SAFETY DATA SHEETS

This SDS packet was issued with item:

078929563

The safety data sheets (SDS) in this packet apply to the individual products listed below. Please refer to invoice for specific item number(s).

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SAFETY DATA SHEET

SECTION 1: IDENTIFICATION

Product Name: Ketoconazole Tablets USP, 200 mg **Product No.:** 51672-4026

Distributor: Taro Pharmaceuticals U.S.A., Inc.
3 Skyline Drive, Hawthorne, New York 10532
Telephone: 1-888-TARO-USA

Recommended Use: Ketoconazole tablets USP, 200 mg should be used only when other effective antifungal therapy is not available or tolerated and the potential benefits are considered to outweigh the potential risks.

Ketoconazole tablets USP, 200 mg are indicated for the treatment of the following systemic fungal infections in patients who have failed or who are intolerant to other therapies: blastomycosis, coccidioidomycosis, histoplasmosis, chromomycosis, and paracoccidioidomycosis. Ketoconazole tablets USP, 200 mg should not be used for fungal meningitis because it penetrates poorly into the cerebrospinal fluid.

Restrictions on Use:

Drug Interactions
Coadministration of a number of CYP3A4 substrates such as dofetilide, quinidine cisapride and pimozide is contraindicated with ketoconazole tablets. Coadministration with ketoconazole can cause elevated plasma concentrations of these drugs and may increase or prolong both therapeutic and adverse effects to such an extent that a potentially serious adverse reaction may occur. For example, increased plasma concentrations of some of these drugs can lead to QT prolongation and sometimes resulting in life-threatening ventricular tachyarrhythmias including occurrences of torsades de pointes, a potentially fatal arrhythmia.

Additionally, the following other drugs are contraindicated with ketoconazole tablets: methadone, disopyramide, dronedarone, ergot alkaloids such as dihydroergotamine, ergometrine, ergotamine, methylergometrine, irinotecan, lurasidone, oral midazolam, alprazolam, triazolam, felodipine, nisoldipine, ranolazine, tolvaptan, eplerenone, lovastatin, simvastatin and colchicine.

Enhanced Sedation
Coadministration of ketoconazole tablets with oral midazolam, oral triazolam or alprazolam has resulted in elevated plasma concentrations of these drugs. This may potentiate and prolong hypnotic and sedative effects, especially with repeated dosing or chronic administration of these agents. Concomitant administration of ketoconazole tablets with oral triazolam, oral midazolam or alprazolam is contraindicated.

Myopathy
Coadministration of CYP3A4 metabolized HMG-CoA reductase inhibitors such as simvastatin, and lovastatin is contraindicated with ketoconazole tablets.

Ergotism
Concomitant administration of ergot alkaloids such as dihydroergotamine and ergotamine with ketoconazole tablets is contraindicated.

Liver Disease
The use of ketoconazole tablets is contraindicated in patients with acute or chronic liver disease.

Hypersensitivity
Ketoconazole tablets USP, 200 mg is contraindicated in patients who have shown hypersensitivity to the drug.

Substance Class: Antifungal

Formula: $C_{26}H_{28}Cl_2N_4O_4$

M.W.: 531.43

SECTION 2: HAZARD(S) IDENTIFICATION

Handling of this product in its final form presents minimal occupational exposure risk.

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient:	Ketoconazole	CAS#: 65277-42-1
Inactive Ingredients:	Colloidal silicon dioxide, corn starch, lactose monohydrate, magnesium stearate, microcrystalline cellulose, and povidone.	

SECTION 4: FIRST-AID MEASURES

Inhalation: If breathing is difficult, remove to fresh air and keep at rest in a position comfortable for breathing. Call a physician if symptoms develop or persist.

Skin Contact: Rinse skin with water/shower. Get medical attention if irritation develops and persists.

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

Ingestion: Rinse mouth. If ingestion of a large amount does occur, call a poison control center immediately.

Most Important Symptoms/Effects, Acute and Delayed: Liver damage.

Indication of Immediate Medical Attention and Special Treatment Needed: Treatment of imidazole antifungal overdose should be symptomatic and supportive and may include the following: Toxicity after ingestion is unlikely. Gastrointestinal decontamination is generally unnecessary. For severe diarrhea or vomiting, monitor and correct fluid status. (Poisindex)

General Information: Remove from exposure. Remove contaminated clothing. For treatment advice, seek guidance from an occupational health physician or other licensed health-care provider familiar with workplace chemical exposures. In the United States, the national poison control center phone number is 1-800-222-1222. If person is not breathing, give artificial respiration. If breathing is difficult, give oxygen if available. Persons developing serious hypersensitivity (anaphylactic) reactions must receive immediate medical attention.

