PRESCRIBING INFORMATION

PrKAYEXALATE®

(Sodium Polystyrene Sulfonate)

Cation - Exchange Resin

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DESCRIPTION

KAYEXALATE (sodium polystyrene sulfonate) is a cream or light brown fine powder of sodium polystyrene sulfonate. KAYEXALATE is a cation-exchange resin prepared in the sodium phase, with an *in vivo* exchange capacity of approximately 1 mmol (*in vitro* approximately 3.1 mmol) of potassium per gram. The sodium content is approximately 4.1 mmol (100 mg) per gram of the drug. KAYEXALATE can be administered either orally or as an enema.

ACTION

Sodium polystyrene sulfonate is not absorbed from the gastrointestinal tract. As the resin passes through the gastrointestinal tract, the resin removes the potassium ions by exchanging it for sodium ions. Most of this action occurs in the large intestine, which excretes potassium ions to a greater degree than does the small intestine. Potassium exchange also occurs in the colon following retention of the resin, when administered as an enema. The efficiency of this process is limited and unpredictable. It commonly approximates the order of 33 per cent but the range is so large that definite indices of electrolyte balance must be clearly monitored. Metabolic data are unavailable.

INDICATION

KAYEXALATE is indicated for the treatment of hyperkalemia.

CONTRAINDICATIONS

KAYEXALATE should not be administered to patients with the following conditions:

- serum potassium <5 mmol/L
- history of hypersensitivity to polystyrene sulfonate resins
- obstructive bowel disease

KAYEXALATE should not be administered ***orally*** to neonates or in neonates with reduced gut motility (postoperatively or drug induced).

WARNINGS AND PRECAUTIONS

Alternative therapy in severe hyperkalemia: Since effective lowering of serum potassium with KAYEXALATE may take hours to days, treatment with this drug alone may be insufficient to rapidly correct severe hyperkalemia associated with states of rapid tissue breakdown (e.g. burns and renal failure). In such instances, some form of dialysis (peritoneal or hemo-) may be imperative.

If hyperkalemia is so marked as to constitute a medical emergency (e.g. serum potassium above 7.5 mmol/liter), immediate treatment with intravenous glucose and insulin, or intravenous sodium bicarbonate may be necessary as a temporary measure to lower serum potassium, while other long term potassium lowering therapy is initiated.

Binding to other orally administered medications: When administered orally, KAYEXALATE may bind to other orally administered medications, which could decrease their gastrointestinal absorption and efficacy. Avoid co-administration of KAYEXALATE with other orally administered medications. Administer KAYEXALATE at least 3 hours before or 3 hours after administration of other oral medications. For patients with gastroparesis, a 6-hour separation should be considered (see DRUG INTERACTIONS and DOSAGE AND ADMINISTRATION, Adults, including the Elderly).

Gastrointestinal injuries: Cases of gastrointestinal stenosis, intestinal ischemia, ischemic colitis, rectal haemorrhage, gastrointestinal necrosis and intestinal perforation with fatal outcomes 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, immunosuppressant therapy, severe burns, and renal insufficiency and failure. Concomitant administration of sorbitol is not recommended (see DRUG INTERACTIONS and ADVERSE REACTIONS).

Hypokalemia: KAYEXALATE therapy can precipitate serious potassium deficiency and the possibility of severe potassium depletion should be considered. It is therefore, imperative, to determine serum potassium levels at least daily and more frequently when indicated. Adequate clinical and biochemical control is essential during treatment especially in patients on digitalis. Therapy should be discontinued as soon as serum potassium falls below 5 mmol/L (see DRUG INTERACTIONS). Since intracellular potassium deficiency is not always reflected by serum potassium levels, the level at which treatment with KAYEXALATE should be discontinued must be determined individually for each patient. The patient's clinical condition and electrocardiogram are important in making this determination.

Early clinical signs of severe hypokalemia include a pattern of irritability, confusion and delayed thought processes. Severe hypokalemia is often associated with a lengthened Q-T interval, widening, flattening or inversion of the T wave, and the appearance of U waves on the ECG. Cardiac arrhythmias such as premature atrial, nodal and ventricular contractions and supra-ventricular and ventricular tachycardias may also occur. Marked hypokalemia can also be manifested by severe muscle weakness, at times extending into frank paralysis. The toxic effects of digitalis on the heart, especially various ventricular arrhythmia and A-V nodal dissociation, are likely to be exaggerated by hypokalemia. These effects can occur even though serum digoxin concentration is within the ‘normal range’.

