

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use KAYEXALATE safely and effectively. See full prescribing information for KAYEXALATE

**KAYEXALATE (sodium polystyrene sulfonate) powder for suspension, for oral or rectal use
Initial U.S. Approval: 1958**

INDICATIONS AND USAGE

KAYEXALATE is a potassium binder indicated for the treatment of hyperkalemia (1).

Limitation of Use:

KAYEXALATE should not be used as an emergency treatment for life threatening hyperkalemia because of its delayed onset of action (1).

DOSAGE AND ADMINISTRATION

Oral: The average total daily adult dose of KAYEXALATE is 15 g to 60 g, administered as a 15-g dose (four level teaspoons), one to four times daily (2.1).

Rectal: The average adult dose is 30 g to 50 g every six hours (2.1).

DOSAGE FORMS AND STRENGTHS

KAYEXALATE is available as a cream to light brown, finely ground powder (3)

CONTRAINDICATIONS

- Hypersensitivity to polystyrene sulfonate resins (4)
- Obstructive bowel disease (4)
- Neonates with reduced gut motility (4)

WARNINGS AND PRECAUTIONS

- Intestinal Necrosis: cases of intestinal necrosis and other serious gastrointestinal events have been reported (5.1).
- Electrolyte Disturbances: Severe hypokalemia can occur. (5.2).
- Fluid overload in patient sensitive to high sodium intake: Monitor patients who are sensitive to sodium intake for signs of fluid overload. (5.3).
- Risk of aspiration: Acute bronchitis or bronchopneumonia caused by inhalation of sodium polystyrene sulfonate particles has been reported. (5.4).

ADVERSE REACTIONS

Adverse reactions reported include: anorexia, constipation, diarrhea, fecal impaction, gastrointestinal concretions (bezoars), ischemic colitis, nausea, vomiting (6).

To report SUSPECTED ADVERSE REACTIONS, contact Concordia Pharmaceutical Inc. at 1-877-370-1142 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Take other orally administered drugs at least 3 hours before or 3 hours after KAYEXALATE (7.1).
- Cation-Donating Antacids: may reduce the resin’s potassium exchange capability and increase risk of systemic alkalosis (7.2).
- Sorbitol: Concomitant use may contribute to the risk of intestinal necrosis and is not recommended (7.3).

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

KAYEXALATE is indicated for the treatment of hyperkalemia.

Limitation of Use:

KAYEXALATE should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action [*see Clinical Pharmacology (12.2)*].

2 DOSAGE AND ADMINISTRATION

2.1 General Information

Administer KAYEXALATE at least 3 hours before or 3 hours after other oral medications. Patients with gastroparesis may require a 6 hour separation [*see Warnings and Precautions (5.5) and Drug Interaction (7)*]

2.2 Recommended Dosage

The intensity and duration of therapy depend upon the severity and resistance of hyperkalemia.

Oral

The average total daily adult dose of KAYEXALATE is 15 g to 60 g, administered as a 15-g dose (four level teaspoons), one to four times daily.

Rectal

The average adult dose is 30 g to 50 g every six hours.

2.3 Preparation and Administration

Prepare suspension fresh and use within 24 hours.

Do not heat KAYEXALATE as it could alter the exchange properties of the resin.

One level teaspoon contains approximately 3.5 g of KAYEXALATE and 15 mEq of sodium.

Oral Suspension

Suspend each dose in a small quantity of water or syrup, approximately 3 to 4 mL of liquid per gram of resin. Administer with patient in an upright position [*see Warnings and Precautions (5.4)*].

Enema

After an initial cleansing enema, insert a soft, large size (French 28) rubber tube into the rectum for a distance of about 20 cm, with the tip well into the sigmoid colon, and tape in place.

Administer as a warm (body temperature) emulsion in 100 mL of aqueous vehicle and flush with 50 to 100 ml of fluid. A somewhat thicker suspension may be used, but do not form a paste.

Agitate the emulsion gently during administration. The resin should be retained for as long as possible and follow by a cleansing enema with a nonsodium containing solution. Ensure an adequate volume of cleansing solution (up to 2 liters) is utilized.

3 DOSAGE FORMS AND STRENGTHS

KAYEXALATE is a cream to light brown, finely ground powder and is available in 453.6 g jars.

