SAFETY DATA SHEET

Carbidopa / Levodopa Formulation

Version: 3.12
Revision Date: 10.10.2020
SDS Number: 50123-00016
Date of last issue: 23.03.2020
Date of first issue: 23.01.2015

Section 1: Identification

Product name: Carbidopa / Levodopa Formulation

Manufacturer or supplier's details
Company: Organon & Co.
Address: 30 Hudson Street, 33nd floor
Jersey City, New Jersey, U.S.A 07302
Telephone: 551-430-6000
Emergency telephone number: 215-631-6999
E-mail address: EHSSTEWARD@organon.com

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

Section 2: Hazard identification

GHS Classification
Acute toxicity (Oral): Category 4
Reproductive toxicity: Category 2
Specific target organ toxicity - repeated exposure (Oral): Category 1 (Central nervous system)

GHS label elements
Hazard pictograms:
Signal word: Danger
Hazard statements:
H302 Harmful if swallowed.
H361d Suspected of damaging the unborn child.
H372 Causes damage to organs (Central nervous system) 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.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P281 Use personal protective equipment as required.
Response:
P301 + P312 + P330 IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell. Rinse mouth.
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
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.

Section 3: Composition/information on ingredients

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levodopa</td>
<td>59-92-7</td>
<td>&gt;= 60 &lt;= 100</td>
</tr>
<tr>
<td>Carbidopa</td>
<td>38821-49-7</td>
<td>&gt;= 10 &lt; 30</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>&lt; 10</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 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. Never give anything by mouth to an unconscious person.

Most important symptoms and effects, both acute and: Harmful if swallowed. Suspected of damaging the unborn child.
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delayed
Causes damage to organs through prolonged or repeated exposure if swallowed. Contact with dust can cause mechanical irritation or drying of the skin. Dust contact with the eyes can lead to mechanical irritation.

Protection of first-aiders:
First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

Notes to physician:
Treat symptomatically and supportively.

Section 5: Fire-fighting 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
- 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.

Section 6: Accidental release measures

Personal precautions, protective equipment and emergency procedures:
- Use personal protective equipment.
- Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

Environmental precautions:
- Avoid release to the environment.
- 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 dis-
posal 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: 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: Use only with adequate ventilation.

Advice on safe handling:
- Do not breathe dust.
- Do not swallow.
- Avoid contact with eyes.
- Avoid prolonged or repeated contact with skin.
- Wash skin thoroughly after handling.
- Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment.
- 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.
- Do not eat, drink or smoke when using this product.
- Take care to prevent spills, waste and minimize release to the environment.

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.

Conditions for safe storage:
- Keep in properly labelled containers.
- Store locked up.
- Store in accordance with the particular national regulations.

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

Section 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>Levodopa</td>
<td>59-92-7</td>
<td>TWA</td>
<td>500 µg/m3 (OEB 2)</td>
<td>Internal</td>
</tr>
</tbody>
</table>
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Carbidopa 38821-49-7  TWA 2,000 µg/m³ (OEB 1)  Internal

Cellulose 9004-34-6  WES-TWA 10 mg/m³  NZ OEL
TWA 10 mg/m³  ACGIH

Starch 9005-25-8  WES-TWA 10 mg/m³  NZ OEL
TWA 10 mg/m³  ACGIH

Magnesium stearate 557-04-0  WES-TWA 10 mg/m³  NZ OEL
TWA (Inhalable particulate matter) 10 mg/m³  ACGIH
TWA (Respirable particulate matter) 3 mg/m³  ACGIH

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.

