OSMOPREP- sodium phosphate, monobasic, monohydrate, sodium phosphate, dibasic anhydrous tablet
Salix Pharmaceuticals, Inc.

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

OsmoPrep® (sodium phosphate monobasic monohydrate, USP and sodium phosphate dibasic anhydrous, USP) Tablets
Initial U.S. Approval: 2006

WARNINGS

There have been rare, but serious reports of acute phosphate nephropathy in patients who received oral sodium phosphate products for colon cleansing prior to colonoscopy. Some cases have resulted in permanent impairment of renal function and some patients required long-term dialysis. While some cases have occurred in patients without identifiable risk factors, patients at increased risk of acute phosphate nephropathy may include those with increased age, hypovolemia, increased bowel transit time (such as bowel obstruction), active colitis, or baseline kidney disease, and those using medicines that affect renal perfusion or function (such as diuretics, angiotensin converting enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs], and possibly nonsteroidal anti-inflammatory drugs [NSAIDs]) *[see Warnings and Precautions (5)]*.

It is important to use the dose and dosing regimen as recommended (pm/am split dose) *[see Dosage and Administration (2)*].

INDICATIONS AND USAGE

OsmoPrep is an osmotic laxative indicated for cleansing of the colon as a preparation for colonoscopy in adults 18 years of age or older (1)

DOSAGE AND ADMINISTRATION

- Evening before colonoscopy: Four tablets with 8 ounces of clear liquids every 15 minutes for a total of 20 tablets (2)
- Next morning: Four tablets with 8 ounces of clear liquids every 15 minutes for a total of 12 tablets (2)

DOSAGE FORMS AND STRENGTHS

Tablet: 1.5 g of sodium phosphate (3)

CONTRAINDICATIONS

- Biopsy-proven acute phosphate nephropathy (4)
- Gastrointestinal (GI) obstruction (4)
- Gastric bypass or stapling surgery (4)
- Bowel perforation (4)
- Toxic colitis (4)
- Toxic megacolon (4)
- Hypersensitivity to any components of OsmoPrep (4)

WARNINGS AND PRECAUTIONS

- Renal impairment may occur. Assess renal function before treatment and during therapy (5.1)
- Seizures due to electrolyte abnormalities can occur (5.3)
- Use caution in patients with higher risk of arrhythmias, e.g., cardiomyopathy, prolonged QT, uncontrolled arrhythmias, or recent MI (5.2)
- Adequately hydrate before, during and after dosing (5.4)
- Use caution in patients with history of Inflammatory Bowel Disease (5.5)

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥3%) are abdominal bloating, abdominal pain, nausea, and vomiting (6)
To report SUSPECTED ADVERSE REACTIONS, contact Salix Pharmaceuticals, Inc. at 1-800-321-4576 or FDA

at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Some drugs increase risks due to fluid and electrolyte changes (7.1)
- Oral medication taken within 1 hour of start of each dose might not be absorbed properly (7.2)

USE IN SPECIFIC POPULATIONS

- Pregnancy: No human or animal data. Use only if clearly needed. (8.1)
- Use with caution in patients with renal disease (5.1)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 8/2016

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

WARNINGS

There have been rare, but serious reports of acute phosphate nephropathy in patients who received oral sodium phosphate products for colon cleansing prior to colonoscopy. Some cases have resulted in permanent impairment of renal function and some patients required long-term dialysis. While some cases have occurred in patients without identifiable risk factors, patients at increased risk of acute phosphate nephropathy may include those with increased age, hypovolemia, increased bowel transit time (such as bowel obstruction), active colitis, or baseline kidney disease, and those using medicines that affect renal perfusion or function (such as diuretics, angiotensin converting enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs], and possibly nonsteroidal anti-inflammatory drugs [NSAIDs]) *[see Warnings and Precautions (5)]*.

It is important to use the dose and dosing regimen as recommended (pm/am split dose) *[see Dosage and Administration (2)*].

1 INDICATIONS AND USAGE

OsmoPrep Tablets are indicated for cleansing of the colon as a preparation for colonoscopy in adults 18 years of age or older.

2 DOSAGE AND ADMINISTRATION

The recommended dose of OsmoPrep Tablets for colon cleansing for adult patients is 32 tablets (48 grams of sodium phosphate) taken orally with a total of 2 quarts of clear liquids in the following manner:

The evening before the colonoscopy: Take 4 OsmoPrep Tablets with 8 ounces of clear liquids every 15 minutes for a total of 20 tablets.

On the day of the colonoscopy: Starting 3-5 hours before the procedure, take 4 OsmoPrep Tablets with 8 ounces of clear liquids every 15 minutes for a total of 12 tablets.

Examples of clear liquids are water, flavored water, lemonade (no pulp), ginger ale or apple juice. Do not drink any liquids colored purple or red.

Patients should be advised of the importance of taking the recommended fluid regimen. It is recommended that patients receiving OsmoPrep be advised to adequately hydrate before, during, and after the use of OsmoPrep.

Patients should not use OsmoPrep for colon cleansing within seven days of previous administration. No additional enema or laxative is required, and patients should be advised NOT to take additional agents, particularly those containing sodium phosphate.

