MOVIPREP - polyethylene glycol 3350, sodium sulfate, sodium chloride, potassium chloride, sodium ascorbate and ascorbic acid
Physicians Total Care, Inc.

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1 INDICATIONS AND USAGE

MoviPrep® is indicated for cleansing of the colon as a preparation for colonoscopy in adults 18 years of age or older.

2 DOSAGE AND ADMINISTRATION

The MoviPrep dose for colon cleansing for adult patients is 2 liters (approximately 64 ounces) of MoviPrep solution (with 1 additional liter of clear fluids) taken orally prior to the colonoscopy in one of the following ways:

1. **Split-dose MoviPrep regimen:** The evening before the colonoscopy, take the first liter of MoviPrep solution over one hour (one 8 ounce glass every 15 minutes) and then drink 0.5 liters (approximately 16 ounces) of clear fluid. Then, on the morning of the colonoscopy, take the second liter of MoviPrep solution over one hour and then drink 0.5 liters of clear liquid at least one hour prior to the start of the colonoscopy; or
2. **Evening only (Full-dose) MoviPrep regimen:** Around 6 PM in the evening before the colonoscopy, take the first liter of MoviPrep solution over one hour (one 8 ounce glass every 15 minutes) and then about 1.5 hours later take the second liter of MoviPrep solution over one hour. In addition, take 1 liter (approximately 32 ounces) of additional clear liquid during the evening before the colonoscopy.

Preparation of the MoviPrep solution:

MoviPrep solution is prepared by emptying the contents of 1 pouch A and 1 pouch B into a suitable glass container (or the container provided) and adding to the container 1 liter of lukewarm water. Mix the solution to ensure that the ingredients are completely dissolved. If the patient prefers, the MoviPrep solution can be refrigerated prior to drinking. The reconstituted solution should be used within 24 hours.

After consumption of the first liter of MoviPrep solution, the above mixing procedure should be repeated with the second pouch A and pouch B to reconstitute the second liter of the MoviPrep solution.

3 DOSAGE FORMS AND STRENGTHS

MoviPrep is available in a carton that contains 4 separate pouches (2 of pouch A and 2 of pouch B). Each pouch A contains 100 grams of polyethylene glycol (PEG) 3350, NF, 7.5 grams of sodium sulfate, USP, 2.691 grams of sodium chloride, USP, and 1.015 grams of potassium chloride, USP, plus the following excipients: aspartame, NF (sweetener), acesulfame potassium, NF (sweetener), and lemon flavoring. Each pouch B contains 4.7 grams of ascorbic acid, USP and 5.9 grams of sodium ascorbate, USP.

4 CONTRAINDICATIONS

MoviPrep is contraindicated in patients who have had a severe hypersensitivity reaction to any of its

components.

5 WARNINGS AND PRECAUTIONS

MoviPrep should be used with caution in patients with severe ulcerative colitis, ileus, gastrointestinal obstruction or perforation, gastric retention, toxic colitis, or toxic megacolon

General

Patients with impaired gag reflex and patients prone to regurgitation or aspiration should be observed during the administration of MoviPrep. If a patient experiences severe bloating, abdominal distention, or abdominal pain, administration should be slowed or temporarily discontinued until the symptoms abate. If gastrointestinal obstruction or perforation is suspected, appropriate tests should be performed to rule out these conditions before administration of MoviPrep®.

Phenylketonurics: MoviPrep contains phenylalanine – a maximum of 2.33 mg of phenylalanine per treatment.

No additional ingredients (e.g., flavorings) should be added to the MoviPrep solution.

Since MoviPrep contains sodium ascorbate and ascorbic acid, MoviPrep should be used with caution in patients with glucose-6-phosphate dehydrogenase (G-6-PD) deficiency especially G-6-PD deficiency patients with an active infection, with a history of hemolysis, or taking concomitant medications known to precipitate hemolytic reactions.

