CALCIUM ACETATE 667 MG- calcium acetate tablet, coated
Pharmin USA, LLC

CALCIUM ACETATE Tablets 667 mg

HIGHLIGHTS OF PRESCRIBING INFORMATION

Dispensed Under Clinical Supervision*

*** Calcium Acetate 667mg Tablets are categorized as a human prescription drug or supplement in the USA. This product should be dispensed under clinical supervision in compliance with all regulations as set forth by the United States Food and Drug Administration.**

1 INDICATIONS AND USAGE

Calcium Acetate Tablet is a phosphate binder indicated to reduce serum phosphorus in patients with end stage renal disease (ESRD).

2 DOSAGE AND ADMINISTRATION

The recommended initial dose of Calcium Acetate Tablets 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 AND STRENGTHS

Tablet: 667 mg calcium acetate per tablet.

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. Avoid the use of calcium supplements, including calcium-based nonprescription antacids, concurrently with calcium acetate.

An overdose of calcium acetate 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 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 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 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 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 mg2/dL2.

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 Trial 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 was 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, nausea, 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-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 is characterized by the potential of calcium to bind to drugs

with anionic functions (e.g., carboxyl and hydroxyl groups). Calcium Acetate Tablet may decrease the bioavailability of tetracyclines or fluoroquinolones via this mechanism.

There are no empirical data on avoiding drug interactions between calcium acetate and most concomitant drugs. When administering an oral medication with calcium acetate 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. 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 Tablets contains calcium acetate. Animal reproduction studies have not been conducted with calcium acetate, and there are no adequate and well controlled studies of calcium acetate 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 treatment, as recommended, is not expected to harm a fetus if maternal calcium levels are properly monitored during and following treatment.

8.2 LABOR AND DELIVERY

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

8.3 Nursing Mothers

Calcium Acetate Tablet Capsule contains calcium acetate and is excreted in human milk. Human milk feeding by a mother receiving calcium acetate 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.

9 GERIATRIC USE

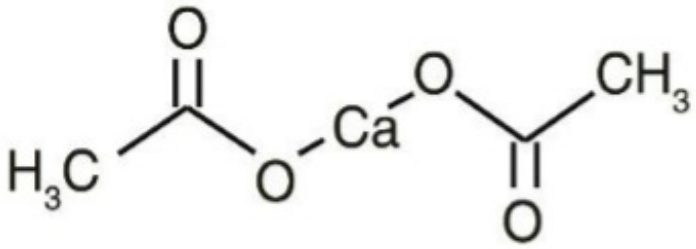
Clinical studies of calcium acetate did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection 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 Tablet in excess of the appropriate daily dosage may result in hypercalcemia *[see Warnings and Precautions (5.1)]*.

11 DESCRIPTION

Calcium Acetate Tablet acts as a phosphate binder. Its chemical name is calcium acetate. Its molecular formula is C4H6CaO4, and its molecular weight is 158.17. Its structural formula is:



Each calcium acetate tablet contains 667 mg of calcium acetate, (anhydrous; Ca (CH3COO)2; MW = 158.17 grams) equal to 169 mg (8.45 mEq) calcium. In addition, each tablet contains following inactive ingredients: powder cellulose, polyethylene glycol, calcium stearate, sodium starch glycolate and hydroxypropyl methylcellulose. Calcium acetate tablets are administered orally for the control of hyperphosphatemia in end stage renal failure.

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, 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 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 tablet [667 mg] 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***	**Week 8**	**Week 12**	**p-value†**
Phosphorus (mg/dL)‡	7.4 ± 0.17	5.9 ± 0.16	5.6 ± 0.17	5.2 ± 0.17	≤0.01
Calcium (mg/dL)‡	8.9 ± 0.09	9.5 ± 0.10	9.7 ± 0.10	9.7 ± 0.10	≤0.01

* Ninety-one patients completed at least 6 weeks of the study.

† ANOVA of difference in values at pre-study and study completion

‡ Values expressed as mean ± SE.

