SAFETY DATA SHEET

Efavirenz Liquid Formulation

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Efavirenz Liquid Formulation

Manufacturer or supplier’s details
Company: MSD
Address: 50 Tuas West Drive
Singapore - Singapore 638408
Telephone: +1-908-740-4000
Emergency telephone number: 65 6697 2111 (24/7/365)
E-mail address: EHSDATASTEWARD@msd.com

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: Category 2 (Central nervous system, Skin)
Long-term (chronic) aquatic hazard: Category 2

GHS label elements
Hazard pictograms: ☑️ ☑️
Signal word: Danger
Hazard statements: H360D May damage the unborn child.
H373 May cause damage to organs (Central nervous system, Skin) through prolonged or repeated exposure.
H411 Toxic to aquatic life with long lasting effects.

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 mist or vapours.
P273 Avoid release to the environment.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.
Response:
P308 + P313 IF exposed or concerned: Get medical advice/attention.
P391 Collect spillage.

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
None known.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efavirenz</td>
<td>154598-52-4</td>
<td>&gt;= 2.5 -&lt; 10</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 : Flush eyes with water as a precaution. 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.

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.

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:
Exposure to combustion products may be a hazard to health.

Hazardous combustion products:
Carbon 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 (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.
Prevent spreading over a wide area (e.g., by containment or oil barriers).
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:
Soak up with inert absorbent material.
For large spills, provide dyking or other appropriate containment to keep material from spreading. If dyked material can be pumped, store recovered material in appropriate container.
Clean up remaining materials from spill with suitable absorbent.
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 determine 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:
See Engineering measures under EXPOSURE CONTROLS/PERSONAL PROTECTION section.

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 mist or vapours.
Do not swallow.
Avoid contact with eyes.
Wash skin thoroughly after handling.
Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment
Keep container tightly closed.
Do not eat, drink or smoke when using this product.
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>Efavirenz</td>
<td>154598-52-4</td>
<td>TWA</td>
<td>100 µg/m3</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Engineering measures:
Minimize workplace exposure concentrations.
If sufficient ventilation is unavailable, use with local exhaust ventilation.

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:
- Combined particulates and organic vapour type

Hand protection
Material:
- Chemical-resistant gloves

Remarks:
- Choose gloves to protect hands against chemicals depending on the concentration and quantity of the hazardous substance and specific to place of work. Breakthrough time is not determined for the product. Change gloves often! For special applications, we recommend clarifying the resistance to chemicals of the aforementioned protective gloves with the glove manufacturer. Wash hands before breaks and at the end of workday.

Eye protection:
- Wear the following personal protective equipment:
  - Safety glasses

Skin and body protection:
- Select appropriate protective clothing based on chemical resistance data and an assessment of the local exposure potential.
  - Skin contact must be avoided by using impervious protective
clothing (gloves, aprons, boots, etc).

Hygiene measures : If exposure to chemical is likely during typical use, provide
eye flushing systems and safety showers close to the work-
ing place.

When using do not eat, drink or smoke.

Wash contaminated clothing before re-use.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance : liquid

Colour : white to off-white

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 : No data available

Evaporation rate : No data available

Flammability (solid, gas) : Not applicable

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

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
6. Viscosity, kinematic: No data available
7. Explosive properties: Not explosive
8. Oxidizing properties: The substance or mixture is not classified as oxidizing.
9. Molecular weight: No data available
10. Particle size: No data available

10. STABILITY AND REACTIVITY
Reactivity: Not classified as a reactivity hazard.
Chemical stability: Stable under normal conditions.
Possibility of hazardous reactions: Can react with strong oxidizing agents.
Conditions to avoid: None known.
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.

Product:
Acute oral toxicity: Acute toxicity estimate: > 2,000 mg/kg
Method: Calculation method

Components:
Efavirenz:
Acute oral toxicity: LD50 (Rat, female): 419 mg/kg
LDLo (Rat, male): 1,000 mg/kg

Skin corrosion/irritation
Not classified based on available information.

Components:
Efavirenz:
Result: Mild skin irritation
Remarks: slight irritation
Serious eye damage/eye irritation
Not classified based on available information.

**Components:**

**Efavirenz:**

**Remarks:** Moderate eye irritation

**Respiratory or skin sensitisation**

**Skin sensitisation**
Not classified based on available information.

**Respiratory sensitisation**
Not classified based on available information.

**Components:**

**Efavirenz:**

**Test Type:** Maximisation Test
**Exposure routes:** Dermal
**Species:** Guinea pig
**Assessment:** Does not cause skin sensitisation.
**Result:** negative

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

**Components:**

**Efavirenz:**

**Genotoxicity in vitro**

**Test Type:** Bacterial reverse mutation assay (AMES)
**Result:** negative

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

**Test Type:** Chromosome aberration test in vitro
**Result:** negative

**Genotoxicity in vivo**

**Test Type:** Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
**Species:** Mouse
**Application Route:** Oral
**Result:** negative

**Germ cell mutagenicity - Assessment**

Weight of evidence does not support classification as a germ cell mutagen.