4 CONTRAINDICATIONS

KAYEXALATE is contraindicated in patients with the following conditions:

- Hypersensitivity to polystyrene sulfonate resins
- Obstructive bowel disease
- Neonates with reduced gut motility

5 WARNINGS AND PRECAUTIONS

5.1 Intestinal Necrosis

Cases of intestinal necrosis, some fatal, and other serious gastrointestinal adverse events (bleeding, ischemic colitis, perforation) have been reported in association with KAYEXALATE use. The majority of these cases reported the concomitant use of sorbitol. Risk factors for gastrointestinal adverse events were present in many of the cases including prematurity, history of intestinal disease or surgery, hypovolemia, and renal insufficiency and failure. Concomitant administration of sorbitol is not recommended.

- Use only in patients who have normal bowel function. Avoid use in patients who have not had a bowel movement post-surgery.
- Avoid use in patients who are at risk for developing constipation or impaction (including those with history of impaction, chronic constipation, inflammatory bowel disease, ischemic colitis, vascular intestinal atherosclerosis, previous bowel resection, or bowel obstruction). Discontinue use in patients who develop constipation.

5.2 Electrolyte Disturbances

Monitor serum potassium during therapy because severe hypokalemia may occur.

KAYEXALATE is not totally selective for potassium, and small amounts of other cations such as magnesium and calcium can also be lost during treatment. Monitor calcium and magnesium in patients receiving KAYEXALATE.

5.3 Fluid Overload in Patients Sensitive to High Sodium Intake

Each 15 g dose of KAYEXALATE contains 1500 mg (60 mEq) of sodium. Monitor patients who are sensitive to sodium intake (heart failure, hypertension, edema) for signs of fluid overload. Adjustment of other sources of sodium may be required.

5.4 Risk of Aspiration

Cases of acute bronchitis or bronchopneumonia caused by inhalation of sodium polystyrene sulfonate particles have been reported. Patients with impaired gag reflex, altered level of consciousness, or patients prone to regurgitation may be at increased risk. Administer KAYEXALATE with the patient in an upright position.

5.5 Binding to Other Orally Administered Medications

KAYEXALATE may bind orally administered medications, which could decrease their gastrointestinal absorption and lead to reduced efficacy. Administer other oral medications at least 3 hours before or 3 hours after KAYEXALATE. Patients with gastroparesis may require a 6 hour separation. [see *Dosage and Administration (2.1) and Drug Interactions (7)*].

6 ADVERSE REACTIONS

The following adverse reactions are discussed elsewhere in the labeling:

- Intestinal Necrosis [see *Warnings and Precautions (5.1)*]
- Electrolyte Disturbances [see *Warnings and Precautions (5.2, 5.3)*]
- Aspiration [see *Warnings and Precautions (5.4)*]

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

Gastrointestinal: anorexia, constipation, diarrhea, fecal impaction, gastrointestinal concretions (bezoars), ischemic colitis, nausea, ulcerations, vomiting, gastric irritation, intestinal obstruction (due to concentration of aluminium hydroxide)

Metabolic: systemic alkalosis

7 DRUG INTERACTIONS

7.1 General Interactions

No formal drug interaction studies have been conducted in humans.

KAYEXALATE has the potential to bind other drugs. In *in vitro* binding studies, KAYEXALATE was shown to significantly bind the oral medications (n=6) that were tested. Decreased absorption of lithium and thyroxine have also been reported with co-administration of KAYEXALATE. Binding of KAYEXALATE to other oral medications could cause decreased gastrointestinal absorption and loss of efficacy when taken close to the time KAYEXALATE is

administered. Administer KAYEXALATE at least 3 hours before or 3 hours after other oral medications. Patients with gastroparesis may require a 6 hour separation. Monitor for clinical response and/or blood levels where possible.

7.2 Cation-Donating Antacids

The simultaneous oral administration of KAYEXALATE with nonabsorbable cation-donating antacids and laxatives may reduce the resin's potassium exchange capability and increase the risk of systemic alkalosis.

7.3 Sorbitol

Sorbitol may contribute to the risk of intestinal necrosis [*see Warnings and Precautions (5.1)*] and concomitant use is not recommended.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

KAYEXALATE is not absorbed systemically following oral or rectal administration and maternal use is not expected to result in fetal risk.

