CMP PHARMA

CaroSpir®
(Spironolactone)
ORAL SUSPENSION
25 mg/5 mL

FDA-Approved Oral Suspension of Spironolactone

For patients with dysphagia who need a liquid form of spironolactone

Dysphagia

& The Need For A Liquid Suspension of Spironolactone

Dysphagia is the medical term used to describe difficulty swallowing. It can include difficulty starting a swallow (oropharyngeal dysphagia), issues in the throat (pharyngeal dysphagia), and the sensation of food being stuck (esophageal dysphagia).

Dysphagic Patients:

2x more likely to die while in the hospital[2]

33% more likely to need nursing home care

3.8 days longer in the hospital on average

$6,243 higher hospital costs on average

It's important to optimize treatment plans for patients with dysphagia given these complications. Dysphagic patients who suffer from chronic heart failure, edema caused by heart or liver failure, and/or hypertension are often prescribed medication that is crushed/compounded from tablets into a liquid form.

69%
OF OLDER PATIENTS REPORT MISSING DOSES OF A TABLET OR CAPSULE DUE TO DIFFICULTIES SWALLOWING

Unfortunately, liquids derived from crushed/compounded tablets raise concerns about patient safety and efficacy, and they have come under increasing scrutiny from the FDA.

PATIENTS WHO MAY NEED AN ORAL LIQUID

- Stroke
- Parkinson's Disease
- ALS
- Multiple Sclerosis
- Cerebral Palsy

READ THIS BEFORE YOU CRUSH/COMPOUND ANOTHER SPIRONOLACTONE TABLET

The Risks and Concerns of Crushing/Compounding

The Challenges of Crushed/Compounded Formulations

Use of crushed/compounded formulations can result in serious risks in addition to being highly inconvenient for patients and caregivers.[2]

Potency

Crushed/compounded formulations can exhibit a wide variation in potency due to non-uniformity of crushed/compounded materials.[2] The dosing inconsistencies of crushed/compounded suspensions have long been a persistent challenge for pharmacists and patients.[2]

FDA Approval and GMP Compliance

Crushed/compounded formulations are not approved by FDA, are not manufactured in GMP facilities, and are not tested to assure potency, uniformity, and sterility/bioburden.[3]

Shelf Life

Crushed/compounded spironolactone can have a variable shelf life. The shelf life for crushed/compounded spironolactone can be as little as 14 days.[4]

NIOSH List Of Hazardous Drugs

Spironolactone is on the NIOSH List of Hazardous Drugs in Healthcare Settings and is subject to legally enforceable regulatory guidelines. Required safety protocols when crushing/compounding spironolactone includes:

- Double chemotherapy gloves
- Protective gowns
- Ventilated engineering control
- Eye/face and respiratory protection (if not crushed/compounded in a control device)

Not following these protocols is a reportable offense.

USP-800

The pharmacy boards of several states have conducted inspections to ensure compliance with USP-797 standards in hospitals. Now compendial with risks of fines and penalties, USP-800 compliance is a top priority by state boards and the FDA.

CaroSpir®

Customized care & consistent dosing

What is CaroSpir?

CaroSpir is the first FDA-approved oral suspension of spironolactone that provides a stable, ready to use, and consistent liquid treatment option for adult patients who have difficulty swallowing, or who cannot swallow tablets, and are suffering from heart failure, edema caused by heart failure and cirrhosis, and hypertension.

CaroSpir addresses the complexities and inconsistencies of crushing/compounding by providing patients with an FDA-approved oral liquid suspension of spironolactone. It eliminates the need for additional preparation by a pharmacist or patient and it does not have special storage requirements.

