SAFETY DATA SHEET
Cimetidine Formulation

Version 1.2  Revision Date: 09/13/2019  SDS Number: 4242357-00003  Date of last issue: 23.05.2019
Date of first issue: 03.05.2019

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Cimetidine Formulation

Manufacturer or supplier's details
Company: MSD
Address: 50 Tuas West Drive
Singapore - Singapore 638408
Telephone: 908-740-4000
Emergency telephone number: 65 6697 2111 (24/7/365)
E-mail address: EHSDATASTEWARD@msd.com
Telefax: 908-735-1496

Recommended use of the chemical and restrictions on use
Recommended use: Pharmaceutical

2. HAZARDS IDENTIFICATION

GHS Classification
Reproductive toxicity: Category 1B
Specific target organ toxicity - repeated exposure (Oral): Category 2 (Liver, Kidney, Testis)

GHS label elements
Hazard pictograms:

Signal word: Danger
Hazard statements:
H360D May damage the unborn child.
H373 May cause damage to organs (Liver, Kidney, Testis) through prolonged or repeated exposure if swallowed.

Precautionary statements:
Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P308 + P313 IF exposed or concerned: Get medical advice/
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Storage:
P405 Store locked up.

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

Additional Labelling
The following percentage of the mixture consists of ingredient(s) with unknown hazards to the aquatic environment: 40 %

Other hazards which do not result in classification
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.
May form explosive dust-air mixture during processing, handling or other means.

3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>cimetidine</td>
<td>51481-61-9</td>
<td>&gt;= 30 - &lt; 50</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Starch</td>
<td>9005-25-8</td>
<td>&gt;= 1 - &lt; 10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>&gt;= 1 - &lt; 10</td>
<td></td>
</tr>
</tbody>
</table>

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: If in eyes, rinse well with water. 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 delayed: May damage the unborn child. May cause damage to organs through prolonged or repeated exposure if swallowed. Contact with dust can cause mechanical irritation or drying of the skin.
5. FIREFIGHTING MEASURES

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

Unsuitable extinguishing media : None known.

Specific hazards during firefighting : Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard.
Exposure to combustion products may be a hazard to health.

Hazardous combustion products : Carbon oxides
Nitrogen oxides (NOx)
Sulphur oxides
Metal 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 firefighters : In the event of fire, wear self-contained breathing apparatus.
Use personal protective equipment.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures : 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.
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 : Sweep up or vacuum up spillage and collect in suitable container for disposal.
Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air).
Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration.
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 deter-
mine which regulations are applicable.
Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

7. HANDLING AND STORAGE

Technical measures: Static electricity may accumulate and ignite suspended dust causing an explosion.
Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation: If sufficient ventilation is unavailable, use with local exhaust ventilation.

Advice on safe handling: Do not get on skin or clothing.
Do not breathe dust.
Do not swallow.
Avoid contact with eyes.
Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment
Keep container tightly closed.
Minimize dust generation and accumulation.
Keep container closed when not in use.
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 labelled containers.
Store locked up.
Keep tightly closed.
Store in accordance with the particular national regulations.

Materials to avoid: Do not store with the following product types:
Strong oxidizing agents

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components 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>cimetidine</td>
<td>51481-61-9</td>
<td>TWA</td>
<td>1000 µg/m3 (OEB 1)</td>
<td></td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>PEL (long term)</td>
<td>10 mg/m3</td>
<td>SG OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m3</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>PEL (long term)</td>
<td>10 mg/m3</td>
<td>SG OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m3</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>PEL (long term)</td>
<td>10 mg/m3</td>
<td>SG OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Inhalable fraction)</td>
<td>10 mg/m3</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Res-)</td>
<td>3 mg/m3</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>
Engineering measures: Use feasible engineering controls to minimize exposure to compound. All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.

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: Particulates type
Hand protection Material: Chemical-resistant gloves

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.

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.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: powder
Colour: No data available
Odour: No data available
Odour Threshold: No data available
pH: No data available
Melting point/freezing point: No data available
Initial boiling point and boiling range: No data available
Flash point: Not applicable
Evaporation rate: Not applicable
10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reactions : May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

Conditions to avoid : Heat, flames and sparks. Avoid dust formation.
Incompatible materials : Oxidizing agents
Hazardous decomposition products : No hazardous decomposition products are known.
11. TOXICOLOGICAL INFORMATION

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

Acute toxicity:
Not classified based on available information.

