



SAFETY DATA SHEET

Safety Data Sheet according to Regulation (EC) No. 1907/2006 (REACH)

Issuing Date 29-Nov-2009

Revision Date 03-Sep-2017

Revision Number 13

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

1.1. Product identifier

Product Name	LEFLUNOMIDE
Chemical Name	5-Methylisoxazole-4-carboxylic acid,4-trifluoromethyl anilide
Synonyms	5-Methyl-N-(4-trifluoromethyl phenyl) isoxazole-4-carboxamide; Isoxazole-4-carboxamide,5-methyl-N-4-trifluoromethyl phenyl,-;Alpha,alpha,alpha,Trifluoro-N-(5-methyl-isoxazole-4-carboxy)-p-toluidine;HWA-486; SU-101:ARAVA
Formula	C ₁₂ H ₉ F ₃ N O ₂
CAS	75706-12-6
EINECS	No information available
Index No	No information available
Reach Registration Number	No information available

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

Identified Use	Active Pharmaceutical Ingredient
Uses advised against	No information available

1.3. Details of the supplier of the safety data sheet

Manufacturer, Supplier	Assia Chemical Industries Ltd. - Teva-Tech site Neot-Hovav Eco-Industrial Park P.O Box 2049, Emek Sara Be'er Sheva 8412316 Israel Tel: 972-8-6509555 Fax: 972-8-6509500
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For further information, please contact

E-mail Address	SDS.TevaIL@teva.co.il
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1.4. Emergency Telephone Number

Emergency Telephone Number	United States/Canada/Puerto Rico: 1-800/424-9300 (Chemtrec) [24-hrs] International: 01-703-527-3887 (Chemtrec) [24-hours]
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SECTION 2: Hazards identification

2.1. Classification of the substance or mixture

Classification according to Regulation (EC) No. 1272/2008

Acute.Tox.4; H302
Eye Irrit.2; H319
STOT SE 2; H335
Skin Irrit.2; H315
Carc.2; H351
Repr.1B; H360D

2.2. Label Elements

Signal Word

Danger



Hazard Statements

H302 - Harmful if swallowed
H319 - Causes serious eye irritation
H335 - May cause respiratory irritation
H315 - Causes skin irritation
H351 - Suspected of causing cancer
H360D - May damage the unborn child

Precautionary Statements

P262 - Do not get in eyes, on skin, or on clothing
P305 + P351 + P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing
P280 - Wear protective gloves/protective clothing/eye protection/face protection
P201 - Obtain special instructions before use

2.3. Other hazards

None known

SECTION 3: Composition/information on ingredients

3.1. Substances

Chemical Name	EC No	REACH Reg. No	CAS-No	Weight %
5-Methylisoxazole-4-carboxylic acid,4-trifluoromethyl anilide	-	Not available	75706-12-6	100

3.2. Mixtures

N.A.

SECTION 4: First aid measures

4.1. Description of first aid measures

Eye Contact	Flush eyes with water for at least 15 minutes. Get medical attention if eye irritation develops or persists.
Skin Contact	Wash off immediately with plenty of water. Get medical advice/attention if you feel unwell.
Ingestion	If swallowed, rinse mouth with water (only if the person is conscious). Do NOT induce vomiting. Get medical advice/attention if you feel unwell.
Inhalation	Remove person to fresh air. If signs/symptoms continue, get medical attention.

4.2. Most important symptoms and effects, both acute and delayed

Irritation	Irritating to eyes, respiratory system and skin.
Corrosivity	No information available.
Eyes	May cause: irritation, blurred vision, Cataracts, Conjunctivitis, Eye disorder.
Skin	May cause: skin rash, dry skin.
Inhalation	May cause: Bronchitis.
Ingestion	May cause: nausea, diarrhea, abdominal pain.

4.3. Indication of immediate medical attention and special treatment needed

Notes to Physician	Treat symptomatically.
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SECTION 5: Fire-fighting measures

5.1. Extinguishing media

Suitable Extinguishing Media

Water spray. Carbon dioxide (CO₂). Foam. Dry powder. Halons.