3 DOSAGE FORMS AND STRENGTHS

Each OsmoPrep Tablet contains 1.102 grams of sodium phosphate monobasic monohydrate, USP and 0.398 grams of sodium phosphate dibasic anhydrous, USP for a total of 1.5 grams of sodium phosphate per tablet.

4 CONTRAINDICATIONS

OsmoPrep Tablets are contraindicated in the following conditions:

- Biopsy-proven acute phosphate nephropathy
- Gastrointestinal (GI) obstruction
- Gastric bypass or stapling surgery
- Bowel perforation
- Toxic colitis
- Toxic megacolon
- Known allergy or hypersensitivity to sodium phosphate salts or any component of OsmoPrep *[see Description* (11)].

5 WARNINGS AND PRECAUTIONS

5.1 Renal Disease, Acute Phosphate Nephropathy, and Electrolyte Disorders

Renal Disease and Acute Phosphate Nephropathy

There have been rare, but serious, reports of renal failure, acute phosphate nephropathy, and nephrocalcinosis in patients who received oral sodium phosphate products (including oral sodium phosphate solutions and tablets) for colon cleansing prior to colonoscopy. These cases often resulted in permanent impairment of renal function and several patients required long-term dialysis. The time to onset is typically within days; however, in some cases, the diagnosis of these events has been delayed up to several months after the ingestion of these products. Patients at increased risk of acute phosphate nephropathy may include patients with the following: hypovolemia, baseline kidney disease, increased age, and patients using medicines that affect renal perfusion or function [such as diuretics, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers, and possibly nonsteroidal anti-inflammatory drugs (NSAIDs).

Use OsmoPrep with caution in patients with impaired renal function (creatinine clearance less than 30 mL/minute), patients with a history of acute phosphate nephropathy, known or suspected electrolyte disturbances (such as dehydration), or people taking concomitant medications that may affect electrolyte levels (such as diuretics). Patients with electrolyte abnormalities such as hypernatremia, hyperphosphatemia, hypokalemia, or hypocalcemia should have their electrolytes corrected before treatment with OsmoPrep Tablets.

Electrolyte Disorders

Advise all patients to hydrate adequately before, during, and after the use of OsmoPrep. If a patient develops significant vomiting or signs of dehydration while or after taking OsmoPrep, consider performing post-colonoscopy lab tests (electrolytes, creatinine, and BUN). Fluid and electrolyte disturbances can lead to serious adverse events including cardiac arrhythmias, seizures and renal impairment [*see Dosage and Administration (2)]*.

Patients with electrolyte abnormalities should have them corrected before treatment with OsmoPrep. In addition, use caution when prescribing OsmoPrep for patients with conditions, or who are using medications, that increase the risk for fluid and electrolyte disturbances or may increase the risk of adverse events of seizure, arrhythmias, and renal impairment *[see Drug Interactions (7.1)*].

Patients should not administer additional laxative or purgative agents, particularly additional sodium phosphate-based purgative or enema products.

5.2 Cardiac Arrhythmias

There have been rare reports of serious arrhythmias associated with the use of ionic osmotic laxative products for bowel preparation. Use caution when prescribing OsmoPrep for patients at increased risk of arrhythmias (e.g., patients with a history of prolonged QT, uncontrolled arrhythmias, recent myocardial infarction, unstable angina, congestive heart failure, or cardiomyopathy). QT prolongation

with sodium phosphate tablets has been associated with electrolyte imbalances, such as hypokalemia and hypocalcemia. OsmoPrep Tablets should be used with caution in patients who are taking medications known to prolong the QT interval, since serious complications may occur. Pre-dose and post-colonoscopy ECGs should be considered in patients at increased risk of serious cardiac arrhythmias.

5.3 Seizures

There have been rare reports of generalized tonic-clonic seizures and/or loss of consciousness associated with use of sodium phosphate osmotic laxative products, such as OsmoPrep, in patients with no prior history of seizures. The seizure cases were associated with electrolyte abnormalities (e.g., hyponatremia, hypokalemia, hypocalcemia, and hypomagnesemia) and low serum osmolality. The neurologic abnormalities resolved with correction of fluid and electrolyte abnormalities. OsmoPrep should be used with caution in patients with a history of seizures and in patients at higher risk of seizure [patients using concomitant medications that lower the seizure threshold (such as tricyclic antidepressants), patients withdrawing from alcohol or benzodiazepines, or patients with known or suspected hyponatremia].

5.4 Use in Patients with Significant Gastrointestinal Disease

If gastrointestinal obstruction or perforation is suspected, perform appropriate diagnostic studies to rule out these conditions before administering OsmoPrep. Use with caution in patients with severe active ulcerative colitis.

5.5 Inflammatory Bowel Disease

Administration of OsmoPrep Tablets may induce colonic mucosal aphthous ulcerations. In the OsmoPrep clinical program, aphthous ulcers were observed in 3% of patients who took the 48 gram OsmoPrep dosing regimen. This colonoscopic finding should be considered in patients with known or suspected inflammatory bowel disease.

Because published data suggest that sodium phosphate absorption may be enhanced in patients experiencing an acute exacerbation of chronic inflammatory bowel disease, OsmoPrep Tablets should be used with caution in such patients.