Other electrolytes disturbances: Like all cation-exchange resins, KAYEXALATE is not totally selective (for potassium) in its actions, and small amounts of other cations such as magnesium

and calcium can also be lost during treatment. Patients receiving KAYEXALATE should be monitored for all applicable electrolyte disturbances.

Other risks: In the event of clinically significant constipation, treatment with the resin should be discontinued until normal bowel motion is resumed. Magnesium-containing laxatives should not be used (see DRUG INTERACTIONS).

The patient should be positioned carefully when ingesting the resin, in order to avoid aspiration, which could lead to bronchopulmonary complications.

Special Populations

Children and neonates: In neonates, KAYEXALATE should not be given by the ***oral*** route. In both children and neonates, particular care should be observed with rectal administration. Excessive dosage or inadequate dilution could result in impaction of the resin.

Due to the risk of gastrointestinal tract hemorrhage, colonic necrosis, or sodium overload, particular care should be observed in premature infants or low birth weight infants.

Patients at risk from an increase in sodium load: During the resin's action in the intestinal tract, sodium is released mole for mole with potassium uptake. A single dose of KAYEXALATE (15 grams) contains approximately 60 mmol of sodium. Since the resin is a source of sodium, caution is advised when KAYEXALATE is administered to patients who cannot tolerate even a small increase in sodium loads and for whom an increase in sodium load may be detrimental (i.e. severe congestive heart failure, severe hypertension, marked edema or renal damage). In such instances compensatory restriction of sodium intake from other sources may be indicated and adequate clinical and biochemical control is essential. The calcium form of the resin may offer advantages in this situation.

DRUG INTERACTIONS

Orally administered medications: When administered orally, KAYEXALATE has the potential to bind to other orally administered medications. Binding of KAYEXALATE to other oral medications could decrease their gastrointestinal absorption and efficacy. Dosing separation of KAYEXALATE from other orally administered medications is recommended (see DOSAGE AND ADMINISTRATION and WARNINGS).

Sorbitol (oral or rectal): Concomitant administration of sorbitol with KAYEXALATE is not recommended due to cases of intestinal necrosis, and other serious gastrointestinal adverse reactions**,** which may be fatal (see WARNINGS and ADVERSE REACTIONS).

To be used with caution:

Cation donating agents: may reduce the effectiveness of the resin in binding potassium.

Aluminum hydroxide: intestinal obstruction due to concretions of aluminum hydroxide has been reported when aluminum hydroxide was combined with the resin.

Digitalis drugs: the toxic effects of digitalis on the heart, especially various ventricular arrhythmias and A-V nodal dissociation, are likely to be exaggerated if hypokalemia is allowed to develop (see WARNINGS).

Non-absorbable cation-donating antacids and laxatives: systemic alkalosis has been reported after cation-exchange resins were administered orally in combination with non-absorbable cation-donating antacids and laxatives such as magnesium hydroxide and aluminum carbonate.

Lithium: possible decrease of lithium absorption.

Thyroxine: possible decrease of thyroxine absorption.

PREGNANCY**:**

KAYEXALATE is not absorbed from the gastrointestinal tract. No data are available concerning the use of polystyrene sulfonate resins in humans during pregnancy.

LACTATION:

KAYEXALATE is not absorbed from the gastrointestinal tract. No data are available concerning the use of polystyrene sulfonate resins in humans during lactation.

OVERDOSAGE

Biochemical disturbances resulting from overdosage may give rise to clinical signs and symptoms of hypokalemia, including irritability, confusion, delayed thought processes, muscle weakness, hyporeflexia, and eventually frank paralysis. Apnea may be a serious consequence of the progression. Electrocardiographic changes may be consistent with hypokalemia; cardiac arrhythmia may occur. Hypocalcemic tetany may occur.

Appropriate measures should be taken to correct serum electrolytes (potassium, calcium). The resin should be removed from the alimentary tract by appropriate use of laxatives or enemas.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

ADVERSE REACTIONS

Gastrointestinal disorders
KAYEXALATE (sodium polystyrene sulfonate) may cause some degree of gastric irritation. Anorexia, nausea, vomiting and constipation may occur especially if high doses are given. Occasionally diarrhea develops.

