

## PhosLo<sup>®</sup> (calcium acetate)

### Frequently Asked Questions

#### Pharmacology

##### **Q. What is PhosLo? How does it work?**

- A. PhosLo (calcium acetate) is an effective intestinal calcium-based phosphate binder indicated for the control of hyperphosphatemia in patients with end-stage renal failure.<sup>1</sup>

When taken with meals, PhosLo combines with dietary phosphate to form insoluble calcium phosphate, which is excreted in the feces.<sup>1</sup>

PhosLo is 10,000 times more soluble than calcium carbonate and dissolves readily in both acid and alkaline solutions.<sup>2</sup> In both normal subjects and patients with chronic renal failure, PhosLo binds twice as much phosphorus as equivalent doses of calcium carbonate.<sup>2, 3</sup> Of additional importance, one-half as much calcium is absorbed from equivalent doses of PhosLo compared with calcium carbonate.<sup>2, 3</sup>

#### Indications

##### **Q. What is PhosLo's indication?**

- A. PhosLo is indicated for control of hyperphosphatemia in end-stage renal failure.<sup>1</sup> Patients with higher-than-normal serum calcium levels should be closely monitored and their dose adjusted or terminated to bring levels to normal.

#### Efficacy

##### **Q. How effective is PhosLo?**

- A. As a phosphate binder, PhosLo effectively controls hyperphosphatemia in patients with end-stage renal failure. In these patients, it is recommended to maintain serum phosphorus levels  $\leq 5.5$  mg/dL and the serum calcium-phosphorus (Ca x P) product  $< 55$  mg<sup>2</sup>/dL<sup>2</sup>.<sup>4</sup> The findings from representative studies of PhosLo in patients with end-stage renal failure are presented below in tabular form followed by a summary of the most recent clinical trial involving PhosLo.

<b>Calcium Acetate Clinical Studies: A Summary of Final Mean Serum Phosphorus, Calcium, and Calcium Phosphorus Product Levels</b>				
<b>Study</b>	<b>PhosLo Therapy (n)</b>	<b>Serum Phosphorus levels (mg/dL)</b>	<b>Serum Ca levels (mg/dL)</b>	<b>Ca·P levels (mg<sup>2</sup>/dL<sup>2</sup>)</b>
CARE, 2002 <sup>5</sup>	48	5.7	9.7	55.6
Bleyer et al, 1999 <sup>6</sup>	80	5.9	9.7	57.1
Delmez et al, 1992 <sup>7</sup>	20	5.3	9.7	51.4
Emmett et al, 1991 <sup>8</sup>	85	5.2	9.7	50.6

**Q. Calcium carbonate is still being prescribed to many patients. What are the advantages for switching a patient over to PhosLo?**

A. There are several factors that healthcare providers should consider when choosing a calcium-based phosphate binder:

1. **Solubility**:<sup>2,3</sup>

PhosLo is 10,000 times more soluble than calcium carbonate and dissolves readily in both acid and alkaline environments.

As for calcium carbonate, it requires an acidic environment for dissolution and is completely insoluble in neutral or basic environments.

2. **Amount of phosphorus binding**:<sup>2,3</sup>

In normal and ESRD patients, PhosLo binds twice as much phosphorus as equivalent doses of calcium carbonate.

As for calcium carbonate, in order for it to effectively bind phosphorus, an alkaline environment is needed which again, is not the case for PhosLo.

3. **Amount of elemental calcium absorbed**:<sup>2,3</sup>

Each PhosLo 667 mg tablet or gelcap contains about 25% elemental calcium compared to each calcium carbonate tablet containing 40% elemental calcium. As a result, almost twice as much calcium is absorbed with calcium carbonate, which can increase the patient's risk for hypercalcemia.

According to Dr. Michael Emmett (Ralph Tompsett Professor of Medicine and Chief of Nephrology/Metabolism Division at Baylor University Medical Center in Houston, Texas) and Dr. Robert Hootkins (Attending Physician at Nephrology/Metabolism Division at Baylor University Medical Center in Houston, Texas), hypercalcemia is an important adverse effect and develops in about one-third of dialysis patients treated with calcium carbonate.

