Drug Monograph

Drug/Drug Class:	**Veltassa™(patiromer) oral powder for suspension/ Potassium binder**
Prepared for:	MO HealthNet
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☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Veltassa™ oral powder for suspension is available in 3 strengths. It is available in 8.4 g/ 1 packet, 16.8 g/1 packet, and 25.2 g/ 1 packet of patiromer, respectively. Manufacturer: Relypsa, Inc., Redwood City, CA 94063
Summary of Findings:	Veltassa™ was evaluated in a multicenter, 2-phase clinical trial that assessed its efficacy in patients with hyperkalemia and chronic kidney disease who were receiving renin-angiotensin-aldosterone system (RAAS) inhibitors (N=243). The percentage of patients achieving target serum potassium levels after 4 weeks of treatment was 76%, with a mean decrease in potassium levels of 1.01 mmol/L. Significantly fewer patients randomized to Veltassa™ experienced a recurrence of hyperkalemia during the randomized, 8-week withdrawal phase compared with placebo (15% vs 60%). In the subgroup of patients with comorbid heart failure, similar results were seen for both phases. In 304 patients with mild or moderate hyperkalemia, chronic kidney disease, and type 2 diabetes mellitus receiving RAAS inhibitors in the AMETHYST-DN trial, the treatment effect was maintained for up to 52 weeks with continued Veltassa™ therapy. There was a significant mean decrease in serum potassium at each monthly assessment from weeks 4 to 52.
Status Recommendation:	☐ Prior Authorization (PA) Required ☒ Open Access ☐ Clinical Edit ☐ PDL
Type of PA Criteria:	☐ Increased Risk of ADE ☐ Preferred Agent ☒ No PA Required ☐ Non-Preferred Agent

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payors are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction[5]

Hyperkalemia is a serious condition in which the amount of potassium in the blood is too high. Delivered to the body by food, potassium is a mineral that is needed for cells to function properly. The kidneys remove potassium from the blood to maintain a proper balance of potassium in the body. The level of potassium can get too high when the kidneys are not able to remove enough potassium from the blood. Hyperkalemia typically occurs in patients with acute or chronic kidney disease or heart failure, particularly in those who are taking drugs that inhibit the renin-angiotensin-aldosterone system, which regulates blood pressure and fluid balance in the body.

Dosage Form(s) [1]

Veltassa™ powder for oral suspension is available in 3 strengths. It is available in 8.4 g/ 1 packet, 16.8 g/1 packet, and 25.2 g/ 1 packet of patiromer, respectively.

Manufacturer [1]

Relypsa, Inc., Redwood City, CA 94063

Indication(s) [1]

Veltassa™ is indicated for the treatment of hyperkalemia. It is not for use as emergency treatment for life-threatening hyperkalemia due to its delayed onset of action.

Clinical Efficacy [1-5] (mechanism of action/pharmacology, comparative efficacy)

Veltassa™ is a cation exchange polymer that does not get absorbed. Potassium is bound in the gastrointestinal tract lumen, which reduces potassium serum levels through increased fecal excretion of potassium.

Pharmacokinetics:
Veltassa™ is excreted in the feces and not systemically absorbed.

Veltassa™ effectively reduced potassium levels and subsequently reduced the recurrence of hyperkalemia when compared with placebo.

STUDY DESIGN	Multicenter, 2-phase (4-week single-group phase followed by an 8-week, randomized, placebo-controlled withdrawal phase) OPAL-HK clinical trial (N=243).

INCLUSION CRITERIA	Adult patients with serum potassium levels of 5.1 to < 6.5 mmol/L and stage 3 or 4 chronic kidney disease who were receiving stable doses of at least 1 RAAS inhibitor.
EXCLUSION CRITERIA	Patients with potassium-related EKG changes, unstable arrhythmias, a recent cardiac surgery, acute coronary syndrome, a recent stroke or transient ischemic attack, severe gastrointestinal disorders, heart or kidney transplantation, a systolic blood pressure of 180 mmHg or higher, a systolic blood pressure of less than 110 mmHg, a diastolic blood pressure of 110 mmHg or higher, or a diastolic blood pressure of less than 60 mmHg.
TREATMENT REGIMEN	Patients were treated with Veltassa™ 4.2 grams or 8.4 grams orally twice daily (adjusted to achieve a target potassium level) for 4 weeks. Those who achieved target potassium levels, and had baseline potassium levels higher than 5.5 mmol/L, were randomized to continue Veltassa or change to placebo for an 8-week withdrawal phase.
RESULTS	At week 4, target serum potassium levels (3.8 to <5.1 mmol/L) were achieved in 76% of patients. Potassium levels were decreased an average of 1.01 mmol/L. For the withdrawal phase, of the 107 patients randomized to Veltassa™ or placebo, significantly fewer patients receiving Veltassa™ experienced a recurrence of hyperkalemia (15% vs 60%) by week 8. After 4 weeks of the withdrawal phase, the median changes in potassium levels were 0 in the Veltassa™ group and +0.72 mmol/L in the placebo group. Similar results were seen in the subgroup of patients with comorbid heart failure for both phases (N=102).
SAFETY	Constipation (11%) was the most common adverse event in the initial phase. Throughout both phases, hypokalemia occurred in 3% of patients who received Veltassa™.