Large doses in elderly individuals may cause fecal impaction. These effects may be obviated through usage of the resin in enemas as described under "Dosage and Administration"'.

Fecal impaction following rectal administration particularly in children and gastrointestinal concretions (bezoars) following oral administration have been reported. Gastrointestinal stenosis and intestinal obstruction have also been reported, possibly due to co-existing pathology or inadequate dilution of the resin. Intestinal obstruction due to concretions of aluminum hydroxide has been reported when aluminum hydroxide was used in combination with KAYEXALATE.

Gastrointestinal ischemia, ischemic colitis, rectal haemorrhage, gastrointestinal tract ulceration or necrosis which could lead to intestinal perforation have been reported, which is sometimes fatal.
The majority of cases have been reported with concomitant use of sorbitol (see WARNINGS and DRUG INTERACTIONS).

Metabolism and nutrition disorders
In accordance with its pharmacological actions, the resin may give rise to sodium retention, hypokalemia and hypocalcemia, and their related clinical manifestations (see WARNINGS and OVERDOSAGE). Cases of hypomagnesemia have been reported.

Respiratory, thoracic and mediastinal disorders
Some cases of acute bronchitis and/or bronchopneumonia associated with inhalation of particles of sodium polystyrene sulfonate have been described.

DOSAGE AND ADMINISTRATION

KAYEXALATE is for oral or rectal administration only. The dosage recommendations given below are approximate. The precise requirements for each individual patient should be determined on the basis of regular clinical and biochemical assessments.

Suspensions of KAYEXALATE should be freshly prepared and not stored beyond 24 hours.

KAYEXALATE powder should not be heated as heating may alter the exchange properties of the resin.

Adults, Including the Elderly:

Oral:
The average daily adult dose of the resin is 15 to 60 grams. This is provided by administering 15 grams (approximately 4 level teaspoons) of KAYEXALATE one to four times daily. 1 gram of KAYEXALATE powder contains 4.1 mmol of sodium; one level teaspoon contains approximately 3.5 grams of KAYEXALATE powder and 15 mmol of sodium. A heaping teaspoon may contain as much as 10-12 grams of KAYEXALATE powder. Since the *in vivo*

efficiency of sodium-potassium exchange resins is approximately 33 per cent, about one third of the resin's actual sodium content is being delivered to the body.

Each dose should be given as a suspension in a small quantity of water or, for greater palatability, in syrup, but not in orange juice or other fruit juices that are known to contain potassium. The amount of fluid usually ranges from 20 to 100 mL, depending on the dose. It may be simply determined by allowing 3 to 4 mL per gram of resin.

Administer KAYEXALATE at least 3 hours before or 3 hours after other oral medications. For patients with gastroparesis, a 6-hour separation should be considered (see WARNINGS and DRUG INTERACTIONS).

The resin may be introduced into the stomach through a plastic tube. If desired, it may be mixed with a diet appropriate for a patient in renal failure.

Rectal:
For adults, the resin may also be given, although with less effective results, in a daily enema. 30 to 50 g of resin is given once or twice daily (at intervals of six hours). Each dose is administered as a warm emulsion (at body temperature) in 150 to 200 mL of aqueous vehicle (such as plain water, 10 per cent dextrose in water or equal parts of water and 2 per cent methylcellulose suspension). The emulsion should be agitated gently during administration. The enema should be retained for as long as possible and should be followed by a cleansing enema.

After the 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. Then tape the tube in place. Suspend the resin in the appropriate amount of water or 10 percent dextrose in water at body temperature. While constantly stirring to keep the particles in suspension, introduce the suspension into the colon by gravitational flow. The suspension should be flushed with 50 or 100 mL of saline solution, following which the tube is clamped and left in place. If back leakage occurs, the hips may be elevated on pillows or a temporary knee-chest position may be taken. A somewhat thicker suspension may be used, but care should be taken that no paste is formed. Paste formation has a greatly reduced exchange surface and is particularly ineffective, if deposited in the rectal ampulla. If possible, keep the suspension in the sigmoid colon for several hours. In order to remove the resin, irrigate the colon with non-sodium containing solution at body temperature. Two quarts of flushing solution may be necessary. The returns should be drained constantly through a Y tube connection. While the use of sorbitol is not recommended, particular attention should be paid to the cleansing enema whenever sorbitol has been used.