SECTION 5: FIRE-FIGHTING MEASURES

Suitable Extinguishing Media: Use fire-extinguishing media appropriate for surrounding materials. Water. Foam. Dry chemical or CO_2.

Unsuitable Extinguishing Media: None known.

Specific Hazards Arising From the Chemical: Explosion hazard: 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.

Special Protective Equipment and Precautions for Firefighters: Wear suitable protective equipment.

Fire-Fighting Equipment/Instructions: Use water spray to cool unopened containers. As with all fires, evacuate personnel to a safe area. Firefighters should use self-contained breathing equipment and protective clothing.

Specific Methods: Use standard firefighting procedures and consider the hazards of other involved materials.

SECTION 6: ACCIDENTAL RELEASE MEASURES

Personal Precautions, Protective Equipment and Emergency Procedures: 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. Keep unnecessary personnel away. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing. Ensure adequate ventilation. Avoid inhalation of dust from the spilled material. Wear appropriate personal protective equipment.

Methods and Materials for Containment and Cleaning Up: Sweep up or vacuum up spillage and collect in suitable container for disposal. Avoid the generation of dusts during clean-up. For waste disposal, see section 13 of the SDS. Clean surface thoroughly to remove residual contamination.

SECTION 7: HANDLING AND STORAGE

Precautions for Safe Handling: As a general rule, when handling USP Reference Standards, avoid all contact and inhalation of dust, mists, and/or vapors associated with the material. Clean equipment and work surfaces with suitable detergent or solvent after use. After removing gloves, wash hands and other exposed skin thoroughly. Combustible dust clouds may be created where operations produce fine material (dust). Avoid significant deposits of material, especially on horizontal surfaces, which may become airborne and form combustible dust clouds and may contribute to secondary explosions.

Conditions for Safe Storage, Including Any Incompatibilities: Store in tight container as defined in the USP-NF. This material should be handled and stored per label instructions to ensure product integrity.

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Limit Values

Industrial Use

Material	Type	Value
Ketoconazole (CAS65277-42-1)	TWA	0.2 mg/m^3

Biological Limit Values: No biological exposure limits noted for the ingredient(s).

Appropriate Engineering Controls: Airborne exposure should be controlled primarily by engineering controls such as general dilution ventilation, local exhaust ventilation, or process enclosure. Local exhaust ventilation is generally preferred to general exhaust because it can control the contaminant at its source, preventing dispersion into the work area. An industrial hygiene survey involving air monitoring may be used to determine the effectiveness of engineering controls. Effectiveness of engineering controls intended for use with highly potent materials should be assessed by use of nontoxic surrogate materials. Local exhaust ventilation such as a laboratory fume hood or other vented enclosure is recommended, particularly for grinding, crushing, weighing, or other dust-generating procedures.

Individual Protection Measures, Such As Personal Protective Equipment

Eye/Face Protection: Safety glasses with sideshields are recommended. Face shields or goggles may be required if splash potential exists or if corrosive materials are present. Approved eye protection (e.g., bearing the ANSI Z87 or CSA stamp) is preferred. Maintain eyewash facilities in the work area.

Skin Protection

Hand Protection: Chemically compatible gloves. For handling solutions, ensure that the glove material is protective against the solvent being used. Use handling practices that minimize direct hand contact. Employees who are sensitive to natural rubber (latex) should use nitrile or other synthetic nonlatex gloves. Use of powdered latex gloves should be avoided due to the risk of latex allergy.

Other: For handling of laboratory scale quantities, a cloth lab coat is recommended. Where significant quantities are handled, work clothing may be necessary to prevent take-home contamination.

Respiratory Protection: Where respirators are deemed necessary to reduce or control occupational exposures, use NIOSH-approved respiratory protection and have an effective respirator program in place (applicable U.S. regulation OSHA 29 CFR 1910.134).

Thermal Hazards: Not available.

General Hygiene Considerations: Handle in accordance with good industrial hygiene and safety practice.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

Boiling Point: Not available.

Physical State (Liquid/Solid/Gas): Solid

Specific Gravity (H_2O = 1): Not available.

Evaporation Rate (Butyl Acetate = 1): Not available.

Solubility: Practically insoluble in water.

Appearance: White to off-white, round, flat tablet. One side scored and engraved "T" above the score and "57" below the score. Other side plain.

