# SAFETY DATA SHEET

## 1. Identification

**Product identifier** **TACROLIMUS CAPSULES**

**Other means of identification**

**Synonyms** Tacrolimus Capsules 0.5 mg * Tacrolimus Capsules 1 mg * Tacrolimus Capsules 5 mg

**Recommended use** This product is a calcineurin-inhibitor immunosuppressant indicated for the prophylaxis of organ rejection in patients receiving allogeneic liver, kidney or heart transplants.

Use concomitantly with adrenal corticosteroids; in kidney and heart transplant, use in conjunction with azathioprine or mycophenolate mofetil.

**Recommended restrictions** None known.

**Manufacturer/Importer/Supplier/Distributor information**

**Distributor**

**Company name** Accord Healthcare, Inc.

**Address** 1009 Slater Road Suite
210-B Durham, NC 27703, USA.

**Telephone number** 1-919-941-7880

**Fax** 1-919-941-7881

**Contact Name** Technical Representative

**Website** www.accord-healthcare.com

**Emergency telephone number** 1-800-424-9300 Call CHEMTREC Day or Night

**Manufacturer**

**Company name** Intas Pharmaceuticals Limited,

**Address** Plot No.: 457 – 458,
Village: Matoda, Taluka: Sanand,
Sarkhej - Bavla Highway,
District: Ahmedabad
Gujarat, India. 382 210

## 2. Hazard(s) identification

**Physical hazards** Not classified.

**Health hazards**

| | |
|---|---|
| Reproductive toxicity | Category 2 |
| Reproductive toxicity | Effects on or via lactation |
| Specific target organ toxicity, repeated exposure | Category 1 (immune system) |

**OSHA defined hazards** Not classified.

**Label elements**

**Signal word** Danger

**Hazard statement** Suspected of damaging fertility or the unborn child. May cause harm to breast-fed children. Causes damage to organs (immune system) through prolonged or repeated exposure.

**Precautionary statement**

| | |
|---|---|
| **Prevention** | Obtain special instructions before use. Do not handle until all safety precautions have been read and understood. Do not breathe dust. Do not eat, drink or smoke when using this product. Avoid contact during pregnancy/while nursing. Wear protective gloves/protective clothing/eye protection/face protection. Wash thoroughly after handling. |
| **Response** | If exposed or concerned: Get medical advice/attention. |
| **Storage** | Store locked up. |
| **Disposal** | Dispose of contents/container in accordance with local/regional/national/international regulations. |

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

**Supplemental information** Finished Pharmaceutical products in their final packages are not subject to OSHA labeling requirements. Handling pharmaceutical products in workplace is subject to OSHA requirements for labeling.

## 3. Composition/information on ingredients

**Mixtures**

| Chemical name | CAS number | % |
|---|---|---|
| CROSCARMELLOSE SODIUM | 74811-65-7 | Proprietary |
| Hydroxy propyl methyl cellulose | 9004-65-3 | Proprietary |
| Lactose monohydrate | 64044-51-5 | Proprietary |
| Magnesium distearate | 557-04-0 | Proprietary |
| TACROLIMUS | 109581-93-3 | Proprietary |

**Composition comments** All concentrations are in percent by weight unless ingredient is a gas. Gas concentrations are in percent by volume.

Active: Tacrolimus.

Inactive: lactose monohydrate, hypromellose E5, croscarmellose sodium, and magnesium stearate .

Capsule shell: gelatin, titanium dioxide and sodium lauryl sulfate (in 0.5/1/5 mg); iron oxide yellow (in 0.5 mg); and iron oxide red (in 5 mg).

## 4. First-aid measures

**Inhalation** Move to fresh air. Oxygen or artificial respiration if needed. Call a physician if symptoms develop or persist.

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

**Eye contact** Do not rub eyes. Rinse with water. Get medical attention if irritation develops and persists.

**Ingestion** Rinse mouth. Never give anything by mouth to a victim who is unconscious or is having convulsions. Do not induce vomiting without advice from poison control center. If vomiting occurs, keep head low so that stomach content doesn't get into the lungs. Get medical attention if symptoms occur.

