

Patiromer (VELTASSA™)**Criteria for Use****March 2016**

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

The Product Information should be consulted for detailed prescribing information. See the VA National PBM-MAP-VPE Monograph on this drug at www.pbm.va.gov or <https://vaww.cmopnational.va.gov/cmop/PBM/default.asp> for further information.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive patiromer*

- History of hypersensitivity to patiromer or any of its components
- Severe constipation, bowel obstruction or impaction, including abnormal post-operative bowel motility disorders, unless corrected (Refer to Issues for Consideration)
- Hyperkalemia requiring emergency intervention (Refer to Issues for Consideration; FDA indication)
- Hypomagnesemia (e.g., serum magnesium < 1.4 mg/dl) (Refer to Monitoring)
- Patient unable to comply with instructions to allow for adequate separation of patiromer and other oral medications [Boxed Warning to administer other oral medications at least 6 hours before or after patiromer] or with required monitoring (Refer to Monitoring)

Inclusion Criteria *The answers to the following must be fulfilled in order to meet criteria for patiromer*

- Persistent or recurrent serum potassium ≥ 5.5 mEq/L despite the following measures to reduce serum potassium:
 - o Review for discontinuation of medications that may contribute to hyperkalemia (e.g., potassium supplements, potassium-sparing diuretics, nonsteroidal anti-inflammatory drugs)
 - o Instruction on a low potassium diet and avoidance of potassium salt substitutes
 - o Initiation or adjustment of diuretic (loop or thiazide) therapy, as appropriate
 - o If considering a renin-angiotensin-aldosterone system (RAAS) inhibitor, or a RAAS inhibitor is part of the current treatment regimen, adjustment of the initial or current angiotensin-converting enzyme inhibitor (ACEI), angiotensin II receptor blocker (ARB) and/or mineralocorticoid receptor antagonist (MRA) dose, as indicated, taking into consideration the risk vs. benefit of continued therapy vs. treatment of hyperkalemia (Refer to Issues for Consideration)
 - o Trial of sodium polystyrene sulfonate, as appropriate (Refer to Issues for Consideration)

Dosage and Administration

- Patiromer should not be taken in dry form. Each dose of patiromer should be prepared immediately prior to administration as follows:
 - Step 1: Add approximately 1 ounce (30 ml) water to an empty glass or cup
 - Step 2: Empty the entire packet(s) contents into the glass or cup
 - Step 3: Stir the mixture thoroughly
 - Step 4: Add an additional 2 ounces (60 ml) of water to the glass or cup that contains the mixture
 - Step 5: Stir the mixture thoroughly (the powder will not dissolve and will appear cloudy)
 - Step 6: Immediately drink the mixture. If some powder remains in the glass, add more water, stir and drink immediately. Repeat as necessary to ensure the entire dose is administered.
- The initial dose of patiromer is 8.4 grams once daily. Serum potassium should be monitored, with the dose of patiromer adjusted based on the potassium level and treatment goal. The dose of patiromer may be increased or decreased, up to a maximum of 25.2 grams once daily, to achieve the desired serum potassium. The dose may be titrated according to serum potassium at intervals of one week or more, by increments of 8.4 grams.
- Patiromer should be administered with food. It should be mixed with water only. Patiromer should not be heated, microwaved, or added to heated foods.
- Patiromer should be stored in the refrigerator. If removed from the refrigerator and stored at room temperature, patiromer should be used within 3 months (but not past the manufacturer expiration date).

Monitoring

- **Serum potassium**
 - o **Efficacy:** In one clinical trial of patients with chronic kidney disease and hyperkalemia (serum potassium ≥ 5.1 to < 6.5 mmol/L [or mEq/L]) on a RAAS inhibitor, patiromer significantly reduced serum potassium (mean -1.01 ± 0.03 mEq/L) at 4 weeks compared to baseline, with 76% of patients achieving target potassium 3.8 to < 5.1 mEq/L. Patients eligible for the 8 week withdrawal phase

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(i.e., those with serum potassium ≥ 5.5 mEq/L at baseline and who achieved target potassium at the end of the initial treatment phase) experienced a significant increase in serum potassium (0.72 mEq/L) on placebo compared to no change in those continued on patiromer, with 60% of patients on placebo compared to 15% of patients on patiromer experiencing a recurrence of hyperkalemia (potassium ≥ 5.5 mEq/L).

