



# HETERO LABS LIMITED

"Hetero Corporate", 7-2-A2, Industrial Estates, Sanath Nagar, Hyderabad - 500 018. A.P., INDIA.  
Tel : 91-40-23704923/24/25, Fax : 91-40-23704926, 23714250  
e-mail : contact@heterodrugs.com URL : http://www.heterodrugs.com

## SAFETY DATA SHEET

| <b>Section 1: Identification</b>                 |  |
|--|--|
| <b>Section 1, Identification</b>                 |  |
| <b>GHS Product identifier</b>                    | Tadalafil Tablets USP, 20 mg.  |
| <b>Trade Name</b>                                | Not Applicable   |
| <b>Other means of identification</b>             | Tadalafil, Finished Product  |
| <b>Synonyms</b>                                  |  |
| <b>Recommended use</b>                           | Pharmaceutical product for the treatment of Pulmonary Arterial Hypertension.   |
| <b>Manufacturer</b>                              | Hetero Labs Limited, Unit-III<br>Plot No. 22-110, Part-II, IDA, Jeedimetla,<br>Hyderabad 500055, Telangana, India (IND). |
| <b>Distributor</b>                               | Camber Pharmaceuticals, Inc., Piscataway, NJ,<br>08854.  |
| <b>Section 2: Hazard(s) Identification</b>       |  |
| <b>Section 2, Hazard(s)identification</b>        |  |
| <b>Physical hazards</b>                          | Not Classified   |
| <b>Health hazards</b>                            | Not Classified   |
| <b>OSHA defined hazards</b>                      | Not Classified   |
| <b>Label elements</b>                            |  |
| <b>Hazard symbol</b>                             | None   |
| <b>Signal word</b>                               | None   |
| <b>Hazard statement</b>                          | The mixture does not meet the criteria for classification.   |
| <b>Precautionary statement</b>                   | Not available  |
| <b>Prevention</b>                                | Not available  |
| <b>Response</b>                                  | Not available  |
| <b>Storage</b>                                   | Not available  |
| <b>Disposal</b>                                  | Not available  |
| <b>Hazard(s) not otherwise classified (HNOC)</b> | None known   |



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## Section 3: Composition/Information on Ingredients

| Chemical Name               | Common Name and Synonym   | CAS         |
|-----------------------------|---|-------------|
| Tadalafil                   | Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione,6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12ahexahydro-2-methyl-(6R-12aR)- | 171596-29-5 |
| <b>Composition comments</b> | Remaining components of this product are non-hazardous and/or are present at concentrations below reportable levels.  |             |

## Section 4: First-Aid Measures

|   |  |
|---|--|
| <b>Inhalation</b>   | Remove to fresh air. If breathing stops, provide artificial respiration. Get medical attention immediately.  |
| <b>Skin Contact</b>   | Wash off immediately with plenty of water. Continue to rinse for at least 15 minutes. Immediately take off all contaminated clothing. Get medical attention if irritation develops and persists. |
| <b>Eye Contact</b>  | In case of eye contact, remove contact lens and rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes. Get medical attention.                                  |
| <b>Ingestion</b>  | Immediately give large quantities of water to drink. Never give anything by mouth to a victim who is unconscious or is having convulsions. Call a physician immediately.                         |
| <b>Most important symptoms/effects, acute and delayed</b>                     | Headache. Flushing.  |
| <b>Indication of immediate medical attention and special treatment needed</b> | Pre-Existing Medical Conditions Which May Be Aggravated By Exposure: Individuals on nitrate or alpha blocker therapy.  |
| <b>General information</b>  | The recommendations in this section are intended for manufacturing or other situations where exposure to contents may occur.   |

## Section 5: Fire-Fighting Measures

|  |  |
|--|--|
| <b>Section 5, Fire-fighting measures</b>                             |  |
| <b>Suitable Extinguishing Media</b>                                  | Carbon dioxide, dry chemical or water.   |
| <b>Unsuitable Extinguishing Media</b>                                | None known   |
| <b>Specific hazards arising from the chemical</b>                    | The recommendations in this section are intended for manufacturing or other situations where exposure to contents may occur.<br>Hazardous decomposition products formed under fire conditions. If small particles are generated during further processing, handling, or by other means, may form combustible dust concentrations in air. |
| <b>Special protective equipment and precautions for firefighters</b> | Wear self-contained breathing apparatus and protective clothing.   |



