CALCIUM ACETATE- calcium acetate capsule
Golden State Medical Supply, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
CALCIUM ACETATE CAPSULES. These highlights do not include all the information needed to use CALCIUM ACETATE CAPSULES safely and effectively. See full prescribing information for CALCIUM ACETATE CAPSULES.

CALCIUM ACETATE capsules, for oral use

Initial U.S. Approval: 1990

INDICATIONS AND USAGE

- Calcium acetate capsules are a phosphate binder indicated for the reduction of serum phosphorus in patients with end stage renal disease. (1)

DOSAGE AND ADMINISTRATION

- Starting dose is 2 capsules with each meal. (2)
- Titrate the dose every 2-3 weeks until acceptable serum phosphorus level is reached. Most patients require 3-4 capsules with each meal. (2)

DOSAGE FORMS AND STRENGTHS

- Capsule: 667 mg calcium acetate (3)

CONTRAINDICATIONS

- Hypercalcemia. (4)

WARNINGS AND PRECAUTIONS

- Treat mild hypercalcemia by reducing or interrupting calcium acetate capsules and Vitamin D. Severe hypercalcemia may require hemodialysis and discontinuation of calcium acetate capsules. (5.1)
- Hypercalcemia may aggravate digitalis toxicity. (5.2)

ADVERSE REACTIONS

- The most common (>10%) adverse reactions are hypercalcemia, nausea, and vomiting. (6.1).
- In clinical studies, patients have occasionally experienced nausea during calcium acetate therapy. (6).

To report SUSPECTED ADVERSE REACTIONS, contact Nostrum Laboratories Inc. at quality@nostrumpharma.com or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

DRUG INTERACTIONS

- Calcium acetate capsules may decrease the bioavailability of tetracyclines or fluoroquinolones. (7)
- When clinically significant drug interactions are expected, administer the drug at least one hour before or at least three hours after calcium acetate capsules, or consider monitoring blood levels of the drug. (7)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS & USAGE

Calcium acetate capsules are a phosphate binder indicated to reduce serum phosphorus in patients with end stage renal disease (ESRD).

2 DOSAGE & ADMINISTRATION

The recommended initial dose of calcium acetate capsules for the adult dialysis patient is 2 capsules with each meal. Increase the dose gradually to lower serum phosphorus levels to the target range, as long as hypercalcemia does not develop. Most patients require 3-4 capsules with each meal.

3 DOSAGE FORMS & STRENGTHS

Capsule: 667 mg calcium acetate, USP per capsule.

4 CONTRAINDICATIONS

Patients with hypercalcemia.

5 WARNINGS AND PRECAUTIONS

5.1 Hypercalcemia

Patients with end stage renal disease may develop hypercalcemia when treated with calcium, including calcium acetate (calcium acetate capsules). Avoid the use of calcium supplements, including calcium-based nonprescription antacids, concurrently with calcium acetate capsules.

An overdose of calcium acetate capsules may lead to progressive hypercalcemia, which may require emergency measures. Therefore, early in the treatment phase during the dosage adjustment period, monitor serum calcium levels twice weekly. Should hypercalcemia develop, reduce the calcium acetate capsules dosage or discontinue the treatment, depending on the severity of hypercalcemia.

More severe hypercalcemia (Ca>12 mg/dL) is associated with confusion, delirium, stupor and coma. Severe hypercalcemia can be treated by acute hemodialysis and discontinuing calcium acetate capsules therapy.

Mild hypercalcemia (10.5 to 11.9 mg/dL) may be asymptomatic or manifest as constipation, anorexia, nausea, and vomiting. Mild hypercalcemia is usually controlled by reducing the calcium acetate capsules dose or temporarily discontinuing therapy. Decreasing or discontinuing Vitamin D therapy is recommended as well.