Section 9: Physical and chemical properties
Appearance: powder
Colour: No data available
Odour: odourless
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
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<tr>
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</tr>
</tbody>
</table>

- **Flash point**: No data available
- **Evaporation rate**: No data available
- **Flammability (solid, gas)**: May form explosive dust-air mixture during processing, handling or other means.
- **Flammability (liquids)**: No data available
- **Upper explosion limit / Upper flammability limit**: No data available
- **Lower explosion limit / Lower flammability limit**: No data available
- **Vapour pressure**: No data available
- **Relative vapour density**: No data available
- **Relative density**: No data available
- **Density**: No data available
- **Solubility(ies)**
  - **Water solubility**: No data available
- **Partition coefficient: n-octanol/water**: No data available
- **Auto-ignition temperature**: No data available
- **Decomposition temperature**: No data available
- **Viscosity**
  - **Viscosity, dynamic**: No data available
  - **Viscosity, kinematic**: No data available
- **Explosive properties**: Not explosive
- **Oxidizing properties**: The substance or mixture is not classified as oxidizing.
- **Molecular weight**: No data available
- **Particle size**: No data available

**Section 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.

Section 11: Toxicological information

Exposure routes: Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity
Harmful if swallowed.

Product:
Acute oral toxicity: Acute toxicity estimate: 1,952 mg/kg
Method: Calculation method

Components:

Levodopa:
Acute oral toxicity: LD50 (Rat): 1,780 mg/kg
LD50 (Mouse): 2,363 mg/kg

Carbidopa:
Acute oral toxicity: LD50 (Rat): 4,810 mg/kg
LD50 (Mouse): 1,750 mg/kg

Cellulose:
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
Acute inhalation toxicity: LC50 (Rat): > 5.8 mg/l
Exposure time: 4 h
Test atmosphere: dust/mist
Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg

Starch:
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg

Magnesium stearate:
Acute oral toxicity: LD50 (Rat): > 2,000 mg/kg
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:**

**Carbidopa:**
Species: Rabbit
Result: No skin irritation

**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:**

**Carbidopa:**
Species: Rabbit
Result: Mild eye irritation

**Starch:**
Species: Rabbit
Result: No eye irritation

**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:**

**Levodopa:**
Species: Guinea pig
Result: Not a skin sensitizer.
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**Carbidopa**:  
Remarks: No data available

**Starch**:  
Test Type: Maximisation Test  
Exposure routes: Skin contact  
Species: Guinea pig  
Result: negative

**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

**Chronic toxicity**

**Germ cell mutagenicity**  
Not classified based on available information.

**Components:**

**Levodopa**:  
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)  
Result: negative  
Test Type: Chromosomal aberration  
Test system: mouse lymphoma cells  
Result: equivocal  
Test Type: Micronucleus test  
Test system: Chinese hamster lung cells  
Result: positive  
Test Type: sister chromatid exchange assay  
Test system: Chinese hamster lung cells  
Result: positive

**Carbidopa**:  
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)  
Result: positive  
Test Type: In vitro mammalian cell gene mutation test  
Result: positive  
Genotoxicity in vivo: Test Type: Micronucleus test  
Species: Mouse  
Application Route: Oral  
Result: negative
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Cellulose:
Genotoxicity in vitro:
- Test Type: Bacterial reverse mutation assay (AMES)
  - Result: negative
- Test Type: In vitro mammalian cell gene mutation test
  - Result: negative

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

Starch:
Genotoxicity in vitro:
- Test Type: Bacterial reverse mutation assay (AMES)
  - 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

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

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

Carcinogenicity
Not classified based on available information.

Components:

Levodopa:
Species: Rat
Application Route: Oral
Exposure time: 2 Years
Result: negative

Carbidopa:
Species: Rat
Application Route: Oral
Exposure time: 96 weeks
  - 135 mg/kg body weight
Result: negative

Cellulose:
Species: Rat
Application Route : Ingestion
Exposure time : 72 weeks
Result : negative

Reproductive toxicity
Suspected of damaging the unborn child.

Components:

**Levodopa:**

Effects on fertility
- Test Type: Fertility
- Species: Rat
- Application Route: Oral
- Fertility: NOAEL: 100 mg/kg body weight
- Result: Animal testing did not show any effects on fertility.