CaroSpir is a safe, ready-made alternative

Spironolactone is NIOSH listed and requires safety protocols when crushing/ compounding

IMPORTANT SAFETY INFORMATION

Contraindications

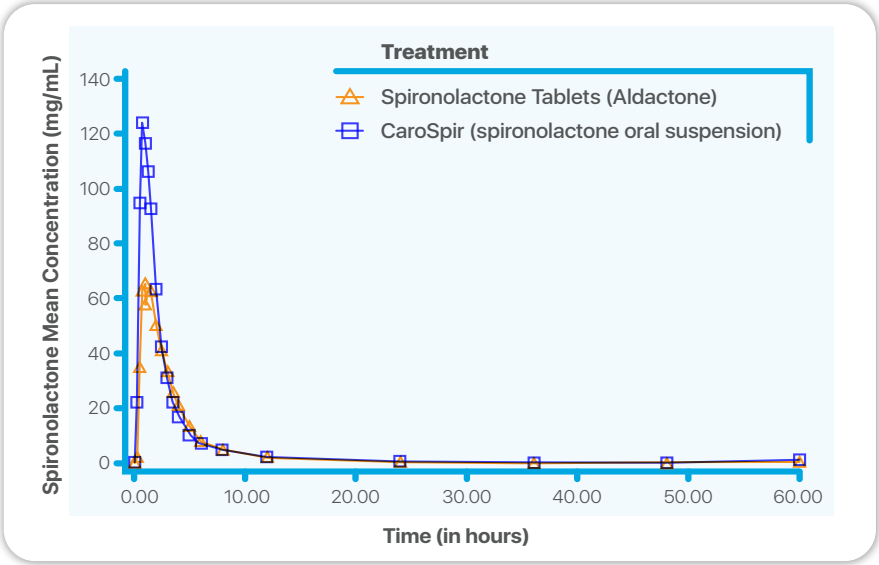
CAROSPIR is contraindicated for patients with the following conditions:
– Hyperkalemia – Addison's disease – Concomitant use of eplerenone

THE RIGHT MEDICATION FOR THE RIGHT PATIENT

Important Pharmacokinetic Differences with CaroSpir

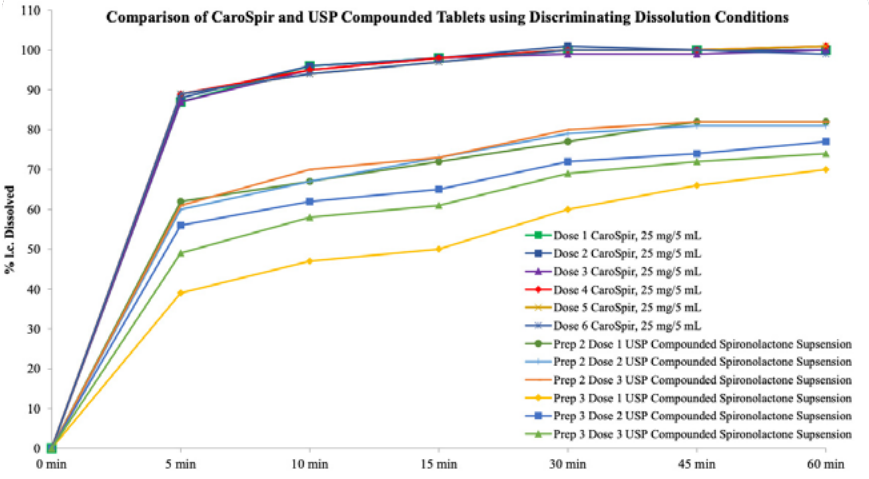
Spironolactone Time vs Mean Concentration Plot Linear Scale[5]

CaroSpir is not therapeutically equivalent to tablet formulations of spironolactone. For an equivalent dose, CaroSpir results in a 15 to 37% higher serum concentration compared to Aldactone (spironolactone) tablets. For dosing information visit: carospir.com/prescribing-information



An open label, randomized, two treatment, two period, two sequence, crossover, single dose, oral pharmacokinetic and comparative bioavailability study of spironolactone suspension 100 mg (20 mL of 25 mg/ 5 mL) with Aldactone® (spironolactone) tablets USP, 100 mg healthy adult subjects under the fasting condition.

CaroSpir delivers a consistent potency of spironolactone compared to compounded preparations



An in-vitro comparison study using a discriminating dissolution method was performed to show the comparison of 100 mg Spironolactone tablets when compounded and made into a suspension liquid according to USP and pharmacy methods and CaroSpir Oral Suspension, 25 mg/5 mL.

