SAFETY DATA SHEETS

This SDS packet was issued with item:

078380724

N/A

SAFETY DATA SHEET

1. Identification

Product identifier **Azathioprine Tablets**

Other means of identification

Product code 50 mg Tablet, debossed with product identification “54 043” on one side, and plain on the other.

Recommended use An adjunct for the prevention of rejection in renal homotransplantation. It is also indicated for the management of active rheumatoid arthritis to reduce signs and symptoms

Recommended restrictions None known.

Manufacturer/Importer/Supplier/Distributor information

Company name Boehringer Ingelheim Roxane Inc.
Address 1809 Wilson Road
Columbus, Ohio 43228
Telephone (614) 276-4000
Emergency phone number (614) 276-4000

2. Hazard(s) identification

Physical hazards Not classified.

Health hazards Carcinogenicity Category 1A

OSHA defined hazards Not classified.

Label elements

Hazard symbol None.

Signal word Warning

Hazard statement This is a pharmaceutical product designed to be prescribed by a licensed health care professional. Should any person while using this product observe any adverse health effects, they should seek medical treatment.

Precautionary statement

Prevention Observe good industrial hygiene practices.

Response Wash hands after handling.

Storage Protect from light. Protect from moisture. Store between 15ºC (59ºF) and 25ºC (77ºF).

Disposal Incineration of waste at an approved USEPA incinerator is recommended.

Hazard(s) not otherwise classified (HNOC) None known.

3. Composition/information on ingredients

Substances

Chemical name	Common name and synonyms	CAS number	%
6-[(1-methyl-4-nitro-1H-imidazol-5-yl)thio]-1H-purine		446-86-6	50 mg

Composition comments Refer to Physician's Desk Reference for common components present at <1%

4. First-aid measures

Inhalation If dust from the material is inhaled, remove the affected person immediately to fresh air. Call a physician if symptoms develop or persist.

Skin contact Wash off with soap and water. Get medical attention if irritation develops and persists.

Eye contact Rinse with water. Get medical attention if irritation develops and persists.

Ingestion Rinse mouth. Get medical attention if symptoms occur. If ingestion of a large amount does occur, call a poison control center immediately.

Most important symptoms/effects, acute and delayed	A gastrointestinal hypersensitivity reaction characterized by severe nausea and vomiting has been reported. These symptoms may also be accompanied by diarrhea, rash, fever, malaise, myalgias, elevations in liver enzymes, and occasionally, hypotension. Additional side effects of low frequency have been reported. These include skin rashes, alopecia, fever, arthralgias, diarrhea, steatorrhea, negative nitrogen balance, and reversible interstitial pneumonitis and hepatosplenic T-cell lymphoma and Sweet's Syndrome (acute febrile neutrophilic dermatosis).
Indication of immediate medical attention and special treatment needed	Treat symptomatically.
General information	Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.

5. Fire-fighting measures

Suitable extinguishing media	Water fog. Foam. Dry chemical powder. Carbon dioxide (CO2).
Unsuitable extinguishing media	Do not use water jet as an extinguisher, as this will spread the fire.
Specific hazards arising from the chemical	During fire, gases hazardous to health may be formed.
Special protective equipment and precautions for firefighters	Self-contained breathing apparatus and full protective clothing must be worn in case of fire.
Fire fighting equipment/instructions	Use water spray to cool unopened containers.
Specific methods	Use standard firefighting procedures and consider the hazards of other involved materials.
General fire hazards	No unusual fire or explosion hazards noted.

6. Accidental release measures

Personal precautions, protective equipment and emergency procedures	Keep unnecessary personnel away. Wear appropriate personal protective equipment (See Section 8).
Methods and materials for containment and cleaning up	Sweep up and place into a proper container for disposal. Minimize dust generation and accumulation. Collect dust using a vacuum cleaner equipped with HEPA filter. Following product recovery, flush area with water. Incineration of waste at an approved USEPA incinerator is recommended.
Environmental precautions	Avoid discharge into drains, water courses or onto the ground.

7. Handling and storage

Precautions for safe handling	Avoid contact with eyes, skin, and clothing. Avoid breathing dust. Wash hands thoroughly after handling.
Conditions for safe storage, including any incompatibilities	Protect from light. Protect from moisture. Store between 15ºC (59ºF) and 25ºC (77ºF). Store away from incompatible materials (see Section 10 of the SDS).

8. Exposure controls/personal protection

Occupational exposure limits	No exposure limits noted for ingredient(s).
Biological limit values	No biological exposure limits noted for the ingredient(s).
Appropriate engineering controls	Ventilation should be matched to conditions.

