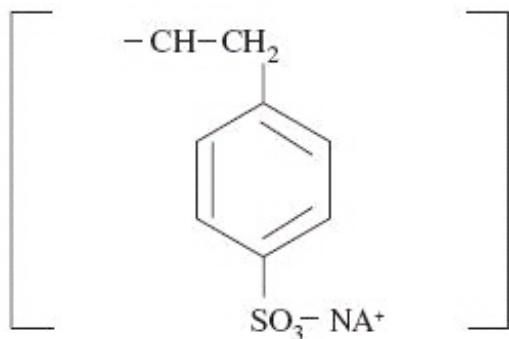


Sodium Polystyrene Sulfonate Suspension, USP
Cation-Exchange Resin
Rx Only

DESCRIPTION

Sodium Polystyrene Sulfonate Suspension, USP can be administered orally or in an enema. It is a suspension containing 15 grams of cation-exchange resin (Sodium Polystyrene Sulfonate, USP) per 60 mL of suspension. Also contains Purified Water, USP; Propylene Glycol, USP; Sodium Saccharin, USP; Methylparaben, NF; Propylparaben, NF; Xanthan Gum, NF; and Citric Acid Anhydrous, USP.

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



The sodium content of the suspension is 1500 mg (65 mEq) per 60 mL. It is a brown, slightly viscous suspension with an *in-vitro* exchange capacity of approximately 3.1 mEq (*in-vivo* approximately 1 mEq) of potassium per 4 mL (1 gram) of suspension. It can be administered orally or in an enema.

CLINICAL PHARMACOLOGY

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. For the most part, this action occurs 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. It commonly approximates the order of 33%, but the range is so large that definitive indices of electrolyte balance must be clearly monitored.

Metabolic data are unavailable.

INDICATION AND USAGE

Sodium Polystyrene Sulfonate Suspension, USP is indicated for the treatment of hyperkalemia.

CONTRAINDICATIONS

Sodium Polystyrene Sulfonate Suspension, USP is contraindicated in the following conditions: patients with hypokalemia, patients with a history of hypersensitivity to polystyrene sulfonate resins, obstructive bowel disease, oral or rectal administration in neonates (See **PRECAUTIONS**).

WARNINGS

Intestinal Necrosis

Cases of intestinal necrosis, which may be fatal, and other serious gastrointestinal adverse events (bleeding, ischemic colitis, perforation) have been reported in association with sodium polystyrene sulfonate 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 additional sorbitol is not recommended (see **PRECAUTIONS, Drug Interactions**).

- 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.

Alternative Therapy in Severe Hyperkalemia

Since the effective lowering of serum potassium with sodium polystyrene sulfonate 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) or hyperkalemia so marked as to constitute a medical emergency.

Therefore, other definitive measures, including dialysis, should always be considered and may be imperative.

Hypokalemia

Serious potassium deficiency can occur from sodium polystyrene sulfonate therapy. The effect must be carefully controlled by frequent serum potassium determinations within each 24 hour period. Since intracellular potassium deficiency is not always reflected by serum potassium levels, the level at which treatment with sodium polystyrene sulfonate

should be discontinued must be determined individually for each patient. Important aids in making this determination are the patient's clinical condition and electrocardiogram. Early clinical signs of severe hypokalemia include a pattern of irritable confusion and delayed thought processes.

Electrocardiographically, severe hypokalemia is often associated with a lengthened Q-T interval, widening, flattening, or inversion of the T wave, and prominent U waves. Also, cardiac arrhythmias may occur, such as premature atrial, nodal, and ventricular contractions, and supraventricular and ventricular tachycardias. The toxic effects of digitalis are likely to be exaggerated. Marked hypokalemia can also be manifested by severe muscle weakness, at times extending into frank paralysis.

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. Accordingly, patients receiving sodium polystyrene sulfonate should be monitored for all applicable electrolyte disturbances.