**Carcinogenicity**
Not classified based on available information.
Components:

Efavirenz:

Species: Mouse
Application Route: Oral
Exposure time: 2 Years
Target Organs: Lungs, Liver
Remarks: The mechanism or mode of action may not be relevant in humans.

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

Reproductive toxicity
May damage the unborn child.

Components:

Efavirenz:

Effects on fertility:
Species: Rat, male and female
Application Route: Oral
Fertility: NOAEL: 200 - 400 mg/kg body weight
Result: No effects on fertility and early embryonic development were detected.

Effects on foetal development:
Test Type: Embryo-foetal development
Species: Rat
Application Route: Oral
Developmental Toxicity: LOAEL: 50 mg/kg body weight
Result: Embryo-foetal toxicity

Test Type: Embryo-foetal development
Species: Monkey
Application Route: Oral
Developmental Toxicity: LOAEL: 60 mg/kg body weight
Symptoms: Malformations were observed.

Test Type: Embryo-foetal development
Species: Rabbit
Application Route: Oral
Developmental Toxicity: NOAEL: 75 mg/kg body weight
Result: No embryotoxic effects

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

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
May cause damage to organs (Central nervous system, Skin) through prolonged or repeated exposure.
Components:

Efavirenz:

Target Organs: Central nervous system
Assessment: Causes damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Efavirenz:

Species: Rat
LOAEL: 50 mg/kg
Application Route: Oral
Exposure time: 3 Months
Target Organs: Kidney

Species: Monkey
LOAEL: 100 mg/kg
Application Route: Oral
Exposure time: 1 - 2 yr
Target Organs: Central nervous system, Liver, Kidney, Thyroid, Adrenal gland

Species: Monkey
LOAEL: 90 mg/kg
Application Route: Oral
Exposure time: 1 Months
Target Organs: Central nervous system
Symptoms: Lethargy, Weakness

Aspiration toxicity

Not classified based on available information.

Experience with human exposure

Components:

Efavirenz:

Ingestion:
Target Organs: Skin
Symptoms: Rash
Target Organs: Central nervous system
Symptoms: Dizziness, insomnia
Target Organs: Heart
Symptoms: irregular heart beat

12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Efavirenz:

Toxicity to fish: LC50 (Lepomis macrochirus (Bluegill sunfish)): 0.85 mg/l
Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 1.1 mg/l
Exposure time: 48 h
Method: FDA 4.08

Toxicity to algae/aquatic plants:
- NOEC (Selenastrum capricornutum (green algae)): 0.026 mg/l
  Exposure time: 12 d
  Method: FDA 4.01
- NOEC (Microcystis aeruginosa (blue-green algae)): 0.76 mg/l
  Exposure time: 12 d
  Method: FDA 4.01

M-Factor (Acute aquatic toxicity): 1
Toxicity to fish (Chronic toxicity):
- NOEC (Pimephales promelas (fathead minnow)): 0.066 mg/l
  Exposure time: 33 d
  Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):
- NOEC (Daphnia magna (Water flea)): 0.16 mg/l
  Exposure time: 21 d
  Method: OECD Test Guideline 211

M-Factor (Chronic aquatic toxicity): 1

**Persistence and degradability**

**Components:**

**Efavirenz:**
Biodegradability: Result: Not readily biodegradable.
  Biodegradation: 11 %
  Exposure time: 32 d
  Method: FDA 3.11

**Bioaccumulative potential**

**Components:**

**Efavirenz:**
Bioaccumulation: Species: Lepomis macrochirus (Bluegill sunfish)
  Bioconcentration factor (BCF): 454
  Method: OECD Test Guideline 305

Partition coefficient: n-octanol/water: log Pow: 5.4

**Mobility in soil**

**Components:**

**Efavirenz:**
Distribution among environ- log Koc: 3.36
11. EFFECTS IN VARIOUS ORGANISMS

mental compartments

Method: FDA 3.08

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
UN number: UN 3082
Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, LIQUID, N.O.S.
   (Efavirenz)
Class: 9
Packing group: III
Labels: 9

IATA-DGR
UN/ID No.: UN 3082
Proper shipping name: Environmentally hazardous substance, liquid, n.o.s.
   (Efavirenz)
Class: 9
Packing group: III
Labels: Miscellaneous
Packing instruction (cargo aircraft): 964
Packing instruction (passenger aircraft): 964
Environmentally hazardous: yes

IMDG-Code
UN number: UN 3082
Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, LIQUID, N.O.S.
   (Efavirenz)
Class: 9
Packing group: III
Labels: 9
EmS Code: F-A, S-F
Marine pollutant: yes

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.
Special precautions for user
The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

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

AICIC - Australian Inventory of Industrial Chemicals; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory con-
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