5.6 Aspiration

Use with caution in patients with impaired gag reflex and patients prone to regurgitation or aspiration. Such patients should be observed during administration of OsmoPrep.

6 ADVERSE REACTIONS

6.1 Clinical Studies 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 clinical practice.

Abdominal bloating, nausea, abdominal pain, and vomiting were the most common adverse events reported with the use of OsmoPrep Tablets. Dizziness and headache were reported less frequently. Since diarrhea was considered as a part of the efficacy of OsmoPrep, diarrhea was not defined as an adverse event in the clinical studies. Table 1 shows the most common adverse events associated with the use of 48 grams of OsmoPrep, 60 grams of OsmoPrep, and 60 grams of Visicol in the colon preparation trials (n= 931).

Table 1: Frequency of Adverse Events of Any Severity Occurring in Greater Than 3% of Patients in the OsmoPrep Trials

	OsmoPrep 32 tabs (48 g) N=272	OsmoPrep 40 tabs (60 g) N=265	Visicol® 40 tabs (60 g) N=268
Bloating	31%	39%	41%
Nausea	26%	37%	30%
Abdominal Pain	23%	24%	25%
Vomiting	4%	10%	9%

6.2 Postmarketing Experience

In addition to adverse events reported from clinical trials, the following adverse events have been identified during post-approval use of OsmoPrep. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. These events have been chosen for inclusion due to either their seriousness, frequency of reporting or causal connection to OsmoPrep, or a combination of these factors.

Body as a Whole: Hypersensitivity reactions including anaphylaxis, rash, pruritus, urticaria, throat tightness, bronchospasm, dyspnea, pharyngeal edema, dysphagia, paresthesia and swelling of the lips and tongue, and facial swelling.

Cardiovascular: Arrhythmias

Nervous system: Seizures

Renal: Renal impairment, increased blood urea nitrogen (BUN), increased creatinine, acute renal failure, acute phosphate nephropathy, nephrocalcinosis, and renal tubular necrosis.

7 DRUG INTERACTIONS

7.1 Drugs That May Increase Risks Due to Fluid and Electrolyte Abnormalities

Use caution when prescribing OsmoPrep for patients with conditions, or who are using medications, that increase the risk for fluid and electrolyte disturbances or may increase the risk of adverse events of seizure, arrhythmias, and prolonged QT in the setting of fluid and electrolyte abnormalities. Consider additional patient evaluations as appropriate [*see Warnings and Precautions (5)*] in patients taking these concomitant medications.

7.2 Potential for Altered Drug Absorption

Oral medication administered within one hour of the start of each OsmoPrep dose may be flushed from the gastrointestinal tract, and the medication may not be absorbed properly.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects: Pregnancy Category C. Animal reproduction studies have not been conducted with OsmoPrep. It is also not known whether OsmoPrep can cause fetal harm when administered to a pregnant woman, or can affect reproduction capacity. OsmoPrep should be given to a pregnant woman only if clearly needed.

8.3 Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when OsmoPrep is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

In controlled colon preparation trials of OsmoPrep, 228 (24%) of 931 patients were 65 years of age or older. In addition, 49 (5%) of the 931 patients were 75 years of age or older.

Of the 228 geriatric patients in the trials, 134 patients (59%) received at least 48 grams of OsmoPrep. Of the 49 patients 75 years old or older in the trials, 27 (55%) patients received at least 48 grams of OsmoPrep. No overall differences in safety or effectiveness were observed between geriatric patients and younger patients. However, the mean phosphate levels in geriatric patients were greater than the phosphate levels in younger patients after OsmoPrep administration. The mean colonoscopy-day phosphate levels in patients 18-64, 65-74, and ≥ 75 years old who received 48 grams of OsmoPrep in the phase 3 study were 7.0, 7.3, and 8.0 mg/dL, respectively. In addition, in all three sodium phosphate treatment groups, the mean phosphate levels in patients 18-64, 65-74, and ≥ 75 years old in the phase 3 study were 7.4, 7.9, and 8.0 mg/dL, respectively, after sodium phosphate administration. Greater sensitivity of some older individuals cannot be ruled out; therefore, OsmoPrep Tablets should be used with caution in geriatric patients.

Sodium phosphate is known to be substantially excreted by the kidney, and the risk of adverse reactions with sodium phosphate may be greater in patients with impaired renal function. Since geriatric patients are more likely to have impaired renal function, consider performing baseline and post-colonoscopy labs (phosphate, calcium, potassium, sodium, creatinine, and BUN) in these patients *[see Warnings and Precautions (5)]*. It is recommended that patients receiving OsmoPrep be advised to adequately hydrate before, during, and after the use of OsmoPrep.

9 DRUG ABUSE AND DEPENDENCE

Laxatives and purgatives (including OsmoPrep) have the potential for abuse by patients who frequently engage in binge eating and vomiting to lose weight.