5.1 Seizures

There have been rare reports of generalized tonic-clonic seizures associated with use of polyethylene glycol colon preparation products in patients with no prior history of seizures. The seizure cases were associated with electrolyte abnormalities (e.g., hyponatremia, hypokalemia). The neurologic abnormalities resolved with correction of fluid and electrolyte abnormalities. Therefore, MoviPrep should be used with caution in patients using concomitant medications that increase the risk of electrolyte abnormalities [such as diuretics or angiotensin converting enzyme (ACE)-inhibitors] or in patients with known or suspected hyponatremia. Consider performing baseline and post-colonoscopy laboratory tests (sodium, potassium, calcium, creatinine, and BUN) in these patients.

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

In the MoviPrep trials, abdominal distension, anal discomfort, thirst, nausea, and abdominal pain were some of the most common adverse reactions to MoviPrep administration. Since diarrhea was considered as a part of the efficacy of MoviPrep, diarrhea was not defined as an adverse reaction in the clinical studies. Tables 1 and 2 display the most common drug-related adverse reactions of MoviPrep and its comparator in the controlled MoviPrep trials.

Table 1: The Most Common Drug-Related Adverse Reactions* (≥ 2%) in the Study of MoviPrep vs. 4 liter Polyethylene Glycol plus Electrolytes Solution

	MoviPrep® (split dose) N=180	**4L PEG + E† N=179**
	n (% = n/N)	n (% = n/N)
Malaise	35 (19.4)	32 (17.9)

Nausea	26 (14.4)	36 (20.1)
Abdominal pain	24 (13.3)	27 (15.1)
Vomiting	14 (7.8)	23 (12.8)
Upper abdominal pain	10 (5.6)	11 (6.1)
Dyspepsia	5 (2.8)	2 (1.1)

* Drug-related adverse reactions were adverse events that were possibly, probably, or definitely related to the study drug.
† 4L PEG + E is 4 liter Polyethylene Glycol plus Electrolytes Solution

Table 2: The Most Common Drug-Related Adverse Reactions* (≥ 5%) in the Study of MoviPrep vs. 90 mL Oral Sodium Phosphate Solution

	MoviPrep® (evening-only) (full dose) N=169	**90 mL OSPS† N=171**
	n (% = n/N)	n (% = n/N)
Abdominal distension	101 (59.8)	70 (40.9)
Anal discomfort	87 (51.5)	89 (52.0)
Thirst	80 (47.3)	112 (65.5)
Nausea	80 (47.3)	80 (46.8)
Abdominal paint	66 (39.1)	55 (32.2)
Sleep disorder	59 (34.9)	49 (28.7)
Rigors	57 (33.7)	51 (29.8)
Hunger	51 (30.2)	121 (70.8)
Malaise	45 (26.6)	90 (52.6)
Vomiting	12 (7.1)	14 (8.2)
Dizziness	11 (6.5)	31 (18.1)
Headache	3 (1.8)	9 (5.3)
Hypokalemia	0 (0)	10 (5.8)
Hyperphosphatemia	0 (0)	10 (5.8)

* Drug-related adverse reactions were adverse events that were possibly, probably, or definitely related to the study drug. In addition to the recording of spontaneous adverse events, patients were also specifically asked about the occurrence of the following symptoms: shivering, anal irritations, abdominal bloating or fullness, sleep loss, nausea, vomiting, weakness, hunger sensation, abdominal cramps or pain, thirst sensation, and dizziness.
† OSPS is Oral Sodium Phosphate Solution

Isolated cases of urticaria, rhinorrhea, dermatitis, and anaphylactic reaction have been reported with PEG-based products and may represent allergic reactions.

Published literature contains isolated reports of serious adverse events following the administration of PEG-based products in patients over 60 years of age. These adverse events included upper gastrointestinal bleeding from a Mallory-Weiss tear, esophageal perforation, asystole, and acute pulmonary edema after aspirating the PEG-based preparation.

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 MoviPrep. 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 MoviPrep, or a combination of these factors.

General: Hypersensitivity reactions including anaphylaxis, rash, urticaria, lip and facial swelling, dyspnea, chest tightness and throat tightness.

7 DRUG INTERACTIONS

Oral medication administered within 1 hour of the start of administration of MoviPrep may be flushed from the gastrointestinal tract and the medication may not be absorbed.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy: Teratogenic Effects

Pregnancy Category C. Animal reproduction studies have not been performed with MoviPrep. It is also not known if MoviPrep can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. MoviPrep should be given to a pregnant woman only if clearly needed.