## Safety

### **Q. What are the side effects of PhosLo?**

A. PhosLo is well tolerated. Nausea, hypercalcemia, and pruritis have occasionally been reported during PhosLo therapy.<sup>1</sup> Please refer to the PhosLo prescribing information for additional information.

### **Q. Can PhosLo be given to pediatric patients?**

A. The safety and effectiveness of PhosLo have not been established in pediatric patients.<sup>1</sup>

### **Q. What is the clinical experience of PhosLo in geriatric patients?**

A. Of the total number of subjects in clinical studies of PhosLo (n = 91), 25% were 65 years and over, while 7% were 75 years and over.<sup>1</sup> No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients. However, greater sensitivity of some older individuals cannot be ruled out.

## Contraindications

### **Q. Are there any contraindications to the use of PhosLo?**

A. PhosLo is contraindicated in patients with hypercalcemia.<sup>1</sup>

Hypercalcemia may occur during treatment with PhosLo. Therefore, early in the treatment during dosage adjustment, serum calcium should be determined twice weekly. Should hypercalcemia develop, the dosage should be reduced or the treatment discontinued immediately, depending upon the severity of hypercalcemia. No other calcium supplements should be given concurrently with PhosLo.

## Dosing

### **Q. What is the recommended dose of PhosLo?**

A. The recommended initial dose for adults is 2 gelcaps with each meal.<sup>1</sup> The dose should be increased gradually to reduce the serum phosphorus to targeted levels  $\leq 5.5$  mg/dL. Most patients will require 3 to 4 gelcaps with each meal.

**Q. When is the optimum time to take PhosLo each day?**

- A. In a study to determine the optimum dose schedule of PhosLo to bind phosphorus, Dr. Schiller and colleagues reported that it made little difference whether the binder was ingested immediately before, after, or during a meal.<sup>9</sup> However, they determined that when PhosLo was given two hours after a meal or when the subject was fasting, phosphorus binding was markedly reduced. Therefore, the investigators concluded that, for the most efficient phosphorus binding, calcium salts should be given with meals.

If possible, it is advisable to adjust the phosphorus binder dose on the basis of the phosphorus content of each meal.<sup>2,9</sup> Dr. Slatopolsky and colleagues determined that the meal content of ingested phosphorus among 20 hemodialysis patients was 245 mg with breakfast, 23 mg with lunch, and 484 mg with dinner, an intermediate dose with breakfast and the smallest dose or none with lunch.<sup>10</sup>

**Q. In regards to tailoring a patient's dose (dose of PhosLo per the phosphorus content of our patients' meals), how much (mg) of phosphorus is bound by one PhosLo (667 mg) gelcap or tablet?**

- A. Based on results of a study in a small number of patients by Mai and colleagues, approximately 18 mg of phosphorus is bound by 1 PhosLo (667 mg) gelcap or tablet.<sup>3</sup> Without getting too bogged down in quantitative determination of PhosLo dosing, a simple rule of thumb can be employed; increase the dose of PhosLo with meals associated with high phosphorus content e.g., lunch and dinner. For additional support, see the recent letter to the editor by Nolan in the 2004 Kidney International issue.<sup>11</sup>

**Q. Can PhosLo tablet or gelcap be chewed before ingestion in patients who have difficulty swallowing oral medications?**

- A. Because PhosLo imparts a vinegar-like taste when chewed, the tablet or gelcap should be swallowed whole. Nabi Biopharmaceuticals has not conducted any pharmacokinetics studies to assess the bioavailability of PhosLo when the tablet or gelcap contents have been triturated and sprinkled on soft food prior to ingestion. However, because both formulations are conventional, immediate-release dosage forms, Nabi Biopharmaceuticals would not anticipate any changes in the pharmacokinetics of PhosLo if the tablet or gelcap was administered in this manner.