Chronic hypercalcemia may lead to vascular calcification and other soft-tissue calcification. Radiographic evaluation of suspected anatomical regions may be helpful in early detection of soft tissue calcification. The long term effect of calcium acetate capsules on the progression of vascular or soft tissue calcification has not been determined.

Hypercalcemia (>11 mg/dL) was reported in 16% of patients in a 3-month study of a solid dose formulation of calcium acetate; all cases resolved upon lowering the dose or discontinuing treatment.

Maintain the serum calcium-phosphorus (Ca x P) product below 55 mg ^{2}/dL ^{2}.

5.2 Concomitant Use with Medications

Hypercalcemia may aggravate digitalis toxicity.

6 ADVERSE REACTIONS

Hypercalcemia is discussed elsewhere [see Warnings and Precautions (5.1)].

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the

clinical trials of another drug and may not reflect the rates observed in practice.

In clinical studies, calcium acetate has been generally well tolerated.

Calcium acetate capsules were studied in a 3-month, open-label, non-randomized study of 98 enrolled ESRD hemodialysis patients and in a two week double-blind, placebo-controlled, cross-over study with 69 enrolled ESRD hemodialysis patients. Adverse reactions (>2% on treatment) from these trials are presented in Table 1.

Table 1: Adverse Reactions in Patients with End-Stage Renal Disease Undergoing Hemodialysis

Preferred Term	**Total adverse reactions reported for calcium acetate n = 167** n (%)	**3-mo, open-label study of calcium acetate n = 98** n (%)	**Double-blind, placebo-controlled, cross-over study of calcium acetate n = 69**	
			Calcium acetate n (%)	**Placebo** n (%)
Nausea	6 (3.6)	6 (6.1)	0 (0.0)	0 (0.0)
Vomiting	4 (2.4)	4 (4.1)	0 (0.0)	0 (0.0)
Hypercalcemia	21 (12.6)	16 (16.3)	5 (7.2)	0 (0.0)

Mild hypercalcemia may be asymptomatic or manifest itself as constipation, anorexia, neusea, and vomiting. More severe hypercalcemia is associated with confusion, delirium, stupor, and coma. Decreasing dialysate calcium concentration could reduce the incidence and severity of calcium acetate capsules induced hypercalcemia. Isolated cases of pruritus have been reported, which may represent allergic reactions.

6.2 Postmarketing Experience

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency or to establish a causal relationship to drug exposure.

The following additional adverse reactions have been identified during post-approval of calcium acetate: dizziness, edema, and weakness.

7 DRUG INTERACTIONS

The drug interaction of calcium acetate capsules is characterized by the potential of calcium to bind to drugs with anionic functions (e.g., carboxyl and hydroxyl groups). Calcium acetate capsules may decrease the bioavailability of tetracyclines or fluoroquinolones via this mechanism.

There are no empirical data on avoiding drug interactions between calcium acetate or calcium acetate capsules and most concomitant drugs. When administering an oral medication with calcium acetate capsules where a reduction in the bioavailability of that medication would have a clinically significant effect on its safety or efficacy, administer the drug one hour before or three hours after calcium acetate capsules or calcium

acetate. Monitor blood levels of the concomitant drugs that have a narrow therapeutic range. Patients taking anti-arrhythmic medications for the control of arrhythmias and anti-seizure medications for the control of seizure disorders were excluded from the clinical trials with all forms of calcium acetate.

7.1 Ciprofloxacin

In a study of 15 healthy subjects, a co-administered single dose of 4 calcium acetate tablets approximately 2.7 g, decreased the bioavailability of ciprofloxacin by approximately 50%.

