Patiromer (Veltassa) for Hyperkalemia

The FDA has approved patiromer (Veltassa – Relypsa), an oral potassium binder, for treatment of hyperkalemia. It is the first drug to be approved for this indication since the cation-exchange resin sodium polystyrene sulfonate (Kayexalate, and others) in 1958. Patiromer is not indicated for emergency correction of life-threatening hyperkalemia. Sodium zirconium cyclosilicate, another oral potassium binder, is currently being reviewed by the FDA; a decision on its approval is expected in May 2016.

**HYPERKALEMIA** – Hyperkalemia (serum potassium level >5.0 mEq/L) can occur in patients with renal disease or in those taking drugs that inhibit the renin-angiotensin-aldosterone system (RAAS) such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), direct renin inhibitors, and aldosterone antagonists. Dosage reduction or discontinuation of RAAS inhibitors because of hyperkalemia is sometimes required in patients with congestive heart failure, chronic kidney disease, or diabetes. Other drugs, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and trimethoprim, can also increase serum potassium levels.

Asymptomatic patients with mild to moderate hyperkalemia not adequately corrected by dietary restrictions and/or treatment with a diuretic are sometimes treated with sodium polystyrene sulfonate, which can cause serious adverse effects. Severe GI toxicity including intestinal necrosis has occurred, particularly with rectal administration of the drug in patients with bowel dysfunction or recent GI surgery.1-3 Taken orally, the drug may bind to other drugs in the gut, preventing their absorption.4 Binding of potassium with sodium polystyrene sulfonate results in a release of sodium; sodium and fluid retention can occur.

**PHARMACOLOGY** – Veltassa is a nonabsorbed anion polymer that exchanges a calcium-sorbitol counterion for potassium cations in the GI lumen. Binding of free potassium in the GI tract leads to a decrease in serum potassium levels.

**CLINICAL STUDIES** – The results of randomized trials evaluating the effects of patiromer on serum potassium levels over a 4-week period are summarized in Table 1.5,6

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Mean Change in [K+] (mEq/L)</th>
<th>Pronunciation Key</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMETHYST-DN (open-label; n=306)1,2</td>
<td></td>
<td>Patiromer: pa teer’ uh mer Veltassa: vel tas’ ah</td>
</tr>
<tr>
<td>Patiromer 8.4 g/d</td>
<td>-0.35</td>
<td>Mild HK(^2) Moderate HK(^1)</td>
</tr>
<tr>
<td>Patiromer 16.8 g/d</td>
<td>-0.51</td>
<td>N/A</td>
</tr>
<tr>
<td>Patiromer 25.2 g/d</td>
<td>-0.55</td>
<td>-0.87</td>
</tr>
<tr>
<td>Patiromer 33.6 g/d</td>
<td>-0.55</td>
<td>N/A</td>
</tr>
<tr>
<td>OPAL-HK (single-blind; n=243)4,5</td>
<td></td>
<td>Mild HK(^5) Moderate–Severe HK(^6)</td>
</tr>
<tr>
<td>Patiromer 8.4 g/d(^7)</td>
<td>-0.65</td>
<td>N/A</td>
</tr>
<tr>
<td>Patiromer 16.8 g/d(^7)</td>
<td>-1.23</td>
<td></td>
</tr>
</tbody>
</table>

HK = hyperkalemia; N/A = dosage not used in this subgroup
2. Patients had HK, type 2 diabetes, and an eGFR 15–<60 mL/min/1.73 m\(^2\), and were taking an ACE inhibitor or ARB.
3. Mild HK = serum potassium level >5.0–5.5 mEq/L; Moderate HK = serum potassium level >5.5–6.0 mEq/L.
5. Patients had HK and an eGFR 15–60 mL/min/1.73 m\(^2\), and were taking a renin-angiotensin-aldosterone system inhibitor.
6. Mild HK = serum potassium level 5.1–5.5 mEq/L; Moderate–Severe HK = serum potassium level 5.5–6.5 mEq/L.
7. Initial dosages; titrated according to a prespecified algorithm.

In the open-label AMETHYST-DN trial, reductions in serum potassium levels achieved with patiromer persisted through 52 weeks of treatment.5

In a continuation phase of the single-blind OPAL-HK trial, 107 patients whose serum potassium levels had fallen below 5.1 mEq/L after 4 weeks of treatment with patiromer were randomized to continue receiving the drug or switch to placebo. The median increase in serum potassium levels after
8 weeks, the primary endpoint, was significantly greater in patients switched to placebo than in those who continued taking the active drug (0.72 vs 0.00 mEq/L). Patients who continued receiving patiromer were less likely to experience recurrent hyperkalemia than those switched to placebo (15% vs 60%) and more likely to remain on a RAAS inhibitor (94% vs 44%).

In another study in 25 patients with hyperkalemia and chronic kidney disease, patiromer 8.4 g twice daily significantly decreased serum potassium levels as early as 7 hours after administration of the first dose (-0.21 mEq/L). After 48 hours, mean levels had dropped by 0.75 mEq/L.

ADVERSE EFFECTS — The most common adverse effects reported with patiromer in clinical trials (occurring in ≥2% of patients) were constipation, hypomagnesemia, diarrhea, nausea, abdominal discomfort, and flatulence. Mild to moderate hypersensitivity reactions have been reported. Severe adverse reactions were uncommon.

Patiromer binds to magnesium in the colon; serum magnesium levels should be monitored and supplementation should be considered if hypomagnesemia occurs.

DRUG INTERACTIONS — Patiromer may bind to some other drugs in the GI tract. Based on in vitro data, the labeling currently recommends that it not be taken within 6 hours of any other oral drug. An FDA review of in vivo data is anticipated.

DOSAGE, ADMINISTRATION, AND COST — Veltassa is supplied in packets containing 8.4, 16.8, or 25.2 grams of patiromer. The recommended starting dosage is 8.4 g once daily with food. The dose should be titrated to achieve the desired serum potassium level; dose increases should occur at ≥1 week intervals in increments of 8.4 g up to a maximum daily dose of 25.2 g. Each dose should be mixed with water as described in the labeling; the turbid suspension should be taken immediately upon preparation. Patiromer should not be used in patients with severe constipation, bowel obstruction, or abnormal postoperative GI motility. The cost for 30 Veltassa packets of any strength is $595.

CONCLUSION — The oral potassium binder patiromer (Veltassa) can reduce serum potassium levels in patients with non-life-threatening hyperkalemia and it appears to be safe. It may allow patients with comorbid conditions such as chronic kidney disease, congestive heart failure, or diabetes to continue taking ACE inhibitors or other drugs that cause hyperkalemia. How patiromer compares to sodium polystyrene sulfonate (Kayexalate, and others) in efficacy and safety remains to be determined.

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