8.2 Lactation

Risk Summary

KAYEXALATE is not absorbed systemically by the mother, so breastfeeding is not expected to result in risk to the infant.

8.4 Pediatric Use

Studies of safety and efficacy have not been conducted in pediatric patients.

In pediatric patients, as in adults, KAYEXALATE is expected to bind potassium at the practical exchange ratio of 1mEq potassium per 1 gram of resin.

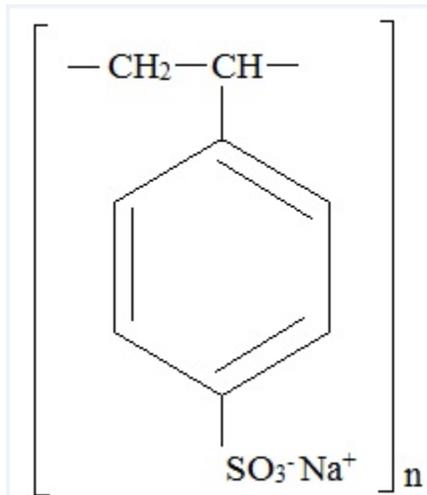
In neonates, KAYEXALATE should not be given by the oral route. In both children and neonates, excessive dosage or inadequate dilution could result in impaction of the resin. Premature infants or low birth weight infants may have an increased risk for gastrointestinal adverse effects with KAYEXALATE. use [*see Warnings and Precautions (5.4)*].

10 OVERDOSAGE

Overdosage may result in electrolyte disturbances including hypokalemia, hypocalcemia, and hypomagnesemia. Appropriate measures should be taken to correct serum electrolytes (potassium, calcium, magnesium), and the resin should be removed from the alimentary tract by appropriate use of laxatives or enemas.

11 DESCRIPTION

KAYEXALATE is a benzene, diethenyl-polymer, with ethenylbenzene, sulfonated, sodium salt and has the following structural formula:



The drug is a cream to light brown finely ground, powdered form of sodium polystyrene sulfonate, a cation-exchange resin prepared in the sodium phase with an *in vitro* exchange capacity of approximately 3.1 mEq (*in vivo* approximately 1 mEq) of potassium per gram. The sodium content is approximately 100 mg (4.1 mEq) per gram of the drug. It can be administered orally or rectally as an enema.

One gram of KAYEXALATE contains 4.1 mEq of sodium.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

KAYEXALATE is a non-absorbed, cation exchange polymer that contains a sodium counterion.

KAYEXALATE increases fecal potassium excretion through binding of potassium in the lumen of the gastrointestinal tract. Binding of potassium reduces the concentration of free potassium in the gastrointestinal lumen, resulting in a reduction of serum potassium levels. The practical exchange ratio is 1 mEq K per 1 gram of resin.

As the resin passes along the intestine or is retained in the colon after administration by enema, the sodium ions are partially released and are replaced by potassium ions. This action occurs primarily in the large intestine, which excretes potassium ions to a greater degree than does the small intestine. The efficiency of this process is limited and unpredictably variable.

12.2 Pharmacodynamics

The effective lowering of serum potassium with KAYEXALATE may take hours to days.

12.3 Pharmacokinetics

The *in vivo* efficiency of sodium-potassium exchange resins is approximately 33 percent; hence, about one third of the resin's actual sodium content is delivered to the body.

KAYEXALATE is not absorbed systemically.

Drug Interactions

In vitro binding studies showed that KAYEXALATE bound significantly to the following tested drugs – warfarin, metoprolol, phenytoin, furosemide, amlodipine and amoxicillin.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies have not been performed.

16 HOW SUPPLIED/STORAGE AND HANDLING

KAYEXALATE is available as a cream to light brown, finely ground powder in jars of 1 pound (453.6 g), NDC 59212-075-01.

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

17 PATIENT COUNSELING INFORMATION

Drug Interactions

Advise patients who are taking other oral medication to separate the dosing of KAYEXALATE by at least 3 hours (before or after) [see *Dosage and Administration (2.1)*, *Warnings and Precautions (5.5)*, and *Drug Interactions (7.1)*]

Rx Only

Manufactured for:

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