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(54) Title: BOWEL CLEANSING COMPOSITIONS AND METHODS

(57) Abstract: Methods and kits aid in preparing a patient for a colon procedure. In some embodiments, an effective amount of sodium phosphate, an effective amount of polyethylene glycol, an effective amount of bisacodyl, and an effective amount of psyllium are administered to the patient during a 24-hour period just prior to the colon procedure to provide a bowel cleansing of the patient for the colon procedure. In some embodiments, a kit includes an effective amount of sodium phosphate, an effective amount of polyethylene glycol, an effective amount of bisacodyl, and an effective amount of psyllium. The methods and kits may optionally include lubiprostone, linaclotide, and/or naloxegol for administration to the patient to provide a more thorough bowel cleansing.

BOWEL CLEANSING COMPOSITIONS AND METHODS

REFERENCE TO RELATED APPLICATIONS

This application claims one or more inventions which were disclosed in Provisional Application Number 62/191,681, filed July 13, 2015, entitled "BOWEL CLEANSING COMPOSITIONS AND METHODS". The benefit under 35 USC §119(e) of the United States provisional application is hereby claimed, and the aforementioned application is hereby incorporated herein by reference.

The subject matter of this application is related to co-pending application serial no. 13/724,931, filed December 21, 2012, entitled "BOWEL CLEANSING COMPOSITION" and application serial no. 10/756,269, filed January 14, 2004, entitled "BOWEL CLEANSING COMPOSITION", now abandoned, which is a continuation-in-part of application serial no. 10/194,251, filed July 15, 2002, entitled "BOWEL CLEANSING COMPOSITION", now U.S. Patent No. 8,361,452, issued January 29, 2013. The aforementioned applications are hereby incorporated herein by reference.

BACKGROUND OF THE INVENTION

FIELD OF THE INVENTION

The invention pertains to the field of medicine. More particularly, the invention pertains to compositions and methods for rapid bowel cleansing which are particularly useful for preparing the bowel prior to surgery or diagnostic procedures such as colonoscopies.

DESCRIPTION OF RELATED ART

Gastrointestinal agents for regulating bowel movement are conveniently placed into two categories: laxatives and bowel cleansers.

Laxatives are formulated for long term use, with the intention of eliminating constipation and obtaining a regular bowel function. Many laxatives work by stimulating bowel motility (peristalsis) in various ways, as by distending the gut with bulking or

osmotic agents, or by directly stimulating the bowel nerves or muscles with stimulant laxatives. Other laxatives function as stool softeners or lubricants. The various types of laxatives are often combined in attempts to maximize efficacy or to reduce side effects of the agents.

Bowel cleansers, also called purgatives, cathartics, and lavages, are formulated for rapid emptying of the bowel and are intended for short-term use only. They are commonly used as "bowel preps" for emptying the bowel prior to surgery, childbirth, or diagnostic procedures and usually include an osmotic or stimulant laxative administered by either the oral route or the anal route. While purgatives formulated for patient use as enemas are often prescribed before examinations, they are awkward to handle and are frequently not properly administered, so orally-administered preparations are generally preferred. Conventional orally-administered compositions for rapid bowel cleansing in common use, however, have disadvantages which discourage patient compliance.

The most commonly prescribed oral bowel preps today for bowel examination include sodium phosphate compositions in varying proportions of mono-and dibasic species and polyethylene glycol (PEG) in combination with electrolytes.

Sodium phosphate is a saline osmotic laxative, sold, for example, under the trademark Fleet Phospho-Soda® (C.B. Fleet Co., Lynchburg, VA), which contains both monobasic and dibasic uncoated sodium phosphate powders. It is also sold under the trademark Visicol® as monobasic and dibasic sodium phosphates in tablet form. This laxative, when formulated and used as a bowel cleanser, is associated with nausea, vomiting, and symptoms of electrolyte imbalance; the product also has an unpleasant taste. As a result, patient compliance is difficult to obtain, particularly when the cleanser is supplemented with, for example, another saline agent such as a magnesium salt, or a bowel stimulant such as bisacodyl.

While PEG is known for its successful use as a long-term osmotic laxative in combination with dietary fiber (as described in U.S. Pat. No. 5,710,183, issued January 20, 1998 to Halow, and incorporated herein by reference), PEG purgatives, such as those sold under the trademark Colyte® (Braintree Laboratories, Braintree, MA), have poor patient compliance. They have an unpleasant taste, and the amount and frequency of fluid the

patient is required to drink, typically eight fluid ounces every ten minutes over several hours, frequently causes severe bloating and attendant nausea. Further, although these purgatives normally include electrolytes to counterbalance electrolyte loss during treatment, symptoms of electrolyte imbalance are, notwithstanding, often experienced by the patient.

SUMMARY OF THE INVENTION

Methods and kits aid in preparing a patient for a colon procedure. In some embodiments, an effective amount of sodium phosphate, an effective amount of polyethylene glycol, an effective amount of bisacodyl, and an effective amount of psyllium are administered to the patient during a 24-hour period just prior to the colon procedure to provide a bowel cleansing of the patient for the colon procedure. In some embodiments, a kit includes an effective amount of sodium phosphate, an effective amount of polyethylene glycol, an effective amount of bisacodyl, and an effective amount of psyllium. The methods and kits may optionally include lubiprostone, linaclotide, and/or naloxegol for administration to the patient to provide a more thorough bowel cleansing.