8.3 Nursing Mothers

Because many drugs are excreted in human milk, caution should be exercised when MoviPrep is administered to a nursing woman.

8.4 Pediatric Use

The safety and effectiveness of MoviPrep in pediatric patients has not been established.

8.5 Geriatric Use

Of the 413 patients in clinical studies receiving MoviPrep, 91 (22%) patients were aged 65 or older, while 25 (6%) patients were over 75 years of age. No overall differences in safety or effectiveness were observed between geriatric patients and younger patients, and other reported clinical experience has not identified differences in responses between geriatric patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

10 OVERDOSAGE

There have been no reported cases of overdose with MoviPrep. Purposeful or gross accidental ingestion of more than the recommended dose of MoviPrep might be expected to lead to severe electrolyte disturbances, including hyponatremia and/or hypokalemia, as well as dehydration and hypovolemia, with signs and symptoms of these disturbances. The patient who has taken an overdose should be monitored carefully, and treated symptomatically for complications until stable.

11 DESCRIPTION

MoviPrep® consists of 4 separate pouches (2 of pouch A and 2 of pouch B) containing white to yellow powder for reconstitution. Each pouch A contains 100 grams of polyethylene glycol (PEG) 3350, NF, 7.5 grams of sodium sulfate, USP, 2.691 grams of sodium chloride, USP, and 1.015 grams of potassium chloride, USP, plus the following excipients: aspartame, NF (sweetener), acesulfame potassium, NF (sweetener), and lemon flavoring. Each pouch B contains 4.7 grams of ascorbic acid, USP and 5.9 grams of sodium ascorbate, USP. When 1 pouch A and 1 pouch B are dissolved together in water to a volume of 1 liter, MoviPrep (PEG-3350, sodium sulfate, sodium chloride, potassium chloride, sodium ascorbate, and ascorbic acid) is an oral solution having a lemon taste.

The entire, reconstituted, 2-liter MoviPrep colon preparation contains 200 grams of PEG-3350, 15 grams of sodium sulfate, 5.38 grams of sodium chloride, 2.03 grams of potassium chloride, 9.4 grams of ascorbic acid, and 11.8 grams of sodium ascorbate plus the following excipients: aspartame (sweetener), acesulfame potassium (sweetener), and lemon flavoring.

12 CLINICAL PHARMACOLOGY

MoviPrep produces a watery stool leading to cleansing of the colon. The osmotic activity of polyethylene glycol 3350, sodium sulfate, sodium chloride, potassium chloride, sodium ascorbate, and ascorbic acid, when taken with 1 liter of additional clear fluid, usually results in no net absorption or excretion of ions or water.

The pharmacokinetics of MoviPrep have not been studied in patients with renal or hepatic insufficiency.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate the carcinogenic potential have not been performed with MoviPrep®. Studies to evaluate potential for impairment of fertility or mutagenic potential have not been performed with MoviPrep®.

14 CLINICAL STUDIES

The colon cleansing efficacy and safety of MoviPrep was evaluated in two randomized, actively-controlled, multi-center, investigator-blinded, phase 3 trials in patients scheduled to have an elective colonoscopy.

In the first study, patients were randomized to one of the following two colon preparation treatments: 1) 2 liters of MoviPrep with 1 additional liter of clear fluid split into two doses (during the evening before and the morning of the colonoscopy) and 2) 4 liters of polyethylene glycol plus electrolytes solution (4L PEG + E) split into two doses (during the evening before and the morning of the colonoscopy). Patients were allowed to have a morning breakfast, a light lunch, clear soup and/or plain yogurt for dinner. Dinner had to be completed at least one hour prior to initiation of the colon preparation administration.

The primary efficacy endpoint was the proportion of patients with effective colon cleansing as judged by blinded gastroenterologists on the basis of videotapes recorded during the colonoscopy. The blinded gastroenterologists graded the colon cleansing twice (during introduction and withdrawal of the colonoscope) and the poorer of the two assessments was used in the primary efficacy analysis.

The efficacy analysis included 308 adult patients who had an elective colonoscopy. Patients ranged in age from 18 to 88 years old (mean age about 59 years old) with 52% female and 48% male patients. Table 3 displays the results.