Components:

Cimetidine:
- Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
  LD50 (Mouse): 2,550 mg/kg
  LD50 (Hamster): > 4,000 mg/kg
- Acute toxicity (other routes of administration):
  LD50 (Rat): 106 mg/kg
  Application Route: Intravenous
  LD50 (Rabbit): 164 mg/kg
  Application Route: Intravenous
  LD50 (Rat): 860 mg/kg
  Application Route: Subcutaneous
  LD50 (Mouse): 437 mg/kg
  Application Route: Subcutaneous
  Symptoms: Convulsions

Cellulose:
- Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg

Starch:
- Acute oral toxicity: LD50 (Mouse): > 5,000 mg/kg

Magnesium stearate:
- Acute oral toxicity:
  Method: OECD Test Guideline 423
  Assessment: The substance or mixture has no acute oral toxicity
  Remarks: Based on data from similar materials
- Acute dermal toxicity:
  LD50 (Rabbit): > 2,000 mg/kg
  Remarks: Based on data from similar materials
Skin corrosion/irritation
Not classified based on available information.

Components:
Magnesium stearate:
  Species: Rabbit
  Result: No skin irritation
  Remarks: Based on data from similar materials

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

Components:
Magnesium stearate:
  Species: Rabbit
  Result: No eye irritation
  Remarks: Based on data from similar materials

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:
Magnesium stearate:
  Test Type: Maximisation Test
  Exposure routes: Skin contact
  Species: Guinea pig
  Method: OECD Test Guideline 406
  Result: negative
  Remarks: Based on data from similar materials

Germ cell mutagenicity
Not classified based on available information.

Components:
cimetidine:
  Genotoxicity in vitro:
    Test Type: Bacterial reverse mutation assay (AMES)
    Result: negative
    Test Type: Chromosomal aberration
    Result: negative
    Test Type: unscheduled DNA synthesis assay
    Test system: rat hepatocytes
    Result: negative
Cimetidine Formulation

Test Type: unscheduled DNA synthesis assay
Result: negative

Cellulose:
Genotoxicity in vitro
: Test Type: Bacterial reverse mutation assay (AMES)
  Result: negative

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

Cellulose:
Genotoxicity in vivo
: Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
  Species: Mouse
  Application Route: Ingestion
  Result: negative

Magnesium stearate:
Genotoxicity in vitro
: Test Type: In vitro mammalian cell gene mutation test
  Result: negative
  Remarks: Based on data from similar materials

Genotoxicity in vitro
: Test Type: Chromosome aberration test in vitro
  Method: OECD Test Guideline 473
  Result: negative
  Remarks: Based on data from similar materials

Genotoxicity in vitro
: Test Type: Bacterial reverse mutation assay (AMES)
  Result: negative
  Remarks: Based on data from similar materials

Carcinogenicity
Not classified based on available information.

Components:
cimetidine:
Species: Rat
Application Route: Oral
Exposure time: 2 Years
Target Organs: Testis
Remarks: Benign tumor(s)
Carcinogenicity - Assessment: No evidence of carcinogenicity in animal studies.

Cellulose:
Species: Rat
Application Route: Ingestion
Exposure time: 72 weeks
Result: negative
Reproductive toxicity
May damage the unborn child.

Components:
cimetidine:
Effects on fertility :
  Test Type: Fertility/early embryonic development
  Species: Rat
  Application Route: Oral
  Fertility: NOAEL: 950 mg/kg body weight
  Result: No effect on reproduction capacity

Effects on foetal development :
  Test Type: Development
  Species: Rat
  Application Route: Oral
  Developmental Toxicity: LOAEL: 17 mg/kg body weight
  Symptoms: male reproductive effects
  Remarks: Adverse effects were observed in males only.

Reproductive toxicity - Assessment :
  May damage the unborn child.

Cellulose:
Effects on fertility :
  Test Type: One-generation reproduction toxicity study
  Species: Rat
  Application Route: Ingestion
  Result: negative

Effects on foetal development :
  Test Type: Fertility/early embryonic development
  Species: Rat
  Application Route: Ingestion
  Result: negative

Magnesium stearate:
Effects on fertility :
  Test Type: Combined repeated dose toxicity study with the
  reproduction/developmental toxicity screening test
  Species: Rat
  Application Route: Ingestion
  Method: OECD Test Guideline 422
  Result: negative
  Remarks: Based on data from similar materials

Effects on foetal development :
  Test Type: Embryo-foetal development
  Species: Rat
  Application Route: Ingestion
  Result: negative
  Remarks: Based on data from similar materials

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
May cause damage to organs (Liver, Kidney, Testis) through prolonged or repeated exposure if swallowed.
Components:

**cimetidine:**
- **Exposure routes:** Oral
- **Target Organs:** Liver, Kidney, Testis
- **Assessment:** May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

**cimetidine:**
- **Species:** Rat
- **LOAEL:** 160 mg/kg
- **Application Route:** Oral
- **Exposure time:** 2 Months
- **Target Organs:** Gastrointestinal tract
- **Remarks:** May cause damage to organs.