Odor Description: Odorless

Melting Point: 298.4-305.6°F (148-152°C)

SECTION 10: STABILITY AND REACTIVITY

Reactivity: No reactivity hazards known.

Chemical Stability: Material is stable under normal conditions.

Possibility of Hazardous Reactions: No dangerous reaction known under conditions of normal use.

Conditions to Avoid: None known.

Incompatible Materials: Acids. Strong bases.

Hazardous Decomposition Products: Cl-. NOx. Irritating and/or toxic fumes or gases. Emits toxic fumes under fire conditions.

SECTION 11: TOXICOLOGICAL INFORMATION

Information on Likely Routes of Exposure

Ingestion: Toxic if swallowed.

Inhalation: Due to lack of data the classification is not possible.

Skin Contact: Due to lack of data the classification is not possible.

Eye Contact: Due to lack of data the classification is not possible.

Symptoms Related to the Physical, Chemical, and Toxicological Characteristics: Imidazole antifungals: Nausea. Vomiting. Diarrhea. Abdominal pain. Headache. Back pain. Fever. Chills. Drowsiness. Fatigue. Dizziness. Skin rash. Itching. Blistering. Burning. Skin redness. Flushing. Constipation. Loss of appetite. Visual disturbances. Yellowed eyes or skin. Swelling in arms or legs. Difficulty breathing. Confusion. Depression. Sedation. Trembling. Convulsions.

Medical Conditions Aggravated By Exposure: Alcoholism. Impaired liver function. Achlorhydria. Porphyria.

Acute Toxicity: Toxic if swallowed.

Product	**Species**	**Test Results**
Ketoconazole (CAS 65277-42-1)		
Acute		
Oral		
LD50	Dog	780 mg/kg
	Guinea pig	202 mg/kg
	Mouse	702 mg/kg
	Rat	227 mg/kg

Skin Corrosion/Irritation: Due to lack of data the classification is not possible.

Serious Eye Damage/Eye Irritation: Due to lack of data the classification is not possible.

Respiratory Sensitization: Due to lack of data the classification is not possible.

Skin Sensitization: Due to lack of data the classification is not possible.

Germ Cell Mutagenicity: Based on available data, the classification criteria are not met.

Mutagenicity:

Dominant lethal test in mice
Result: Negative.

Carcinogenicity: Based on available data, the classification criteria are not met. This material is not considered to be a carcinogen by IARC, NTP, or OSHA.

<80 mg/kg/day Carcinogenicity study
Result: No evidence of carcinogenicity was seen in rats or mice in a long-term feeding study.

SECTION 12: ECOLOGICAL INFORMATION

Ecotoxicity: No ecotoxicity data noted for the ingredient(s).

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

Bioaccumulative Potential: Not available.

Mobility in Soil: Not available.

Other Adverse Effects: Not available.

SECTION 13: DISPOSAL CONSIDERATIONS

Disposal Instructions: Dispose in accordance with all applicable regulations. Under RCRA, it is the responsibility of the user of the product to determine, at the time of disposal, whether the product meets RCRA criteria for hazardous waste.

Local Disposal Regulations: Not available.

Hazardous Waste Code: Not available.

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.

SECTION 14: TRANSPORT INFORMATION

Transportation and shipping of this product is not restricted. It has no known, significant hazards requiring special packaging or labeling for air, maritime, US or European ground transport purposes.

SECTION 15: REGULATORY INFORMATION

US Federal Regulations: CERCLA/SARA Hazardous Substances - Not applicable.
One or more components are not listed on TSCA.

Superfund Amendments and Reauthorization Act of 1986 (SARA)

Hazard Categories: Immediate Hazard - Yes
Delayed Hazard - No

Fire Hazard - No
Pressure Hazard - No
Reactivity Hazard – No

SARA 302 Extremely Hazardous Substance: No

SARA 311/312 Hazardous Chemical: No

Other Federal Regulations

Safe Drinking Water Act (SDWA): Not regulated.

Food and Drug Administration (FDA): Not regulated.

U.S. State Regulations: California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65): This material is not known to contain any chemicals currently listed as carcinogens or reproductive toxins.

SECTION 16: OTHER INFORMATION

Contact: Taro Pharmaceuticals U.S.A., Inc., Regulatory Affairs Department
3 Skyline Drive, Hawthorne, NY 10532

Preparation and/or Revision Date: November 2017

D I S C L A I M E R

The above information has been obtained from a number of sources and its accuracy cannot be guaranteed. It is the user's responsibility to evaluate the information and use it in a prudent manner for its particular purpose. Taro Pharmaceuticals assumes no responsibility for the use of this information.