It should be noted that the rectal route of administration should be reserved for patients who are vomiting or who have upper gastrointestinal tract problems, including paralytic ileus. The rectal route may also be used simultaneously with oral administration in cases where more rapid initial results are desirable. If both routes are used initially, it is probably unnecessary to continue rectal administration once the oral resin has reached the rectum.

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

Children:

Oral:
In smaller children and infants correspondingly lower doses should be employed. Calculation of the dose may be based upon the exchange rate of 1 mmol of potassium per g of resin. An appropriate initial dose is 1 g/kg body weight daily in divided doses in acute hyperkalemia. For maintenance therapy, dosage may be reduced to 0.5 g/kg body weight daily.

Rectal:
When refused by mouth, the resin may be given rectally using a dose at least as great as that which would have been given orally. The resin should be suspended in a proportional amount of 10% dextrose in water. Following retention of the enema, the colon should be irrigated to ensure adequate removal of the resin (see WARNINGS).

Neonates:

Rectal:
Since it is advised that the oral route should not be employed, only rectal administration should be considered. With rectal administration, the minimum effective dosage within the range of 0.5 to 1 g/kg of resin should be employed. The resultant suspension should be diluted as for adults. Following administration of the resin, the colon should be adequately irrigated to ensure recovery of the resin (see WARNINGS).

HOW SUPPLIED

In white opaque HDPE jars of 454g.

STORAGE

Store at room temperature (15 to 30 °C).

CONSUMER INFORMATION

PrKAYEXALATE®
(sodium polystyrene sulfonate powder)

This KAYEXALATE® leaflet is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about KAYEXALATE. Contact your doctor, nurse or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
KAYEXALATE is used to remove high amounts of potassium from the blood.

What it does:
KAYEXALATE attaches to the extra potassium in the body, particularly in the large intestine, so it can be removed from the body in the stool.

When it should not be used:

Do not take KAYELAXATE if:

- You have a bowel obstruction (blocked intestine).
- You have low levels of potassium in your blood.
- If you are allergic to sodium polystyrene sulfonate

Do not use KAYEXALATE in newborn babies who have slowed movements in their gut (caused by other medications or following surgery).
Do not give KAYEXALATE by mouth to newborn babies. KAYEXALATE should only be given rectally to newborns.

What the medicinal ingredient is:
Sodium polystyrene sulfonate

What the non-medicinal ingredients are:
None

What dosage forms it comes in:
Powder

WARNINGS AND PRECAUTIONS

BEFORE you use KAYEXALATE, talk to your doctor, nurse or pharmacist if you have or have had any medical conditions, especially the following:

- Heart problems
- High blood pressure
- Problems with your bowel or constipation
- Severe burns
- Low blood volume, which can occur with dehydration or bleeding
- Electrolyte imbalance. KAYEXALATE therapy can worsen these imbalances. Your doctor may want to check the levels of the electrolytes in your blood more frequently during treatment.
- Kidney problems
- Edema (swelling of the face, hands or feet with fluid)
- You require low salt diet.
- You are pregnant or intend to become pregnant.
- You are breastfeeding. It is not known if KAYEXALATE passes into breast milk.

When taken by mouth, avoid taking KAYEXALATE at the same time as other orally administered medications (see "PROPER USE OF THIS MEDICATION").

Magnesium containing laxatives should not be used with KAYEXALATE.

INTERACTIONS WITH THIS MEDICATION

As with most medicines, interactions with other drugs are possible. Tell your doctor, nurse or pharmacist about all the medicines you take, including drugs prescribed by other doctors, vitamins, minerals, natural supplements or alternative medicines (non-prescription drugs or over the counter drugs).

When taken by mouth, KAYEXALATE may interfere with how other oral medicines are absorbed (see "PROPER USE OF THIS MEDICATION").

The following may interact with KAYEXALATE:

- Digoxin, a medicine used for heart problems.
- Laxatives such as magnesium hydroxide or aluminium carbonate

- Thyroxine, a medicine for hypothyroidism
- Lithium, a medicine which can be used to treat bipolar disorder.
- Antacids containing aluminium or magnesium
- Sorbitol (a 'sugar free' sweetener used to sweeten food).
- Immunosuppressant drugs

PROPER USE OF THIS MEDICATION

Usual dose:
KAYEXALATE can be given by mouth or in the rectum.