8 USE IN SPECIFIC POPULATIONS

8.1 PREGNANCY

Pregnancy Category C

Calcium acetate capsules contains calcium acetate. Animal reproduction studies have not been conducted with calcium acetate capsules, and there are no adequate and well controlled studies of calcium acetate capsules use in pregnant women. Patients with end stage renal disease may develop hypercalcemia with calcium acetate treatment *[see Warnings and Precautions (5.1)]*. Maintenance of normal serum calcium levels is important for maternal and fetal well being. Hypercalcemia during pregnancy may increase the risk for maternal and neonatal complications such as stillbirth, preterm delivery, and neonatal hypocalcemia and hypoparathyroidism. Calcium acetate capsules treatment, as recommended, is not expected to harm a fetus if maternal calcium levels are properly monitored during and following treatment.

8.2 LABOR & DELIVERY

The effects of calcium acetate capsules on labor and delivery are unknown.

8.3 NURSING MOTHERS

Calcium acetate capsules contains calcium acetate and is excreted in human milk. Human milk feeding by a mother receiving calcium acetate capsules is not expected to harm an infant, provided maternal serum calcium levels are appropriately monitored.

8.4 PEDIATRIC USE

Safety and effectiveness in pediatric patients have not been established.

8.5 GERIATRIC USE

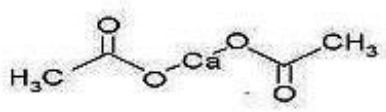
Clinical studies of calcium acetate did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

10 OVERDOSAGE

Administration of calcium acetate capsules in excess of the appropriate daily dosage may result in hypercalcemia *[see Warnings and Precautions (5.1)].*

11 DESCRIPTION

Calcium acetate capsules, USP act as a phosphate binder. Its chemical name is calcium acetate. Its molecular formula is $C_4H_6CaO_4$, and its molecular weight is 158.17. Its structural formula is:



Each capsule for oral administration contains 667 mg of calcium acetate, USP (anhydrous; $Ca(CH_3COO)_2$; MW=158.17 grams) equivalent to 169 mg (8.45 mEq) of calcium and and the inactive ingredients magnesium stearate and polyethylene glycol.

The capsules are size 00EL with light green opaque cap and white opaque body with black imprint on cap “NC” above “667”. The gelatin capsules contain D&C Yellow #10, FD&C Blue #1, FD&C Red # 40, titanium dioxide and gelatin

The imprinting ink contains the following: black iron oxide, D&C Yellow # 10 Aluminium Lake, FD&C Blue #1/ Brilliant Blue FCF Aluminum Lake, FD&C Blue #2/ Indigo Carmine Aluminum Lake, FD&C Red # 40/ Allura Red AC Aluminum Lake, propylene glycol and shellac glaze.

USP dissolution test is pending.

12 CLINICAL PHARMACOLOGY

Patients with ESRD retain phosphorus and can develop hyperphosphatemia. High serum phosphorus can precipitate serum calcium resulting in ectopic calcification. Hyperphosphatemia also plays a role in the development of secondary hyperparathyroidism in patients with ESRD.

12.1 MECHANISM OF ACTION

Calcium acetate, (calcium acetate capsules) when taken with meals, combines with dietary phosphate to form an insoluble calcium phosphate complex, which is excreted in the feces, resulting in decreased serum phosphorus concentration.

12.2 PHARMACODYNAMICS

Orally administered calcium acetate from pharmaceutical dosage forms is systemically absorbed up to approximately 40% under fasting conditions and up to approximately 30% under non-fasting conditions. This range represents data from both healthy

subjects and renal dialysis patients under various conditions.

13 NONCLINICAL TOXICOLOGY

13.1 CARCINOGENESIS & MUTAGENESIS & IMPAIRMENT OF FERTILITY

No carcinogenicity, mutagenicity, or fertility studies have been conducted with calcium acetate.

14 CLINICAL STUDIES

Effectiveness of calcium acetate in decreasing serum phosphorus has been demonstrated in two studies of the calcium acetate solid oral dosage form.

Ninety-one patients with end-stage renal disease who were undergoing hemodialysis and were hyperphosphatemic (serum phosphorus >5.5 mg/dL) following a 1-week phosphate binder washout period contributed efficacy data to an open-label, non-randomized study.

