

PRESCRIBING INFORMATION

RESONIUM CALCIUM[®]

(calcium polystyrene sulfonate)

Cation-Exchange Resin

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ACTIONS AND CLINICAL PHARMACOLOGY

RESONIUM CALCIUM (calcium polystyrene sulfonate) is a cation exchange resin prepared in the calcium phase. Each gram of resin has a theoretical *in vitro* exchange capacity of about 1.3 to 2 millimoles (mmol) of potassium (K⁺). *In vivo*, the actual amount of potassium bound will be less than this. The sodium (Na⁺) content of the resin is less than 1 mg/g. The calcium content is 1.6 to 2.4 mmol/g. The resin is insoluble in water. Calcium polystyrene sulfonate is not absorbed from the gastrointestinal tract.

RESONIUM CALCIUM acts by a cumulative process throughout the gastrointestinal tract, removing potassium ions which are excreted in the feces.

As the resin passes through the colon, it comes into contact with fluids containing increasing amounts of potassium. In the cecum the concentration of Na⁺ and K⁺ are similar to those in the small intestine. In the stool water of the sigmoid colon there may be 6-38 mmol/L sodium and 14-44 mmol/L potassium. The result is that potassium is taken up in increasing amounts in exchange for calcium ions. The length of time the resin remains in the body is a decisive factor in its effectiveness. For this reason oral administration is more effective than the use of enemas which should, if possible, be retained for 9 hours. The efficiency of potassium exchange is unpredictably variable. The resin is not selective for potassium.

INDICATIONS

RESONIUM CALCIUM is indicated in patients with hyperkalemia associated with anuria or severe oliguria. It reduces serum levels of potassium and removes excess potassium from the body. RESONIUM CALCIUM is indicated in all states of hyperkalemia due to acute and chronic renal failure; examples include use following abortion, complicated labor, incompatible blood transfusion, crush injury, prostatectomy, severe burns, surgical shock, and in cases of severe glomerulonephritis and pyelonephritis.

RESONIUM CALCIUM can also be useful in patients requiring dialysis. Serum potassium levels in acute renal failure often reach dangerous heights before a rise in blood urea indicates the need for hemodialysis. RESONIUM CALCIUM can be used to reduce these potassium levels and thereby postpone the need for the use of the artificial kidney machine until other causes make it necessary.

Patients on regular hemodialysis therapy may develop shunt difficulties and underdialysis occurs, resulting in serious hyperkalemia. In these circumstances it is advisable to give the resin to control hyperkalemia during the period of underdialysis. Monitoring serum potassium and calcium levels should be undertaken at regular intervals.

When patients on routine hemodialysis present a dietary management problem and tend towards hyperkalemia, RESONIUM CALCIUM can be used to control blood potassium levels. Similarly, patients on prolonged peritoneal dialysis may develop intermittent hyperkalemia after a few weeks, possibly due to dietary problems. These patients also can be satisfactorily controlled with

RESONIUM CALCIUM.

CONTRAINDICATIONS

RESONIUM CALCIUM should not be administered to patients with:

- Serum potassium < 5 mmol/L
- Conditions associated with hypercalcemia (e.g. hyperparathyroidism, multiple myeloma, sarcoidosis or metastatic carcinoma)
- A history of hypersensitivity to polystyrene sulfonate resins
- Obstructive bowel disease
- Oral administration of RESONIUM CALCIUM is contraindicated in neonates. Administration of the resin in neonates with reduced gut motility (postoperatively or drug induced) is contraindicated.

WARNINGS

In neonates, RESONIUM CALCIUM should not be given by the oral route (see CONTRAINDICATIONS).

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 RESONIUM CALCIUM 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).

PRECAUTIONS

Hypokalemia

During treatment with RESONIUM CALCIUM the possibility of severe potassium depletion should be considered. Adequate clinical control, as well as biochemical control by daily estimation of serum electrolytes and blood urea levels, is essential during treatment especially in patients on digitalis. To prevent serious hypokalemia, administration of the resin should be discontinued as soon as the serum potassium level falls to 5 mmol/L (see DRUG INTERACTIONS).