In one embodiment, a method of preparing a patient for a colon procedure includes administering, to the patient during a 24-hour period just prior to the colon procedure, an effective amount of sodium phosphate, an effective amount of polyethylene glycol, an effective amount of bisacodyl, an effective amount of psyllium and an effective amount of lubiprostone to provide a bowel cleansing of the patient for the colon procedure.

In another embodiment, a method of preparing a patient for a colon procedure includes administering, to the patient during a 24-hour period just prior to the colon procedure, an effective amount of sodium phosphate, an effective amount of polyethylene glycol, an effective amount of bisacodyl, an effective amount of psyllium and an effective amount of linaclotide to provide a bowel cleansing of the patient for the colon procedure.

In yet another embodiment, a method of preparing a patient for a colon procedure includes administering to the patient during a 24-hour period just prior to the colon procedure, an effective amount of naloxegol and, after administering the effective amount of naloxegol, administering an effective amount of sodium phosphate, an effective amount

of polyethylene glycol, an effective amount of bisacodyl, and an effective amount of psyllium to provide a bowel cleansing of the patient for the colon procedure.

In another embodiment, a method of preparing a patient for a colon procedure includes administering to the patient during a 24-hour period just prior to the colon procedure, an effective amount of sodium phosphate, an effective amount of polyethylene glycol, an effective amount of bisacodyl, and an effective amount of psyllium to provide a bowel cleansing of the patient for the colon procedure; and administering to the patient a low-residue meal after administering at least one dose of the effective amount of sodium phosphate, the effective amount of polyethylene glycol, the effective amount of bisacodyl, and the effective amount of psyllium, but prior to the colon procedure.

In another embodiment, a method of preparing a patient for a colon procedure includes administering to the patient during a 24-hour period just prior to the colon procedure, an effective amount of sodium phosphate, an effective amount of polyethylene glycol, an effective amount of bisacodyl, and an effective amount of psyllium, and flushing a lining of the bowel with carbonated water.

In another embodiment, a method of preparing a child or adolescent patient between 8 and 18 years of age for a colon procedure includes administering to the patient during a 24-hour period just prior to the colon procedure about 2 to 7.5 grams of sodium phosphate, about 1.2 to 1.8 grams of polyethylene glycol per kilogram of weight of the patient, about 5 to 15 mg of bisacodyl, and about 1.5 to 4 grams of psyllium to provide a bowel cleansing of the patient for the colon procedure.

In another embodiment, a kit for cleansing a bowel of a renal patient for a colon procedure, the kit includes an effective amount of magnesium citrate (1:1), an effective amount of polyethylene glycol, an effective amount of bisacodyl, and an effective amount of psyllium, where administration of the effective amount of sodium phosphate, the effective amount of polyethylene glycol, the effective amount of bisacodyl, and the effective amount of psyllium to the patient during a 24-hour period provides a bowel cleansing of the renal patient.

In yet another embodiment, a method of preparing a renal patient for a colon procedure includes administering to the patient during a 24-hour period just prior to the

colon procedure, an effective amount of magnesium citrate (1:1), an effective amount of polyethylene glycol, an effective amount of bisacodyl, and an effective amount of psyllium to provide a bowel cleansing of the patient for the colon procedure.

In another embodiment, a kit for cleansing a bowel of a patient for a colon procedure, the kit includes an effective amount of sodium phosphate, an effective amount of polyethylene glycol, an effective amount of bisacodyl, an effective amount of psyllium, and at least one additional component selected from the group consisting of an effective amount of lubiprostone, an effective amount of linaclotide, and an effective amount of naloxegol. Administration of the effective amount of sodium phosphate, the effective amount of polyethylene glycol, the effective amount of bisacodyl, the effective amount of psyllium and the at least one additional component to the patient during a 24-hour period just prior to the colon procedure provides a bowel cleansing of the patient.

DETAILED DESCRIPTION OF THE INVENTION

Administration of an effective amount of sodium phosphate, an effective amount of polyethylene glycol, an effective amount of bisacodyl, and an effective amount of psyllium to a patient during a 24-hour period prior to a colon procedure preferably provides a bowel cleansing of the patient for the colon procedure. In some embodiments, lubiprostone or linaclotide are also administered to the patient prior to the colon procedure.

The compositions described herein stimulate the small bowel and the small bowel helps flush the colon without irritating the bowel. This results in a better, less irritating bowel cleansing than prior art compositions.