- **Monitoring frequency:** In this short-term trial, serum potassium was measured at baseline, day 3 of each phase, and weekly thereafter; in a long-term study, serum potassium was measured at day 3, then weekly for the first 8 weeks, then monthly thereafter up to 52 weeks.
- **Hypomagnesemia:** Reported in 9% (as an adverse reaction in 5.3%) of patients in clinical trials. Monitor serum magnesium (e.g., every 2 weeks for 2 months, then monthly thereafter up to 52 weeks, as per one long-term study); consider magnesium supplementation or risk vs. benefit of continued treatment with patiromer, in patients who develop hypomagnesemia on patiromer.
- **Drug Interactions**
 - **Boxed Warning:** It is recommended to administer other oral medications at least 6 hours before or 6 hours after patiromer, due to the potential binding of patiromer to other orally administered medications that could result in decreased gastrointestinal absorption and reduced efficacy if taken within a short period of time of each other; the warning also recommends to choose patiromer or the other oral medication if adequate dosing separation is not possible.
 - According to *in vitro* data, about half of the medications studied demonstrated binding to patiromer. Data from drug interaction studies in healthy volunteers have become available since the approval of patiromer and are pending additional review.

Issues for Consideration

- **FDA indication:** Patiromer is indicated for the treatment of hyperkalemia. It should not be used as an emergency treatment for life-threatening hyperkalemia due to its delayed onset of action.
 - Patiromer has not been studied nor is it FDA approved for the management of acute hyperkalemia requiring intervention. Clinical trials of patiromer included patients with potassium < 6.5 mEq/L. According to the product information, a statistically significant reduction in serum potassium was noted at 7 hours after the first dose of patiromer. If being considered for adjunctive therapy in the acute management of hyperkalemia (as where sodium polystyrene sulfonate has been used), this should be determined on a case by case basis, after first considering sodium polystyrene sulfonate, as appropriate.
- **Consultation with Nephrology:** Patiromer was studied primarily in patients with chronic kidney disease. Consultation with nephrology is strongly recommended either prior to or during treatment with patiromer to evaluate or confirm etiology of hyperkalemia, and to recommend or support appropriate management.
- **Warning/precaution for worsening of gastrointestinal motility:** Patients with a history of bowel obstruction or major gastrointestinal surgery, severe gastrointestinal disorders, diabetic gastroparesis, or swallowing disorders were not included in the clinical trials of patiromer. Evaluate for tolerability if used in patients with difficulty swallowing.
- **Risk vs. benefit of continued RAAS inhibitor therapy:** The long-term outcome benefits of patiromer with continued RAAS inhibitor therapy vs. adjustment of RAAS inhibitor treatment to manage hyperkalemia has not been studied. Therefore, the risk vs. outcome benefit of continuing the RAAS inhibitor (e.g. clinical practice guidelines recommend treatment with an ACEI or ARB in patients with chronic kidney disease and macroalbuminuria [Grade 1B]; an ACEI [or ARB if ACEI intolerant] and a MRA in patients with heart failure with reduced ejection fraction [Class IA]) in the presence of hyperkalemia needs to be taken into consideration. It is noted that approximately 42% of patients had concomitant heart failure that were enrolled in the clinical trial of patiromer in patients with chronic kidney disease. Patiromer has not been specifically studied in patients with heart failure with reduced ejection fraction (without chronic kidney disease) for treatment of hyperkalemia on a RAAS inhibitor.
- **Sodium polystyrene sulfonate:** Although there is also a lack of long-term outcome data with sodium polystyrene sulfonate, it has frequently been used to manage hyperkalemia, either orally or as an enema. As sodium polystyrene sulfonate is a cation exchange resin that exchanges sodium for potassium in the colon, the potential for edema as a result of sodium retention (each 15 gram dose of sodium polystyrene sulfonate contains approximately 1.5 grams sodium, with approximately 33% efficiency of sodium for potassium exchange, estimating approximately 500 mg of sodium released into the body) may be a consideration in some patients at risk for or from sodium or fluid overload. Intestinal necrosis, although uncommon, may be fatal; concerns for which resulted in changes to the product labeling to warn against use in patients at increased risk of developing constipation or impaction (e.g., history of impaction, chronic constipation, inflammatory bowel disease, ischemic colitis, vascular intestinal atherosclerosis, previous bowel resection, bowel obstruction, as well as postoperative patients who have not had a bowel movement after surgery) and to caution against use of sodium polystyrene sulfonate with additional sorbitol, as concomitant use has been associated with cases of intestinal necrosis. It should be noted that the FDA has also recommended potential drug interaction studies be undertaken for sodium polystyrene sulfonate, and that there be a separation of 6 hours between sodium polystyrene sulfonate and other oral medications.

Discontinuation Criteria

- Patient does not respond to therapy with patiromer with an acceptable reduction in serum potassium
- Patient is unable to manage the recommended spacing interval of patiromer with other oral medications
- Patient is not tolerating therapy with patiromer
- Patient develops severe constipation or worsening gastrointestinal motility
- Re-evaluate need for continued therapy and discontinue if treatment with patiromer is no longer required to manage hyperkalemia

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