Other electrolyte disturbances

Like all cation-exchange resins, RESONIUM CALCIUM is not totally selective for potassium. Hypomagnesemia and/or hypercalcemia may occur. Accordingly, patients should be monitored for all applicable electrolyte disturbances.

Hypercalcemia has been reported in well dialysed patients receiving calcium resin, and

occasionally in patients with chronic renal failure. Many patients in chronic renal failure have low serum calcium and high serum phosphate, but some, who cannot be screened out beforehand, show a sudden rise in serum calcium to high levels after therapy with calcium resin. The risk emphasizes the need for adequate biochemical control. Serum calcium levels should be estimated at weekly intervals to detect the early development of hypercalcemia. The dose of administered calcium resin should be reduced to levels at which hypercalcemia and hypokalemia are prevented (see REFERENCES).

Other risks

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

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

Children and neonates:

In neonates, RESONIUM CALCIUM should not be given by the oral route (see CONTRAINDICATIONS).

In both children and neonates, particular care should be observed with rectal administration, as excessive dosage or inadequate dilution could result in impaction of the resin.

Due to the risk of gastrointestinal tract hemorrhage or colonic necrosis, 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 RESONIUM CALCIUM 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:

Digitalic drugs: The toxic effects of digitalis on the heart, especially various ventricular arrhythmias and atrioventricular (A-V) nodal dissociation, are likely to be exaggerated if hypokalemia and/or hypercalcemia develop, even in the face of serum digoxin concentrations in the 'normal range' (see PRECAUTIONS).

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

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.

Aluminum hydroxide: Intestinal obstruction due to concretions of aluminum hydroxide has been reported when aluminum hydroxide was combined with the resin (sodium form).

Lithium: Possible decrease of lithium absorption.

Thyroxine: Possible decrease of thyroxine absorption.

PREGNANCY

RESONIUM CALCIUM is not absorbed from the gastrointestinal tract. No data are available about the use of polystyrene sulfonate resins in human pregnancy.

LACTATION

RESONIUM CALCIUM is not absorbed from the gastrointestinal tract. No data are available about the use of polystyrene sulfonate resins in human lactation.

ADVERSE REACTIONS

Gastrointestinal disorders:

Intestinal intolerance due to the gritty consistency and bulk of the resin may be manifested by the appearance of general adverse effects including nausea, vomiting, gastric irritation, anorexia, constipation and occasionally, diarrhea. These adverse effects may be relieved by intermittent therapy and the use of mild laxatives where constipation is a factor.

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. This could possibly due to co-existing pathology or inadequate dilution of the resin.

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, RESONIUM CALCIUM may give rise to hypokalemia and hypercalcemia and their related clinical manifestations (see PRECAUTIONS and OVERDOSAGE). Cases of hypomagnesemia have been reported.

Hypercalcemia has been reported in well dialysed patients receiving calcium resin, and occasionally in patients with chronic renal failure (see PRECAUTIONS).

Respiratory, thoracic and mediastinal disorders:

Some cases of acute bronchitis and/or bronchopneumonia associated with inhalation of particles of calcium polystyrene sulfonate have been described.

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 this progression. Electrocardiographic changes may be consistent with hypokalemia or hypercalcemia; cardiac arrhythmia 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.

DOSAGE AND ADMINISTRATION

Treatment with the resin should be given as soon as the serum potassium level rises above 6 mmol/L (23.5 mg per 100 mL). The action may be delayed for one or two days since maximal exchange probably takes place in the colon. Exchange will continue until all the resin has been voided (this may be one or two days after administration has been discontinued). For this reason, resin therapy should be stopped when the serum potassium level has fallen to 5 mmol/L, otherwise, the continued action may lead to potassium depletion.

RESONIUM CALCIUM is for oral or rectal administration only. The following doses are suggested only as a general guide. The precise daily dose should be decided on the basis of regular clinical and serum electrolyte determination.

The amount of potassium taken up by the resin will be largely determined by the length of time it is exposed to the high potassium concentration in the fecal water in the colon. For this reason, a tendency towards constipation should be encouraged and purgative drugs should be avoided.