Systemic Alkalosis

Systemic alkalosis has been reported after cation-exchange resins were administered orally in combination with nonabsorbable cation-donating antacids and laxatives such as magnesium hydroxide and aluminum carbonate. Magnesium hydroxide should not be administered with sodium polystyrene sulfonate. One case of grand mal seizure has been reported in a patient with chronic hypocalcemia of renal failure who was given sodium polystyrene sulfonate with magnesium hydroxide as a laxative (See **PRECAUTIONS, Drug Interactions**).

Risk of Aspiration

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

Binding to Other Orally Administered Medications

Sodium polystyrene sulfonate suspension 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 sodium polystyrene sulfonate suspension. Patients with gastroparesis may require a 6 hour separation (see **DOSAGE AND ADMINISTRATION** and **PRECAUTIONS, Drug Interactions**).

PRECAUTIONS

Caution is advised when sodium polystyrene sulfonate is administered to patients who cannot tolerate even a small increase in sodium loads (i.e., severe congestive heart failure, severe hypertension, or marked edema). In such instances compensatory restriction of sodium intake from other sources may be indicated.

Precautions should be taken to ensure the use of adequate volumes of sodium-free cleansing enemas after rectal administration.

In the event of clinically significant constipation, treatment with Sodium Polystyrene Sulfonate Suspension, USP should be discontinued until normal bowel motion is resumed (See **WARNINGS, Intestinal Necrosis**).

Drug Interactions

General Interactions

No formal drug interaction studies have been conducted in humans. Sodium polystyrene sulfonate suspension has the potential to bind other drugs. In *in-vitro* binding studies, sodium polystyrene sulfonate 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 sodium polystyrene sulfonate. Binding of sodium polystyrene sulfonate suspension to other oral medications could cause decreased gastrointestinal absorption and loss of efficacy when taken close to the time sodium polystyrene sulfonate suspension is administered. Administer sodium polystyrene sulfonate suspension 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.

Antacids

The simultaneous oral administration of sodium polystyrene sulfonate with nonabsorbable cation-donating antacids and laxatives may reduce the resin's potassium exchange capability.

Nonabsorbable cation-donating antacids and laxatives

Systemic alkalosis has been reported after cation exchange resins were administered orally in combination with nonabsorbable cation-donating antacids and laxatives such as magnesium hydroxide and aluminum carbonate. Magnesium hydroxide should not be administered with sodium polystyrene sulfonate. One case of grand mal seizure has been reported in a patient with chronic hypocalcemia of renal failure who was given sodium polystyrene sulfonate with magnesium hydroxide as a laxative.

Intestinal obstruction due to concretions of aluminum hydroxide when used in combination with sodium polystyrene sulfonate has been reported.

Digitalis

The toxic effects of digitalis on the heart, especially various ventricular arrhythmias and A-V nodal dissociation, are likely to be exaggerated by hypokalemia, even in the face of serum digoxin concentrations in the "normal range" (See **WARNINGS**).

Sorbitol

Concomitant use of sorbitol with sodium polystyrene sulfonate has been implicated in cases of intestinal necrosis, which may be fatal (See **WARNINGS**).

Lithium

Sodium Polystyrene Sulfonate Suspension, USP may decrease absorption of lithium.

Thyroxine

Sodium Polystyrene Sulfonate Suspension, USP may decrease absorption of thyroxine.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies have not been performed.

Pregnancy

Animal reproduction studies have not been conducted with sodium polystyrene sulfonate. It is also not known whether sodium polystyrene sulfonate can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Sodium polystyrene sulfonate should be given to a pregnant woman only if clearly needed.

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 sodium polystyrene sulfonate is administered to a nursing woman.

Pediatric Use

The effectiveness of Sodium Polystyrene Sulfonate Suspension, USP in pediatric patients has not been established. **The use of Sodium Polystyrene Sulfonate Suspension, USP is contraindicated in neonates and especially in premature infants.** In children and neonates, particular care should be observed with rectal administration, as excessive dosage could result in impaction of the resin. **Precautions should be taken to ensure the use of adequate volumes of sodium-free cleansing enemas after rectal administration.**

ADVERSE REACTIONS

Sodium Polystyrene Sulfonate Suspension, USP may cause some degree of gastric irritation. Anorexia, nausea, vomiting, and constipation may occur especially if high doses are given. Also, hypokalemia, hypocalcemia, hypomagnesemia and significant sodium retention, and their related clinical manifestations, may occur (See **WARNINGS**). Occasionally diarrhea develops. Large doses in elderly individuals may cause fecal impaction (See **PRECAUTIONS**). Rare instances of intestinal necrosis have been reported. Intestinal obstruction due to concretions of aluminum hydroxide, when used in combination with sodium polystyrene sulfonate, has been reported.

