READ THIS BEFORE YOU CRUSH/COMPOUND ANOTHER SPIRONOLACTONE TABLET

- Spironolactone tablets appear on the NIOSH list of Hazardous Drugs in Healthcare Settings and require special safety protocols when crushed/compounded.
- Required safety protocols when crushing/compounding spironolactone tablets include double chemotherapy gloves, protective gowns, ventilated engineering control, and—if not crushed/compounded in a control device—eye/face and respiratory protection. Not following these protocols is a reportable offense.
- Spironolactone tablets are subject to legally enforceable regulatory guidelines such as USP-797 and the upcoming USP-800. The pharmacy boards of several states have conducted inspections to ensure compliance with USP-797 standards in hospitals. It is expected that USP-800 will result in pharmacy inspections by both state boards and the FDA.
- Crushed/compounded formulations are not approved by the FDA. The FDA has recently issued stricter guidance about the use of crushed/compounded products, recommending that drugs not be crushed/compounded if FDA-approved alternatives exist.

CaroSpir®
Spironolactone
(25mg/5mL Oral Suspension)

The First & Only FDA-approved Spironolactone Oral Suspension

For patients with dysphagia who need a liquid form of spironolactone

Exclusively from

CMP PHARMA

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

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 in the neck or chest (esophageal dysphagia).

Though dysphagia is uncomfortable for patients and leads to a lower quality of life, it can also lead to serious health risks and complications. Dysphagic patients are nearly twice as likely to die while in the hospital, their average stays are 3.8 days longer, and their bills are an average of $6,243 higher. Dysphagic patients are also 33% more likely to need nursing home care.

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

Dysphagia has shown to be responsible for a sharp decrease in adherence to treatment, as patients delay or even skip doses of prescribed medication. In fact, 69% of older patients report missing or skipping medication doses because of discomfort due to difficulties swallowing.

Dysphagic patients who suffer from chronic heart failure, edema caused by heart or liver failure, and/or hypertension are often prescribed the potassium-sparing diuretic spironolactone, crushed/compounded from tablets into a liquid form.

Unfortunately, liquids derived from crushed/compounded tablets raise concerns about patient safety and efficacy, and they have come under increasing scrutiny from the FDA, which recently released stricter guidance regarding crushing/compounding in general.

SPIRONOLACTONE COMPARISON MATRIX	CAROSPIR	CRUSHED/ COMPOUNDED SPIRONOLACTONE
FDA-Approved	☑	⊗
Tested to ensure potency and consistency in dosing	☑	⊗
Tested and proven to ensure proper dosing for bioequivalence	☑	⊗
24-month shelf life	☑	⊗
No black box warning	☑	⊗
Manufactured in GMP-compliant facility	☑	⊗
Has no special handling or storage requirements	☑	⊗
Additional preparation required by pharmacist / patient / caregiver	⊗	☑
On NIOSH List of Hazardous Drugs In Workplace Settings	⊗	☑
Requires special safety protocols when crushed or compounded	⊗	☑

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

READ THIS BEFORE YOU CRUSH/COMPOUND ANOTHER SPIRONOLACTONE TABLET

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 tablets are on the NIOSH List of Hazardous Drugs in Healthcare Settings, and are subject to legally enforceable regulatory guidelines. Required safety protocols when crushing/compounding spironolactone tablets include:

- 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. It is expected that the upcoming USP-800 will result in pharmacy inspections by both state boards and the FDA.

CaroSpir does not appear on the NIOSH list and does not have a black box warning. The guidelines for handling hazardous drugs like spironolactone tablets do not apply to CaroSpir.

CaroSpir®

The Formulation That's Easy

Easy To Swallow

CaroSpir 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.

In clinical studies, spironolactone has demonstrated significant mortality benefits and reduced the risk of hospitalization for cardiac causes.

Easy To Prescribe

CaroSpir addresses the complexities and inconsistencies of crushing/compounding by providing patients with an FDA-approved oral liquid suspension of spironolactone.

– CaroSpir oral suspension ensures a stable and consistent dose every time.

– CaroSpir is manufactured in CMP Pharma's high-quality GMP facility.

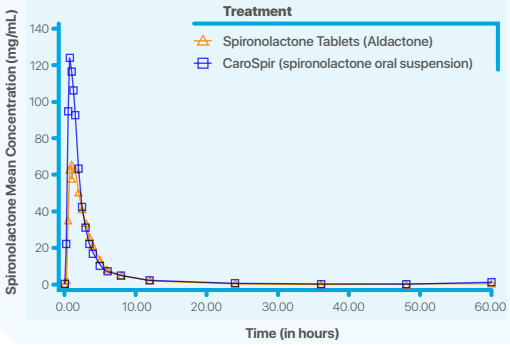
– 118 mL and 473 mL bottles of CaroSpir provide a shelf life of 24 months.

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.

Important Pharmacokinetic Differences with CaroSpir

Spironolactone Time vs Mean Concentration Plot Linear Scale[5]

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.



If you crush/compound spironolactone, does it behave like the tablet or like our liquid?

IMPORTANT SAFETY INFORMATION

Contraindications

CAROSPIR is contraindicated for patients with the following conditions:

– Hyperkalemia – Addison's disease – Concomitant use of eplerenone

Easy To Fill

- CaroSpir oral suspension eliminates the need for additional preparation by the pharmacist or patient.
- 118 mL and 473 mL bottles of CaroSpir have a 24-month shelf life.
- Unlike all other spironolactone dosage forms on the market, CaroSpir does not have a black box warning.
- There are no special handling and storage requirements with CaroSpir.

Easy To Afford

We want every patient who needs CaroSpir to have access to it. That's why we've created the EasyPay Program, so your patients can lower their out-of-pocket costs associated with a CaroSpir prescription.

EasyPay PROGRAM

Order your EasyPay Program co-pay cards for your patients by calling (844) 567-9503 or by visiting CaroSpir.com/EasyPay.

IMPORTANT SAFETY INFORMATION

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.
- Cholestyramine: Hyperkalemic metabolic acidosis has been reported with concomitant use.
- Acetylsalicylic Acid (ASA): ASA may reduce the efficacy of spironolactone.

CaroSpir®
Spironolactone
(25mg/5mL Oral Suspension)

The First & Only FDA-approved Spironolactone Oral Suspension

- CaroSpir® is the first and only FDA-approved oral liquid of spironolactone.
- CaroSpir provides a stable, ready to use and consistent liquid treatment option for adult patients, including those who have difficulty swallowing, or who cannot swallow tablets.
- CaroSpir provides consistent bioavailability as demonstrated in studies.
- 118 mL and 473 mL bottles of CaroSpir provide a shelf life of 24 months
- CaroSpir does NOT carry a black box warning.

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

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.
- 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.

For additional important safety information, please visit www.carospir.com/prescribing-information for the Full Prescribing Information