide solution: soluble

SECTION 10: Stability and reactivity

10.1. Reactivity
N/D

10.2 Chemical stability
Stable under the recommended storage conditions.

10.3. Possibility of hazardous reactions
N/D

10.4. Conditions to be avoided
Avoid humidity.

10.5. Incompatible materials
Strong oxidising agents, strong bases

10.6. Hazardous decomposition products
Other hazardous decomposition products – no information available
In case of fire: see section 5

SECTION 11: Toxicological information

11.1. Information on the toxicological effects
a) Acute toxicity: *Oral:* DL50 (rat): 70 mg/kg
DL50 (mouse, female): 38 mg/kg
other administration routes: DL50 (rat, Intraperitoneal): 50,350 mg/kg
DL50 (mouse, Intraperitoneal): 53 mg/kg
b) Skin corrosion/irritation: N/D
c) Serious eye damage/serious eye irritation: N/D
d) Respiratory or skin sensitisation: N/D
e) Geminal cell mutagenicity: This substance resulted positive in a battery of genotoxicity tests both *in vivo* and *in vitro*.
f) Carcinogenicity: This product is, or contains, a component deemed to be a possible carcinogenic agent according to its IARC, OSHA, ACGIH, NTP or EPA classification.
Possible carcinogen for humans
IARC: 2A - Group 2A: Probably carcinogenic for humans (Lomustine)
g) Reproductive toxicity: *Reproductive Toxicity Test:* Studies on animals indicate that there may be effects on reproduction.
Developmental toxicity test: Several studies have been conducted on development. Birth defects were observed in studies on animals.
h) Specific target organ toxicity (STOT) – single exposure: N/D
i) Specific target organ toxicity (STOT) – repeated exposure: N/D
j) Hazard in the event of aspiration: N/D

further information
RTECS: YS4900000

Potential health consequences:
General effects from therapeutic use – Symptoms: nausea, vomiting, diarrhoea, loss of appetite, inflammation of the stomach, death, burning, pain, redness and swelling of the skin, bruising, bleeding, loss of hair, infection, fever, chills, sore throat, jaundice, shortness of breath, coughing, swelling, neurological effects, confusion, ocular effects, changes to dermal pigments and changes in the blood vessels. Other effects include: bone marrow suppression, decrease white blood cell count, decrease of red blood cell count, cancer, pulmonary toxicity, pulmonary fibrosis, increase in liver enzymes, liver toxicity, kidney toxicity.

Causal relationship(s): Symptoms: skin sensitisation. The use of topical products containing this substance has produced sensitisation in humans.

SECTION 12: Ecological information

12.1. Toxicity
ACUTE (SHORT TERM) TOXICITY:
N/D
CHRONIC (LONG TERM) TOXICITY:
N/D

12.2. Persistence and degradability
N/D

12.3 Bioaccumulative potential
N/D

12.4 Mobility in soil
N/D:

12.5. Results of PBT and vPvB assessment
N/D

12.6. Other harmful effects
N/D

SECTION 13: Disposal considerations

13.1. Waste treatment methods
Product
Assign non-recyclable waste and surpluses to an authorised waste disposal company.
Solubilise or mix the product with a combustible solvent, then burn in an incinerator for chemical products equipped with an afterburner and scrubber.
Contaminated containers
Dispose of as an unused product.

SECTION 14: Transport information

14.1. UN number
ADR/RID: 2811 IMDG: 2811 IATA: 2811

14.2 UN proper shipping name.
ADR/RID: TOXIC SOLID, ORGANIC N.A.S. (Lomustine)
IMDG: TOXIC SOLID, ORGANIC, N.O.S. (Lomustine)
IATA: Toxic solid, organic, n.o.s. (Lomustine)

14.3. Hazard classes connected to transport
ADR/RID: 6.1 IMDG: 6.1 IATA: 6.1

14.4. Packaging group
ADR/RID: III IMDG: III IATA: III

14.5 Environmental hazards
ADR/RID: no IMDG Marine pollutant: no IATA: no

14.6. Special precautions for users.
N/D

14.7. Transport in bulk according to attachment II of MARPOL 73/78 and the IBC code
N/D

SECTION 15: Regulatory information

This safety sheet respects the instructions of (EC) Regulation Number 1907/2006

15.1. Specific regulations and laws on health, safety and the environment for the substance or the mixture
N/D

15.2. Chemical safety assessment
A chemical safety assessment was not carried out.

SECTION 16: Other information

Complete text of the hazard indications (H) referred to in sections 2 – 3.
Acute Tox.3; Acute toxicity (Category 3)
Carc. 1B; Carcinogen (Category 1B)
Muta. 1B; Mutagenicity on germinal cells (Category 1B)
STOT RE 1; Specific target organ toxicity – Repeated exposure (Category 1)
Repr. 1A; Reproductive toxicity (Category 1)
H301 Toxic if swallowed.
H350 May cause cancer.
H340: May cause generic defects <state the route of exposure if it is confirmed that no other route of exposure method carries the same hazard>.

H372: Causes damage to organs <or state all the organs concerned, if known> through prolonged or repeated exposure <state the route of exposure if confirmed that no other route of exposure carried the same hazard>.
H360FD: May damage fertility or the unborn child.

Full text of R phrases referred to in Sections 2 and 3
T Toxic
R25 Toxic if swallowed.
R45 May cause cancer.

The above information is held to be correct but it cannot be exhaustive and therefore must be considered purely indicative.

Bibliography
[1] MSDS Bristol Myers Squibb