Disparities in dosing potency are dependent upon many variables including the consistency of the preparation and are influenced by the compounding procedure, person compounding, and compounding vehicles.

Results demonstrated that CaroSpir, the first and only FDA approved spironolactone oral suspension, delivered a consistent potency of spironolactone dose to dose, compared to compounded preparations that routinely showed potency inconsistencies.

SPIRONOLACTONE COMPARISON MATRIX	CaroSpir® (Spironolactone) ORAL SUSPENSION 25 mg/5 mL	CRUSHED/ COMPOUNDED SPIRONOLACTONE
FDA-approved	✔	✖
Tested to ensure potency and consistency in dosing	✔	✖
Tested and proven to ensure proper dosing for bioequivalence	✔	✖
Shelf life of 24-30 months*	✔	✖
Manufactured in GMP-compliant facility	✔	✖
Additional preparation required by pharmacist / patient / caregiver	✖	✔
Requires special safety protocols when crushed or compounded	✖	✔

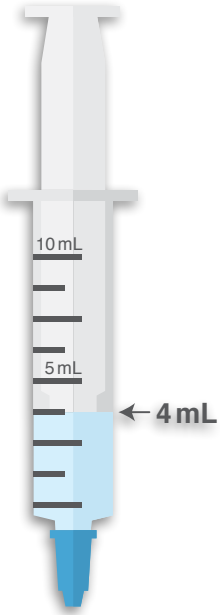
***Shelf life of CaroSpir:**

- **10 X 5mL unit dose cups (24 months)** | NDC: 46287-020-50
- **118mL bottle (24 months)** | NDC: 46287-020-04
- **473mL bottle (30 months)** | NDC: 46287-020-01

- Agents increasing serum potassium: Concomitant administration can lead to hyperkalemia.
- Lithium: Increased risk of lithium toxicity.
- NSAIDs: May reduce the diuretic, natriuretic and antihypertensive effect of CAROSPIR.
- Digoxin: CAROSPIR can interfere with radioimmunologic assays of digoxin.Spironolactone and its metabolites increase the apparent exposure to digoxin.
- Cholestyramine: Hyperkalemic metabolic acidosis has been reported with concomitant use.
- Acetylsalicylic Acid (ASA): ASA may reduce the efficacy of spironolactone.

Dosing & Administration

CAROSPIR is not therapeutically equivalent to Aldactone tablets.



HEART FAILURE

- Initiate treatment at 20 mg (4 mL) once daily.
- In patients with serum potassium ≤5.0 mEq/L and eGFR >50 mL/min/1.73m^2, initiate treatment at 20 mg (4 mL) once daily.
  - Patients who tolerate 20 mg (4 mL) once daily may have their dosage increased to 37.5 mg (7.5 mL) once daily as clinically indicated.
  - Patients who develop hyperkalemia on 20 mg (4 mL) once daily may have their dosage reduced to 20 mg (4 mL) every other day.
- In patients with an eGFR between 30 and 50 mL/min/1.73m^2, consider initiating treatment at 10 mg (2 mL) because of the risk of hyperkalemia.

ESSENTIAL HYPERTENSION

- The recommended initial daily dose is 20 mg (4 mL) to 75 mg (15 mL) administered in either single or divided doses.
- Dosage can be titrated at two-week intervals.
- Doses >75 mg/day generally do not provide additional reductions in blood pressure.

EDEMA ASSOCIATED WITH HEPATIC CIRRHOSIS

- Initiate therapy in a hospital setting and titrate slowly.
- The recommended initial daily dose is 75 mg (15 mL).
- The recommended initial daily dose should be administered in either single or divided doses.
- In patients requiring titration above 100 mg, use another formulation. When given as the sole agent for diuresis, administer for at least five days before increasing dose to obtain desired effect.

PLEASE CLICK LINK FOR FULL IMPORTANT SAFETY INFORMATION AND FULL PRESCRIBING INFORMATION:
https://carospir.com/prescribing-information/

CaroSpir®
(Spironolactone)
ORAL SUSPENSION
25 mg/5 mL

Healthcare providers can help their patients pay as little as $0* on each prescription using the EasyPay Card.