| | |
|---|---|
| **Most important symptoms/effects, acute and delayed** | Dusts may irritate the respiratory tract, skin and eyes. Swallowing may cause gastrointestinal irritation. Prolonged exposure may cause chronic effects.<br><br>Adverse effects may include nausea; diarrhea; muscle or joint pain; dizziness; difficulty sleeping; flushing; itching or rash; trembling; headache; tingling, prickling, or numbness of skin; high blood pressure; kidney problems; and seizures. Possible allergic reaction to material if inhaled, ingested or in contact with skin.<br><br>Kidney Transplant: The most common adverse reactions ( ≥ 30%) were infection, tremor, hypertension, abnormal renal function, constipation, diarrhea, headache, abdominal pain, insomnia, nausea, hypomagnesemia, urinary tract infection, hypophosphatemia, peripheral edema, asthenia, pain, hyperlipidemia, hyperkalemia and anemia.<br><br>Liver Transplant: The most common adverse reactions (≥ 40%) were tremor, headache, diarrhea, hypertension, nausea, abnormal renal function, abdominal pain, insomnia, paresthesia, anemia, pain, fever, asthenia, hyperkalemia, hypomagnesemia, and hyperglycemia.<br><br>Heart Transplant: The most common adverse reactions ( ≥ 15%) were abnormal renal function, hypertension, diabetes mellitus, CMV infection, tremor, hyperglycemia, leukopenia, infection, anemia, bronchitis, pericardial effusion, urinary tract infection and hyperlipemia.<br><br>Overdose effects may include coma and delirium. |
| **Indication of immediate medical attention and special treatment needed** | Provide general supportive measures and treat symptomatically. Keep victim under observation. Symptoms may be delayed.<br><br>Persons developing anaphylactic (life threatening) reactions, such a as difficulty in breathing or unconsciousness, must receive immediate medical attention.<br><br>PRE-EXISTING MEDICAL CONDITIONS WHICH MAY BE AGGRAVATED BY EXPOSURE: Hypersensitivity to material, Netherton's syndrome, and impaired liver or kidney function. |
| **General information** | IF exposed or concerned: Get medical advice/attention. If you feel unwell, seek medical advice (show the label where possible). Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves. Show this safety data sheet to the doctor in attendance. |

## 5. Fire-fighting measures

| | |
|---|---|
| **Suitable extinguishing media** | Water spray. Dry chemical. Carbon dioxide (CO2). Foam. |
| **Unsuitable extinguishing media** | None known. |
| **Specific hazards arising from the chemical** | The product may form dust and can accumulate electrostatic charges, which may cause an electrical spark (ignition source). Use proper grounding procedures. During fire, gases hazardous to health may be formed. Product in its powder form in sufficient quantity can cause a dust combustion / explosion hazards. |
| **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** | Evacuate personnel to safe area. Use water spray to cool unopened containers. |
| **Specific methods** | Use standard firefighting procedures and consider the hazards of other involved materials. |
| **General fire hazards** | May form combustible dust concentrations in air. |

## 6. Accidental release measures

| | |
|---|---|
| **Personal precautions, protective equipment and emergency procedures** | Keep unnecessary personnel away. Keep people away from and upwind of spill/leak. Wear appropriate protective equipment and clothing during clean-up. Do not breathe dust. Use a NIOSH/MSHA approved respirator if there is a risk of exposure to dust/fume at levels exceeding the exposure limits. Ensure adequate ventilation. Local authorities should be advised if significant spillages cannot be contained. For personal protection, see section 8 of the SDS. |
| **Methods and materials for containment and cleaning up** | Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air). Collect dust using a vacuum cleaner equipped with HEPA filter. The product is immiscible with water and will spread on the water surface. Stop the flow of material, if this is without risk.<br><br>Large Spills: Wet down with water and dike for later disposal. Shovel the material into waste container. Following product recovery, flush area with water.<br><br>Small Spills: Sweep up or vacuum up spillage and collect in suitable container for disposal.<br><br>Never return spills to original containers for re-use. For waste disposal, see section 13 of the SDS. |

**Environmental precautions** Avoid discharge into drains, water courses or onto the ground.

## 7. Handling and storage

**Precautions for safe handling** Obtain special instructions before use. Do not handle until all safety precautions have been read and understood. Minimize dust generation and accumulation. Provide appropriate exhaust ventilation at places where dust is formed. Do not breathe dust. Avoid contact with eyes, skin, and clothing. Avoid prolonged exposure. When using, do not eat, drink or smoke. Pregnant or breastfeeding women must not handle this product. Should be handled in closed systems, if possible. Wear appropriate personal protective equipment. Wash thoroughly after handling. Observe good industrial hygiene practices.