In some embodiments, any food-grade or pharmaceutical-grade PEG may be used in a bowel cleansing composition. For convenience of use in preparing and using the bowel cleansing composition, polymers having molecular weights above about 900, which are solid at room temperature and soluble in or miscible with water, are preferred. Polymers having average molecular weights between about 3000 and 8000 are exemplary; PEG 4000, which is nearly odorless and tasteless and widely available in “pharmaceutical grade”/United States Pharmacopeia (USP) grade, or PEG 3350, are very suitable. A

proprietary laxative, sold under the trademark MiraLax® (Braintree Laboratories, Braintree, MA), is a useful source of PEG 3350 powder readily soluble in water. Other suitable PEG powders are commercially available, as from the Spectrum Chemical Mfg. Company, Gardena, CA. Non-powdered PEG is preferably comminuted to a particle size that is readily soluble in water before use.

The bowel cleansing composition preferably includes a sodium phosphate powder in the form of a pharmaceutical USP grade free flowing powder of anhydrous dibasic sodium phosphate (Na_2HPO_4, disodium phosphate), optionally in combination with monobasic sodium phosphate monohydrate ($NaH_2PO_4 \cdot H_2O$, monosodium phosphate), or anhydrous, such as conventionally used in saline laxatives, for example, the powders described in the Fleet Phospho-Soda® laxative composition discussed above. The phosphate powder provides a bowel cleansing composition with a saline osmotic effect, which complements the effect of the PEG component and is used in amounts which provide the desired osmolarity for this purpose.

To administer the bowel cleansing composition, the phosphate and PEG powders are preferably dissolved by mixing into an aqueous carrier, which may be any appropriate predetermined desired aqueous carrier, such as water or juice.

PEG and phosphate powder are combined in amounts that provide a bowel cleansing composition, which preferably evacuates the bowel in the course of a few (3-4) hours. In some embodiments, a dry preparation bowel cleansing composition contains about 60 to 80% by weight PEG and 20 to 40% by weight of phosphate component. The term "phosphate component", as used herein, refers to either disodium phosphate alone, or disodium phosphate in combination with monosodium phosphate. In some embodiments, the amount of PEG in a bowel cleansing composition is about 70 to 80% by weight, and 20 to 30% by weight sodium phosphate, based on the total amount of PEG and phosphate; the combined PEG and phosphate should make up no less than about 80% by weight of a bowel cleansing composition containing additives for optimum results. Compositions containing about 75 to 80% by weight PEG and 20 to 25% by weight phosphate are particularly contemplated. Generally, at least a majority (greater than about 50% by weight) of the phosphate present is disodium phosphate; if monosodium phosphate is

included in the composition, it should usually make up less than one-half, and preferably less than one-quarter, of the phosphate content of the composition.

To formulate a convenient single dosage drink, a dry prep composition containing from about 45 to 70 grams powdered PEG and 10 to 30 grams phosphate powder, preferably about 55 to 65 grams PEG and 15 to 25 grams phosphate powder, is dissolved or suspended in an aqueous liquid of choice, such as water, tea, or juice. In an exemplary drink formulation, a single dose dry prep composition containing from about 58 to 63 gram PEG and from about 15 to 20 grams phosphate powder, for example, 60 grams powdered PEG and 18 grams sodium phosphate powder, preferably disodium phosphate powder, is dissolved in about 1 to 1.5 quarts of water or other aqueous liquid, for oral ingestion. Alternatively, the compositions may be dissolved in a smaller portion of water, such as eight fluid ounces, and the remainder of the liquid taken in conjunction with this solution. The amount of water or other aqueous medium, in which the dry prep composition is dissolved or which is taken with the dry prep composition, is not critical; however, for optimum bowel cleansing, at least about a pint should be used, and preferably at least a quart, depending upon the patient's total liquid intake during the treatment.

In some embodiments, lower molecular weight PEG polymers such as PEG 400, which are liquid at room temperature, may be used as a base, and the phosphate powder dissolved or dispersed therein; the solution may then be diluted to taste with the desired aqueous liquid.

The single dosage drinks so prepared are taken from twice per day to four times per day on the day preceding the colonoscopy or other procedure, depending upon the degree of clean-out required and the presence of complicating bowel conditions such as constipation.

For a typical patient, taking the bowel cleansing composition twice per day for one day provides the desired result. If, however, the patient has failed a standard preparation, a two day preparation is recommended. Preferably, the patient is restricted to a clear liquid diet while on the regimen, i.e., a diet of liquids containing no significant solid material. Suitable clear liquids include, but are not limited to, apple juice, tea, plain gelatin, 7-Up®

soft drink, Sprite® soft drink, chicken broth, and beef broth. If the patient receives a sufficient amount of liquids containing sodium and potassium ions to satisfy hunger, no supplemental electrolytes need be used with the PEG/phosphate compositions.

For added potency in certain clinical applications, the compositions may be taken in conjunction with a bowel stimulant such as bisacodyl, generally available over-the-counter in products sold, for example, under the trademarks Dulcolax® or BiscoLax®. In some embodiments, bisacodyl should not be taken in powder form to avoid neutralization with stomach acids. Enteric-coated 10 milligram tablets once or twice a day may be suitable. Two 5-mg tablets may be taken as an alternative to one 10-mg tablet.

The bowel cleansing compositions may include, or be taken in conjunction with, conventional additives such as flavoring or coloring agents. While not presently recommended, an herbal bowel stimulant such as Cascara sagrada may also be included in or taken in conjunction with the bowel cleansing compositions. Additionally, psyllium or other fiber commonly used as a stool-bulking agent may be optionally added to or taken with the bowel cleansing compositions, both for its laxative properties and its potential ability to counteract any adverse effects of the other components.