The following events have been reported from worldwide post marketing experience:

- Fecal impaction following rectal administration, particularly in children;
- Gastrointestinal concretions (bezoars) following oral administration;
- Ischemic colitis, gastrointestinal tract ulceration or necrosis which could lead to intestinal perforation; and
- Rare cases of acute bronchitis and/or bronchopneumonia associated with inhalation of particles of polystyrene sulfonate (see **WARNINGS**).

To report SUSPECTED ADVERSE REACTIONS, contact Burel Pharmaceuticals, LLC at 1-844-436-7010 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

OVERDOSAGE

Overdosage may result in electrolyte disturbances including hypokalemia, hypocalcemia, and hypomagnesemia. Biochemical disturbances resulting from overdosage may give rise to clinical signs and symptoms of hypokalemia, including: irritability, confusion, delayed thought processes, muscle weakness, hyporeflexia, which may progress to frank paralysis and/or apnea. Tetany may occur. Electrocardiographic changes may be consistent with hypokalemia or hypocalcemia; cardiac arrhythmias may occur. 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.

DOSAGE AND ADMINISTRATION

Administer sodium polystyrene sulfonate suspension 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, Drug Interactions**).

The average daily adult dose is 15 g (60 mL) to 60 g (240 mL) of suspension. This is best provided by administering 15 g (60 mL) of Sodium Polystyrene Sulfonate Suspension, USP one to four times daily. Each 60 mL of Sodium Polystyrene Sulfonate Suspension, USP contains 1500 mg (65 mEq) of sodium. Since the *in-vivo* efficiency of sodium-potassium exchange resins is approximately 33%, about one-third of the resin's actual sodium content is being delivered to the body.

In smaller children and infants, lower doses should be employed by using as a guide a rate of 1 mEq of potassium per gram of resin as the basis for calculation. Administer with patient in an upright position (see **WARNINGS**).

Sodium Polystyrene Sulfonate Suspension, USP may be introduced into the stomach through a plastic tube and, if desired, given with a diet appropriate for a patient in renal failure.

Sodium Polystyrene Sulfonate Suspension, USP may also be given, although with less effective results, as an enema consisting (for adults) of 30 g (120 mL) to 50 g (200 mL) every six hours. The enema should be retained as long as possible and followed by a cleansing enema.

After an initial cleansing enema, a soft, large size (French 28) rubber tube is inserted into the rectum for a distance of about 20 cm, with the tip well into the sigmoid colon, and taped into place. The suspension is introduced at body temperature by gravity. The suspension is flushed with 50 or 100 mL of fluid, following which the tube is clamped and left in place. If back leakage occurs, the hips are elevated on pillows or a knee-chest position is taken temporarily. The suspension is kept in the sigmoid colon for several hours, if possible. **Then the colon is irrigated with a sodium-free cleansing enema at body temperature in order to remove the resin. Two quarts of flushing solution may be necessary. The returns are drained constantly**

through a Y tube connection.

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

Sodium Polystyrene Sulfonate Suspension, USP should not be heated for to do so may alter the exchange properties of the resin.

HOW SUPPLIED

Sodium Polystyrene Sulfonate Suspension, USP is a light brown suspension supplied in pint (473 mL) bottles (NDC 35573-108-57), and 60 mL unit dose bottles, 10 bottles per carton (NDC 35573-108-14).

Dispense in a tight container, as defined in the USP. If repackaging into other containers, store in refrigerator and use within 14 days of packaging.

SHAKE WELL BEFORE USING.

Store at 20°-25°C (68°-77°F); excursions permitted to 15°-30°C (59°-86°F). [See USP Controlled Room Temperature].

Manufactured for:

Burel Pharmaceuticals, LLC

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