10 OVERDOSAGE

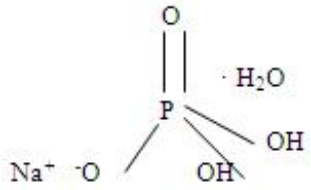
There have been no reported cases of overdosage with OsmoPrep Tablets. Purposeful or accidental ingestion of more than the recommended dosage of OsmoPrep Tablets might be expected to lead to severe electrolyte disturbances, including hyperphosphatemia, hypocalcemia, hypernatremia, or hypokalemia, as well as dehydration and hypovolemia, with attendant signs and symptoms of these disturbances. Certain severe electrolyte disturbances resulting from overdose may lead to cardiac arrhythmias, seizure, renal failure, and death. The patient who has taken an overdosage should be monitored carefully, and treated symptomatically for complications until stable.

11 DESCRIPTION

OsmoPrep (sodium phosphate monobasic monohydrate, USP, and sodium phosphate dibasic anhydrous, USP) is an osmotic laxative used to clean the colon prior to colonoscopy. OsmoPrep is manufactured with a highly soluble tablet binder and does not contain microcrystalline cellulose (MCC). OsmoPrep Tablets are oval, white to off-white compressed tablets, debossed with “SLX” on one side of the bisect and “102” on the other side of the bisect. Each OsmoPrep tablet contains 1.102 grams of sodium phosphate monobasic monohydrate, USP and 0.398 grams of sodium phosphate dibasic anhydrous, USP for a total of 1.5 grams of sodium phosphate per tablet. Inert ingredients include polyethylene glycol 8000, NF; and magnesium stearate, NF. OsmoPrep is gluten-free.

The structural and molecular formulae and molecular weights of the active ingredients are shown below:

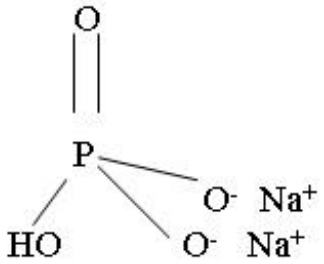
- Sodium phosphate monobasic monohydrate, USP



Molecular Formula: NaH2PO4\\· H2O

Molecular Weight: 137.99

- Sodium phosphate dibasic anhydrous, USP



Molecular Formula: Na_2HPO_4

Molecular Weight: 141.96

OsmoPrep Tablets are for oral administration only.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

OsmoPrep Tablets, a dosing regimen containing 48 grams of sodium phosphate (32 tablets), induces diarrhea. Each administration has a purgative effect for approximately 1 to 3 hours. The primary mode of action is thought to be through the osmotic effect of sodium, causing large amounts of water to be drawn into the colon, promoting evacuation.

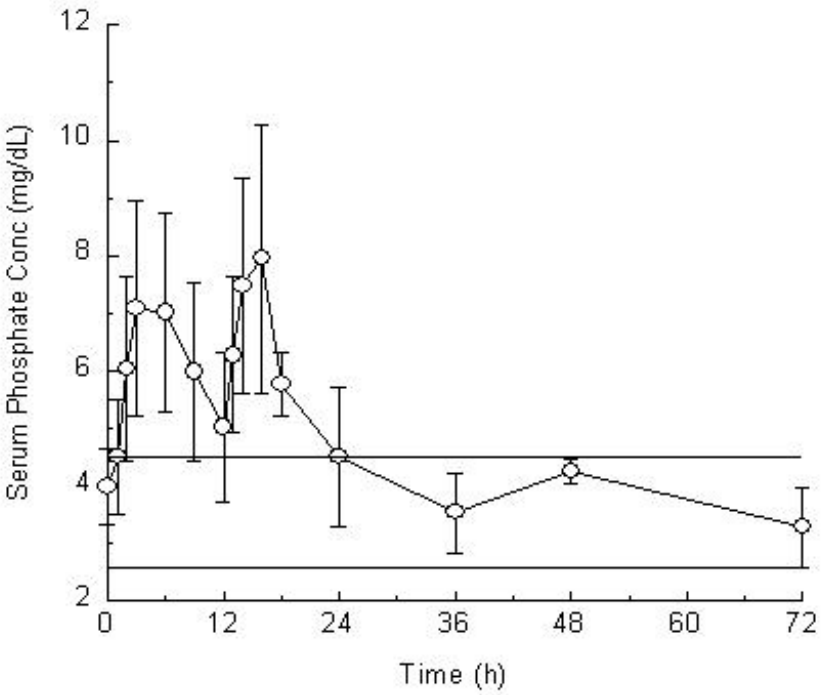
12.3 Pharmacokinetics

Pharmacokinetic studies with OsmoPrep have not been conducted. However, the following pharmacokinetic study was conducted with Visicol tablets which contain the same active ingredients (sodium phosphate) as OsmoPrep. In addition, Visicol is administered at a dose that is 25% greater than the OsmoPrep dose.

An open-label pharmacokinetic study of Visicol in healthy volunteers was performed to determine the concentration-time profile of serum inorganic phosphorus levels after Visicol administration. All subjects received the approved Visicol dosing regimen (60 grams of sodium phosphate with a total liquid volume of 3.6 quarts) for colon cleansing. A 30 gram dose (20 tablets given as 3 tablets every 15 minutes with 8 ounces of clear liquids) was given beginning at 6 PM in the evening. The 30 gram dose (20 tablets given as 3 tablets every 15 minutes with 8 ounces of clear liquids) was repeated the following morning beginning at 6 AM.

