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PRESCRIBING ALERT[®]

Dear Healthcare Professional,

At *MPR*, we strive to bring you important drug information in a concise and timely fashion. In keeping with this goal, we are pleased to bring you this PRESCRIBING ALERT highlighting important updated labeling information about **OsmoPrep[®] (sodium phosphate monobasic monohydrate, USP, and sodium phosphate dibasic anhydrous, USP) Tablets** from **Salix Pharmaceuticals, Inc.**

All prescription oral sodium phosphate products for bowel cleansing prior to colonoscopy, including OsmoPrep Tablets, have added a Boxed Warning to the labeling. The final Boxed Warning label is below.

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]). It is important to use the dose and dosing regimen as recommended (PM/AM split dose).¹

OsmoPrep Tablets are indicated to cleanse the colon as a preparation for colonoscopy in adults 18 years of age or older.¹ This unique, virtually tasteless tablet formulation can be taken with any clear liquid, an attribute that may help to enhance patient compliance and satisfaction.² In clinical trials, 97% of patients were fully compliant with the OsmoPrep regimen.³ OsmoPrep has demonstrated consistently acceptable efficacy, resulting in a 100% *excellent or good* rating in ascending colon cleansing when used with the PM/AM split dosing regimen.^{4,*} It is important to use the dose and dosing regimen as recommended (PM/AM split dose) and patients should be advised to adequately hydrate before, during, and after the use of OsmoPrep.¹ To date, over four million prescriptions of sodium phosphate tablets have been written.³

* Data taken from a phase 2, randomized, investigator-blinded study with 12 study arms comparing various dosing regimens of sodium phosphate tablets. A rating of "excellent" or "good" was considered a response. The results reported here are from 1 arm (n=33), with a 32-tablet, split-dose regimen of OsmoPrep.

More information about the use of OsmoPrep Tablets is available in the current edition of *MPR*.

For your reference, please see enclosed full Prescribing Information, including the Boxed Warning, for OsmoPrep Tablets.

Sincerely,



Grace L. McBride
Editorial Director,
MPR Custom Programs

REFERENCES

1. OsmoPrep Tablets [package insert]. Morrisville, NC: Salix Pharmaceuticals, Inc; 2009.
2. Rex DK, Schwartz H, Goldstein M, et al. Safety and colon-cleansing efficacy of a new residue-free formulation of sodium phosphate tablets. *Am J Gastroenterol.* 2006;101(11):2594-2604.
3. Data on file, Salix Pharmaceuticals, Inc.
4. Wruble L, DeMicco M, Medoff J, et al. Residue-free sodium phosphate tablets (OsmoPrep) versus Visicol for colon cleansing: a randomized, investigator-blinded trial. *Gastrointest Endosc.* 2007;65(4):660-670.

Important Safety Information

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]).

It is important to use the dose and dosing regimen as recommended (PM/AM split dose).

Please see enclosed full Prescribing Information for OsmoPrep, including BOXED WARNINGS.

OsmoPrep[®] (sodium phosphate monobasic monohydrate, USP, and sodium phosphate dibasic anhydrous, USP) Tablets are indicated for cleansing of the colon as a preparation for colonoscopy in adults 18 years of age or older. Considerable caution should be advised before OsmoPrep is used in patients with severe renal insufficiency, congestive heart failure, ascites, unstable angina, gastric retention, ileus, severe chronic constipation, bowel perforation, toxic megacolon, gastric bypass or stapling surgery, or hypomotility syndrome. Use with caution in patients with impaired renal function, patients with a history of seizures or at higher risk of seizure, patients with higher risk of cardiac arrhythmias, known or suspected electrolyte disturbances (such as dehydration), or people taking drugs that affect electrolyte levels. Patients with electrolyte abnormalities such as hypernatremia, hyperphosphatemia, hypokalemia, or hypocalcemia should have their electrolytes corrected before treatment with OsmoPrep.

OsmoPrep is contraindicated in patients with a known allergy or hypersensitivity to sodium phosphate salts or any of its ingredients, and in patients with biopsy-proven acute phosphate nephropathy. In clinical trials, the most commonly reported adverse reactions (reporting frequency >3%) were abdominal bloating, nausea, abdominal pain, and vomiting. It is recommended that patients receiving OsmoPrep be advised to adequately hydrate before, during, and after the use of OsmoPrep.