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## Section 6: Accidental Release Measures

| Section 6, Accidental release measures                                     |   |
|--|---|
| <b>Personal precautions, protective equipment and emergency procedures</b> | Wear suitable protective clothing, gloves and eye/face protection. See Section 8 of the SDS for Personal Protective Equipment.  |
| <b>Methods and materials for containment and cleaning up</b>               | The recommendations in this section are intended for manufacturing or other situations where exposure to contents may occur.<br>Do not sweep. Collect spill using a vacuum cleaner with a HEPA filter. Be aware of potential for dust explosion when using electrical equipment. If vacuum is not available, lightly mist/wet material and remove by mopping or wet wiping. |
| <b>Environmental precautions</b>   | Avoid discharge into drains, water courses or onto the ground.  |

## Section 7: Handling and Storage

| Section 7, Handling and storage                                     |  |
|---|--|
| <b>Precautions for safe handling</b>                                | Avoid contact with eyes, skin, and clothing. Wash hands thoroughly after handling. See Section 8 of the SDS for Personal Protective Equipment. |
| <b>Conditions for safe storage, including any incompatibilities</b> | Store at 20°C to 25°C (68°F to 77°F); [see USP Controlled Room Temperature]. Keep out of reach of children.                                    |

## Section 8: Exposure Controls/Personal Protection

| Section 8, Exposure controls/personal protection                             |  |              |
|--|--|--------------|
| <b>Occupational exposure limits</b>  |  |              |
| <b>Lilly (LEG) Components</b>  | <b>Type</b>  | <b>Value</b> |
| Tadalafil (CAS 171596-29-5)  | TWA (12 hrs)   | 13 ug/m3     |
|  | TWA (8hrs)   | 20 ug/m3     |
| <b>Biological limit values</b>   | No biological exposure limits noted for the ingredient(s)  |              |
| <b>Appropriate engineering controls</b>                                      | The recommendations in this section are intended for manufacturing or other situations where exposure to contents may occur.   |              |
|  | Open handling is not recommended. Use appropriate control measures such as fume hood, ventilated enclosure, isolator (i.e. glove bag/glove box) and/or closed transfers to maintain airborne levels below occupational exposure level (OEL). |              |
| <b>Individual protection measures, such as personal protective equipment</b> |  |              |
| <b>Eye/ Face protection</b>  | Safety glasses with side shields recommended. If splash potential or dusty operations, wear goggles/face shield.   |              |
| <b>Skin protection</b>   |  |              |
| <b>Hand protection</b>   | Chemical resistant gloves.   |              |
| <b>Other</b>   | Chemical-resistant gloves and impermeable body covering to minimize skin contact.  |              |



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|                                       |  |
|---------------------------------------|--|
| <b>Respiratory protection</b>         | If the applicable occupational exposure level (OEL) is anticipated to be exceeded, wear an approved respirator with sufficient protection factor to control exposure below the OEL.  |
| <b>Thermal hazards</b>                | Not available  |
| <b>General hygiene considerations</b> | Engineering controls should be used as the primary means to control workplace exposures. Follow good workplace hygiene practices such as washing hands after handling this material. |

## Section 9: Physical and Chemical Properties

### Section 9, Physical and chemical properties

#### Appearance

|                       |   |
|-----------------------|---|
| <b>Physical State</b> | <b>Solid</b>  |
| <b>Form</b>           | <b>Tablets</b>  |
| <b>Colour</b>         | <b>white</b>  |
| <b>Odor</b>           | <b>Not Available</b>  |
| <b>Description</b>    | <b>Tadalafil Tablets 20 mg</b><br>White colour, capsule shaped, biconvex, film-coated tablets debossed with 'T15' on one side and 'H' on the other side.<br><br>Bottles of 30 Tablets (NDC 31722-647-30)<br>Carton of 100 (10x10) (NDC 31722-647-31)<br>Unit-dose tablets |