Contraindications [(1)]

- History of hypersensitivity reaction to Veltassa™ or any product components.

Warnings and Precautions [(1)]

- Binding to orally administered medications may occur, resulting in decreased absorption and reduced effectiveness of other medications; administer other oral medications at least 6 hours before or 6 hours after Veltassa™; choose Veltassa™ or the other oral medication if adequate dosing separation is not possible.
- Hypomagnesemia may occur; monitoring recommended and magnesium supplementation may be required.
- Gastrointestinal conditions may worsen and result in decreased efficacy; avoid use in patients with severe constipation, bowel obstruction, or bowel impaction, including

abnormal postoperative bowel motility disorders.

Adverse Effects [1]

Most Common, ≥ 2%	Veltassa™ (n=666)
Constipation	7.2%
Hypomagnesemia	5.3%
Diarrhea	4.8%
Nausea	2.3%
Abdominal discomfort	2.0%
Flatulence	2.0%

Drug Interactions [1]

No drug interaction studies have been conducted, although it is known that Veltassa™ binds to other oral medications.

Dosage and Administration [1]

Recommended dosage: 8.4 grams orally once daily with food; administer at least 6 hours before or 6 hours after other oral medications. Adjust dosage in increments of 8.4 grams at 1-week or longer intervals to reach desired serum potassium level; maximum dosage: 25.2 grams once daily.

Cost

GENERIC NAME	BRAND NAME	MANUFACTURER	STRENGTH	DOSE	COST*/ MONTH
Patiromer	Veltassa	Relypsa	8.4 g/ packet, powder for suspension	8.4 g daily	$594.90
			16.8 g/ packet, powder for suspension	16.8 g daily	$594.90
			25.2 g/ packet, powder for suspension	25.2 g daily	$594.90

* Wholesale Acquisition Cost

Conclusion

Veltassa™ is a non-absorbed, oral potassium-binding agent indicated for the treatment of hyperkalemia in adults. It is not for use as an emergency treatment for life-threatening hyperkalemia due to its delayed onset of action. In a multicenter, 2-phase clinical trial of patients with hyperkalemia and chronic kidney disease who were receiving at least 1 RAAS inhibitor (N=243), treatment with Veltassa™ resulted in a mean decrease of 1.01 mmol/L in potassium levels and 76% of patients achieving target serum potassium levels. Veltassa™ also significantly reduced the recurrence of hyperkalemia compared with placebo (15% vs 60%). The treatment effect was maintained for up to 52 weeks with continued Veltassa™ therapy in a long term trial in patients with type 2 diabetes mellitus who were receiving RAAS inhibitors. Veltassa™ is well tolerated, with the most common adverse effects including constipation, hypomagnesemia, and diarrhea. The administration of concomitant oral medications must be separated by at least 6 hours from Veltassa™.

Recommendation

MO HealthNet Division recommends Open Access status for this product.

References

1. Product Information: Veltassa™, patiromer suspension. Relypsa, Inc, Redwood City, CA, 10/2015.
2. Weir MR, Bakris GL, Bushinsky DA et al: Patiromer in patients with kidney disease and hyperkalemia receiving RAAS inhibitors. N Engl J Med 2015; 372(3):211-221.
3. Pitt B, Bakris GL, Bushinsky DA et al: Effect of patiromer on reducing serum potassium and preventing recurrent hyperkalaemia in patients with heart failure and chronic kidney disease on RAAS inhibitors. Eur J Heart Fail 2015; 17(10):1057-1065.
4. Bakris GL, Pitt B, Weir MR et al: Effect of patiromer on serum potassium level in patients with hyperkalemia and diabetic kidney disease: The AMETHYST-DN randomized clinical trial. JAMA 2015; 314(2):151-161.
5. FDA approves new drug to treat hyperkalemia. Retrieved 02/12/2016 from: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm468546.htm

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