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

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

* ANOVA of calcium acetate vs. placebo after 2 weeks of treatment.

Overall, 2 weeks of treatment with calcium acetate statistically significantly ($p<0.01$) 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 Tablet , intended for oral administration, is white, round white coated tablet. Each calcium acetate tablet contains 667 mg of calcium acetate (anhydrous Ca(CH3COO)2; MW=158.17 grams) equal to 169 mg (8.45 mEq) calcium and are supplied as follows:

NDC 70586-1347-5 Bottles of 180 Tablets **RX only** (Pharmacies)

NDC 70586-1347-1 Bottles of 180 Tablets **Supplement*** (Hospitals & Medical Facilities)

***Dispensed under clinical supervision.**

STORAGE:

Store at 20° to 25°C (68° to 77°F) excursions permitted between 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Inform patients to take calcium acetate tablets 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 tablets.

Manufactured by:

Formulation Technology Incorporation

Oakdale, California 95361
United States of America

Manufactured For:

Pharmin USA, LLC

San Jose, California 95128
United States of America

Address inquiries to Pharmin USA, LLC , info@pharminusa.com, Tel: 1-949-545-9700

www.pharminusa.com

Made in USA

Package label principal display panel (180 Tablets)

NDC 70586-1347-1

Lic. No: 94-532, 02/26/2008

DISPENSED UNDER CLINICAL SUPERVISION

DIRECTIONS: SWALLOW TABLETS. DO NOT CHEW. Take as directed by your physician.

Supplement Facts* Serving Size: One Tablet	
Each Tablet Contains:	Amount/Serving
Calcium Acetate	667 mg

Packaging

NDC 70586-1347-1

Supplement Facts*	
Serving Size: One Tablet	
Each Tablet Contains:	Amount/Serving
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MANUFACTURED BY:
Formulation Technology Inc.
Oakdale, California 95361
United States of America

MANUFACTURED FOR:
Pharmin USA, LLC
San Jose, California 95128
United States of America
www.pharminusa.com

Made in USA

PHARMIN

CALCIUM ACETATE
Tablets

667 mg*

DISPENSED UNDER CLINICAL SUPERVISION

180 Tablets

DIRECTIONS:
SWALLOW TABLETS. DO NOT CHEW.
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KEEP THIS AND ALL MEDICATIONS OUT OF REACH OF CHILDREN.

Store at 20° to 25°C (68° to 77°F) excursions permitted between 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].

1 70586-1347-5 5

NDC 70586-1347-5

*Each tablet contains 667 mg calcium acetate equivalent to 169 mg calcium.

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Oakdale, California 95361
United States of America

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PHARMIN

CALCIUM ACETATE
Tablets

667 mg*

Rx only

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180 Tablets

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1 70586-1347-5 5

CALCIUM ACETATE 667 MG

calcium acetate tablet, coated

Product Information			
Product Type	DIETARY SUPPLEMENT	**Item Code (Source)**	NHRIC:70586-1347
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**
POWDERED CELLULOSE (UNII: SMD1X3XO9M)	

POLYETHYLENE GLYCOLS (UNII: 3WJQ0SDW1A)	
CALCIUM STEARATE (UNII: 776XM7047L)	
SODIUM STARCH GLYCOLATE TYPE A CORN (UNII: AG9B65PV6B)	
HYPROMELLOSES (UNII: 3NXW29V3WO)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NHRIC:70586-1347-5	180 in 1 BOTTLE, PLASTIC		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
dietary supplement		02/26/2008	

Supplement Facts

Serving Size : **Serving per Container :**

	Amount Per Serving	% Daily Value
color		
shape		
size (solid drugs)	13 mm	
scoring	1	

Labeler - Pharmin USA, LLC (025964216)

Establishment

Name	Address	ID/FEI	Business Operations
Formulation Technology Incorporated		062525910	manufacture(70586-1347)

Revised: 12/2017 Pharmin USA, LLC