## Section 10: Stability and Reactivity

### Section 10, Stability and reactivity

|   |   |
|---|---|
| <b>Reactivity</b>                         | Not water reactive  |
| <b>Chemical stability</b>                 | Material is stable under normal conditions                    |
| <b>Possibility of hazardous reactions</b> | Hazardous polymerization does not occur                       |
| <b>Conditions to avoid</b>                | None known  |
| <b>Incompatible materials</b>             | Strong oxidizing substances                                   |
| <b>Hazardous decomposition products</b>   | Hazardous decomposition products formed under fire conditions |

## Section 11: Toxicological Information

### Information on toxicological effects

#### Acute toxicity

| Components                  | Species | Test Results                            |
|-----------------------------|---------|---|
| Tadalafil (CAS 171596-29-5) |         |   |
| <b>Acute</b>                |         |   |
| Dermal - LD                 | Rabbit  | > 1000 mg/kg No mortality. No toxicity. |
| Oral - LD                   | Rat     | > 2000 mg/kg No mortality. No toxicity. |



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|   |     |  |
|---|-----|--|
| Other - LD  | Rat | > 62.5 mg/kg (Intravenous) No mortality. Convulsions.  |
| <b>Skin corrosion/irritation</b>                                      |     | Rabbit: Slight irritation  |
| <b>Serious eye damage/eye irritation</b>                              |     | Rabbit: Slightly irritating.<br>Based on available data, the classification criteria are not met.  |
| <b>Respiratory or skin sensitization</b>                              |     |  |
| <b>Respiratory sensitization</b>                                      |     | Due to lack of data the classification is not possible   |
| <b>Skin sensitization</b>   |     | Due to lack of data the classification is not possible   |
| <b>Germ cell mutagenicity</b>   |     | Result in genetic toxicity assays (in vitro and in vivo): Negative Based on available data, the classification criteria are not met.   |
| <b>Carcinogenicity</b>  |     | Not listed by ACGIH, IARC, NIOSH, NTP OR OSHA. Based on available data, the classification criteria are not met.   |
| <b>IARC Monographs. Overall Evaluation of Carcinogenicity</b>         |     | Not listed   |
| <b>OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)</b> |     | Not regulated  |
| <b>US. National Toxicology Program (NTP) Report on Carcinogens</b>    |     | Not listed   |
| <b>Reproductive toxicity</b>  |     | There was no impairment of fertility in male and female rats. In beagle dogs given Tadalafil daily for 6 to 12 months at doses of 25 mg/kg/day and above, there were alterations to the seminiferous tubular epithelium that resulted in a decrease in spermatogenesis in some dogs. These findings were not observed in rats or mice. Furthermore, in men taking Tadalafil 10 or 20 mg/daily for 6 months, there were no clinically relevant effects on sperm concentration, count, motility, or morphology. Additionally, there were no significant effects of serum levels of testosterone, luteinizing hormone, or follicle stimulating hormone. There was no evidence of teratogenicity, embryo toxicity or fetotoxicity in rats or mice that received up to 1000 mg/kg/day. In a rat pre- and postnatal development study, the observed no effect dose was 30 mg/kg/day. Based on available data, the classification criteria are not met. |
| <b>Specific target organ toxicity - single exposure</b>               |     | Due to lack of data the classification is not possible.  |
| <b>Specific target organ toxicity - repeated exposure</b>             |     | Repeated oral doses of Tadalafil for more than six months resulted in decreased testicular weight in dogs. The decreased testes weights (reported at doses of 25 mg/kg/day and above in the 12-month study) correlated with degeneration and atrophy of the seminiferous epithelium. Decreased sperm in the epididymes was also reported with aspermia in the most severely affected dogs. No effects on semen parameters reported in humans after six-months of daily dosing (10 or 20 mg/day). When administered orally for 5 or 28 days at 5 mg/kg/day, blood pressure was reduced in rats. No significant findings were reported in rats or mice administered  |