Unsuitable extinguishing media

No information available.

5.2. Special hazards arising from the substance or mixture

Thermal decomposition can lead to release of irritating gases and vapors. Combustible material.

5.3. Advice for firefighters

Special protective equipment for firefighters

As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear.

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

Use personal protective equipment. Avoid contact with dusts/fumes/mists/vapors. Avoid all unnecessary contact.

6.1.1. For non-emergency personnel

Protective equipment See section 8

Emergency procedures Evacuate the danger area and alert emergency team

6.1.2. For emergency responders

See section 8

6.2. Environmental Precautions

Prevent entry into waterways, sewers, basements or confined areas. Prevent further leakage or spillage if safe to do so. Report according to local regulations.

6.3. Methods and materials for containment and cleaning up

6.3.1. Methods for Containment

No information available.

6.3.2. For cleaning up

Take up mechanically and collect in suitable container for disposal.

6.3.3. Other information

No information available

6.4. Reference to other sections

See Sections 8 & 13 for additional information.

SECTION 7: Handling and storage

7.1. Precautions for Safe Handling

Handling

Avoid contact with skin, eyes and clothing. Handle in accordance with good industrial hygiene and safety practice. Do not breathe vapors/dust. Provide appropriate exhaust ventilation at places where dust is formed.

Hygiene Measures

Handle in accordance with good industrial hygiene and safety practice.

7.2. Conditions for safe storage, including any incompatibilities

Keep in properly labeled containers. See product quality documents and/or label for the correct storage conditions of this product.

7.3. Specific end use(s)

Exposure Scenario

No information available.

Other Guidelines

No information available.

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

Exposure Limits Teva OEL (8hr-TWA): 5 µg/m³

Biological occupational exposure limits No information available.

Derived No Effect Level (DNEL) No information available.

Predicted No Effect Concentration (PNEC) No information available.

8.2. Exposure controls

Engineering Measures Appropriate Engineering Controls.

Personal protective equipment

Eye/face protection Use eye protection appropriate for the task.

Skin protection:

- Body protection

Use protective clothing appropriate for the task.

- Hand protection

Use appropriate protective gloves.

Respiratory Protection

Use appropriate respiratory protection.

Environmental exposure controls No information available.

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Appearance

Color

Off-white to pink

Physical State

, crystalline powder

Odor

Odourless

Odor Threshold

No information available

pH

No information available

Melting Point/Range

162-169 °C

Boiling Point/Range

No information available

Flash Point

No information available

Evaporation Rate

No information available

Flammability (solid, gas)

No information available

Flammability Limits in Air

Upper

No information available

Lower

No information available

Vapor Pressure

No information available

Vapor Density

No information available

Relative Density

No information available

Solubility

Soluble in Alcohols, Chloroform, Dichloromethane, Halogenated solvents Insoluble in Hexanes, non polar solvents

Water Solubility

Insoluble in water

Octanol/water Partition Coefficient (Log Kow)

2.8

Autoignition Temperature

No information available

Decomposition Temperature

No information available

Viscosity

No information available

Explosive Properties

No information available

Oxidizing Properties

No information available

9.2. Other information

Molecular Weight 270.2

SECTION 10: Stability and reactivity

10.1. Reactivity

No information available.

10.2. Chemical Stability

Stable under normal conditions.

10.3. Possibility of hazardous reactions

Hazardous polymerization does not occur.

10.4. Conditions to avoid

All sources of ignition, Moisture, Excessive light.

10.5. Incompatible materials.

Strong oxidizing agents.

10.6. Hazardous decomposition products

Toxic fumes of: Nitrogen oxides (NOx), carbon oxides, Hydrogen fluoride.