Twenty-three healthy subjects (mean age 57 years old; 57% male and 43% female; and 65% Hispanic, 30% Caucasian, and 4% African-American) participated in this pharmacokinetic study. The serum phosphorus level rose from a mean (± standard deviation) baseline of 4.0 (± 0.7) mg/dL to 7.7 (± 1.6 mg/dL), at a median of 3 hours after the administration of the first 30-gram dose of sodium phosphate tablets (see Figure 1). The serum phosphorus level rose to a mean of 8.4 (± 1.9) mg/dL, at a median of 4 hours after the administration of the second 30-gram dose of sodium phosphate tablets. The serum phosphorus level remained above baseline for a median of 24 hours after the administration of the initial dose of sodium phosphate tablets (range 16 to 48 hours).

Figure 1. Mean (±standard deviation) serum phosphorus concentrations



The upper (4.5 mg/dL) and lower (2.6 mg/dL) reference limits for serum phosphate are represented by solid bars.

Special Populations

Renal Insufficiency: The effect of renal dysfunction on the pharmacokinetics of OsmoPrep Tablets has not been studied. Since the inorganic form of phosphate in the circulating plasma is excreted almost entirely by the kidneys, patients with renal disease may have difficulty excreting a large phosphate load. Thus, OsmoPrep Tablets should be used with caution in patients with impaired renal function *[see Warnings and Precautions (5)]*.

Hepatic Insufficiency: OsmoPrep Tablets have not been investigated in patients with hepatic failure.

Geriatric: In a single pharmacokinetic study of sodium phosphate tablets, which included 6 elderly volunteers, plasma half-life increased two-fold in subjects > 70 years of age compared to subjects < 50 years of age (3 subjects and 5 subjects, respectively).

Gender: No difference in serum phosphate AUC values were observed in the single pharmacokinetic study conducted with sodium phosphate tablets in 13 male and 10 female healthy volunteers.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals have not been performed to evaluate the carcinogenic potential of OsmoPrep. Studies to evaluate the possible impairment of fertility or mutagenic potential of OsmoPrep have not been performed.

14 CLINICAL STUDIES

The colon cleansing efficacy and safety of OsmoPrep was evaluated in 2 randomized, investigator-blinded, actively controlled, multicenter, U.S. trials in patients scheduled to have an elective colonoscopy. The trials consisted of a dose ranging and a confirmatory phase 3 study.

In the phase 3 trial, patients were randomized into one of the following three sodium phosphate treatment groups: 1) Visicol containing 60 grams of sodium phosphate given in split doses (30 grams in the evening before the colonoscopy and 30 grams on the next day) with at least 3.6 quarts of clear liquids; 2) OsmoPrep containing 60 grams of sodium phosphate given in split doses (30 grams in the evening before the colonoscopy and 30 grams on the next day) with 2.5 quarts of clear liquids; and 3) OsmoPrep containing 48 grams of sodium phosphate (30 grams in the evening before the colonoscopy and 18 grams on the next day) with 2 quarts of clear liquids. Patients were instructed to eat a light breakfast before noon on the day prior to the colonoscopy and then were told to drink only clear liquids after noon on the day prior to the colonoscopy.

The primary efficacy endpoint was the overall colon cleansing response rate in the 4-point Colonic Contents Scale. Response was defined as a rating of "excellent" or "good" on the 4-point scale as determined by the blinded colonoscopist. This phase 3 study was planned to assess the non-inferiority of the two OsmoPrep groups compared to the Visicol group.

The efficacy analysis included 704 adult patients who had an elective colonoscopy. Patients ranged in age from 21 to 89 years old (mean age 56 years old) with 55% female and 45% male patients. Race was distributed as follows: 87% Caucasian, 10% African American, and 3% other race. The OsmoPrep 60 gram and 48 gram treatment groups demonstrated non-inferiority compared to Visicol. See Table 2 for the results.

Table 2: Phase 3 Study – Overall Colon Content Cleansing Response Rates*

Treatment Arm (grams of sodium phosphate)	No. of tablets taken at 6 PM on the day prior to colonoscopy	No. of tablets taken the next day†	Excellent	Good	Fair	Inadequate	Overall Response Rate (Excellent or Good)
OsmoPrep 32 tabs (48 g) n=236	20	12	76%	19%	3%	2%	95%
OsmoPrep 40 tabs (60 g) n=233	20	20	73%	24%	2%	1%	97%
Visicol 40 tabs (60 g) n=235	20	20	51%	43%	6%	0%	94%

* Colon cleansing efficacy was based on response rate to treatment. A patient was considered to be a responder if overall colon cleansing was rated as "excellent" or "good" on a 4-point scale based on the amount of retained "colonic contents". Excellent was defined as >90% of mucosa seen, mostly liquid stool, minimal suctioning needed for adequate visualization. Good was defined as >90% of mucosa seen, mostly liquid stool, significant suctioning needed for adequate visualization. Fair was defined as >90% of mucosa seen, mixture of liquid and

semisolid stool, could be suctioned and/or washed. Inadequate was defined as <90% of mucosa seen, mixture of semisolid and solid stool which could not be suctioned or washed.