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|                            |  |
|----------------------------|--|
|                            | up to 800 mg/kg by oral gavage for up to 3 months. Based on available data, the classification criteria are not met.   |
| <b>Aspiration hazard</b>   | Not applicable   |
| <b>Further information</b> | Based on animal studies with Tadalafil, chronic overexposure by ingestion may cause testicular tissue changes and decreased sperm production. However, two six-month human clinical studies reported no changes in sperm parameters. The most common adverse effects related to drug treatment were headache, lower back pain, and vasodilation (flushing), which can result in transient decreases in blood pressure. |

## Section 12: Ecological Information

Ectotoxicity: Harmful to aquatic life with long lasting effects.

| Components                           | Species  | Test Results   |
|--------------------------------------|--|--|
| Tadalafil (CAS 171596-29-5)          |  |  |
| <b>Acute</b>                         |  |  |
| EC50                                 |  | > 1000 mg/l, 3 hr<br>(Respiration inhibition of activated sludge)  |
| Other                                | Pseudokirchnerella subcapitata   | > 1200 µg/l, 72 hr (yield)   |
| <b>Chronic</b>                       |  |  |
| NOEC                                 |  | 1000 mg/l, 3 hr<br>(Respiration inhibition of activated sludge) (highest concentration tested)                   |
|                                      | Chironomus riparius (sediment dwelling midge)  | 250 mg/kg, 28 d (sediment exposure)  |
| Other - NOEC                         | Pseudokirchnerella subcapitata   | 1200 µg/l, 72 hr<br>(average specific growth rate) (highest concentration tested)<br>300 µg/l, 72 hr (yield)     |
|                                      |  | > 62.5 mg/kg (Intravenous) No mortality. Convulsions.  |
| <b>Aquatic</b>                       |  |  |
| Acute                                |  |  |
| Crustacea                            | EC50   | Daphnia magna<br>> 2000 mg/l, 48 hr  |
|                                      | NOEC   | Daphnia magna<br>1200 µg/l, 21 d (Full Life-Cycle Toxicity)  |
| Fish                                 | LC50   | Rainbow trout, donaldson trout (Oncorhynchus mykiss)<br>> 2100 µg/l, 96 hr                                       |
| Chronic Crustacea                    | LOEC   | Daphnia magna<br>1200 µg/l, 21 d (Full Life-Cycle Toxicity)  |
|                                      | NOEC   | Daphnia magna<br>2000 µg/l, 48 hr<br>(highest concentration tested)  |
| Fish                                 | NOEC   | Fathead minnow (Pimephales promelas)<br>1200 µg/l (embryo and 28 days post hatch) (highest concentration tested) |
|                                      | Rainbow trout, Donaldson trout (Oncorhynchus mykiss)   | 2100 µg/l, 96 hr (highest concentration tested)  |
| <b>Persistence and degradability</b> | Additional ecological information<br>Tadalafil<br>24-Hour municipal sewage sludge Kd (g total suspended solids/L): 180 |  |



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|  |   |
|--|---|
|  | <p>24-Hour biodegradation in municipal sewage sludge (g total suspended solids/L): none<br/>         Log Koc: 1.95<br/>         Adsorption to sewage sludge after 4 hours, Kd: 183 to 644 (determined at a range of sludge concentrations from 313 to 2500 mg/L)<br/>         Biodegradation in Sludge:<br/>         DT50: 9 days<br/>         Degradation in Aquatic Sediments (108 day aerobic incubation):<br/>         DT50 from overlying water: 3.8 to 4.6 days<br/>         DT50 from water/sediment systems: 70 to 117 days<br/>         24-Hour municipal sewage sludge Kd (g total suspended solids/L): 180<br/>         24-Hour biodegradation in municipal sewage sludge (g total suspended solids/L): none</p> |
| <b>Bioaccumulative potential</b>                         | No data available on bioaccumulation.   |
| <b>Partition coefficient n-octanol / water (log Kow)</b> |   |
| Tadalafil  | 2.32  |
| Mobility in soil   | No data available   |
| <b>Adsorption</b>  |   |
| <b>Soil/sediment sorption - log Koc</b>                  |   |
| Tadalafil  | 1.95  |
| Other adverse effects                                    | Not available   |
| <b>Eco toxicological Properties</b>                      |   |
| Drinking Water   |   |
| <b>Components</b>  | <b>Test Results</b>   |
| Tadalafil  | 2.5 µg/l, (Lilly Aquatic Exposure Guideline)  |
| <b>Chronic Exposure of Aquatic Organisms</b>             |   |
| Tadalafil  | 200 µg/l, (Lilly Aquatic Exposure Guideline)  |
| <b>Acute Exposure of Aquatic Organisms</b>               |   |
| Tadalafil  | 1000 µg/l, (Lilly Aquatic Exposure Guideline)   |