SECTION 11: Toxicological information

11.1. Information on toxicological effects

acute toxicity

LD50 Oral rat 235 mg/kg

LD50 Oral mouse 445 mg/kg

skin corrosion/irritation No information available.

serious eye damage/irritation No information available.

respiratory or skin sensitization No information available.

germ cell mutagenicity

Ames test negative . Not clastogenic in in-vivo mice micronucleus assay.

carcinogenicity

In a 2-year bioassay, male mice exhibited an increased incidence in lymphoma at an oral dose of 15 mg/kg , and female mice exhibited an increased incidence of bronchoalveolar adenomas/carcinomas beginning at 1.5 mg/kg.

reproductive toxicity

Animal studies suggest a risk for fetal death and/or teratogenic effects at an oral dose of 15 mg/kg. No antifertility action in either male or female rat at oral doses up to 4mg/kg; no inhibition of reproductive performance.

STOT - single exposure

No information available.

STOT - repeated exposures

No information available.

aspiration hazard

No information available.

Other Information

Target Organ Effects

Liver. (increased liver enzyme, reversible).

Musculoskeletal System

May cause: myalgia.

Central nervous system

May cause headache, May cause dizziness.

Cardiovascular system

May cause: chest pain, hypertension.

Body as a whole

May cause: Weight loss, fever, Back/muscle/bone/extremities pain.

SECTION 12: Ecological information

12.1. Toxicity

Ecotoxicity effects

No information available.

12.2. Persistence and degradability

No information available.

12.3. Bioaccumulative potential

Half-Life Elimination in Human: 2 weeks. Not expected to bioaccumulate : Log Po/w <3 (EC) or <4 (GHS).

12.4. Mobility in soil

No information available.

12.5. Results of PBT and vPvB assessment

No information available.

12.6. Other adverse effects

No information available.

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Waste from Residues/Unused Products

Dispose of in accordance with local regulations.

Contaminated Packaging

Empty containers should be taken for local recycling, recovery or waste disposal.

SECTION 14: Transport information

14.1.

UN-No 2811

14.2.

Proper Shipping Name Toxic solid, organic, n.o.s (Leflunomide)

14.3. Transport hazard class(es)

ADR / RID / ADN (land transport) 6.1
IMDG (sea transport) 6.1
IATA / ICAO (air transport) 6.1
DOT 6.1

14.4.

Packing Group III

14.5. Environmental hazards

Marine Pollutant -

14.6. Special precautions for user

Emergency No. F-A, S-F
ADR/RID-Labels -

14.7.

Technical name -
Ship type -
Annex II -

SECTION 15: Regulatory information

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

- Regulation 1907/2006/EC (REACH) and successive modifications
- Regulation 1272/2008 (CLP) and successive modifications
- D.Lgs. 81/2008 and successive modifications and Dir. 2009/161/EU
- REGULATION (EU) 2015/830

This safety data sheet complies with the requirements of: GHS

15.2. Chemical Safety Assessment

No information available

SECTION 16: Other information

CLP/GHS - Regulation

Hazard Statements

- H302 - Harmful if swallowed
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- H360D - May damage the unborn child

Training appropriate for workers is required to ensure protection of human health and environment.

Application/Drug Class Anti-inflammatory; anti-arthritis.

Source of data

R.T.E.C.S. - REGISTRY OF TOXIC EFFECTS OF CHEMICAL SUBSTANCES
A.C.G.I.H. - AMERICAN CONFERENCE OF INDUSTRIAL HYGIENISTS
H.S.D.B. - HAZARDOUS SUBSTANCES DATA BANK
N.I.O.S.H. - NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
N.T.P. - NATIONAL TOXICOLOGY PROGRAM
I.A.R.C. - INTERNATIONAL AGENCY FOR RESEARCH ON CANCER
ECHA (European chemicals agency) databases
FDA (Food & Drug administration) database
EMA (European Medicines agency) documents
ChemAdvisor
Chemspider database

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Revision Note

7.2 SDS section updated

Disclaimer

The information provided on this SDS is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guide for safe handling, use, processing, storage, transportation, and disposal of the designated material and is not to be considered as a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other material or in any process, unless specified in the text.

End of Safety Data Sheet