**Conditions for safe storage, including any incompatibilities** Store locked up. Store in original tightly closed container. Store in a well-ventilated place. Store at 25ºC (77ºF); excursions permitted to 15 - 30 °C (59 - 86 ºF). Store away from incompatible materials (see Section 10 of the SDS).

## 8. Exposure controls/personal protection

**Occupational exposure limits**

**US. ACGIH Threshold Limit Values**

| Components | Type | Value |
|---|---|---|
| Magnesium distearate (CAS 557-04-0) | TWA | 10 mg/m3 |

**Biological limit values** No biological exposure limits noted for the ingredient(s).

**Appropriate engineering controls** Good general ventilation (typically 10 air changes per hour) should be used. Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits. If exposure limits have not been established, maintain airborne levels to an acceptable level. If engineering measures are not sufficient to maintain concentrations of dust particulates below the Occupational Exposure Limit (OEL), suitable respiratory protection must be worn. If material is ground, cut, or used in any operation which may generate dusts, use appropriate local exhaust ventilation to keep exposures below the recommended exposure limits.

**Individual protection measures, such as personal protective equipment**

**Eye/face protection** Wear safety glasses with side shields (or goggles).

**Skin protection**

**Hand protection** Wear appropriate chemical resistant gloves. Suitable gloves can be recommended by the glove supplier.

**Skin protection**

**Other** Wear appropriate chemical resistant clothing. Use of an impervious apron is recommended.

**Respiratory protection** Use a NIOSH/MSHA approved respirator if there is a risk of exposure to dust/fume at levels exceeding the exposure limits.

**Thermal hazards** Wear appropriate thermal protective clothing, when necessary.

**General hygiene considerations** When using, do not eat, drink or smoke. 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. Observe any medical surveillance requirements.

## 9. Physical and chemical properties

**Appearance** Solid / Hard gelatin capsule containing white to off granular powder.

**Physical state** Solid.

**Form** Capsule.

**Color** White to off-white.

**Odor** Not available.

**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)** | API: Insoluble in water. |
| **Solubility (other)** | API: Soluble in Acetone, chloroform and ethyl acetate. |
| **Partition coefficient (n-octanol/water)** | Not available. |
| **Auto-ignition temperature** | Not available. |
| **Decomposition temperature** | Not available. |
| **Viscosity** | Not available. |

## 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** | Will not occur. |
| **Conditions to avoid** | Avoid generation of dust. Light. Heat. Contact with incompatible materials. |
| **Incompatible materials** | Strong oxidizing agents. |
| **Hazardous decomposition products** | Nitrogen oxides (NOx). |

## 11. Toxicological information

**Information on likely routes of exposure**

| | |
|---|---|
| **Inhalation** | Dust may irritate respiratory system. |
| **Skin contact** | Dust or powder may irritate the skin. |
| **Eye contact** | Dust may irritate the eyes. |
| **Ingestion** | Swallowing may cause gastrointestinal irritation. |

**Symptoms related to the physical, chemical and toxicological characteristics**

Dusts may irritate the respiratory tract, skin and eyes. Swallowing may cause gastrointestinal irritation.

Adverse effects may include nausea; diarrhea; muscle or joint pain; dizziness; difficulty sleeping; flushing; itching or rash; trembling; headache; tingling, prickling, or numbness of skin; high blood pressure; kidney problems; and seizures. Possible allergic reaction to material if inhaled, ingested or in contact with skin.

Kidney Transplant: The most common adverse reactions ( ≥ 30%) were infection, tremor, hypertension, abnormal renal function, constipation, diarrhea, headache, abdominal pain, insomnia, nausea, hypomagnesemia, urinary tract infection, hypophosphatemia, peripheral edema, asthenia, pain, hyperlipidemia, hyperkalemia and anemia.

Liver Transplant: The most common adverse reactions (≥ 40%) were tremor, headache, diarrhea, hypertension, nausea, abnormal renal function, abdominal pain, insomnia, paresthesia, anemia, pain, fever, asthenia, hyperkalemia, hypomagnesemia, and hyperglycemia.

Heart Transplant: The most common adverse reactions ( ≥ 15%) were abnormal renal function, hypertension, diabetes mellitus, CMV infection, tremor, hyperglycemia, leukopenia, infection, anemia, bronchitis, pericardial effusion, urinary tract infection and hyperlipemia.

Overdose effects may include coma and delirium.