Patients were prepared for colonoscopy with a bowel cleansing composition of 60 grams PEG powder and 18 grams disodium phosphate powder per dose.

Each patient was given two single-dose packets of bowel cleansing composition for self-administration on the day preceding the colonoscopy, with instructions to dissolve each dose in water and drink the first dose at 10 a.m. and the second at 4 p.m. For each patient, a clear liquid diet was prescribed for that day. A flavor packet containing powdered Crystal Light® iced tea was provided for use as desired with the bowel cleansing composition to encourage drinking.

A 61 year-old female had weight loss and decrease in appetite. She underwent a clear liquid diet the day before with bowel cleansing composition taken at 10 a.m. and at 4 p.m. Good prep and adequate view of the colon was verified by multiple photographs, including a view of the transverse colon, during colonoscopy. She had no complaints of cramping or complaints of nausea but a mild dislike of taste.

An 86 year-old female with a history of anemia underwent bowel prep, taking a bowel cleansing composition twice the day before examination with a clear liquid diet. There was adequate clean out and a good view of the entire colon, including the sigmoid colon, with no abnormalities found in the colon.

A 62 year-old male with a hemorrhoidal bleed and diarrhea underwent a colonoscopy. A bowel cleansing composition at 10 a.m. and 4 p.m. and a clear liquid diet were prescribed. He had no complaints of nausea, vomiting, or discomfort and no complaints of taste abnormalities. He was given a flavor packet to use as needed.

A 74 year-old male with a history of colon polyps, scheduled for a surveillance colonoscopy, underwent bowel prep and clean out the day before using the bowel cleansing composition at 10 a.m. and 4 p.m. with one Dulcolax 10 milligram tablet. Adequate clean out showed diverticulosis at the sigmoid colon. Mild rectal irritation and inflammation with a good view of the entire colon were verified by video photographs, including the descending colon, taken during colonoscopy. Tolerance of the prep and slight complaint about taste, but no cramping sensation. No nausea and vomiting occurred that he has had with other preps.

A 50 year-old female with a first degree relative with colon cancer underwent surveillance colonoscopy. The patient took the bowel cleansing composition at 10 a.m. and 4 p.m.; some stool was found in the sigmoid colon. There was no liquid, able to suction out completely and got a good visualization of the entire colon verified by video photographs, including the transverse colon, during the colonoscopy with the patient having no complaints of product tolerance. No nausea and no vomiting with diarrhea and no crampy sensation were reported.

A 50 year-old female presented with diarrhea for a colonoscopy. The bowel cleansing composition was taken at 10 a.m. and 4 p.m. on the day before the exam, with a clear liquid diet. The bowel prep was good, with adequate view of colon, including the transverse colon. The patient had no complaints.

In some embodiments, a bowel cleansing composition includes PEG, monobasic and/or dibasic sodium phosphate, bisacodyl, psyllium, optionally lubiprostone, and optionally linaclotide.

In some embodiments, the bowel cleansing composition is tailored toward adult usage. In some embodiments, adult bowel cleansing is accomplished by administration of 10 to 30 g of sodium phosphate, 45 to 70 g of PEG, 5 to 30 mg of bisacodyl, 2.5 to 30 g of psyllium, optionally 12 to 60 µg of lubiprostone, and optionally 145 to 290 µg of linaclotide, preferably administered in two separate doses the day before the procedure, as described above. The lubiprostone dosage is more preferably in the range of 24 to 48 µg and the linaclotide dosage is more preferably about 145 µg or about 290 µg. The sodium phosphate and PEG are preferably dissolved in up to two quarts of water or a flavored water beverage. The biscodyl, psyllium, lubiprostone, and/or linaclotide may be administered simultaneously with the sodium phosphate and PEG or at a different time during the administration period. The biscodyl, psyllium, lubiprostone, and linaclotide may be dissolved or dispersed in the same aqueous carrier as the sodium phosphate and PEG or may be taken in other aqueous carriers or taken in another form, such as, for example, a pill or a capsule.

In some preferred embodiments, the bowel cleansing composition includes 16 to 18 grams sodium phosphate, 60 g polyethylene glycol, 10 mg bisacodyl, and 1 teaspoon psyllium (3 to 5 g). This composition is preferably administered twice during the administration period. Additional components in this composition may include linaclotide and lubiprostone. Naloxegol may also be administered to the patient.

In some preferred embodiments, each dose administered to the patient contains less than 20 grams of sodium phosphate and the patient is preferably administered two doses during the administration period.

At least 30 different adult patients with written consent have been administered a bowel cleansing composition as described above, including sodium phosphate, polyethylene glycol, bisacodyl, and psyllium. Two have been given an evening meal including buttered toast. Four have been given an evening meal pancakes with syrup. At least 70 different adult patients in total have been administered a bowel cleansing composition as described above, including sodium phosphate, polyethylene glycol, bisacodyl, and psyllium. All of the patients have done well.