The patients received calcium acetate 667 mg tablets at each meal for a period of 12 weeks. The initial starting dose was 2 tablets per meal for 3 meals a day, and the dose was adjusted as necessary to control serum phosphorus levels. The average final dose after 12 weeks of treatment was 3.4 tablets per meal. Although there was a decrease in serum phosphorus, in the absence of a control group the true magnitude of effect is uncertain.

The data presented in Table 2 demonstrate the efficacy of calcium acetate in the treatment of hyperphosphatemia in end-stage renal disease patients. The effects on serum calcium levels are also presented.

Table 2: Average Serum Phosphorous and Calcium Levels at Pre-Study, Interim, and Study Completion Time points

Parameter	Pre-Study	Week 4[b]	Week 8	Week 12	p-value[c]
Phosphorus (mg/dL) [a]	7.4 ± 0.17	5.9 ± 0.16	5.6 ± 0.17	5.2 ± 0.17	≤0.01
Calcium (mg/dL) [a]	8.9 ± 0.09	9.5 ± 0.10	9.7 ± 0.10	9.7 ± 0.10	≤0.01

[a] Values expressed as mean ± SE.

[b] Ninety-one patients completed at least 6 weeks of the study.

[c] ANOVA of difference in values at pre-study and study completion.

There was a 30% decrease in serum phosphorus levels during the 12 week study period ($p<0.01$). Two-thirds of the decline occurred in the first month of the study. Serum calcium increased 9% during the study mostly in the first month of the study.

Treatment with the phosphate binder was discontinued for patients from the open-label study, and those patients whose serum phosphorus exceeded 5.5 mg/dL were eligible for entry into a double-blind, placebo-controlled, cross-over study. Patients were

randomized to receive calcium acetate or placebo, and each continued to receive the same number of tablets as had been individually established during the previous study. Following 2 weeks of treatment, patients switched to the alternative therapy for an additional 2 weeks.

The phosphate binding effect of calcium acetate is shown in the Table 3.

Table 3: Serum Phosphorus and Calcium Levels at Study Initiation and After Completion of Each Treatment Arm

		Post-Treatment		
Parameter	**Pre-Study**	*Calcium Acetate*	*Placebo*	**p-value[b]**
Phosphorus (mg/dL) [a]	7.3 ± 0.18	5.9 ± 0.24	7.8 ± 0.22	<0.01
Calcium (mg/dL) [a]	8.9 ± 0.11	9.5 ± 0.13	8.8 ± 0.12	<0.01

[a] Values expressed as mean ± SE.

[b] ANOVA of calcium acetate vs. placebo after 2 weeks of treatment.

Overall, 2 weeks of treatment with calcium acetate statistically significantally ($p<0.01$) decreased serum phosphorus by a mean of 19% and increased serum calcium by a statistically significant ($p<0.01$) but clinically unimportant mean of 7%.

16 HOW SUPPLIED/STORAGE AND HANDLING

Each calcium acetate capsule USP, for oral administration contains 667 mg of Calcium Acetate, USP (anhydrous $Ca(CH_3COO)_2$; MW=158.17 grams) equivalent to 169 mg (8.45 mEq) of calcium. The capsules are size 00EL with light green opaque cap and white opaque body with black imprint on cap “NC” above “667”.

NDC 60429-491-02 Bottles of 200

STORAGE: Store at 20-25°C (68-77°F); excursions permitted to 15-30°C (59-86°F) [See USP “Controlled Room Temperature”].

17 PATIENT COUNSELING INFORMATION

Inform patients to take calcium acetate capsules with meals, adhere to their prescribed diets, and avoid the use of calcium supplements including nonprescription antacids. Inform the patients about the symptoms of hypercalcemia *[see Warnings and Precautions (5.1) and Adverse Reactions (6.1)]*

Advise patients who are taking an oral medication where reduction in the bioavailability of that medication would have clinically significant effect on its safety and efficacy to take the drug one hour before or three hours after calcium acetate capsules.

