SAFETY DATA SHEETS

This SDS packet was issued with item:

078934522

N/A

SAFETY DATA SHEET

SPIRONOLACTONE TABLETS USP

Strength: 25 mg, 50 mg and 100 mg
Pack Size: HDPE bottle packs of 30, 90, 100, 500 and 1000 Tablets
Blister Pack of 10 Tablets

Revision No.: 00

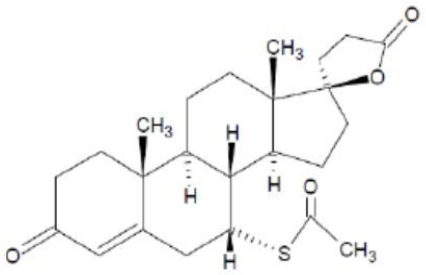
EMERGENCY OVERVIEW

Each Spironolactone Tablets USP intended for oral administration contains Spironolactone and excipients generally considered to be non- toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.

Section 1. IDENTIFICATION

Identification of the product

Product Name: Spironolactone Tablets USP 25 mg, 50 mg and 100 mg
Formula: $C_{24}H_{32}O_4S$
Chemical Name: 17-Hydroxy-7α-mercapto-3-oxo-17α-pregn-4-ene-21- carboxylic acidγ-lactone acetate.



Manufacturer / supplier identification

Company:	**Cadila Healthcare Limited Baddi, India**
Address:	Cadila Healthcare Limited, Swaraj Majra, Judi Kalan, Post - Baddi, Tehsil - Nalagarh, District - Solan, Himachal Pradesh 173205.
Contact for information:	Tel: +91-1795-246841 Fax: +91-1795-246842
Emergency Telephone No.	Tel: +91-1795-246841
Recommended use / Therapeutic Category	Orally /Diuretics
Restriction on Use / Contraindications:	Spironolactone Tablets are contraindicated for patients with anuria, acute renal insufficiency, significant impairment of renal excretory function, hyperkalemia, Addison's disease, and with concomitant use of eplerenone.

Section 2. HAZARD(S) IDENTIFICATION

Dose and Administration

Dosage should be individualized with careful monitoring of patient response.

Oral Administration:

Primary hyperaldosteronism. Spironolactone may be employed as an initial diagnostic measure to provide presumptive evidence of primary hyperaldosteronism while patients are on normal diets.

Long test: Spironolactone is administered at a daily dosage of 400 mg for three to four weeks. Correction of hypokalemia and of hypertension provides presumptive evidence for the diagnosis of primary hyperaldosteronism.

Short test: Spironolactone is administered at a daily dosage of 400 mg for four days. If serum potassium increases during spironolactone administration but drops when spironolactone is discontinued, a presumptive diagnosis of primary hyperaldosteronism should be considered.

After the diagnosis of hyperaldosteronism has been established by more definitive testing procedures, spironolactone may be administered in doses of 100 to 400 mg daily in preparation for surgery. For patients who are considered unsuitable for surgery, spironolactone may be employed for long-term maintenance therapy at the lowest effective dosage determined for the individual patient.

Edema in adults *(congestive heart failure, hepatic cirrhosis, or nephrotic syndrome).*

An initial daily dosage of 100 mg of spironolactone administered in either single or divided doses is recommended, but may range from 25 to 200 mg daily. When given as the sole agent for diuresis, spironolactone should be continued for at least five days at the initial dosage level, after which it may be adjusted to the optimal therapeutic or maintenance level administered in either single or divided daily doses. If, after five days, an adequate diuretic response to spironolactone has not occurred, a second diuretic that acts more proximally in the renal tubule may be added to the regimen. Because of the additive effect of spironolactone when administered concurrently with such diuretics, an enhanced diuresis usually begins on the first day of combined treatment; combined therapy is indicated when more rapid diuresis is desired. The dosage of spironolactone should remain unchanged when other diuretic therapy is added.

Essential hypertension. For adults, an initial daily dosage of 50 to 100 mg of spironolactone administered in either single or divided doses is recommended. Spironolactone may also be given with diuretics that act more proximally in the renal tubule or with other antihypertensive agents. Treatment with spironolactone should be continued for at least two weeks since the maximum response may not occur before this time. Subsequently, dosage should be adjusted according to the response of the patient.

Hypokalemia. Spironolactone in a dosage ranging from 25 mg to 100 mg daily is useful in treating a diuretic-induced hypokalemia, when oral potassium supplements or other potassium-sparing regimens are considered inappropriate.