For some of the above-described adult patients, the bowel cleansing composition has additionally included at least one of lubiprostone, linaclotide, and naloxegol. All of the patients receiving a bowel cleansing composition containing at least one of these additional components have done well.

The administration of sodium phosphate, PEG, bisacodyl, and psyllium has been observed to produce better bowel cleanout than administration of sodium phosphate and PEG without bisacodyl and psyllium. More specifically, the psyllium has been observed to bind bile salts to better clean out bile from the bowel, such as by a flush with water by the scope during a colonoscopy.

In some embodiments, the bowel cleansing composition and method are adapted for a patient with certain predetermined conditions. For renal patients, which may be any patient suffering from any kind of kidney disease, the bowel cleansing composition is preferably as disclosed above, with the exception that the sodium phosphate is replaced with magnesium citrate (1:1). 12 to 25 grams of magnesium citrate is preferably administered in place of the sodium phosphate in the split doses. More preferably, the amount of magnesium citrate is in the range of 16 to 17 grams. In some embodiments, the amount of PEG is 60 grams. These compositions and methods may also optionally include one or more of the following components discussed herein: lubiprostone, linaclotide, and naloxegol.

Opioids, a class of drugs for pain treatment and management, are known for reducing the motility of the gastrointestinal tract, leading to opioid-induced constipation. Opioids are commonly given to treat both acute and chronic pain, including, but not limited to, pain associated with terminal conditions and degenerative conditions, such as, for example, rheumatoid arthritis. Bowel cleansings for patients with opioid-induced constipation tend to be particularly difficult. In addition to the components of the bowel cleansing compositions described above, a patient with opioid-induced constipation is preferably given 10 to 40 mg of naloxegol, currently marketed under the trademark Movantik® (AstraZeneca AB Corp., Södertälje, Sweden), in one dose, preferably in the morning the day before the procedure, and more preferably first thing in the morning the day before the procedure. In some embodiments, the dosage of naloxegol is about 25 mg.

For a morning colon procedure, the patient is preferably maintained on a clear liquid diet at least from the morning of the day before the colon procedure up to the evening before the colon procedure as part of the bowel cleansing procedure. In some embodiments, the patient may eat a predetermined evening meal (preferably a low-residue meal) the evening before the colon procedure. A low-residue meal, as defined herein, is a meal with foods that are acceptable for a low-residue diet, which is a diet designed to reduce the frequency and volume of stools while prolonging intestinal transit time. The evening meal may include, but is not limited to, buttered toast or pancakes with syrup.

In some embodiments, a patient who has a procedure scheduled in the afternoon may take a portion of the bowel cleansing composition the day before the procedure, and the remaining portion of the bowel cleansing composition the morning of the procedure (at least four hours before the procedure). In some of these embodiments, the patients take half (typically a quart) of the bowel cleansing composition the day before the procedure and the other half (typically a quart) the morning of the procedure. In some of these embodiments, the patients may also eat an evening meal (preferably a low-residue meal consistent with a low-residue diet) the evening before the procedure. For example, the evening meal may include, but is not limited to, pancakes with syrup or buttered toast.

In some embodiments, the bowel cleansing composition is for an adolescent or a child. The PEG dosage is preferably 1.2 to 1.8 grams, and more preferably about 1.5 grams, per kilogram of weight of the adolescent up to a maximum of 100 grams or of weight of the child up to a maximum of 30 grams. In addition to the PEG, an adolescent bowel cleansing composition for an adolescent 12 to 18 years of age preferably includes 4.5 to 7.5 g, and more preferably about 6 g, of sodium phosphate; 2 to 4 g, and more preferably about 3 g, of psyllium; and 5 to 15 mg, and more preferably about 10 mg, of bisacodyl. In addition to the PEG, a child bowel cleansing composition for a child 8 to 12 years of age preferably includes 2 to 4 g, and more preferably about 3 g, of sodium phosphate; 1.5 to 2.5 g, and more preferably about 2 g, of psyllium; and 5 to 15 mg, and more preferably about 10 mg, of bisacodyl.

Any of the bowel cleansing compositions described herein may be administered to the patient with no supplemental electrolytes.

Any of the bowel cleansing compositions described herein may be administered as described additionally to the patient for a second day prior to the colon procedure to assure a thorough bowel cleansing.

In situations with a gastrointestinal (GI) bleeder patient, the bowel of the patient may be black as a result of the bleeder, making imaging of the bowel during a colonoscopy difficult. In some embodiments, preparation of a GI bleeder patient for a colonoscopy includes, in addition to the previously-described administration of a bowel cleansing composition, the use of carbonated water in place of non-carbonated water in flushing the bowel lining prior to imaging. The carbonated water cleans the bowel lining better than non-carbonated water by removing more of the black coloration from the GI bleeder to allow for better imaging of the bowel during a colonoscopy. The carbonated water is preferably seltzer water. Alternatively, club soda may be use as the carbonated water.

Accordingly, it is to be understood that the embodiments of the invention herein described are merely illustrative of the application of the principles of the invention. Reference herein to details of the illustrated embodiments is not intended to limit the scope of the claims, which themselves recite those features regarded as essential to the invention.