Adults, Including the Elderly:

a) Oral: For adults the usual dose is 15 g, 3 or 4 times a day. The resin is given by mouth as a suspension in a little water, or for greater palatability, the resin may be made into a paste with some sweetened vehicle, but not orange juice or other fruit juices that are known to contain potassium. The amount of fluid usually ranges from 3 to 4 mL per gram of resin. If there is difficulty with swallowing, it may be given through a gastric tube, 2 to 3 mm in diameter.

b) Rectal: In cases where vomiting may make oral administration difficult or in patients who have upper gastrointestinal tract problems, including paralytic ileus, the resin may be given rectally as a suspension of 30 g resin in 100 mL of 2% methylcellulose and 100 mL of water, as a daily retention enema. In the initial stages, administration by this route as well as orally may help to achieve a more rapid lowering of the serum potassium level.

Since the rectal route is less effective than the oral route, the longer the resin is retained the greater is the amount of potassium removed. The enema should, if possible, be retained for at least nine hours and then the colon irrigated to remove the resin. If both routes are used initially, it is probably unnecessary to continue rectal administration once the oral resin has reached the rectum.

Children:

a) Oral: In smaller children and infants correspondingly smaller doses should be employed by using as a guide a rate of 1mEq of potassium per gram of resin as the basis for calculation. Children should be given 1 g/kg body weight of RESONIUM CALCIUM daily in divided doses, in acute hyperkalemia. In maintenance therapy the dose may be reduced to 0.5 g/kg body weight daily in divided doses. RESONIUM CALCIUM should be given orally, preferably with a drink or a little jam or honey. It should not be given in fruit drinks and some carbonated beverages, since these have a high potassium content.

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

Neonates:

Oral administration of RESONIUM CALCIUM is contraindicated in neonates. Administration of the resin in neonates with reduced gut motility (postoperatively or drug-induced) is contraindicated (see CONTRAINDICATIONS). Only rectal administration should be considered. With rectal administration, the minimum effective dosage within the range of 0.5 g/kg to 1 g/kg should be employed, diluted as for adults and with adequate irrigation to ensure recovery of the resin (see WARNINGS and PRECAUTIONS).

STORAGE

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

AVAILABILITY

RESONIUM CALCIUM is supplied in a white opaque HDPE jar containing 300 g. A plastic measure is included which holds 15 g of resin.

CHEMISTRY

RESONIUM CALCIUM (calcium polystyrene sulfonate), is a solid substance, cream to light brown fine powder with vanilla odor.

RESONIUM CALCIUM bears the chemical name of cross-linked polystyrene calcium sulfonate.

RESONIUM CALCIUM is a sulfonic acid resin in the calcium phase containing about 8% calcium. Its average binding capacity is 1.6 mmol of potassium per gram of resin. This implies a binding of 96 mmol of potassium by a daily dose of 60 g RESONIUM CALCIUM. The sodium content of the anhydrous resin is not more than 1 mg per gram.

Non medicinal ingredients:

Saccharin, vanillin

TOXICOLOGY

Segal et al demonstrated that amberlite IR-4 (a general range of cation exchange resins), could be fed to rats for eight months without any adverse effects on their growth and well-being, except that on the 20% dietary resin regime the growth of male rats was slightly inhibited (see REFERENCES).

McChesney and McAuliff carried out a similar study with sulfonic acid resins at a 10% dietary level and found the growth of male rats, but not of females, was slightly inhibited. The male rats however, thrived on sodium resins which led McChesney and McAuliff to conclude that the inhibition was related to acidosis or sodium deprivation (see REFERENCES).

Symptoms indicative of sodium depletion (excessive weight loss and weakness) or of potassium depletion (muscle weakness, mental confusion and apathy) may occur without adequate biochemical control. No studies have been published carried out in healthy volunteers.