Individual protection measures, such as personal protective equipment

Eye/face protection	None required for consumer use. In laboratory, medical or industrial settings, safety glasses with side shields are recommended. The use of goggles or full face protection may be required depending on the industrial exposure setting. Contact a health and safety professional for specific information.
Skin protection	
Hand protection	For consumer use, no unusual precautions are necessary.
Other	None required for consumer use. In laboratory, medical or industrial settings, gloves and lab coats are recommended. The use of additional personal protective equipment such as shoe coverings, gauntlets, hood or head coverings may be necessary. Contact a health and safety professional for specific information.

Respiratory protection	None required for consumer use. Respirators may be required for certain laboratory and manufacturing tasks if engineering controls do not maintain airborne concentrations below recommended exposure limits (where applicable) or to an acceptable level (where exposure limits have not been established). Workplace risk assessments should be completed before specifying and implementing respirator usage. All respirators must conform to specifications for efficiency and performance. In the United States of America, if respirators are used, a program should be instituted to assure compliance with OSHA Standard 29 CFR 1910.134. Respirator type: Air-purifying respirator with an appropriate, air-purifying filter, cartridge or canister. Contact a health and safety professional or manufacturer for specific information.
Thermal hazards	Wear appropriate thermal protective clothing, when necessary.
General hygiene considerations	Always observe good personal hygiene measures, such as washing after handling the material and before eating, drinking, and/or smoking. Routinely wash work clothing and protective equipment to remove contaminants.

9. Physical and chemical properties

Appearance	Yellow, round, scored tablets
Physical state	Solid.
Form	Tablet.
Color	Yellow.
Odor	None.
Odor threshold	Not available.
pH	Not available.
Melting point/freezing point	Not available.
Initial boiling point and boiling range	Not available.
Flash point	Not available.
Evaporation rate	Not available.
Flammability (solid, gas)	Not available.
Upper/lower flammability or explosive limits	
Flammability limit - lower (%)	Not available.
Flammability limit - upper (%)	Not available.
Explosive limit - lower (%)	Not available.
Explosive limit - upper (%)	Not available.
Vapor pressure	Not available.
Vapor density	Not available.
Relative density	Not available.
Solubility(ies)	
Solubility (water)	Insoluble
Partition coefficient (n-octanol/water)	Not available.
Auto-ignition temperature	Not available.
Decomposition temperature	Not available.
Viscosity	Not available.
Other information	
Molecular formula	C25H43NO18
Molecular weight	645.6

10. Stability and reactivity

Reactivity	The product is stable and non-reactive under normal conditions of use, storage and transport.
Chemical stability	Material is stable under normal conditions.
Possibility of hazardous reactions	No dangerous reaction known under conditions of normal use.

Conditions to avoid	Contact with incompatible materials. Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air).
Incompatible materials	Strong oxidizing agents.
Hazardous decomposition products	No hazardous decomposition products are known.

11. Toxicological information

Information on likely routes of exposure

Inhalation	Not expected to be hazardous in final pharmaceutical form. Mechanical processing may generate dust. Inhalation of dusts may cause respiratory irritation.
Skin contact	Not expected to be hazardous in final pharmaceutical form. Mechanical processing may generate dust. Dust or powder may irritate the skin.
Eye contact	Not expected to be hazardous in final pharmaceutical form. Mechanical processing may generate dust. Dust may irritate the eyes.
Ingestion	Ingestion may cause irritation and malaise.
Symptoms related to the physical, chemical and toxicological characteristics	A gastrointestinal hypersensitivity reaction characterized by severe nausea and vomiting has been reported. These symptoms may also be accompanied by diarrhea, rash, fever, malaise, myalgias, elevations in liver enzymes, and occasionally, hypotension Additional side effects of low frequency have been reported. These include skin rashes, alopecia, fever, arthralgias, diarrhea, steatorrhea, negative nitrogen balance, and reversible interstitial pneumonitis and hepatosplenic T-cell lymphoma. (see Warnings – Malignancy), and Sweet's Syndrome (acute febrile neutrophilic dermatosis).

Information on toxicological effects

Acute toxicity	The oral LD50s for single doses of azathioprine in mice and rats are 2500 mg/kg and 400 mg/kg, respectively. Very large doses of this antimetabolite may lead to marrow hypoplasia, bleeding, infection, and death
Skin corrosion/irritation	Prolonged skin contact may cause temporary irritation.
Serious eye damage/eye irritation	Dust may irritate the eyes.