What is claimed is:

1. A method of preparing a patient for a colon procedure comprising:

administering, to the patient during a 24-hour period just prior to the colon procedure, an effective amount of sodium phosphate, an effective amount of polyethylene glycol, an effective amount of bisacodyl, an effective amount of psyllium and an effective amount of lubiprostone to provide a bowel cleansing of the patient for the colon procedure.

2. The method of claim 1, wherein the effective amount of sodium phosphate is less than 20 g.

3. The method of claim 1, wherein the effective amount of lubiprostone is in the range of 24 to 48 μg.

4. The method of claim 1, further comprising administering an effective amount of linaclotide to the patient during the 24-hour period just prior to the colon procedure.

5. The method of claim 4, wherein the effective amount of linaclotide is in the range of 145 to 290 μg.

6. The method of claim 1, further comprising administering an effective amount of naloxegol to the patient a day before the colon procedure and prior to administering the effective amount of sodium phosphate, the effective amount of polyethylene glycol, the effective amount of bisacodyl, the effective amount of psyllium and the effective amount of lubiprostone.

7. The method of claim 6, wherein the effective amount of naloxegol is in the range of 15 to 40 mg.

8. The method of claim 1, wherein the effective amount of sodium phosphate, the effective amount of polyethylene glycol, the effective amount of bisacodyl, the effective amount of psyllium and the effective amount of lubiprostone are divided and

administered as a first dose and a second dose during the 24-hour period just prior to the colon procedure.

9. The method of claim 1, further comprising:

administering to the patient a low-residue meal after administering at least one dose of the effective amount of sodium phosphate, the effective amount of polyethylene glycol, the effective amount of bisacodyl, the effective amount of psyllium and the effective amount of lubiprostone, but prior to the colon procedure.

10. The method of claim 1, further comprising:

flushing a lining of the bowel with carbonated water.

11. The method of claim 1, wherein the effective amount of sodium phosphate is in the range of 10 to 30 g, the effective amount of polyethylene glycol is in the range of 45 to 70 g, the effective amount of bisacodyl is in the range of 5 to 30 mg, and the effective amount of psyllium is in the range of 2.5 to 30 g.

12. The method of claim 11, wherein the effective amount of sodium phosphate is in the range of 16 to 18 g, the effective amount of polyethylene glycol is about 60 g, the effective amount of bisacodyl is about 10 mg, and the effective amount of psyllium is in the range of 3 to 5 g.

13. A method of preparing a patient for a colon procedure comprising:

administering, to the patient during a 24-hour period just prior to the colon procedure, an effective amount of sodium phosphate, an effective amount of polyethylene glycol, an effective amount of bisacodyl, an effective amount of psyllium and an effective amount of linaclotide to provide a bowel cleansing of the patient for the colon procedure.

14. The method of claim 13, wherein the effective amount of sodium phosphate is less than 20 g.

15. The method of claim 13, wherein the effective amount of linaclotide is in the range of 145 to 290 µg.

16. The method of claim 13, further comprising administering an effective amount of naloxegol to the patient a day before the colon procedure and prior to administering the effective amount of sodium phosphate, the effective amount of polyethylene glycol, the effective amount of bisacodyl, the effective amount of psyllium and the effective amount of linaclotide.

17. The method of claim 16, wherein the effective amount of naloxegol is in the range of 15 to 40 mg.

18. The method of claim 13, wherein the effective amount of sodium phosphate, the effective amount of polyethylene glycol, the effective amount of bisacodyl, the effective amount of psyllium and the effective amount of linaclotide are divided and administered as a first dose and a second dose during the 24-hour period just prior to the colon procedure.

19. The method of claim 13, further comprising:

administering to the patient a low-residue meal after administering at least one dose of the effective amount of sodium phosphate, the effective amount of polyethylene glycol, the effective amount of bisacodyl, the effective amount of psyllium and the effective amount of linaclotide, but prior to the colon procedure.

20. The method of claim 13, further comprising:

flushing a lining of the bowel with carbonated water.

21. The method of claim 13, wherein the effective amount of sodium phosphate is in the range of 10 to 30 g, the effective amount of polyethylene glycol is in the range of 45 to 70 g, the effective amount of bisacodyl is in the range of 5 to 30 mg, and the effective amount of psyllium is in the range of 2.5 to 30 g.

22. The method of claim 21, wherein the effective amount of sodium phosphate is in the range of 16 to18 g, the effective amount of polyethylene glycol is about 60 g, the effective amount of bisacodyl is about 10 mg, and the effective amount of psyllium is in the range of 3 to 5 g.

23. A method of preparing a patient for a colon procedure comprising:

administering to the patient during a 24-hour period just prior to the colon procedure, an effective amount of naloxegol and, after administering the effective amount of naloxegol, administering an effective amount of sodium phosphate, an effective amount of polyethylene glycol, an effective amount of bisacodyl, and an effective amount of psyllium to provide a bowel cleansing of the patient for the colon procedure.