## Section 13: Disposal Considerations

|  |  |
|--|--|
| <b>Disposal instructions</b>                 | Dispose in accordance with all applicable regulations. |
| <b>Waste from residues / unused products</b> | Not available  |
| <b>Contaminated packaging</b>                | Not available  |

## Section 14: Transport Information

|   |               |
|---|---------------|
| <b>DOT</b>  |               |
| Not regulated as dangerous goods  |               |
| <b>IATA</b>   |               |
| Not regulated as dangerous goods.   |               |
| <b>IMDG</b>   |               |
| Not regulated as dangerous goods  |               |
| <b>Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code</b> | Not available |

## Section 15: Regulatory Information

|                               |   |
|-------------------------------|---|
| <b>US federal regulations</b> | This product is not known to be a "Hazardous Chemical" as defined by the OSHA Hazard Communication Standard, 29 CFR 1910.1200. One or more components are not listed on TSCA. |
|-------------------------------|---|



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|   |  |                               |
|---|--|-------------------------------|
| <b>TSCA Section 12(b) Export Notification (40 CFR 707, Subpt. D)</b>  | Not regulated  |                               |
| <b>CERCLA Hazardous Substance List (40 CFR 302.4)</b>   | Not listed   |                               |
| <b>SARA 304 Emergency release notification</b>  | Not regulated  |                               |
| <b>Superfund Amendments and Reauthorization Act of 1986 (SARA)</b>  |  |                               |
| <b>Hazard categories</b>  | No   |                               |
| Immediate Hazard  | No   |                               |
| Delayed Hazard  | No   |                               |
| Fire Hazard   | No   |                               |
| Pressure Hazard   | No   |                               |
| Reactivity Hazard   | No   |                               |
| <b>SARA 313 (TRI reporting)</b>   | Not regulated  |                               |
| <b>Other federal regulations</b>  |  |                               |
| <b>Clean Air Act (CAA) Section 112 Hazardous Air Pollutants (HAPs) List</b>   | Not regulated  |                               |
| <b>Clean Air Act (CAA) Section 112(r) Accidental Release Prevention (40 CFR 68.130)</b>   | Not regulated  |                               |
| <b>Safe Drinking Water Act (SDWA)</b>   | Not regulated  |                               |
| <b>US state regulations</b>   | 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. |                               |
| <b>International Inventories</b>  |  |                               |
| <b>Country(s) or region</b>   | <b>Inventory name</b>  | <b>On inventory (yes/no)*</b> |
| Canada  | Domestic Substances List (DSL)   | No                            |
| Canada  | Non-Domestic Substances List (NDSL)  | No                            |
| United States & Puerto Rico   | Toxic Substances Control Act (TSCA) Inventory  | No                            |
| <p>*A "Yes" indicates that all components of this product comply with the inventory requirements administered by the governing country(s)<br/>         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).</p>   |  |                               |
| <b>Section 16: Other Information, including date of preparation or last revision</b>  |  |                               |
| <b>Issue Date: 28-01-2019</b>   |  |                               |
| <b>Version: 00</b>  |  |                               |
| <b>Revision note: New</b>   |  |                               |
| <p>The information and recommendations in this safety data sheet are, to the best of our knowledge, accurate as of the date of issue. Nothing herein shall be deemed to create any warranty, express or implied. It is the responsibility of the user to determine the applicability of this information and the suitability of the material or product for any particular purpose.</p> <p>Hetero Labs Limited shall not be held liable for any damage resulting from handling or from contact with the above product. Hetero Labs Limited reserves the right to revise this SDS.</p> |  |                               |