† On the day of the colonoscopy, study medication was taken 3 to 5 hours before the start of the colonoscopy.

Electrolyte Changes

In the OsmoPrep clinical studies, expected serum electrolyte changes (including phosphate, calcium, potassium, and sodium levels) have been observed in patients taking OsmoPrep.

In the OsmoPrep phase 3 study, 96%, 96%, and 93% of patients who took 60 grams of Visicol, 60 grams of OsmoPrep, and 48 grams of OsmoPrep, respectively, developed hyperphosphatemia (defined as phosphate level > 5.1 mg/dL) on the day of the colonoscopy. In this study, patients who took 60 grams of Visicol, 60 grams of OsmoPrep, and 48 grams of OsmoPrep had baseline mean phosphate levels of 3.5, 3.5, and 3.6 mg/dL and subsequently developed mean phosphate levels of 7.6, 7.9, and 7.1 mg/dL, respectively, on the day of the colonoscopy.

In the OsmoPrep phase 3 study, 20%, 22%, and 18% of patients who took 60 grams of Visicol, 60 grams of OsmoPrep, and 48 grams of OsmoPrep, respectively, developed hypokalemia (defined as a potassium level < 3.4 mEq/L) on the day of the colonoscopy. In this study, patients who took 60 grams of Visicol, 60 grams of OsmoPrep, and 48 grams of OsmoPrep all had baseline potassium levels of about 4.3 mEq/L and then developed a mean potassium level of 3.7 mEq/L on the day of the colonoscopy.

In the OsmoPrep phase 3 trial, several patients on all three sodium phosphate regimens developed hypocalcemia and hypernatremia that did not require treatment.

16 HOW SUPPLIED/STORAGE AND HANDLING

NDC 65649-701-41, multi-dose, child-resistant bottle containing 100 tablets.

Each bottle contains two silica desiccant packets, which should not be ingested.

Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Discard any unused portion.

17 PATIENT COUNSELING INFORMATION

[See Medication Guide]

OsmoPrep can cause serious kidney problems and/or severe fluid loss. Consider performing baseline and post-colonoscopy laboratory studies (phosphate, calcium, potassium, sodium, creatinine and BUN). It is important to:

- Instruct patients to tell their healthcare provider if they have a history of kidney disease or take medications for blood pressure, heart disease, or kidney disease.
- Advise patients of the importance of taking the recommended fluid regimen. Advise them to hydrate adequately before, during, and after the use of OsmoPrep.
- Instruct patients to tell their healthcare provider if they experience symptoms of dehydration.
- Instruct patients to contact a healthcare provider if they experience a worsening of bloating, abdominal pain, nausea, vomiting, or headache.
- Instruct patients not to take OsmoPrep with other laxatives or enemas made with sodium phosphate, because it could lead to complications.

Manufactured for:
Salix Pharmaceuticals, a division of
Valeant Pharmaceuticals North America LLC

Bridgewater, NJ 08807 USA

9516400
70011844 (Outsert)

9516500
70011847 (Topsert)

Rev. 08/2016

Medication Guide

OsmoPrep® (AhZ-MŌ-prĕp)

(sodium phosphate monobasic monohydrate, and sodium phosphate dibasic anhydrous) Tablets

Read this Medication Guide before you start taking OsmoPrep each time you get a new prescription. There may be new information. This Medication Guide does not take the place of talking with your doctor about your medical condition or your treatment.

What is the most important information I should know about OsmoPrep?

OsmoPrep can cause serious side effects, including:

Serious kidney problems. Rare, but serious kidney problems can happen in people who take medicines made with sodium phosphate, including OsmoPrep, to clean the colon before colonoscopy. These kidney problems can sometimes lead to kidney failure or the need for dialysis for a long time. These problems often happen within a few days, but sometimes may happen several months after taking OsmoPrep.

Conditions that can make you more at risk for having serious kidney problems with OsmoPrep include if you:

- lose too much body fluid (dehydration)
- have slow moving bowels
- have bowels blocked with stool (constipation)
- have severe stomach pain or bloating
- have any disease that causes bowel inflammation (colitis)
- have kidney disease or kidney problems
- have heart failure
- take water pills or non-steroidal anti-inflammatory drugs (NSAIDs)

Your age may also affect your risk for having kidney problems with OsmoPrep.

Before you start taking OsmoPrep, tell your doctor if you:

- have kidney problems
- take any medicines for blood pressure, heart disease, or kidney disease.

Severe fluid loss and severe changes in body salts in the blood (electroytes). People who take

medicines that contain sodium phosphate can have severe loss of body fluid, with severe changes in body salts in the blood. These changes can be serious and can cause:

- abnormal heart rhythms
- seizures
- kidney problems

Tell your doctor if you have any of these symptoms of loss of too much body fluid (dehydration) while taking OsmoPrep:

- vomiting
- dizziness
- urinating less often than normal
- headache

See "What are the possible side effects of OsmoPrep?" for more information about side effects.

What is OsmoPrep?

OsmoPrep is a prescription medicine used in adults 18 years and older to clean your colon before a colonoscopy. OsmoPrep cleans your colon by causing you to have diarrhea. Cleaning your colon helps your doctor see the inside of your colon more clearly during the colonoscopy.