Effects on foetal development
- Test Type: Development
- Species: Rabbit
- Application Route: Oral
- Developmental Toxicity: LOAEL: 125 mg/kg body weight
- Symptoms: Skeletal malformations, Visceral malformations
- Result: positive

- Test Type: Development
- Species: Rat
- Application Route: Oral
- Developmental Toxicity: LOAEL: 10 mg/kg body weight

- Test Type: Development
- Species: Mouse
- Application Route: Oral
- Developmental Toxicity: LOAEL: 500 mg/kg body weight
- Symptoms: Effects on foetal development
- Result: positive

Reproductive toxicity - Assessment
- Some evidence of adverse effects on development, based on animal experiments.

**Carbidopa:**

Effects on fertility
- Test Type: Fertility
- Species: Rat
- Application Route: Oral
- Fertility: NOAEL: 120 mg/kg body weight
- Symptoms: Reduced body weight
- Result: Animal testing did not show any effects on fertility.

Effects on foetal development
- Test Type: Development
- Species: Mouse
- Application Route: Oral
- Developmental Toxicity: NOAEL: 120 mg/kg body weight
- Result: No teratogenic effects

- Test Type: Development
- Species: Rabbit
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Application Route: Oral
Developmental Toxicity: NOAEL: 120 mg/kg body weight
Result: No teratogenic effects

**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**
Causes damage to organs (Central nervous system) through prolonged or repeated exposure if swallowed.

**Components:**

**Levodopa:**
Exposure routes : Oral
Target Organs : Central nervous system
Assessment : Causes damage to organs through prolonged or repeated exposure.

**Repeated dose toxicity**

**Components:**

**Levodopa:**
Species : Rat
LOAEL : 100 mg/kg
Application Route : Oral
Exposure time: 106 Weeks  
Target Organs: Central nervous system  
Symptoms: Salivation  
Species: Monkey  
LOAEL: 100 mg/kg  
Application Route: Oral  
Exposure time: 22 Weeks  
Target Organs: Central nervous system

**Carbidopa:**
Species: Rat  
LOAEL: 25 mg/kg  
Application Route: Oral  
Exposure time: 96 Weeks  
Remarks: No significant adverse effects were reported

Species: Monkey  
NOAEL: 135 mg/kg  
Application Route: Oral  
Exposure time: 1 yr  
Remarks: No significant adverse effects were reported

Species: Dog  
NOAEL: 5 mg/kg  
LOAEL: 15 mg/kg  
Application Route: Oral  
Exposure time: 238 d  
Symptoms: Diarrhoea, Vomiting, Tremors

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

**Starch:**
Species: Rat  
NOAEL: >= 2,000 mg/kg  
Application Route: Skin contact  
Exposure time: 28 Days  
Method: OECD Test Guideline 410

**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:

Levodopa:
Ingestion: Symptoms: Nausea, central nervous system effects, Drowsiness

Carbidopa:
Ingestion: Symptoms: involuntary movement

Section 12: Ecological information

Ecotoxicity

Components:

Levodopa:
Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 16 mg/l
Exposure time: 48 h

Carbidopa:
Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 35.3 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202

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
### 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:**

**Levodopa:**
- **Partition coefficient: n-octanol/water:** $\log P_{ow} = -2.39$

**Magnesium stearate:**
- **Partition coefficient: n-octanol/water:** $\log P_{ow} > 4$

**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.
  - If not otherwise specified: Dispose of as unused product.
Section 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.

National Regulations

NZS 5433
Not regulated as a dangerous good

Section 15: Regulatory information

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

HSNO Approval Number
HSR100425 Pharmaceutical Active Ingredients Group Standard 2017

HSW Controls
Certified handler certificate not required.
Tracking hazardous substance not required.
Refer to the Health and Safety at Work (Hazardous Substances) Regulations 2017, for further information.

The components of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
IECSC : not determined

Section 16: Other information

Further information
Date format : dd.mm.yyyy

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
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NZ OEL: New Zealand. Workplace Exposure Standards for Atmospheric Contaminants

ACGIH / TWA: 8-hour, time-weighted average
NZ OEL / WES-TWA: Workplace Exposure Standard - Time Weighted average

All abbreviations are defined within the SDS, including NZ OEL, ACGIH, and various other acronyms related to safety and regulations.