**Q. Can PhosLo tablets or gelcaps be crushed?**

- A. Nabi Biopharmaceuticals has not conducted any pharmacokinetics studies to assess the bioavailability of PhosLo when the tablet or gelcap contents has been triturated and sprinkled on soft food prior to ingestion. However, because both formulations are conventional, immediate-release dosage forms, Nabi Biopharmaceuticals would not anticipate any changes in the pharmacokinetics of PhosLo if the tablet or gelcap is administered in this manner. There is no concern that crushing either the PhosLo tablet or gelcap will alter the drug's pharmacokinetic profile. The tablet or gelcap, which is essentially an encapsulated tablet, can indeed be crushed for administration via a nasogastric tube or in pudding. The only concern is that of palatability—PhosLo when crushed imparts a distinct vinegar-like taste.

Supply Information

**Q. How is PhosLo supplied?**

- A. Be advised that effective immediately, Nabi Biopharmaceuticals will discontinue distribution of PhosLo® Tablets (NDC 59730-6401-01). Rest assured that, Nabi will be focused on supporting the supply of PhosLo in the Gelcap formulation (NDC 59730-6402-01)—an encapsulated version of the PhosLo tablet. This decision is in large part due to results of a clinical study evaluating the use of PhosLo tablets versus gelcaps in End Stage Renal Disease (ESRD) patients receiving hemodialysis. An overwhelming 90% of patients indicated a preference for PhosLo Gelcaps over the tablet formulation.<sup>12</sup>

PhosLo Gelcaps and tablets are identical in terms of:<sup>1</sup>

- Active ingredient
- Proven efficacy
- Demonstrated safety profile
- Convenient dosing

**Q. How do I order PhosLo?**

- A. Please contact Nabi Biopharmaceuticals Customer Operations at 1-800-327-7106 for a list of authorized wholesalers and distributors. The NDC number for PhosLo Gelcaps (bottles of 200) is 59730-6402-1.

**Q. Recently, patients have been informed by their retail pharmacists that PhosLo tablets are on back order. This has made patient access to PhosLo tablets increasingly difficult. What is going on?**

A. As already evident, Nabi Biopharmaceuticals will gradually be phasing out the PhosLo tablets. However, Nabi will be supporting the supply of the PhosLo gelcap formulation, which is simply an encapsulated version of the PhosLo tablet. This decision was in large part due to the results of a clinical study, the Preference Study, which indicated that 90% of the studied ESRD patients receiving hemodialysis favored the PhosLo gelcap formulation over the tablets.<sup>12</sup> Overall, this preference for the PhosLo gelcaps led to increased compliance in this patient population, and improved control of serum P levels.<sup>12</sup>

PhosLo Gelcaps and tablets are identical in terms of:<sup>1</sup>

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If you have additional questions, please call Nabi Biopharmaceuticals Medical Affairs Department at 1-800-458-4244, or visit our website at [www.nabi.com](http://www.nabi.com).

PhosLo is indicated for control of hyperphosphatemia in end-stage renal failure. Patients with higher-than-normal serum calcium levels should be closely monitored and their dose adjusted or terminated to bring levels to normal. PhosLo is contraindicated in patients with hypercalcemia. No other calcium supplements should be given concurrently with PhosLo.

**References:**

1. PhosLo Prescribing Information, Nabi Biopharmaceuticals.
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3. Mai et al. Calcium acetate, an effective phosphorus binder in patients with renal failure. *Kidney International* 36: 690-695, 1989.
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7. Delmez et al: *J Am Soc Nephrol* 3: 96-102, 1992.
8. Emmett et al: Calcium acetate control of phosphorus in hemodialysis patients. *Am J Kidney Dis* 17: 544-550, 1991.
9. Schiller et al: Effect of the time of administration of calcium acetate on phosphorus binding. *NEJM* 320 (17): 544-550, 1989.

10. Slatopolsky et al: Calcium carbonate as a phosphate binder in patients with chronic renal failure undergoing dialysis. *NEJM* 315 (3): 157-161, 1986.
11. Nolan et al: Phosphate intake and the CARE study (letters to the editors). *Kidney International* 66: 2088-2089, 2004.
12. Kaplan, MR et al: A preference study: calcium acetate tablets versus gelcaps in hemodialysis patients. *Nephrol Nurs J* 29: 363-365, 2002.