REFERENCES

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4. Wootton FT, Rhodes DF, Lee WM, Fitts CT. Colonic necrosis with Kayexalate-sorbitol enemas after renal transplantation. *Ann Intern Med* 1989;111(11):947-9.
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7. McChesney EW, McAuliff JP. Effects of some ion-exchange resins on the mineral metabolism of rats. *Am J Physiol* 1950;160: 264-276.

IMPORTANT: PLEASE READ

CONSUMER INFORMATION RESONIUM CALCIUM® (calcium polystyrene sulfonate powder)

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

ABOUT THIS MEDICATION

What the medication is used for:

RESONIUM CALCIUM is used to remove high amounts of potassium from the blood.

What it does:

RESONIUM CALCIUM 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 RESONIUM CALCIUM if:

- You have a bowel obstruction (blocked intestine).
- You have medical conditions, such as thyroid problems or some types of cancer that result in high levels of calcium in your blood.
- You have low levels of potassium in your blood.
- You are allergic to calcium polystyrene sulfonate or any of the ingredients in the product (**see What the non-medical ingredients are**).

Do not give RESONIUM CALCIUM by mouth to newborn babies. RESONIUM CALCIUM should only be given rectally to newborns.

Do not use RESONIUM CALCIUM in newborn babies who have slowed movements in their gut (caused by other medications or following surgery).

What the medicinal ingredient is:

Calcium polystyrene sulfonate

What the non-medical ingredients are:

Saccharin, vanillin

What dosage forms it comes in:

Powder

WARNINGS AND PRECAUTIONS

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

- Problems with your bowel or constipation

- **Kidney problems**
- **Severe burns**
- **You are taking drugs that suppress your immune system**
- **You have heart problems and are taking the drug digitalis**
- Low blood volume, which can occur with dehydration or bleeding.
- **Electrolyte imbalance.** RESONIUM CALCIUM therapy can worsen these imbalances. Your doctor may want to check the levels of the electrolytes in your blood more frequently during treatment.
- **Breathing, lung or chest problems:** Accidental inhalation of the drug may cause acute bronchitis and/or pneumonia. Caution is advised not to inhale the medicine when ingesting it.
- You are pregnant or intend to become pregnant.
- You are breastfeeding. It is not known if RESONIUM CALCIUM passes into breast milk.

Magnesium containing laxatives should not be used with RESONIUM CALCIUM.

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).

The following may interact with RESONIUM CALCIUM:

- 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).

PROPER USE OF THIS MEDICATION

Usual dose:

RESONIUM CALCIUM can be given by mouth or in the rectum.

IMPORTANT: PLEASE READ

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

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

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

ORAL DOSING

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

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

Adults, including the elderly:

15 g three to four times daily as indicated above. The spoon provided in the jar contains 15 g of powder when filled level.

Children:

You should follow the dosing recommended by your doctor.

For children, RESONIUM CALCIUM 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)

RESONIUM CALCIUM 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. If possible, the enema should be retained in the rectum for at least nine hours. Afterwards, the colon needs to be washed out to remove RESONIUM CALCIUM.

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 RESONIUM CALCIUM.

Overdose:

Taking too much RESONIUM CALCIUM may reduce your potassium in your blood below the normal level. If you take too much, 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	
Abdominal pain (pain in your stomach and rectum)			x
Allergic reaction (rash; itching; swelling of the face, tongue and throat; severe dizziness and trouble breathing)			x
Constipation (bloating and swelling of the abdomen)			x
Stomach irritation and bleeding (vomit that looks like coffee grounds)			x
Rectal bleeding (black bloody or tarry stools)			x
High level of calcium (nausea, constipation, loss of appetite, confusion, memory loss)		x	

IMPORTANT: PLEASE READ

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	
Low level of potassium (muscle cramps, feeling tired, confused, having muscle weakness or change in the heart rate)		x	
Low level of magnesium: abnormal eye movements, seizures, feeling tired, muscle spasms or cramps, muscle weakness, numbness		x	
Fecal Impaction (a hard lump of stools causing leaking liquid stool, stomach pain, feeling the need to push, nausea, vomiting, loss of appetite) following rectal administration particularly in children,			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 RESONIUM CALCIUM, 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 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.

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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