The amount of KAYEXALATE you need to take will depend upon the amount of potassium in your blood.

Once the mixture has been prepared, it should be used straight away. If it needs to be stored, it should be stored for no longer than 24 hours. Do not heat KAYEXALATE.

Your doctor will decide exactly how much KAYEXALATE you need to take. The usual doses are:

ORAL DOSING

When taken by mouth, KAYEXALATE should be taken at least 3 hours before or 3 hours after other oral medications. For patients with gastroparesis (a condition preventing your stomach from emptying properly), a 6-hour separation should be considered. Consult your health care provider for recommendations (see "WARNINGS AND PRECAUTIONS and INTERACTIONS WITH THIS MEDICATION").

KAYEXALATE powder is usually given by mouth mixed in a small amount of water. It can also be mixed with food or sweetened liquid Do NOT mix KEYEXALATE with orange juice or fruit juice which contains potassium.

KAYEXALATE is a powder. Be careful not to inhale it accidentally. Breathing in the powder may cause coughing and shortness of breath.

Your doctor will regularly check the potassium, calcium and magnesium levels in your blood. The doctor may change the dose or stop the KAYEXALATE depending on what the results of these blood tests are.

Adults, including the elderly:
15 g one to four times daily as indicated above.

Children:
You should follow the dosing recommended by your doctor.
For children, KEYAXALATE is preferably given with a drink (NOT a fruit juice because of the high potassium content) or a little jam or honey.

Newborn babies (neonates)
KAYEXALATE should not be given by mouth.

RECTAL DOSING

The enema is usually given by a doctor or nurse.

Adults:
The enema should be prepared by the pharmacist or the nurse. The dosage should be administered once or twice daily at interval of six hours. The enema should be retained in the rectum for as long as possible. Afterwards, the colon needs to be washed out to remove KAYEXALATE.

Children and newborn babies (neonates):
The enema should be prepared by the pharmacist or the nurse. The enema should be retained in the rectum for as long as possible. Afterwards, the colon needs to be washed out to remove KAYEXALATE.

Overdose:
Taking too much KAYEXALATE may reduce your potassium in your blood below the normal level. If you take too much of this medication, you may feel irritable, confused, have muscle weakness, have diminished reflexes or paralysis.

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:
Do not take a double dose to make up for the dose you have missed. If it is almost time for the dose, skip the dose you missed and take the next dose when you are meant to.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Side effects may include:

- Nausea and vomiting
- Diarrhea
- Loss of appetite

If any of these affects you severely, tell your doctor, nurse or pharmacist.

SERIOUS SIDE EFFECTS, AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if severe	In all cases	
Constipation (bloating and swelling of the abdomen)			x
Abdominal pain (pain in your stomach and rectum)			x
Stomach irritation and bleeding (vomit that looks like coffee grounds)			x
Rectal bleeding (black bloody or tarry stools)			x
Allergic reaction (rash; itching; swelling of the face, tongue and throat; severe dizziness and trouble breathing)			x
High level of sodium (swelling)		x	
Low level of potassium (muscle cramps, feeling tired, confused, having muscle weakness or change in the heart rate)		x	
Low level of calcium (feeling nervous or unable to relax, having fits, or muscle cramps)		x	

SERIOUS SIDE EFFECTS, AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if severe	In all cases	
Fecal Impaction (leaking liquid stool, stomach pain, feeling the need to push, nausea, vomiting, loss of appetite)			x
Bowel obstruction (cramping, severe stomach pain, vomiting, bloating, constipation, inability to pass gas)			x
Bowel perforation (severe stomach pain, chills, fever, nausea vomiting)			x

This is not a complete list of side effects. For any unexpected effects while taking KAYEXALATE, contact your doctor or pharmacist.

HOW TO STORE IT

Store at room temperature (15 to 30 °C).

Keep out of reach and sight of children.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

IMPORTANT: PLEASE READ

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at: www.sanofi.ca or by contacting the sponsor, sanofi-aventis Canada Inc., at: 1-800-265-7927

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