Table 3: Effectiveness of Overall Colon Cleansing in the Study of MoviPrep vs 4 Liter Polyethylene Glycol plus Electrolytes Solution

	Responders A* or B† (%)	**C‡ (%)**	**D§ (%)**
MoviPrep® (N=153)	88.9	9.8	1.3

4L PEG + E¶ (N=155)	94.8	4.5	0.6

* A: colon empty and clean or presence of clear liquid, but easily removed by suction
† B: brown liquid or semisolid remaining amounts of stool, fully removable by suction or displaceable, thus allowing a complete visualization of the gut mucosa
‡ C: semisolid amounts of stool, only partially removable with a risk of incomplete visualization of the gut mucosa
§ D: semisolid or solid amounts of stool; consequently colonoscopy incomplete or needed to be terminated. 4 L PEG+E's responder rate was not significantly higher than MoviPrep's responder rate.
¶ 4L PEG + E is 4 Liter Polyethylene Glycol plus Electrolytes Solution

In the second study, patients were randomized to one of the following two colon preparation treatments: 1) 2 liters of MoviPrep with 1 additional liter of clear fluid in the evening prior to the colonoscopy and 2) 90 mL of oral sodium phosphate solution (90 mL OSPS) with at least 2 liters of additional clear fluid during the day and evening prior to the colonoscopy. Patients randomized to MoviPrep therapy were allowed to have a morning breakfast; a light lunch; and clear soup and/or plain yogurt for dinner. Dinner had to be completed at least one hour prior to initiation of the colon preparation administration.

The primary efficacy endpoint was the proportion of patients with effective colon cleansing as judged by the colonoscopist and one blinded gastroenterologist (on the basis of videotapes recorded during the colonoscopy). In case of a discrepancy between the colonoscopist and the blinded gastroenterologist, a second blinded gastroenterologist made the final efficacy determination.
The efficacy analysis included 280 adult patients who had an elective colonoscopy. Patients ranged in age from 21 to 76 years old (mean age about 53 years old) with 47% female and 53% male patients. Table 4 displays the results.

Table 4: Effectiveness of Overall Colon Cleansing in the Study of MoviPrep vs 90mL Oral Sodium Phosphate Solution

	Responders A* or B† (%)	**C‡ (%)**	D§ (%)
MoviPrep® (N=137)	73.0	23.4	3.6
90 mL OSPS¶ (N=143)	64.4	29.4	6.3

* A: empty and clean or clear liquid (transparent, yellow, or green)
† B: brown liquid or semisolid remaining small amounts of stool, fully removable by suction or displaceable allowing a complete visualization of the underlying mucosa
‡ C: semi solid only partially removable/displaceable stools; risk of incomplete examination of the underlying mucosa
§ D: heavy and hard stool making the segment examination uninterpretable and, consequently, the colonoscopy needed to be terminated
¶
OSPS is Oral Sodium Phosphate Solution
MoviPrep's responder rate was not significantly higher than OSPS's responder rate.

16 HOW SUPPLIED/STORAGE AND HANDLING

MoviPrep® is supplied in powdered form. MoviPrep is administered as an oral solution after reconstitution.

NDC 54868-5890-0, MoviPrep, single use carton.

Each carton contains a disposable container for reconstitution of MoviPrep® and an inner carton containing 4 pouches (2 of pouch A and 2 of pouch B).

Rx only

STORAGE

Store carton/container at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). When reconstituted, store upright and keep solution refrigerated. Use within 24 hours.

17 PATIENT COUNSELING INFORMATION

Important Precautions Regarding MOVIPREP

MoviPrep produces a watery stool which cleanses the colon before colonoscopy. It is recommended that patients receiving MoviPrep be advised to adequately hydrate before, during, and after the use of MoviPrep. Patients may have clear soup and/or plain yogurt for dinner, finishing the evening meal at least one hour prior to the start of MoviPrep treatment. No solid food should be taken from the start of MoviPrep treatment until after the colonoscopy.

What Patients Should Know About Adverse Reactions

The first bowel movement may occur approximately 1 hour after the start of MoviPrep administration. Abdominal bloating and distention may occur before the first bowel movement. If severe abdominal discomfort or distention occurs, stop drinking temporarily or drink each portion at longer intervals until these symptoms disappear.

