MEROKEN

Powder for preparation of a lemon-flavored solution

PER OS

Active Ingredients:

Polyethylene Glycol 3350, 315.0 g

Sodium Chloride, 8.424 g

Sodium Bicarbonate, 4.284 g

Potassium Chloride, 1.118 g

PRESCRIBING INFORMATION

1. INDICATIONS AND USAGE

Meroken is indicated for bowel cleansing prior to colonoscopy and barium enema x-ray examinations.

2. DOSAGE AND ADMINISTRATION

2.1 Dosage Overview

Meroken, supplied as a powder, must be reconstituted with water before its use; it is not for direct ingestion *[see Dosage and Administration (2.2), Warnings and Precautions (5.8)]*.

Do not reconstitute with other liquids and/or add starch-based thickeners to the mixing container *[see Warnings and Precautions (5.7)]*.

2.2 Administration Instructions Prior to Dosage

It is preferable not to eat solid food the day before the examination and 3-4 hours before drinking the solution.

It is essential not to eat two hours before drinking the solution and until the examination is completed.

Only drink clear fluids:

- On the day before the examination
- When drinking the solution
- After finishing drinking the solution until 2 hours before the colonoscopy

The pharmacist should open the bottle, add 2.7 liters of tap water or up to the line marked 3 liters at the top of the bottle, close the bottle and shake well until completely dissolved.

2.3 Dosage

The following is the recommended dose of reconstituted Meroken solution for adults.

Instruct patients they may consume water or clear liquids during the bowel preparation and after completion of the bowel preparation up until 2 hours before the time of the colonoscopy.

The solution is more palatable if chilled prior to administration.

Instruct patients to drink the 3 liters of solution at a rate of one glass (240 ml) every 10 minutes until the solution is consumed. It is recommended to drink each glass all at once.

The solution is lemon-flavored. Do not add any flavorings or any other supplements to the solution.

The first bowel movements should occur approximately one hour after the start of Meroken administration. The patient should continue drinking until the watery stool is clear and free of solid matter.

3. DOSAGE FORM

Powder for oral solution.

4. CONTRAINDICATIONS

Meroken is contraindicated in the following conditions:

- Gastrointestinal (GI) obstruction, ileus, or gastric retention
- Bowel perforation
- Toxic colitis or toxic megacolon
- Known allergy or hypersensitivity to active ingredients or to any of the excipients of Meroken [*see How Supplied/Storage and Handling (16)*]

5. WARNINGS AND PRECAUTIONS

5.1 Serious Fluid and Serum Chemistry Abnormalities

Advise patients to hydrate adequately before, during, and after the use of Meroken. Use caution in patients with congestive heart failure when replacing fluids. If a patient develops significant vomiting or signs of dehydration including signs of orthostatic hypotension after taking Meroken, consider performing post-colonoscopy lab tests (electrolytes, creatinine, and BUN) and treat accordingly. Fluid and electrolyte disturbances can lead to serious adverse events including cardiac arrhythmias, seizures and renal impairment. Fluid and electrolyte abnormalities should be corrected before treatment with Meroken.

In addition, use caution when prescribing Meroken for patients who have 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)].

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 Meroken 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). Pre-dose and post-colonoscopy ECGs should be considered in patients at increased risk of serious cardiac arrhythmias.

5.3 Seizures

There have been reports of generalized tonic-clonic seizures and/or loss of consciousness associated with use of bowel preparation products 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.

Use caution when prescribing Meroken for patients with a history of seizures and in patients at increased risk of seizure, such as patients taking medications that lower the seizure threshold (e.g., tricyclic antidepressants), patients withdrawing from alcohol or benzodiazepines, or patients with known or suspected hyponatremia.

5.4 Renal Impairment

Use caution when prescribing Meroken for patients with impaired renal function or patients taking concomitant medications that may affect renal function (such as diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, or non-steroidal anti-inflammatory drugs). Advise these patients of the importance of adequate hydration, and consider performing baseline and postcolonoscopy laboratory tests (electrolytes, creatinine, and BUN) in these patients.

5.5 Colonic Mucosal Ulcerations and Ischemic Colitis

Administration of osmotic laxative products may produce colonic mucosal aphthous ulcerations, and there have been reports of more serious cases of ischemic colitis requiring hospitalization. Concurrent use of stimulant laxatives and Meroken may increase this risk. The potential for mucosal ulcerations resulting from the bowel preparation should be considered when interpreting colonoscopy findings in patients with known or suspect inflammatory bowel disease (IBD).

5.6 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 Meroken. If a patient experiences severe bloating, distention or abdominal pain, administration should be slowed or temporarily discontinued until the symptoms abate. If gastrointestinal obstruction or perforation is suspected, appropriate studies should be performed to rule out these conditions before administration of Meroken. Use with caution in patients with severe active ulcerative colitis.

5.7 Aspiration

Use with caution in patients with impaired gag reflex, unconscious, or semiconscious patients, and patients prone to regurgitation or aspiration. Such patients should be observed during administration of Meroken, especially if it is administered via nasogastric tube.

Do not combine Meroken with starch-based thickeners [see Dosage and Administration (2.1)]. Polyethylene glycol (PEG), a component of Meroken, when mixed with starch-thickened liquids reduces the viscosity of the starch-thickened liquid. When a PEG-based product used for another indication was mixed in starch-based pre-thickened liquids used in patients with dysphagia, thinning of the liquid occurred and cases of choking and potential aspiration were reported.