24. The method of claim 23, wherein the effective amount of naloxegol is in the range of 15 to 40 mg.

25. The method of claim 23, wherein the effective amount of sodium phosphate is less than 20 g.

26. The method of claim 23 further comprising:

administering to the patient a low-residue meal after administering at least one dose of the effective amount of naloxegol, the effective amount of sodium phosphate, the effective amount of polyethylene glycol, the effective amount of bisacodyl, the effective amount of psyllium and the effective amount of linaclotide, but prior to the colon procedure.

27. The method of claim 23, further comprising:

flushing a lining of the bowel with carbonated water.

28. The method of claim 23, wherein the effective amount of sodium phosphate is in the range of 10 to 30 g, the effective amount of polyethylene glycol is in the range of

45 to 70 g, the effective amount of bisacodyl is in the range of 5 to 30 mg, and the effective amount of psyllium is in the range of 2.5 to 30 g.

29. The method of claim 28, wherein the effective amount of sodium phosphate is in the range of 16 to 18 g, the effective amount of polyethylene glycol is about 60 g, the effective amount of bisacodyl is about 10 mg, and the effective amount of psyllium is in the range of 3 to 5 g.

30. A method of preparing a patient for a colon procedure comprising:

administering to the patient during a 24-hour period just prior to the colon procedure, an effective amount of sodium phosphate, an effective amount of polyethylene glycol, an effective amount of bisacodyl, and an effective amount of psyllium to provide a bowel cleansing of the patient for the colon procedure; and

administering to the patient a low-residue meal after administering at least one dose of the effective amount of sodium phosphate, the effective amount of polyethylene glycol, the effective amount of bisacodyl, and the effective amount of psyllium, but prior to the colon procedure.

31. The method of claim 30, further comprising:

flushing a lining of the bowel with carbonated water.

32. The method of claim 30, wherein the effective amount of sodium phosphate is in the range of 10 to 30 g, the effective amount of polyethylene glycol is in the range of 45 to 70 g, the effective amount of bisacodyl is in the range of 5 to 30 mg, and the effective amount of psyllium is in the range of 2.5 to 30 g.

33. The method of claim 32, wherein the effective amount of sodium phosphate is in the range of 16 to 18 g, the effective amount of polyethylene glycol is about 60 g, the effective amount of bisacodyl is about 10 mg, and the effective amount of psyllium is in the range of 3 to 5 g.

34. The method of claim 30, wherein the effective amount of sodium phosphate is less than 20 g.

35. A method of preparing a patient for a colon procedure comprising:

administering to the patient during a 24-hour period just prior to the colon procedure, an effective amount of sodium phosphate, an effective amount of polyethylene glycol, an effective amount of bisacodyl, and an effective amount of psyllium; and

flushing a lining of the bowel with carbonated water.

36. The method of claim 35, wherein the effective amount of sodium phosphate is less than 20 g.

37. The method of claim 35, wherein the effective amount of sodium phosphate is in the range of 10 to 30 g, the effective amount of polyethylene glycol is in the range of 45 to 70 g, the effective amount of bisacodyl is in the range of 5 to 30 mg, and the effective amount of psyllium is in the range of 2.5 to 30 g.

38. The method of claim 37, wherein the effective amount of sodium phosphate is in the range of 16 to 18 g, the effective amount of polyethylene glycol is about 60 g, the effective amount of bisacodyl is about 10 mg, and the effective amount of psyllium is in the range of 3 to 5 g.

39. A method of preparing a child or adolescent patient between 8 and 18 years of age for a colon procedure comprising:

administering to the patient during a 24-hour period just prior to the colon procedure about 2 to 7.5 grams of sodium phosphate, about 1.2 to 1.8 grams of polyethylene glycol per kilogram of weight of the patient, about 5 to 15 mg of bisacodyl, and about 1.5 to 4 grams of psyllium to provide a bowel cleansing of the patient for the colon procedure.

40. The method of claim 39, wherein the patient is between 12 and 18 years of age and about 4.5 to 7.5 grams of sodium phosphate, about 1.2 to 1.8 grams of polyethylene glycol per kilogram of weight of the patient, about 5 to 15 mg of bisacodyl, and about 2 to 4 grams of psyllium are administered to the patient.

41. The method of claim 39, wherein the patient is between 8 and 12 years of age and about 2 to 4 grams of sodium phosphate, about 1.2 to 1.8 grams of polyethylene glycol per kilogram of weight of the patient, about 5 to 15 mg of bisacodyl, and about 1.5 to 2.5 grams of psyllium are administered to the patient.

42. A kit for cleansing a bowel of a renal patient for a colon procedure, the kit comprising:

a) an effective amount of magnesium citrate (1:1);

b) an effective amount of polyethylene glycol;

c) an effective amount of bisacodyl; and

d) an effective amount of psyllium;

wherein administration of the effective amount of sodium phosphate, the effective amount of polyethylene glycol, the effective amount of bisacodyl, and the effective amount of psyllium to the patient during a 24-hour period provides a bowel cleansing of the renal patient.

43. The kit of claim 42, wherein the effective amount of magnesium citrate (1:1) is in the range of 12 to 25 g.

44. The kit of claim 42, further comprising at least one additional component selected from the group consisting of:

i) an effective amount of lubiprostone;

ii) an effective amount of linaclotide; and

iii) an effective amount of naloxegol.