To learn more, visit **cmppharma.com/easypay**

Terms and Conditions

* Void where prohibited by law. CMP Pharma reserves the right to rescind, revoke or amend this program without notice. Offer not valid for patients eligible for benefits under Medicaid (including Medicaid managed care), Medicare, TRICARE, Veterans Affairs, FEHBP, or similar state or federal programs. Offer void where prohibited, taxed, or otherwise restricted. Offer good only in the U.S.A. No generic substitution with this offer.

IMPORTANT SAFETY INFORMATION

INDICATIONS AND USAGE
CAROSPIR is an antagonist of aldosterone indicated for:
- the treatment of NYHA Class III-IV heart failure and reduced ejection fraction to increase survival, manage edema, and to reduce the need for hospitalization for heart failure
- use as an add-on therapy for the treatment of hypertension, to lower blood pressure in adult patients. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions
- the management of edema in adult cirrhotic patients when edema is not responsive to fluid and sodium restrictions

CONTRAINDICATIONS
CAROSPIR is contraindicated for patients with the following conditions:
- Hyperkalemia
- Addison's disease
- Concomitant use of eplerenone

WARNINGS AND PRECAUTIONS/ ADVERSE REACTIONS
CAROSPIR may cause the following conditions:
- Hyperkalemia
- Hypotension and Worsening Renal Function
- Electrolyte and Metabolic Abnormalities
- Gynecomastia
- Impaired neurological function/ coma in patients with hepatic impairment, cirrhosis and ascites

The most common adverse reaction (incidence > 5%) with CAROSPIR treatment is the increased occurrence of gynecomastia in men.

Talk to your healthcare provider about other possible side effects with CAROSPIR. To report SUSPECTED ADVERSE REACTIONS, contact CMP Pharma, Inc. at 1-844-321-1443, or FDA at 1-800-FDA-1088 or www.fda.gov/MedWatch.

DRUG INTERACTIONS
- Agents increasing serum potassium: Concomitant administration can lead to hyperkalemia.
- Lithium: Increased risk of lithium toxicity.
- NSAIDs: May reduce the diuretic, natriuretic and antihypertensive effect of CAROSPIR.
- Digoxin: CAROSPIR can interfere with radioimmunologic assays of digoxin. Spironolactone and its metabolites increase the apparent exposure to digoxin.
- Cholestyramine: Hyperkalemic metabolic acidosis has been reported with concomitant use.
- Acetylsalicylic Acid (ASA): ASA may reduce the efficacy of spironolactone.

ADMINISTRATION
CAROSPIR oral suspension, 25 mg/5 mL, is not therapeutically equivalent to tablet forms of spironolactone. Follow dosing instructions for CAROSPIR. In patients requiring a dose greater than 100 mg, use another formulation of spironolactone. Doses of CAROSPIR suspension greater than 100 mg may result in spironolactone concentrations higher than expected.

Please Click Link for Full Important Safety Information and Full Prescribing Information:
https://carospir.com/prescribing-information/

CaroSpir®

(Spironolactone)

ORAL SUSPENSION

25 mg/5 mL

Why CaroSpir?

- **Eliminates NIOSH Risks of Crushing/Compounding**
- **Customized Dosing Reduces Time and Product Waste**
- **Consistent Dosing and Efficacy**
- **Available as Convenient 10 Pack-5mL Unit Dose Cups**

For more information visit

CaroSpir.com

Exclusively from

CMP PHARMA

References: 1. Takizawa, C., Gemmell, E., Kenworthy, J. et al. Dysphagia (2016) 31: 434. https://doi.org/10.1007/s00455-016-9695-9 **2.** Kindy K, Sun L, Crites A. Compounding pharmacies have been linked to deaths, illnesses for years. Washington Post. February 7, 2013. http://www.washingtonpost.com. Accessed October 2, 2017. **3.** Food Drug Administration Center for Drug Evaluation & Research (2016). Guidance for Industry: Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act (FDA Maryland). **4.** Food Drug Administration Center for Drug Evaluation & Research (2017). Repackaging of Certain Human Drug Products by Pharmacies and Outsourcing Facilities (FDA Maryland). **5.** Data on file, CMP Pharma, Inc.: 2017