PDL DRUG REVIEW

Proprietary Name: Veltassa®
Common Name: patiromer sorbitex calcium
PDL Category: K Removing Resins

Comparable Products	Preferred Drug List Status
Sodium Polystyrene Sulfonate	Preferred

Summary

Pharmacology/Usage: Patiromer sorbitex calcium, the active ingredient of Veltassa®, consists of the active moiety patiromer, which is a non-absorbed potassium-binding polymer, and a calcium-sorbitol counterion. Each gram of patiromer is equivalent to a nominal amount of 2g of patiromer sorbitex calcium. Veltassa® is a non-absorbed, cation exchange polymer that increases fecal potassium excretion through binding of potassium in the lumen of the GI tract, resulting in a reduction of serum potassium levels.

Indication: For the treatment of hyperkalemia. Veltassa® should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action.

There is no pregnancy category listed with this product; however, the risk summary indicates that Veltassa® is not absorbed systemically after oral administration and maternal use is not expected to result in fetal risk. The safety and efficacy of use in the pediatric population have not been established.

Dosage Forms: Powder for oral suspension in single-use packets containing: 8.4g, 16.8g, or 25.2g of patiromer

Recommended Dosage: Start at 8.4g once daily with food. Do not heat Veltassa® (e.g. microwave) or add to heated foods or liquids. Monitor serum potassium and adjust the dose based on serum potassium levels and the desired target range up to a maximum dose of 25.2g once daily.

To prepare Veltassa®, add the entire contents of one Veltassa® package to about 1 ounce of water and stir thoroughly. Then add an additional 2 ounces of water and stir the mixture thoroughly. Drink the mixture immediately and if some residual powder remains then add more water, stir and drink.

Drug Interactions: There were no formal drug interactions studies performed in humans. However, *in vitro* studies suggested that Veltassa® was seen to bind about half of the oral medications that were tested, which could result in decreased GI absorption and loss of efficacy of the oral medications. It is recommended to administer other oral medications at least 6 hours before or 6 hours after Veltassa®. In addition, monitor for clinical response and/or blood levels when possible. A box warning regarding the binding to other oral medications adds that one should choose Veltassa® or the other oral medication if adequate dosing separation is not possible.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Veltassa®). There was no placebo data to compare to.* The most frequently reported adverse events included constipation (7.2%), hypomagnesemia (5.3%), diarrhea (4.8%), nausea (2.3%), abdominal discomfort (2%), and

flatulence (2%). Reported lab abnormalities included hypokalemia with a serum potassium value <3.5mEq/L (4.7%) and hypomagnesemia with a serum magnesium value <1.4mg/dl (9%).

As hypomagnesemia can occur with Veltassa® use, it is recommended to monitor serum magnesium and to consider magnesium supplementation in patients who develop low serum magnesium levels on Veltassa®.

It is recommended to avoid Veltassa® use in patients with severe constipation, bowel obstruction, or impaction, including abnormal post-op bowel motility disorders.

Contraindications: In patients with a history of a hypersensitivity reaction to Veltassa® or any component of the compound

Manufacturer: Relypsa, Inc

Analysis: The efficacy of Veltassa® was assessed in a two-part, single-blind, randomized withdrawal study that evaluated Veltassa® in hyperkalemic patients with chronic kidney disease (CKD) on stable doses of ≥1 renin-angiotensin-aldosterone system inhibitor (RAAS; i.e. ACE inhibitor, ARB, or aldosterone antagonist). In Part A, patients (N=243) were treated with Veltassa® for 4 weeks, with the dose based on serum potassium levels. The results of the primary endpoint, the change in serum potassium from baseline to week 4, are illustrated in the table below.

Study	Baseline Potassium		Overall Population (N=237)
	5.1 to <5.5mEq/L (N=90)	5.5 to <6.5mEq/L (N=147)	
	Serum Potassium (mEq/L)		
Baseline, mean	5.31	5.74	5.58
Week 4 change from baseline, mean	-0.65	-1.23	-1.01
p-value			<0.001

At week 4, 76% of patients had a serum potassium in the target range of 3.8mEq/L to <5.1mEq/L, which was a secondary outcome.

In Part B of the study, 107 patients with a Part A baseline serum potassium of 5.5mEq/L to <6.5mEq/L and whose serum potassium was in the target range (3.8mEq/L to <5.1mEq/L) at Part A week 4 and were still receiving RAAS inhibitor medication were then randomized to continue Veltassa® or to receive placebo. The primary outcome was the change in serum potassium from Part B baseline to the earliest visit at which the patient's serum potassium was first outside the range of 3.8mEq/L to <5.5mEq/L, or to Part B week 4 if the patient's serum potassium remained in the range. Results are illustrated in the table below.

	Placebo (N=52)	Veltassa® (N=55)	Difference	
			Estimate	p-value
Estimated Median Change in serum potassium from baseline (mEq/L)	0.72	0.00	0.72	<0.001

In addition, significantly more placebo patients (91%) developed a serum potassium ≥5.1mEq/L at any time during Part B than Veltassa® patients (43%; p<0.001). Significantly more in the placebo group (60%) developed serum potassium ≥5.5mEq/L at any time during Part B than Veltassa® patients (15%; p<0.001).

Veltassa® was also assessed in up to a one-year open-label study that included hyperkalemic patients (N=304) with CKD and type 2 DM on RAAS inhibitor therapy. The treatment effect on serum potassium was maintained during continued therapy.

Place in Therapy: Hyperkalemia is a common condition generally "...due to impaired urinary potassium excretion due to acute or chronic kidney disease (CKD) and/or disorders or drugs that inhibit the renin-angiotension-

aldosterone axis."[2] Valtessa® is a non-absorbed cation exchange polymer that is indicated for the treatment of hyperkalemia.

There is no evidence at this time to support that Veltassa® is safer or more effective than the currently available, more cost effective medications. It is therefore recommended that Veltassa® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred**

References

[1] Veltassa [package insert]. Redwood City, CA: Relypsa, Inc; 2015.
[2] UpToDate desktop. Treatment and prevention of hyperkalemia in adults. Accessed February 2016.