Respiratory or skin sensitization

Respiratory sensitization	Not a respiratory sensitizer.
Skin sensitization	This product is not expected to cause skin sensitization.
Germ cell mutagenicity	This product is not expected to be mutagenic.
Carcinogenicity	Patients receiving immunosuppressants are at increased risk of developing lymphoma and other malignancies, particularly of the skin

IARC Monographs. Overall Evaluation of Carcinogenicity

6-[(1-methyl-4-nitro-1H-imidazol-5-yl)thio]-1H-purine (CAS 446-86-6)	1 Carcinogenic to humans.

NTP Report on Carcinogens

6-[(1-methyl-4-nitro-1H-imidazol-5-yl)thio]-1H-purine (CAS 446-86-6)	Known To Be Human Carcinogen.

OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)

Not listed.

Reproductive toxicity	This product has been rated Pregnancy Category D-POSITIVE EVIDENCE OR RISK, There is a risk to fetus after drug is administered, but under certain circumstances (e.g., treatment of life threatening illnesses) the benefits can outweigh the risk. Animal reproduction studies have not been conducted with product Avoid contact during pregnancy/while nursing.
Specific target organ toxicity - single exposure	Not classified.
Specific target organ toxicity - repeated exposure	Not classified.
Aspiration hazard	Due to the physical form of the product it is not an aspiration hazard.
Further information	See package insert.

12. Ecological information

Ecotoxicity	The product is not classified as environmentally hazardous.

Persistence and degradability No data is available on the degradability of this product.

Bioaccumulative potential No data available.

Partition coefficient n-octanol / water (log Kow)

6-[(1-methyl-4-nitro-1H-imidazol-5-yl)thio]-1H-purine (CAS 446-86-6)	0.1

Mobility in soil No data available.

Other adverse effects None.

13. Disposal considerations

Disposal instructions Collect and reclaim or dispose in sealed containers at licensed waste disposal site. Dispense in a tight, light-resistant container as defined in the USP/NF.

Local disposal regulations Dispose in accordance with all applicable regulations.

Hazardous waste code The waste code should be assigned in discussion between the user, the producer and the waste disposal company.

Waste from residues / unused products Dispose of in accordance with local regulations. Empty containers or liners may retain some product residues. This material and its container must be disposed of in a safe manner (see: Disposal instructions).

Contaminated packaging Empty containers should be taken to an approved waste handling site for recycling or disposal. Since emptied containers may retain product residue, follow label warnings even after container is emptied.

14. Transport information

DOT

Not regulated as dangerous goods.

IATA

Not regulated as dangerous goods.

IMDG

Not regulated as dangerous goods.

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

15. Regulatory information

US federal regulations This material is not listed on the US TSCA Inventory. Therefore, it can only be used for TSCA exempt purposes such as R&D or drug use.

TSCA Section 12(b) Export Notification (40 CFR 707, Subpt. D)

Not regulated.

OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)

Not listed.

CERCLA Hazardous Substance List (40 CFR 302.4)

Not listed.

Superfund Amendments and Reauthorization Act of 1986 (SARA)

Hazard categories

Immediate Hazard - No
Delayed Hazard - Yes
Fire Hazard - No
Pressure Hazard - No
Reactivity Hazard - No

SARA 302 Extremely hazardous substance

Not listed.

SARA 311/312 Hazardous chemical No

SARA 313 (TRI reporting)

Not regulated.

Other federal regulations

Clean Air Act (CAA) Section 112 Hazardous Air Pollutants (HAPs) List

Not regulated.

Clean Air Act (CAA) Section 112(r) Accidental Release Prevention (40 CFR 68.130)

Not regulated.

Safe Drinking Water Act (SDWA) Not regulated.

Not listed.

US state regulations

US. Massachusetts RTK - Substance List

6-[(1-methyl-4-nitro-1H-imidazol-5-yl)thio]-1H-purine (CAS 446-86-6)

US. New Jersey Worker and Community Right-to-Know Act

Not listed.

US. Pennsylvania Worker and Community Right-to-Know Law

6-[(1-methyl-4-nitro-1H-imidazol-5-yl)thio]-1H-purine (CAS 446-86-6)

US. Rhode Island RTK

Not regulated.

US. California Proposition 65

WARNING: This product contains chemicals known to the State of California to cause cancer.