Manufactured by:

Nostrum Laboratories Inc.

Kansas City, MO 64120

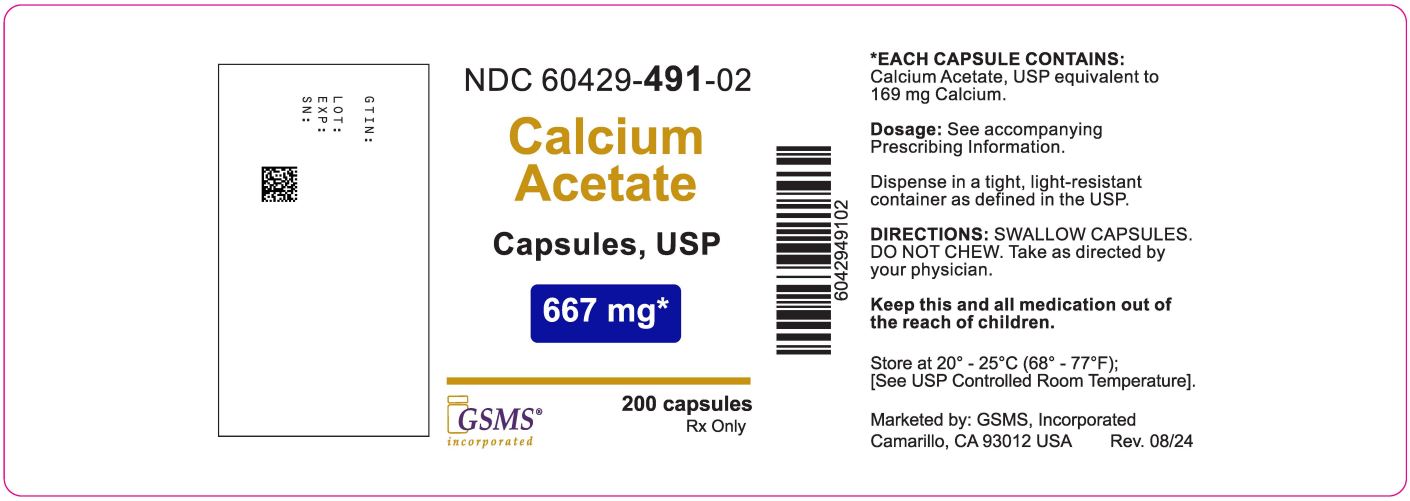
Aug 2020

Marketed by:

GSMS, Inc.

Camarillo, CA 93012 USA

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL



CALCIUM ACETATE

calcium acetate capsule

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:60429-491(NDC:29033-026)
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
CALCIUM ACETATE (UNII: Y882YXF34X) (CALCIUM CATION - UNII:2M83C4R6ZB)	CALCIUM ACETATE	667 mg

Inactive Ingredients	
Ingredient Name	**Strength**
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
GELATIN (UNII: 2G86QN327L)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYETHYLENE GLYCOL 8000 (UNII: Q662QK8M3B)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
FD&C BLUE NO. 2 (UNII: L06K8R7DQK)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
SHELLAC (UNII: 46N107B71O)	

Product Characteristics			
Color	green, white	**Score**	no score
Shape	CAPSULE	**Size**	25mm
Flavor		**Imprint Code**	NC;667mg
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:60429-491-02	200 in 1 BOTTLE; Type 0: Not a Combination Product	06/01/2017	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA203179	10/26/2015	

Labeler - Golden State Medical Supply, Inc. (603184490)

Establishment

Name	Address	ID/FEI	Business Operations
Golden State Medical Supply, Inc.		603184490	relabel(60429-491) , repack(60429-491)

Revised: 9/2024 Golden State Medical Supply, Inc.