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OSMOPREP[®] TABLETS

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

Company: Salix Pharmaceuticals R

Pharmacologic class: Osmotic bowel cleanser

Indications: Bowel cleansing prior to colonoscopy.

Adults: ≥18yrs: Evening before colonoscopy: 4 tablets with 8 ounces of clear liquid every 15 minutes for a total of 20 tablets; repeat on day of colonoscopy 3–5 hours before procedure for a total of 12 tablets. Wait 7 days before retreating.

Children: <18yrs: not recommended

Contraindications: Allergy or hypersensitivity to sodium phosphate salts or any of its ingredients. Biopsy-proven acute phosphate nephropathy.

Precautions: Increased age, hypovolemia, increased bowel transit time, active colitis, baseline kidney disease: increased risk of acute phosphate nephropathy. Severe renal insufficiency (CrCl<30mL/min). Impaired renal function. History of acute phosphate nephropathy. CHF. Unstable angina. Arrhythmias (consider pre-dose and post-colonoscopy ECGs). History of cardiomyopathy. Prolonged QT. Recent MI. Ascites. Gastric retention. Ileus or acute obstruction or pseudo-obstruction. Gastric bypass or stapling surgery. Severe chronic constipation. Bowel perforation. Toxic megacolon. Hypomotility syndrome. Inflammatory bowel disease. Correct electrolyte abnormalities before use.



For bowel cleansing prior to colonoscopy

Consider doing baseline and post-colonoscopy labs in patients at increased risk. History or risk of seizures. Maintain adequate hydration. Pregnancy (Cat.C).

Interactions: Avoid concomitant purgative agents (esp. sodium phosphate). Caution with drugs that prolong QT interval, affect electrolytes or renal function (eg, diuretics, ACEIs, ARBs, NSAIDs), or lower seizure threshold. May reduce absorption of concomitantly administered drugs.

Adverse Reactions: Abdominal bloating/pain, nausea, vomiting, dizziness, headache; rare: renal failure, acute phosphate nephropathy, nephrocalcinosis.

How Supplied: Tabs—100

 **OsmoPrep Tablets have never been recalled or withdrawn from the market**

Please see Important Safety Information on the last page.

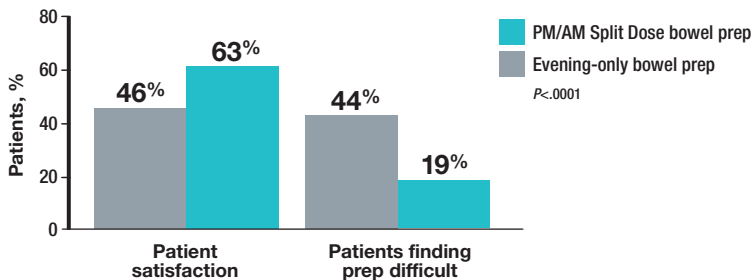
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ADDITIONAL INFORMATION ABOUT BOXED WARNING

- ✓ **No specific age restrictions are associated with Boxed Warning**
 - Patients at an increased age have an increased risk of acute phosphate nephropathy. Physicians should consider a patient's age, kidney function, and concomitant conditions before prescribing OsmoPrep Tablets¹
 - ✓ **Contraindications have changed**
 - OsmoPrep Tablets are contraindicated in patients with biopsy-proven acute phosphate nephropathy and in patients with a known allergy or hypersensitivity to sodium phosphate salts or any of its ingredients¹
 - ✓ **PM/AM split dosing**
 - OsmoPrep's boxed warning mandates PM/AM split dosing, which helps to minimize peak phosphate loads by separating the two doses of OsmoPrep Tablets¹
 - OsmoPrep's PM/AM split dosing aligns with the new 2008 ACG Guidelines for Colorectal Cancer Screening, which recommends that bowel preparations be given in split doses (half of the dose is given on the day of the procedure)²
-
- ✓ **Patients found PM/AM split dosing more satisfying and less difficult³**
 - 8 to 12 hours may elapse between last dose of an evening-only prep and colonoscopy during which chyme can reaccumulate in the ascending colon and obscure adequate visualization of the bowel⁴
 - Prep quality is inadequate for 1 in 4 patients, hindering detection of smaller lesions⁵
 - Procedures in poorly prepped patients are longer, more difficult, and more often incomplete⁶
 - PM/AM split dosing may improve patient tolerability and compliance by splitting the preparation process into two stages

PATIENTS REPORTED GREATER SATISFACTION AND LESS DIFFICULTY WITH PM/AM SPLIT DOSING



Source: Khan MA, et al.³

Please see Important Safety Information on the last page.