Severe heart failure in conjunction with standard therapy (NYHA class III – IV). Treatment should be initiated with spironolactone 25 mg once daily if the patient's serum potassium is ≤ 5 mEq/L and the patient's serum creatinine is ≤ 2.5 mg/dL. Patients who tolerate 25 mg once daily may have their dosage increased to 50 mg once daily as clinically indicated. Patients who do not tolerate 25 mg once daily may have their dosage reduced to 25 mg every other day.

Adverse Effects

The following adverse reactions have been reported and, within each category (body system), are listed in order of decreasing severity.

Digestive: Gastric bleeding, ulceration, gastritis, diarrhea and cramping, nausea, vomiting.

Reproductive: Gynecomastia (see Precautions), inability to achieve or maintain erection, irregular menses or amenorrhea, postmenopausal bleeding, breast pain. Carcinoma of the breast has been reported in patients taking spironolactone but a cause and effect relationship has not been established.

Hematologic: Leukopenia(including granulocytosis), thrombocytopenia.

Hypersensitivity: Fever,urticaria,maculopapular or erythematous cutaneous eruptions, anaphylactic reactions, vasculitis.

Metabolism: Hyperkalemia, electrolyte disturbances.

Musculoskeletal: Leg cramps.

Nervous system /psychiatric: Lethargy, mental confusion, ataxia, dizziness, headache, drowsiness.

Liver / biliary: A very few cases of mixed cholestatic/hepatocellular toxicity, with one reported fatality, have been reported with spironolactone administration.

Renal: Renal dysfunction (including renal failure).

Skin: Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), drug rash with eosinophilia and systemic symptoms (DRESS), alopecia, pruritis.

Over Dose Effect

The oral LD50 of Spironolactone is greater than 1000 mg/kg in mice, rats, and rabbits.

Acute overdosage of spironolactone may be manifested by drowsiness, mental confusion, maculopapular or erythematous rash, nausea, vomiting, dizziness, or diarrhea. Rarely, instances of hyponatremia, hyperkalemia, or hepatic coma may occur in patients with severe liver disease, but these are unlikely due to acute overdosage. Hyperkalemia may occur, especially in patients with impaired renal function.

Contraindications

Spironolactone tablets are contraindicated for patients with anuria, acute renal insufficiency, significant impairment of renal excretory function, hyperkalemia, Addison's disease, and with concomitant use of eplerenone.

Pregnancy Comments	There are no adequate and well-controlled studies with spironolactone in pregnant women. Spironolactone has known endocrine effects in animals including progestational and antiandrogenic effects. The antiandrogenic effects can result in apparent estrogenic side effects in humans, such as gynecomastia. Therefore, the use of spironolactone in pregnant women requires that the anticipated benefit be weighed against the possible hazards to the fetus.
Pregnancy Category	Pregnancy Category C

Section 3. COMPOSITION / INFORMATION ON INGREDIENTS

Component	Exposure Limit	CAS No.
Principle Component:		
Spironolactone	Not Found	52-01-7
Inactive Ingredients:		
Calcium sulfate dihydrate	Not Found	10101-41-4
Colloidal silicon dioxide	Not Found	7631-86-9
Corn Starch	Not Found	9005-25-8
Croscarmellose sodium	Not Found	74811-65-7
Magnesium stearate	Not Found	557-04-0
Microcrystalline cellulose	Not Found	9004-34-6
Peppermint flavor	Not Found	8006-90-4
Povidone	Not Found	9003-39-8
Sodium Lauryl Sulfate	Not Found	151-21-3
Additionally each tablet contains opadry II white 33F28398 which contains		
Hydroxylpropyl methyl cellulose	Not Found	9004-65-3
Lactose monohydrate	Not Found	5989-81-1
Polyethylene glycol	Not Found	25322-68-3
Talc	Not Found	14807-96-6
Titanium Dioxide	Not Found	13463-67-7

Section 4. FIRST -AID MEASURES

Inhalation	Remove to fresh air. If discomfort occurs or persists, get medical attention.
Skin contact	Remove contaminated clothing and shoes. Wash skin with soap and plenty of water. If irritation occurs or persists, get medical attention. Wash clothing and shoes before reuse.
Eye contact	Immediately flush eyes with plenty of water. If irritation occurs or persists, get medical attention.
Ingestion	If large quantities of this material are swallowed, get medical attention immediately. If swallowed, rinse mouth with water (only if the person is conscious). Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

Section 5. FIRE FIGHTING MEASURES

Flash Point	Not applicable
Extinguishing Media	Water, Carbon Dioxide, Dry Chemical, Foam.
Unusual Fire and Explosion Hazards	Toxic emissions may be given off in a fire.
Fire Fighting Instructions	Wear NIOSH/MSHA approved positive pressure, self-contained breathing apparatus and full protective turn out gear. Use caution in approaching fire. Use water to keep fire exposed containers cool.

