

PRESCRIBING INFORMATION

Pr SOLYSTAT®

Sodium Polystyrene Sulfonate, USP

Powder for Suspension
Oral Suspension 250 mg/mL
Rectal Suspension (Retention Enema) 250 mg/mL

Cation Exchange Resin

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THERAPEUTIC CLASSIFICATION

Cation exchange resin

DESCRIPTION

Powder for Oral Suspension

Each gram of light brown, finely ground powder contains 1 gram of sodium polystyrene sulfonate. The sodium content is approximately 4.1 mmol (94.3 mg) per gram of the drug. SOLYSTAT is a cation exchange resin prepared in the sodium phase. Exchange capacity: approximately 3 mmol of potassium per gram *in vitro* and approximately 1 mmol of potassium per gram *in vivo*. SOLYSTAT can be administered either orally or as an enema.

Oral Suspension

Each 60 mL of brown, cherry-flavored suspension contains 15 g of sodium polystyrene sulfonate USP and 14.1 g of sorbitol. Also contains methylparaben and propylparaben as preservatives. The sodium content is 65 mmol (1.5 g)/60 mL. Exchange capacity: approximately 3 mmol of potassium per 4 mL (per gram of resin) of suspension *in vitro* and approximately 1 mmol *in vivo*.

Retention Enema

Each 120 mL of brown suspension contains 30 g of sodium polystyrene sulfonate USP and 28.2 g of sorbitol. Also contains methylparaben and propylparaben as preservatives. The sodium content is 65 mmol (1.5 g)/60 mL. Exchange capacity: approximately 3 mmol of potassium per 4 mL (per gram of resin) of suspension *in vitro* and approximately 1 mmol *in vivo*.

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 them 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

SOLYSTAT (sodium polystyrene sulfonate) is indicated for the treatment of hyperkalemia.

CONTRAINDICATIONS

SOLYSTAT (sodium polystyrene sulfonate) 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

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

WARNINGS

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 the use of sodium polystyrene sulfonate. 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).

Alternative therapy in severe hyperkalemia: Since effective lowering of serum potassium with SOLYSTAT 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.

Hypokalemia: SOLYSTAT 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 SOLYSTAT 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 electrocardiogram (ECG). Cardiac arrhythmias such as premature atrial, nodal and ventricular contractions, and supraventricular 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'.

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 sodium polystyrene sulfonate (15 grams) contains approximately 60 mmol of sodium. Since the resin is a source of sodium, caution is advised when SOLYSTAT 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.

Other electrolyte disturbances: Like all cation-exchange resins, sodium polystyrene sulfonate 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 SOLYSTAT 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.

Children and neonates: In neonates, SOLYSTAT 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.

DRUG INTERACTIONS

Concomitant use not recommended:

Sorbitol (oral or rectal): Concomitant administration of sorbitol with SOLYSTAT 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

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

LACTATION

Sodium polystyrene sulfonate 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

SOLYSTAT (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 sodium polystyrene sulfonate.

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.

Reporting Suspected Side Effects

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to:
Canada Vigilance Program
Health Canada
Postal Locator 0701E
Ottawa, Ontario
K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

DOSAGE AND ADMINISTRATION

SOLYSTAT (sodium polystyrene sulfonate) 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.

Powder for Suspension

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

SOLYSTAT 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 SOLYSTAT one to four times daily. One gram of SOLYSTAT powder contains 4.1 mmol of sodium; one level teaspoon contains approximately 3.5 grams of SOLYSTAT powder and 15 mmol of sodium. A heaping teaspoon may contain as much as 10-12 grams of SOLYSTAT 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.

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. Thirty (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 gram 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).

Oral Suspension and Retention Enema**Adults, Including the Elderly**

Oral: 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.

The average daily adult dose of the resin is 15 to 60 grams (60 to 240 mL). This is provided by administering 60 mL (15 grams) of SOLYSTAT™ one to four times daily. 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.

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: The suspension may be given as a retention enema, but due to less effective potassium exchange, it is recommended that 120 to 200 mL of suspension should be used (30 g to 50 g resin) given once or twice daily (at intervals of six hours).

120 ml Enema Bottle (Retention Enema):

Directions – the following steps should be performed for the proper rectal use of the enema bottle.

1. Administer a cleansing enema.
2. Insert a rubber catheter into the rectum so that it is well into the sigmoid colon. (about 20 cm)
3. Shake bottle well, remove shield from tip and insert tip firmly into catheter.
4. Squeeze bottle to release suspension, then remove tip from catheter.
5. Retain enema if possible for several hours.
6. Administer up to two quarts of a non-sodium containing cleansing enema after administration of this drug in order to remove the resin.

The suspension should be administered 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. 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. 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.

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 (4 mL/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.

AVAILABILITY

Powder for Suspension

Supplied in jars of 454 g.

Oral Suspension

Unit dose plastic bottles of 60 mL and plastic bottles of 500 mL.

Retention Enema

Thin plastic bottles of 120 mL with special enema tip.

STORAGE

Powder for Suspension

Store between 15°C and 30°C (59°F and 86°F). Store in a well-closed container.

Oral Suspension and Retention Enema

Store between 15°C and 30°C (59°F and 86°F). Store in a well-closed container. Protect from freezing and from excessive heat.