US - California Proposition 65 - Carcinogens & Reproductive Toxicity (CRT): Listed substance

6-[(1-methyl-4-nitro-1H-imidazol-5-yl)thio]-1H-purine (CAS 446-86-6)

International Inventories

Country(s) or region	Inventory name	On inventory (yes/no)*
Canada	Domestic Substances List (DSL)	Yes
United States & Puerto Rico	Toxic Substances Control Act (TSCA) Inventory	No

*A "Yes" indicates this product complies with the inventory requirements administered by the governing country(s).
A "No" indicates that one or more components of the product are not listed or exempt from listing on the inventory administered by the governing country(s).

16. Other information, including date of preparation or last revision

Issue date 11-November-2014

Revision date -

Version # 01

References

1) Azathioprine Tablets USP, Package Insert, Roxane Laboratories, Inc. , Columbus, Ohio.

2) PDR – Physicians Desk Reference.

3) Ariel Webinsight. Regulatory and ChemExpert Database.

Disclaimer

Boehringer Ingelheim Roxane Inc. cannot anticipate all conditions under which this information and its product, or the products of other manufacturers in combination with its product, may be used. It is the user's responsibility to ensure safe conditions for handling, storage and disposal of the product, and to assume liability for loss, injury, damage or expense due to improper use. The information in the sheet was written based on the best knowledge and experience currently available.

IN CASE OF EMERGENCY
Emergency Phone: (614) 276-4000

Boehringer Ingelheim
Roxane Laboratories

Material Safety Data Sheet

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Common/Trade Name: Azathioprine Tablets USP
Chemical Name: 1H-Purine, 6-[(1-methyl-4-nitro-1H-imidazol-5-yl)thio]-
Synonyms: None
Molecular Formula: $C_9H_7N_7O_2S$
Molecular Weight: 277.26
CAS No: 446-86-6
Chemical Family: Immunosuppressive antimetabolite
Product Use: Prevents rejection in renal transplant patients or management of active rheumatoid arthritis

Manufacturer's Name: Boehringer Ingelheim Roxane Inc.
Address: 1809 Wilson Road
Columbus, Ohio 43228

2. COMPOSITION / INFORMATION ON INGREDIENTS

Composition	CAS#	Exposure Limit
Azathioprine (active ingredient)	446-86-6	None established

REFER to PHYSICIAN'S DESK REFERENCE for common components present as <1%

3. HAZARDS IDENTIFICATION

Emergency Overview	**Physical State: Round, scored tablets** **The 50 mg tablets are yellow with "54 043" engraved on one side and a scored line on the other.** **Odor: No data available** **DANGER!** **Product contains a known cancer causing agent.** **May be harmful if swallowed.** **Accidental ingestion of large amounts may be harmful.**
Primary Route(s) of Entry	**Ingestion**
Potential Health Effects:	**Inhalation: Not expected to be an inhalation hazard in final pharmaceutical form.** **Eye Contact: Not expected to be a hazard to the eye in final pharmaceutical form.** **Skin Contact: Not expected to be a hazard to the skin. Can cause hypersensitive reactions resulting in rash, redness, itching and inflammation.** **Ingestion: May be harmful if ingested. Ingestion may cause nausea, vomiting, fever, fast heartbeat, low blood pressure and unusual bleeding.**
Toxicity Data:	**See Section 11**
Effects of Overexposure:	**The potential for exposure is reduced in finished pharmaceutical form.** **Contains azathioprine, a known cancer causing agent. Overexposure by ingestion may cause excessive bleeding, liver toxicity and death. Other chronic conditions of azathioprine may include bone marrow depression, immunosuppression, liver problems, pancreatitis, and cancer.**
Target Organs:	**Immune system, bone marrow, blood**

4. FIRST AID MEASURES

Eye Exposure	**Any material that contacts the eye should be washed out immediately with water. If easy to do, remove contact lenses if worn. Get medical attention if symptoms persist.**
Skin Exposure	**Wash with soap and water. Get medical attention if symptoms occur.**
Ingestion	**Call a physician or poison control center immediately.**
Inhalation	**Should not pose a hazard in the final form. If breathing is difficult, move to fresh air. Get medical attention immediately.**

5. FIRE AND EXPLOSION HAZARDS

Flammability	**Lower: N/A Upper: N/A**
Flash Point	**Not Applicable**
Extinguishing Media	**Use water spray, dry chemical, carbon dioxide, foam or material appropriate for fire in surrounding area**
Special Fire Fighting Procedures	**Wear full protective clothing and self-contained breathing apparatus.**
Unusual Fire/Explosion Hazards	**Not Applicable**
Hazardous Combustion Products	**Carbon dioxide, carbon monoxide, oxides of nitrogen, oxides of sulfur**

6. ACCIDENTAL RELEASE INFORMATION

STEPS TO BE TAKEN IF SIGNIFICANT QUANTITIES OF PRODUCT IS SPILLED:
Use appropriate personal protective equipment (see Section 8). Sweep up and containerize spill material in a compatible container. Dispose according to applicable regulations. Incineration of the waste at an approved facility is recommended.