Section 6. ACCIDENTAL RELEASE MEASURES

Spill Clean Up Procedures	Use proper personal protective equipment and clothing. Shut off the source of the spill or leak if it is safe to do so. Scoop or shovel spilled material into a suitable labeled open head drum. Secure the drum cover and move the container to a safe holding area. Wash spill area thoroughly with soapy water.
Treatment and Disposal	Decontaminate equipment. Dispose of protective clothing with spilled material.
Environmental precautions	Avoid release to the environment. Prevent further leakage or spillage if safe to do so. Avoid discharge into drains, water courses or onto the ground. Inform appropriate managerial or supervisory personnel of all environmental releases.

Section 7. HANDLING AND STORAGE

Storage	Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Protect from light. Dispense in a tight, light resistant container (USP).

Precautions for safe handling	Avoid contact with eyes. Avoid breathing dust. Use with adequate ventilation. When handling, use proper personal protective equipment. Wash thoroughly after handling. Keep container tightly closed when not in in use. Store in a dry area at room temperature.

Section 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Respiratory Protection	Use a NIOSH/MSHA approved respirator if there is a risk of exposure to dust/fume at levels exceeding the exposure limits. No personal respiratory protective equipment normally required.
Skin protection	For prolonged or repeated skin contact use suitable protective gloves.
Eye/face protection	If contact is likely, safety glasses with side shields are recommended.
Protective Clothing	Protective clothing is not normally necessary, however it is good practice to use apron.
Biological limit values	No biological exposure limits noted for the ingredient(s).
Exposure guidelines	General ventilation normally adequate.
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. For advice on suitable monitoring methods, seek guidance from a qualified environment, health and safety professional.
Engineering controls	Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Section 9. PHYSICAL AND CHEMICAL PROPERTIES

Physical state	Tablets
Color	White to off white
Odor	Odorless
Pure/Mixture	Mixture

Section 10. STABILITY AND REACTIVITY

Stability	Normally stable but formation of toxic gases is possible during heating or in case of fire.
Incompatibility materials to avoid	Strong Oxidizing agents
Polymerization	No
Conditions of Polymerization	Will not occur

Section 11. TOXICOLOGICAL INFORMATION

Spironolactone
Irritation Skin

May cause skin reaction.

Reproductive

In a three-litter reproduction study in which female rats received dietary doses of 15 and 50 mg spironolactone/kg/day, there were no effects on mating and fertility, but there was a small increase in incidence of stillborn pups at 50 mg/kg/day. When injected into female rats (100 mg/kg/day for 7 days, i.p.), spironolactone was found to increase the length of the estrous cycle by prolonging diestrus during treatment and inducing constant diestrus during a two-week post-treatment observation period.

Teratogenicity

Teratology studies with Spironolactone have been carried out in mice and rabbits at doses of up to 20 mg/kg/day. On a body surface area basis, this dose in the mouse is substantially below the maximum recommended human dose and, in the rabbit, approximates the maximum recommended human dose. No teratogenic or other embryotoxic effects were observed in mice, but the 20 mg/kg dose caused an increased rate of resorption and a lower number of live fetuses in rabbits.

Carcinogenicity and Mutagenicity

In an 18-month study using doses of about 50, 150, and 500 mg/kg/day, there were statistically significant increases in benign adenomas of the thyroid and testes and, in male rats, a dose-related increase in proliferative changes in the liver (including hepatocytomegaly and hyperplastic nodules). In a 24-month study in which the same strain of rat was administered doses of about 10, 30, 100, and 150 mg spironolactone /kg/day, the range of proliferative effects included significant increases in hepatocellular adenomas and testicular interstitial cell tumors in males, and significant increases in thyroid follicular cell adenomas and carcinomas in both sexes. In the presence of metabolic activation, spironolactone has been reported to be negative in some mammalian mutagenicity tests in vitro and inconclusive (but slightly positive) for mutagenicity in other mammalian tests in vitro.

Section 12. ECOLOGICAL INFORMATION

Do not allow product to enter drinking water supplies, waste water or soil.

Section 13. DISPOSAL CONSIDERATION

Disposal Recommendations Dispose the waste in accordance with all applicable Federal, State and local laws.

Section 14. TRANSPORT INFORMATION

The product is not hazardous when shipping via air (IATA), ground (DOT), or sea (IMDG).

Section 15. REGULATORY INFORMATION

Generic Medicine, ANDA Number 205936

Section 16. OTHER INFORMATION

Additional Information

NFPA Rating: These ratings are based on NFPA code 704 and are intended for use by emergency personnel to determine the immediate hazards of a material
Health……..1
Fire……..1
Reactivity…0

Date of issue: January 30, 2017 **Supersedes edition:** New Edition