Manufactured by:
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Netherlands

For:
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Morrisville, NC 27560

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VENART xxx-x/June 09

Product protected by U.S. Patent No. 7169381 and other pending applications

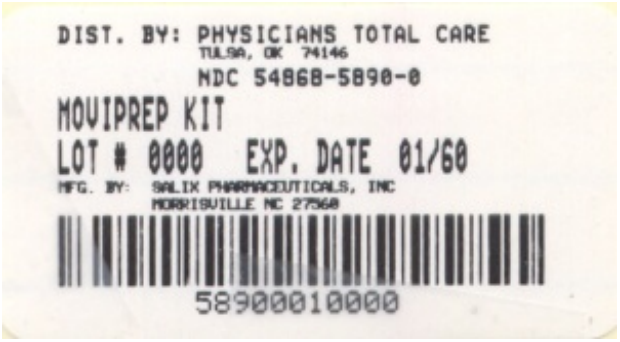
PRINCIPAL DISPLAY PANEL

MoviPrep®
(PEG-3350, Sodium Sulfate, Sodium Chloride, Potassium Chloride, Sodium Ascorbate and Ascorbic

Acid for Oral Solution)

Phenylketonurics:
contains phenylalanine – a maximum of 2.33 mg per course of treatment.

This carton contains
One container for reconstitution of **MoviPrep®**



MOVIPREP

polyethylene glycol 3350, sodium sulfate, sodium chloride, potassium chloride, sodium ascorbate and ascorbic acid kit

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:54868-5890(NDC:65649-201)

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:54868-5890-0	1 in 1 CONTAINER		

Quantity of Parts		
Part #	**Package Quantity**	**Total Product Quantity**
Part 1	2 POUCH	2 L
Part 2	2 POUCH	2 L

Part 1 of 2

POUCH A

polyethylene glycol 3350,sodium sulfate,anhydrous,sodium chloride,potassium chloride solution

Product Information	
Item Code (Source)	NDC:54868-5890
Route of Administration	ORAL

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
POLYETHYLENE GLYCOL 3350 (UNII: G2M7P15E5P) (POLYETHYLENE GLYCOL 3350 - UNII:G2M7P15E5P)	POLYETHYLENE GLYCOL 3350	100 g in 1 L
SODIUM SULFATE (UNII: 0YPR65R21J) (SODIUM CATION - UNII:LYR4M0NH37)	SODIUM SULFATE	7.5 g in 1 L
SODIUM CHLORIDE (UNII: 451W47IQ8X) (SODIUM CATION - UNII:LYR4M0NH37)	SODIUM CHLORIDE	2.69 g in 1 L
POTASSIUM CHLORIDE (UNII: 660YQ98I10) (POTASSIUM CATION - UNII:295O53K152)	POTASSIUM CHLORIDE	1.015 g in 1 L

Inactive Ingredients

Ingredient Name	Strength
ASPARTAME (UNII: Z0H242BBR1)	
LEMON (UNII: 24RS0A988O)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1		1 L in 1 POUCH		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021881	05/30/2008	

Part 2 of 2

POUCH B

ascorbic acid, sodium ascorbate solution

Product Information

Item Code (Source)	NDC:54868-5890
Route of Administration	ORAL

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ASCORBIC ACID (UNII: PQ6CK8PD0R) (ASCORBIC ACID - UNII:PQ6CK8PD0R)	ASCORBIC ACID	4.7 g in 1 L
SODIUM ASCORBATE (UNII: S033EH8359) (SODIUM CATION - UNII:LYR4M0NH37)	SODIUM ASCORBATE	5.9 g in 1 L

Inactive Ingredients

Ingredient Name	Strength
ACESULFAME POTASSIUM (UNII: 23OV73Q5G9)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1		1 L in 1 POUCH		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021881	05/30/2008	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021881	05/30/2008	

Labeler - Physicians Total Care, Inc. (194123980)

Establishment

Name	Address	ID/FEI	Business Operations
Physicians Total Care, Inc.		194123980	relabel

Revised: 11/2009 Physicians Total Care, Inc.