- **Species:** Rat
  - **NOAEL:** 200 mg/kg
  - **Application Route:** Oral
  - **Exposure time:** 12 Months
  - **Symptoms:** No adverse effects

- **Species:** Rat
  - **LOAEL:** 950 mg/kg
  - **Application Route:** Oral
  - **Exposure time:** 2 yr
  - **Target Organs:** Liver, Testis, Prostate
  - **Remarks:** May cause damage to organs.

- **Species:** Dog
  - **NOAEL:** 366 mg/kg
  - **Application Route:** Oral
  - **Exposure time:** 12 Months
  - **Target Organs:** Liver, Kidney, Prostate
  - **Remarks:** May cause damage to organs.

- **Species:** Dog
  - **NOAEL:** 144 mg/kg
  - **Application Route:** Oral
  - **Exposure time:** 4 yr
  - **Symptoms:** No adverse effects

**Cellulose:**
- **Species:** Rat
  - **NOAEL:** >= 9,000 mg/kg
  - **Application Route:** Ingestion
  - **Exposure time:** 90 Days

**Magnesium stearate:**
Species: Rat
NOAEL: > 100 mg/kg
Application Route: Ingestion
Exposure time: 90 Days
Remarks: Based on data from similar materials

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:
cimetidine:
Ingestion: Symptoms: The most common side effects are: Headache, Dizziness, Nausea, skin rash, Itching, May cause, central nervous system effects, gynecomastia, impotence, kidney effects
Remarks: May cause harm to breast-fed children.

12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:
cimetidine:
Ecotoxicology Assessment
Acute aquatic toxicity: Toxic effects cannot be excluded
Chronic aquatic toxicity: Toxic effects cannot be excluded

Cellulose:
Toxicity to fish: LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l
Exposure time: 48 h
Remarks: Based on data from similar materials

Magnesium stearate:
Toxicity to fish: LC50 (Leuciscus idus (Golden orfe)): > 100 mg/l
Exposure time: 48 h
Method: DIN 38412
Remarks: Based on data from similar materials

Toxicity to daphnia and other aquatic invertebrates: EL50 (Daphnia magna (Water flea)): > 1 mg/l
Exposure time: 47 h
Test substance: Water Accommodated Fraction
Remarks: Based on data from similar materials
No toxicity at the limit of solubility

Toxicity to algae/aquatic plants: EL50 (Pseudokirchneriella subcapitata (green algae)): > 1 mg/l
Exposure time: 72 h
Test substance: Water Accommodated Fraction
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials
No toxicity at the limit of solubility

NOELR (Pseudokirchneriella subcapitata (green algae)): > 1 mg/l
Exposure time: 72 h
Test substance: Water Accommodated Fraction
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials

Toxicity to microorganisms: EC10 (Pseudomonas putida): > 100 mg/l
Exposure time: 16 h
Test substance: Water Accommodated Fraction
Remarks: Based on data from similar materials

Persistence and degradability

Components:

Cellulose:
Biodegradability: Result: Readily biodegradable.

Magnesium stearate:
Biodegradability: Result: Not biodegradable
Remarks: Based on data from similar materials

Bioaccumulative potential

Components:

cimetidine:
Partition coefficient: n-octanol/water: log Pow: 0.40

Magnesium stearate:
Partition coefficient: n-octanol/water: log Pow: > 4

Mobility in soil
No data available

Other adverse effects
No data available

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.
If not otherwise specified: Dispose of as unused product.
14. TRANSPORT INFORMATION

International Regulations

UNRTDG
Not regulated as a dangerous good

IATA-DGR
Not regulated as a dangerous good

IMDG-Code
Not regulated as a dangerous good

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

15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture

Workplace Safety and Health Act and Workplace Safety and Health (General Provisions) Regulations: This product is subjected to the SDS, labelling, PEL and other requirements in the Act/Regulations.

Environmental Protection and Management Act and Environmental Protection and Management (Hazardous Substances) Regulations : Not applicable

Fire Safety (Petroleum and Flammable Materials) Regulations : Not applicable

The components of this product are reported in the following inventories:

AICS : not determined

DSL : not determined

IECSC : not determined

16. OTHER INFORMATION

Further information


Date format : dd.mm.yyyy

Full text of other abbreviations

ACGIH : USA. ACGIH Threshold Limit Values (TLV)

SG OEL : Singapore. Workplace Safety and Health Act - First Schedule Permissible Exposure Limits of Toxic Substances
ACGIH / TWA : 8-hour, time-weighted average
SG OEL / PEL (long term) : Permissible Exposure Level (PEL) Long Term

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.

SG / EN