It is not known if OsmoPrep is safe and effective in children under age 18.

Who should not take OsmoPrep?

Do not take OsmoPrep if:

- you have had a kidney biopsy that shows you have kidney problems because of too much phosphate
- impairment of the bowels or bowel function
- had stomach surgery involving stapling or bypass
- significant irritation of the bowels such as toxic megacolon
- you are allergic to sodium phosphate salts or any of the ingredients in OsmoPrep. See the end of this Medication Guide for a list of ingredients in OsmoPrep.

What should I tell my doctor before taking OsmoPrep?

Before you take OsmoPrep, tell your doctor if you:

- have kidney problems
- have heart problems
- have a history of seizures
- have had stomach surgery
- have stomach or bowel problems
- have ulcerative colitis
- have problems with swallowing or gastric reflux
- drink alcohol or are withdrawing from alcohol use
- have any other medical conditions
- are on a low salt diet
- are pregnant. It is not known if OsmoPrep will harm your unborn baby. Talk to your doctor if you are pregnant or plan to become pregnant

- are breastfeeding or plan to breast-feed. It is not known if OsmoPrep passes into your breast milk. You and your doctor should decide if you will take OsmoPrep while breastfeeding.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

OsmoPrep may affect how other medicines work. Medicines taken by mouth may not be absorbed properly when taken within 1 hour before the start of OsmoPrep.

Especially tell your doctor if you take:

- water pills (diuretics)
- medicines for blood pressure or heart problems
- medicines for kidney problems
- medicines for pain, such as aspirin or a non-steroidal anti-inflammatory drug (NSAID)
- medicine for seizures
- a laxative for constipation in the last 7 days. You should not take another medicine that contains sodium phosphate while you take OsmoPrep.

Ask your doctor or pharmacist if you are not sure if you take any of the medicines listed above.

Know the medicines you take. Keep a list of your medicines to show your doctor or pharmacist when you get a new prescription.

How should I take OsmoPrep?

- Take OsmoPrep exactly as prescribed by your doctor.
- **It is important for you to drink clear liquids before, during, and after taking OsmoPrep. This may help prevent kidney damage.** Examples of **clear liquids** are water, flavored water, lemonade (no pulp), ginger ale or apple juice. Do not drink any liquids colored purple or red.

You must read, understand, and follow these instructions to take OsmoPrep the right way:

On the evening before your colonoscopy, you will take a total of 20 OsmoPrep tablets, as follows:

1. Take 4 OsmoPrep tablets with 8 ounces of **clear liquids**.
2. **Wait 15 minutes.**
3. Take 4 more OsmoPrep tablets with 8 ounces of **clear liquids.**
4. Repeat steps 2 and 3 above, three more times. Make sure you wait 15 minutes after each time.

On the day of your colonoscopy, you will take a total of 12 OsmoPrep tablets, starting about 3 to 5 hours before your colonoscopy, as follows:

1. Take 4 OsmoPrep tablets with 8 ounces of **clear liquids.**
2. **Wait 15 minutes.**
3. Take 4 more OsmoPrep tablets with 8 ounces of **clear liquids.**
4. Repeat steps 2 and 3 one more time.

If you take too much OsmoPrep, call your doctor or get medical help right away.

What should I avoid while taking OsmoPrep?

- You should not take other laxatives or enemas made with sodium phosphate, while taking OsmoPrep.
- You should not use OsmoPrep if you have already used it in the last 7 days.

What are the possible side effects of OsmoPrep?

OsmoPrep can cause serious side effects, including:

- **See "What is the most important information I should know about OsmoPrep?"**
- **Changes in your blood tests.** Your doctor may do blood tests after you take OsmoPrep to check your levels of calcium, phosphate, potassium, and sodium in your blood. Tell your doctor if you have any symptoms of too much fluid loss, including:
  - vomiting
  - nausea
- Abnormal heart beat (arrhythmias)
- **Seizures or fainting (black-outs).** People who take a medicine that contains sodium phosphate, such as OsmoPrep, can have seizures or faint (become unconscious) even if they have not had seizures before. Tell your doctor right away if you have a seizure or faint while taking OsmoPrep.
- **Inflammatory bowel disease.**

The most common side effects of OsmoPrep are:

- bloating
- stomach (abdominal) pain
- nausea
- vomiting

Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of OsmoPrep. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store OsmoPrep?

- Store OsmoPrep at room temperature, between 15º to 30°C (59º to 86°F).
- Throw away any OsmoPrep that is not needed.

Keep OsmoPrep and all medicines out of the reach of children.

General information about OsmoPrep.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use OsmoPrep for a condition for which it was not prescribed. Do not give OsmoPrep to other people, even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about OsmoPrep. If you would like more information about OsmoPrep, talk with your doctor or pharmacist. You can ask your doctor or pharmacist for information that is written for healthcare professionals.

For more information, call 1-800-321-4576 (toll-free) or go to www.Salix.com.

What are the ingredients in OsmoPrep?

