Material Safety Data Sheet

PREPARATION DATE: July 10, 2003
This revision replaces MSDS dated June 1, 1998

SECTION 1: Chemical Product and Company Identification

Brand Name: (used on the label)	Arava
Active Ingredient (name and synonyms)	Leflunomide, HWA486, RU66063
Chemical Name (Active):	N-(4-trifluoromethylphenyl)-5-methylisoxazol-4-carboxamide
Chemical Formula (Active):	$C_{12}H_9F_3N_2O_2$
CAS Number (Active):	75706-12-6
Product Use:	For the treatment of active rheumatoid arthritis

Manufacturer: **Aventis Pharmaceuticals, Inc.**
Address: **Route 202-206**
Bridgewater, NJ 08807-0800

Technical Information, M-F, 8 AM – 5 PM EST: **(908) 231-4829**
24-Hour Transport Emergency, US (Chemtrec): **(800) 424-9300**
24-Hour Transport Emergency, outside US (Chemtrec): **(703) 527-3887**
24-Hour Emergency, Aventis: **(908) 231-2666**

SECTION 2: Composition/Information on Ingredients

Leflunomide (Active Ingredient) CAS Number 75706-12-6
Concentration of active in each tablet: 10 mg, 20 mg, or 100 mg
Each Tablet also contains pharmaceutical excipients (inactive ingredients).

Product not considered OSHA hazardous according to 29 CFR 1910.1200.

SECTION 3: Hazards Identification

Emergency Overview:

In the healthcare environment, dispensing Arava presents no occupational exposure hazards.

Data for Leflunomide:

SECTION 3: Hazards Identification (continued)

Carcinogenic: Two year carcinogenicity studies in mice and rats were conducted. Results in the mouse carcinogenicity study showed increased incidences of malignant lymphomas (males, high dose 15 mg/kg/day) and lung adenoma/carcinoma (females). The incidence for the latter, however was within the spontaneous range knows for the mouse strain (CD-1). Results from the rat carcinogenicity study did not indicate a carcinogenic potential of leflunomide (6mg/kg/day).

Leflunomide listed as a carcinogen or potential carcinogen: No.
NTP: No.
IARC: No.
OSHA: No.

SECTION 4: First Aid Measures

If exposed to dust from broken tablets:
Skin: Wash contacted skin with soap and water.
Eyes: Flush eyes with water for fifteen minutes. Get immediate medical attention.

Ingestion: In case of accidental ingestion, consult a physician and show the package insert or a copy of this MSDS.

SECTION 5: Fire Fighting Measures

Hazardous combustion products: In case of fire, hazardous gases may be formed, including carbon monoxide, carbon dioxide, oxides of nitrogen and hydrogen fluoride.

Personal protective equipment: Wear full bunker gear, including SCBA, when responding to fires where this product is stored.

Extinguisher media: Carbon Dioxide, Dry Chemical Powder, Foam. Water may be effective for cooling.

SECTION 6: Accidental Release Measures

Spilled tablets should be scooped or shoveled up and placed in a suitable waste container. Dispose of in accordance with applicable federal, state and local regulations.

SECTION 7: Handling and Storage

Store at controlled room temperature 20-25°C (68-77°F). Protect from light.

SECTION 8: Exposure Controls/Personal Protection

OSHA Permissible Exposure Limit: Not available.
The dispensing of Arava Tablets requires no specialized exposure controls or personal protective equipment.

SECTION 9: Physical and Chemical Properties

Appearance:
10 mg is a white, round film-coated tablet embossed with "ZBN" on one side.
20 mg is a yellow, triangular film-coated tablet embossed with "ZBO" on one side.
100 mg is a white, round film-coated tablet embossed with "ZBP" on one side.
10 mg tablets supplied in bottles of 30, 100 and 1,000
20 mg tablets supplied in bottles of 30, 100 and 1,000

SECTION 10: Stability and Reactivity

Material is stable under normal conditions.

SECTION 11: Toxicological Information

Data for Leflunomide:

Acute oral toxicity for leflunomide:
Oral LD50, rat: 100-250 mg/kg.
Oral LD50, mouse: 200-500 mg/kg.

Irritation:
Not a skin irritant.
Slight eye irritant.

Mutagenicity:
Ames Test: Negative
HGPRT: Negative
UDS: Negative
Mouse Micronucleus Test (in vivo): Negative

Teratogenicity: There are no adequate and well-controlled studies evaluating Arava (leflunomide) in pregnant women. However, based on animal studies, leflunomide may cause fetal or teratogenic effects when administered to a pregnant woman.

SECTION 11: Toxicological Information (continued)

Carcinogenicity: Two-year carcinogenicity studies in mice and rats were conducted. Results in the mouse carcinogenicity study showed increased incidences of malignant lymphomas (males, high dose 15 mg/kg/day) and lung adenoma/carcinoma (females). The incidence for the latter, however, was within the spontaneous range known for the mouse strain (CD-1). Results from the rat carcinogenicity study did not indicate a carcinogenic potential of leflunomide (6 mg/kg/day).

SECTION 12: Ecological Information

Do not allow spilled tablets to enter sewers or waterways.

SECTION 13: Disposal Considerations

This material should be disposed of in accordance with federal, state and local regulations.

SECTION 14: Transportation Information

This material is not regulated as a hazardous material by transportation regulations.

SECTION 15: Regulatory Information

No additional information.

SECTION 16: Other Information

The information provided in this Material Safety Data Sheet has been compiled from our experience and the data presented in various technical publications. It is the users responsibility to determine the suitability of this information for the adoption of safety precautions as may be necessary. We reserve the right to revise the Material Safety Data Sheets from time to time as new information becomes available. It is recommended that the user contact the company to make sure the sheet is the latest one issued.