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✓ **AM dose works quickly and results are of short duration⁷**

RESULTS OF THE AM SERIES OF PM/AM SPLIT DOSE

Average onset of action	0.7 hours
Patients needing to evacuate bowels in transit	3 out of 200

Source: Linden TB, et al.⁷

- In a separate prospective observational study of 412 patients, the percentage of patients who took a PM/AM split dose prep and needed to make a restroom stop en route to their colonoscopy was not significantly different from patients who followed a single-dose regimen ($P=NS$)³

✓ **A clean colon provides greater visibility to detect abnormal growths⁸**

- Makes it easier to identify flat lesions, which are difficult to detect and are 10 times more likely to be cancerous than polyps
- Results of a cross-sectional study showed that 8.58% of patients in the study were found to have flat lesions
- About one third of flat lesions were found in the ascending colon, where chyme typically accumulates following evening-only preps⁴

Clean colon

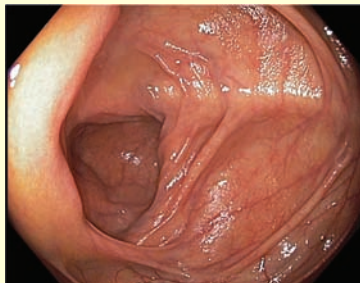


Image courtesy of Douglas K. Rex, MD
Indiana University School of Medicine.

Dirty colon

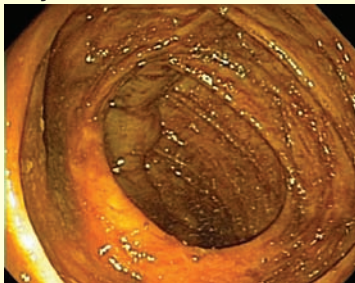


Image courtesy of Douglas K. Rex, MD
Indiana University School of Medicine.

✓ **Supports appropriate dosing while fostering hydration**

- Adequate hydration is recommended before, during, and after the use of OsmoPrep[®] (sodium phosphate monobasic monohydrate, USP, and sodium phosphate dibasic anhydrous, USP)¹
- Concomitant liquid consumption contributes to improved safety of sodium phosphate preparations¹
- Choice of clear liquid enhances tolerability and patient compliance⁹
- OsmoPrep has the lowest approved sodium phosphate content of any marketed sodium phosphate bowel regimen¹

Please see Important Safety Information on the last page.

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REFERENCES

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2. Rex DK et al. American College of Gastroenterology Guidelines for Colorectal Cancer Screening 2008. *Am J Gastroenterol* advance online publication, February 24, 2009;doi:10.1038/ajg.2009.104.
3. Khan MA, Wasiuddin N, Brown M. Patient acceptance, convenience, and efficacy of one-day versus two-day colonoscopy bowel preparation. Poster presented at: Digestive Disease Week; May 20, 2008; San Diego, CA.
4. Johanson J, Popp J, Cohen L, et al. A randomized, multicenter study comparing the safety and efficacy of sodium phosphate tablets with 2L polyethylene glycol solution plus bisacodyl tablets for colon cleansing. *Am J Gastroenterol*. 2007;102(10):2238-2246.
5. Harewood G, Sharma VK, de Garmo P. Impact of colonoscopy preparation quality on detection of suspected colonic neoplasia. *Gastrointest Endosc*. 2003;58(1):76-79.
6. Froelich F, Wietlisbach V, Gonvers J-J, Burnand B, Vader J-P. Impact of colonic cleansing on quality and diagnostic yield of colonoscopy: the European Panel of Appropriateness of Gastrointestinal Endoscopy European multicenter study. *Gastrointest Endosc*. 2005;61(3):378-384.
7. Linden TB, Wayne JD. Sodium phosphate preparation for colonoscopy: onset and duration of bowel activity. *Gastrointest Endosc*. 1999;50(6):811-813.
8. Soetikno RM, Kaltenbach T, Rouse RV, et al. Prevalence of nonpolypoid (flat and depressed) colorectal neoplasms in asymptomatic and symptomatic adults. *JAMA*. 2008;299(9):1027-1035.
9. Wruble L, Demicco M, Medoff J, et al. Residue-free sodium phosphate tablets (OsmoPrep) versus Viscol for colon cleansing: a randomized, investigator-blinded trial. *Gastrointest Endosc*. 2007;65(4):660-670.