Active ingredients: sodium phosphate monobasic monohydrate and sodium phosphate dibasic anhydrous

Inactive ingredients: polyethylene glycol 8000 and magnesium stearate

OsmoPrep is gluten-free.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured for:
Salix Pharmaceuticals, a division of
Valeant Pharmaceuticals North America LLC
Bridgewater, NJ 08807 USA

9516400
70011844 (Outsert)

9516500
70011847 (Topsert)

Rev. 08/2016

PRINCIPAL DISPLAY PANEL - OsmoPrep 100 Tablet Bottle Label

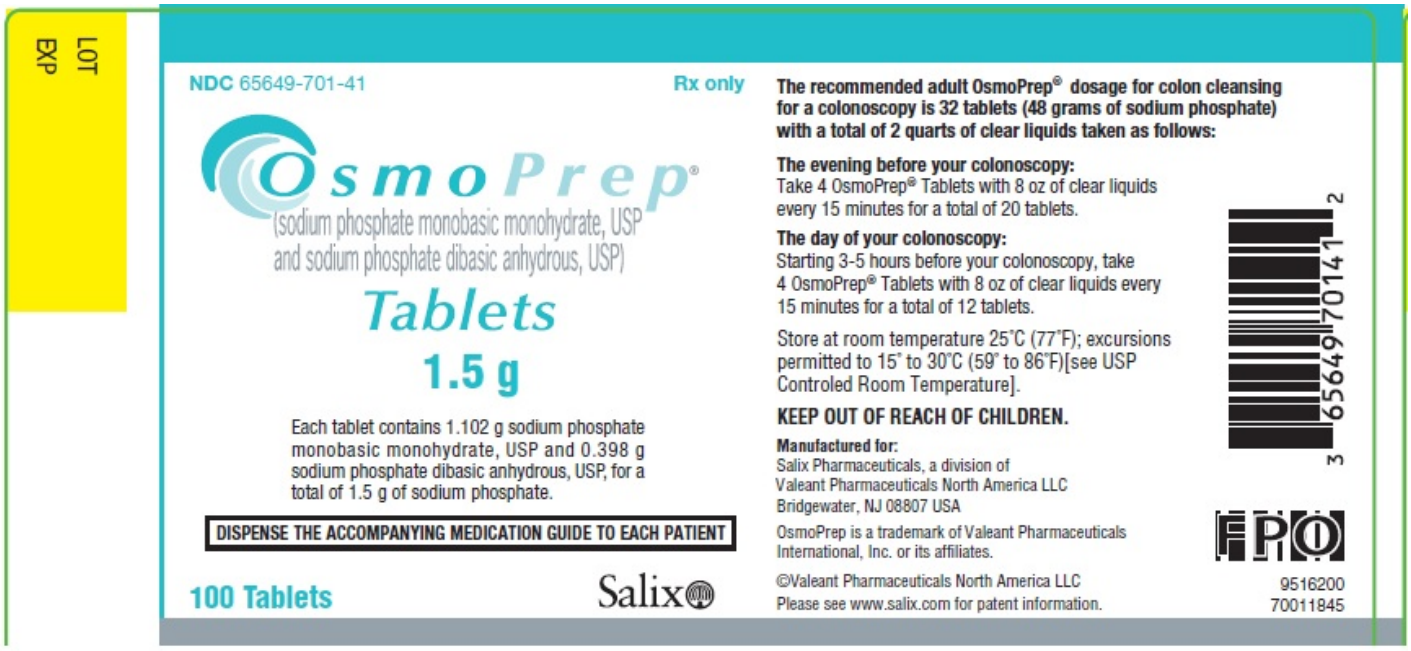
NDC 65649-701-41
Rx only

OsmoPrep®
(sodium phosphate monobasic monohydrate, USP
and sodium phosphate dibasic anhydrous, USP)
Tablets

1.5 g

DISPENSE THE ACCOMPANYING MEDICATION GUIDE TO EACH PATIENT

100 Tablets



OSMOPREP

sodium phosphate, monobasic, monohydrate, sodium phosphate, dibasic anhydrous tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:65649-701
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
SODIUM PHOSPHATE, MONOBASIC, MONOHYDRATE (UNII: 593YOG76RN) (PHOSPHATE ION - UNII:NK08V8K8HR)	SODIUM PHOSPHATE, MONOBASIC, MONOHYDRATE	1.102 g
SODIUM PHOSPHATE, DIBASIC, ANHYDROUS (UNII: 22ADO53M6F) (PHOSPHATE ION - UNII:NK08V8K8HR)	SODIUM PHOSPHATE, DIBASIC, ANHYDROUS	0.398 g

Inactive Ingredients

Ingredient Name	Strength
POLYETHYLENE GLYCOL 8000 (UNII: Q662QK8M3B)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	

Product Characteristics

Color	WHITE	**Score**	2 pieces
Shape	OVAL	**Size**	18mm
Flavor		**Imprint Code**	SLX;102
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:65649-701-41	100 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	05/15/2006	
2	NDC:65649-701-32	32 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	05/15/2006	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021892	05/15/2006	

Labeler - Salix Pharmaceuticals, Inc. (793108036)

Establishment

Name	Address	ID/FEI	Business Operations
Novel Laboratories, Inc.		793518643	MANUFACTURE(65649-701)