45. A method of preparing a renal patient for a colon procedure comprising:

administering to the patient during a 24-hour period just prior to the colon procedure, an effective amount of magnesium citrate (1:1), an effective amount of polyethylene glycol, an effective amount of bisacodyl, and an effective amount of psyllium to provide a bowel cleansing of the patient for the colon procedure.

46. The method of claim 45, wherein the effective amount of magnesium citrate (1:1) is in the range of 12 to 25 g.

47. The method of claim 45, further comprising administering to the patient at least one additional component selected from the group consisting of:

i) an effective amount of lubiprostone;

ii) an effective amount of linaclotide; and

iii) an effective amount of naloxegol.

48. A kit for cleansing a bowel of a patient for a colon procedure, the kit comprising:

a) an effective amount of sodium phosphate;

b) an effective amount of polyethylene glycol;

c) an effective amount of bisacodyl;

d) an effective amount of psyllium; and

e) at least one additional component selected from the group consisting of:

i) an effective amount of lubiprostone;

ii) an effective amount of linaclotide; and

iii) an effective amount of naloxegol;

wherein administration of the effective amount of sodium phosphate, the effective amount of polyethylene glycol, the effective amount of bisacodyl, the effective amount of psyllium and the at least one additional component to the patient

during a 24-hour period just prior to the colon procedure provides a bowel cleansing of the patient.

49. The kit of claim 48, wherein the effective amount of sodium phosphate is less than 20 g.

50. The kit of claim 48, wherein the effective amount of lubiprostone is in the range of 24 to 48 µg.

51. The kit of claim 48, wherein the effective amount of linaclotide is in the range of 145 to 290 µg.

52. The kit of claim 48, wherein the effective amount of naloxegol is in the range of 15 to 40 mg.

53. The kit of claim 48, further comprising carbonated water.

54. The kit of claim 48, wherein the effective amount of sodium phosphate is in the range of 10 to 30 g, the effective amount of polyethylene glycol is in the range of 45 to 70 g, the effective amount of bisacodyl is in the range of 5 to 30 mg, and the effective amount of psyllium is in the range of 2.5 to 30 g.

55. The kit of claim 54, wherein the effective amount of sodium phosphate is in the range of 16 to 18 g, the effective amount of polyethylene glycol is about 60 g, the effective amount of bisacodyl is about 10 mg, and the effective amount of psyllium is in the range of 3 to 5 g.

INTERNATIONAL SEARCH REPORT

International application No.
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A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 31/4402; A61K 31/765; A61K 33/42 (2016.01)
CPC - A61K 9/0053; A61K 9/0095; A61K 9/08; A61K 31/4402; A61K 31/765; A61K 33/42 (2016.08)
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - A61K 31/4402; A61K 31/765; A61K 33/42 (2016.01)
CPC - A61K 9/0053; A61K 9/0095; A61K 9/08; A61K 31/4402; A61K 31/765; A61K 33/42 (2016.08)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 424/78.01; 424/601; 424/606; IPC(8) - A61K 31/4402; A61K 31/765; A61K 33/42; CPC - A61K 9/0053; A61K 9/0095; A61K 9/08; A61K 31/4402; A61K 31/765; A61K 33/42 (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Orbit, Google Patents, Google
Search terms used: colon, bowel, cleanse, GI, prep+, PEG, bisacodyl, polyethylene glycol, psyllium, lubiprostone, Amitiza, naloxegol, carbonated water, seltzer, soda, bowel lining

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2014/0242124 A1 (SYNERGY PHARMACEUTICALS INC) 28 August 2014 (28.08.2014) entire document	1, 4, 5, 8, 9, 13, 15, 18, 19, 30
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Y		2, 3, 10-12, 14, 20-22, 31-41, 44, 47
X	US 2010/0159026 A1 (SKIENDZIELEWSKI et al) 24 June 2010 (24.06.2010) entire document	42, 43, 45, 46
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Y		44, 47
Y	US 2014/0178492 A1 (HALOW) 26 June 2014 (26.06.2014) entire document	2, 11, 12, 14, 21, 22, 32-34, 36-38
Y	GRIGG et al., Lubiprostone Used With Polyethylene Glycol in Diabetic Patients Enhances Colonoscopy Preparation Quality, World Journal of Gastrointestinal Endoscopy, Vol. 1, Issue 7, 16 July 2010, [retrieved on 26 August 2016]. Retrieved from the Internet <URL: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2998835/pdf/WJGE-2-263.pdf>, Pgs. 263-267	3
Y	CA 2 927 719 A1 (KANG et al) 23 April 2015 (23.04.2015) entire document	10, 20, 31, 35-38
Y	US 5,173,296 A (ANDRE et al) 22 December 1992 (22.12.1992) entire document	11, 12, 21, 22, 32, 33, 37-41
Y	US 2005/0244368 A1 (PASHANKAR) 03 November 2005 (03.11.2005) entire document	39-41

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
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"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30 August 2016	23 SEP 2016
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	Authorized officer Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774