**Information on toxicological effects**

**Acute toxicity** Swallowing may cause gastrointestinal irritation.

| Components | Species | Test Results |
|---|---|---|
| TACROLIMUS (CAS 109581-93-3) | | |
| **Acute** | | |
| *Oral* | | |
| LD50 | Mouse | 194 mg/kg, (female) |
| | | 134 mg/kg, (male) |
| | Rat | 134 mg/kg |

**Skin corrosion/irritation** May cause skin irritation.

**Serious eye damage/eye irritation** Direct contact with eyes may cause temporary irritation.

**Respiratory or skin sensitization**

**Respiratory sensitization** Not available.

**Skin sensitization** This product is not expected to cause skin sensitization.

**Germ cell mutagenicity** No data available to indicate product or any components present at greater than 0.1% are mutagenic or genotoxic.

**Carcinogenicity** WARNING! Increased risk of development of lymphoma and other malignancies, particularly of the skin, due to immunosuppression. Avoid prolonged exposure to UV light and sunlight.

**IARC Monographs. Overall Evaluation of Carcinogenicity**

Not listed.

**NTP Report on Carcinogens**

Not listed.

**OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)**

Not regulated.

**Reproductive toxicity** May cause harm to breastfed babies. Suspected of damaging fertility or the unborn child.

In animal studies, embryo-fetal toxicity occurred. Only take during pregnancy if the potential benefit justifies the potential risk to the fetus.

This product is excreted into human milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother's health.

**Specific target organ toxicity - single exposure** Not classified.

**Specific target organ toxicity - repeated exposure** Causes damage to organs (immune system) through prolonged or repeated exposure.

**Aspiration hazard** Not available.

**Chronic effects** Possible hypersensitization (development of abnormal sensitivity).

**Further information** WARNING! Increased susceptibility to bacterial, viral, fungal, and protozoal infections, including opportunistic infections.

Hepatic/Renal impaired patients: Administer at the lower end of the recommended starting dose. Monitor renal function in patients with impaired renal function.

## 12. Ecological information

**Ecotoxicity** The product is not classified as environmentally hazardous. However, this does not exclude the possibility that large or frequent spills can have a harmful or damaging effect on the environment.

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

**Bioaccumulative potential** No data available.

**Mobility in soil** No data available.

**Other adverse effects** No other adverse environmental effects (e.g. ozone depletion, photochemical ozone creation potential, endocrine disruption, global warming potential) are expected from this component.

## 13. Disposal considerations

**Disposal instructions** Collect and reclaim or dispose in sealed containers at licensed waste disposal site. Dispose of contents/container in accordance with local/regional/national/international regulations.

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

## 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 product is a "Hazardous Chemical" as defined by the OSHA Hazard Communication Standard, 29 CFR 1910.1200.

This product is exempt from SARA 311/312 reporting requirements when used as a food, food additive, color additive, drug or cosmetic under 40CFR370.13(a).

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

Not regulated.

**OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)**

Not regulated.

**CERCLA Hazardous Substance List (40 CFR 302.4)**

Not listed.

**Superfund Amendments and Reauthorization Act of 1986 (SARA)**

| | |
|---|---|
| **Hazard categories** | Immediate Hazard - No<br>Delayed Hazard - Yes<br>Fire Hazard - No<br>Pressure Hazard - No<br>Reactivity Hazard - No |

**SARA 302 Extremely hazardous substance**

Not listed.

| | |
|---|---|
| **SARA 311/312 Hazardous chemical** | Yes |

**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. |

**US state regulations**

**US. Massachusetts RTK - Substance List**

Not regulated.

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

Not listed.

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

Not listed.

**US. Rhode Island RTK**

Not regulated.

**US. California Proposition 65**

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.

**International Inventories**

| Country(s) or region | Inventory name | On inventory (yes/no)* |
|---|---|---|
| Australia | Australian Inventory of Chemical Substances (AICS) | No |
| Canada | Domestic Substances List (DSL) | No |
| Canada | Non-Domestic Substances List (NDSL) | No |
| China | Inventory of Existing Chemical Substances in China (IECSC) | No |
| Europe | European Inventory of Existing Commercial Chemical Substances (EINECS) | No |
| Europe | European List of Notified Chemical Substances (ELINCS) | No |
| Japan | Inventory of Existing and New Chemical Substances (ENCS) | No |
| Korea | Existing Chemicals List (ECL) | No |
| New Zealand | New Zealand Inventory | No |
| Philippines | Philippine Inventory of Chemicals and Chemical Substances (PICCS) | No |
| 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** 09-December-2015

**Revision date** -

**Version #** 01

**NFPA ratings**


**Disclaimer**

Accord Healthcare, 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.