5.8 Not for Direct Ingestion

The contents of each bottle must be diluted with water to a final volume of 3 liters and ingestion of additional water is important to patient tolerance. Direct ingestion of the undissolved powder may increase the risk of nausea, vomiting, dehydration, and electrolyte disturbances.

6. ADVERSE REACTIONS

The following adverse reactions have been identified during post-approval use of Meroken. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Nausea, abdominal fullness and bloating are the most common adverse reactions (occurred in up to 50% of patients) to administration of Meroken. Abdominal cramps, vomiting and anal irritation occur less frequently. These adverse reactions are transient and usually subside rapidly. Isolated cases of urticaria, rhinorrhea, dermatitis and (rarely) anaphylactic reaction have been reported which may represent allergic reactions.

Published literature contains isolated reports of serious adverse reactions following the administration of PEG-electrolyte solution products in patients over 60 years of age. These adverse events include upper GI bleeding from Mallory-Weiss Tear, esophageal perforation, asystole, sudden dyspnea with pulmonary edema, and “butterfly-like” infiltrates on chest X-ray after vomiting and aspirating PEG.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: https://sideeffects.health.gov.il.

7. DRUG INTERACTIONS

7.1 Drugs that May Lead to Fluid and Electrolyte Abnormalities

Use caution when prescribing Meroken for patients 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 (5.1, 5.2, 5.3, and 5.4)*] in patients taking these concomitant medications.

7.2 Potential for Altered Drug Absorption

Oral medication administered within one hour of the start of administration of Meroken may be flushed from the gastrointestinal tract and the medication may not be absorbed properly.

7.3 Stimulant Laxatives

Concurrent use of stimulant laxatives and Meroken may increase the risk of mucosal ulceration or ischemic colitis. Avoid use of stimulant laxatives (e.g., bisacodyl, sodium picosulfate) while taking Meroken.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C.

Animal reproduction studies have not been conducted with Meroken. It is also not known whether Meroken can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Meroken 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 Meroken is administered to a nursing woman.

8.4 Pediatric Use

The medicine is not usually intended for children and/or infants

8.5 Geriatric Use

Clinical studies of Meroken did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

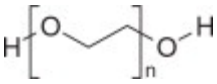
11. DESCRIPTION

For oral solution: Each 3 liter (3L) Meroken bottle contains a white to cream-colored powder for reconstitution. Meroken is a combination of polyethylene glycol 3350, an osmotic

laxative, and electrolytes (sodium chloride, sodium bicarbonate and potassium chloride) for oral solution.

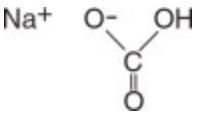
Each 3 liter bottle contains: polyethylene glycol 3350 315 g, sodium bicarbonate 4.284 g, sodium chloride 8.424 g, potassium chloride 1.118 g. The solution is clear and colorless when reconstituted to a final volume of 3 liters with water.

Polyethylene Glycol 3350



Sodium Bicarbonate

The chemical name is $NaHCO_3$. The average Molecular Weight is 84.01. The structural formula is:



Sodium Chloride

The chemical name is NaCl. The average Molecular Weight: 58.44. The structural formula is:

Na+ Cl-

Potassium Chloride

The chemical name is KCl. The average Molecular Weight: 74.55. The structural formula is:

K-Cl

12. CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The primary mode of action is thought to be through the osmotic effect of polyethylene glycol 3350 which causes water to be retained in the colon and produces a watery stool.

12.2 Pharmacodynamics

Meroken induces as diarrhea which rapidly cleanses the bowel, usually within four hours.

12.3 Pharmacokinetics

The pharmacokinetics of PEG3350 following administration of Meroken were not assessed. Available pharmacokinetic information for oral PEG3350 suggests that it is poorly absorbed.

13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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

16. HOW SUPPLIED/STORAGE AND HANDLING

The powder is packaged in a plastic bottle (HDPE) with a plastic cap.

The powder is intended to be dissolved in tap water to obtain a 3 liter solution ready for drinking.

STORAGE:

The expiry date of the product is indicated on the packaging materials.

Store below 25°C.

When reconstituted, keep solution refrigerated (2-8° C). Use within 14 days. Discard unused portion.

Store in original container.

LIST OF EXCIPIENTS:

Sucralose powder**,** Lemon Flavor 58.3520.1P PHA.

17. PATIENT COUNSELING INFORMATION

Instruct patients:

- To let you know if they have trouble swallowing or are prone to regurgitation or aspiration.
- Not to take other laxatives while they are taking Meroken.
- To consume water or clear liquids during the bowel preparation and after completion of the bowel preparation up until 2 hours before the time of the colonoscopy.
- That if they experience severe bloating, distention or abdominal pain, the administration of the solution should be slowed or temporarily discontinued until the symptoms abate. Advise patients to report these events to their health care provider.
- That if they have hives, rashes, or any allergic reaction, they should discontinue the medication and contact their health care provider. Medication should be discontinued until they speak to their physician.
- To contact their healthcare provider if they develop signs and symptoms of dehydration. [*see Warnings and Precautions (5.1)*].
- That oral medication administered within one hour of the start of administration of Meroken solution may be flushed from the GI tract and the medication may not be absorbed completely.

MANUFACTURER AND MARKETING AUTHORISATION HOLDER

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AUTHORISATION NUMBER:

062-36-27922

Revised in August 2021 according to MOHs guidelines