7. PRECAUTIONS FOR SAFE HANDLING AND USE

Precautions Handling Significant Quantities:	**Avoid contact with eyes, skin and clothing. Wash thoroughly after handling.**
Storage	**Store at 15° to 25°C (59° to 77°F). Keep container closed tightly. Protect from light and moisture. Store away from foodstuffs.**

8. CONTROL MEASURES AND PERSONAL PROTECTIVE EQUIPMENT

Exposure Limits	**None**
Engineering Controls	**Not required when handling tablets or containers. Ventilation should be matched to conditions.**
Respiratory Protection	**Not required when handling tablets or containers. NIOSH/MSHA approved respirators for protection should be used if respirators are found to be necessary. Ventilation should be matched to conditions.**
Personal Protection	**If containers are compromised or exposure is likely wear: Goggles, Lab Coat, Gloves**
Recommended Facilities	**Eye wash, washing facilities**

9. PHYSICAL / CHEMICAL CHARACTERISTICS

Appearance	**Yellow, round, scored tablets**	**Melting point**	**Not available**	**Solubility in water**	**Insoluble**
Odor	**Not available**	**Boiling point**	**Not available**	**Specific Gravity**	**Not available**
Taste	**Not available**	**Vapor Pressure**	**Not available**	**Flashpoint**	**Not available**
pH	**Not available**	**Density**	**Not available**	**Flammability Limits**	**Not available**

10. STABILITY AND REACTIVITY DATA

Stability	**Stable**
Incompatibility	**None known**
Hazardous Decomposition	**Oxides of carbon, oxides of nitrogen, oxides of sulfur**
Conditions to Avoid	**Excessive heat, light**
Hazardous Polymerization	**Will not occur.**

11. TOXICOLOGICAL INFORMATION

Acute Toxicity:

Active Ingredient:
LD50 Oral (rat): 400 mg/kg
LD50 Oral (mouse): 1389 mg/kg

Azathioprine is carcinogenic, mutagenic and teratogenic in animals and humans.

Carcinogenicity: Azathioprine is listed as an IARC 1 Carcinogen (Carcinogenic to Humans) and a NTP Known Carcinogen.

12. ENVIRONMENTAL IMPACT INFORMATION

No information is currently available on the environmental impact of this product.

13. DISPOSAL INFORMATION

Waste Disposal Considerations: Dispose of material according to federal, state and local disposal regulations or company operating procedures. Disposal by incineration is recommended.
At home: Discard away from children's reach.

14. TRANSPORTATION INFORMATION

This product is not subject to the regulations for the safe transport of hazardous chemicals.
DOT: Not regulated
TDG: Not regulated
IATA: Not regulated
IMDG: Not regulated

15. REGULATORY INFORMATION

DEA: Azathioprine is not a controlled substance.

FDA: Azathioprine is an approved prescription medication.

Inventory Status:
This material is not listed on the US TSCA Inventory. Therefore, it can only be used for TSCA exempt purposes such as R&D or drug use.
This material is not listed on the DSL Inventory but is exempt.

16. OTHER DATA

ABBEVIATIONS:
N/A – not applicable

Prepared by: Boehringer Ingelheim Roxane, Inc.

References:

1. **Azathioprine Tablets USP, Package Insert, Boehringer Ingelheim Roxane, Inc., Columbus, Ohio**
2. **RTECS No. UO8925000 – Purine, 6-((1-methyl-4-nitroimidazol-5-yl)thio)-**
3. **Ariel Webinsight. Regulatory and ChemExpert Database.**
4. **PDR – Physicians Desk Reference**

Date: 09/13/2008 - New MSDS

SEE CURRENT PACKAGE INSERT FOR FURTHER INFORMATION

The information provided is believed to be complete and accurate. If this product is combined with other materials, deteriorates or becomes contaminated, it may pose hazards not mentioned in this MSDS. It is the users' responsibility to use the information according to the application. Boehringer Ingelheim Roxane, Inc. assumes no responsibility or liability resulting from the use of this information.