OVERVIEW

Chronic kidney disease (CKD) is a public health problem with an overall prevalence of 14% in the United States.\(^1\) It is associated with poor prognosis and high healthcare costs and may lead to complications that result in higher hospitalizations, morbidity, and mortality rates. Disorders of renal tubular reabsorption and secretion can cause electrolyte disturbances, which are markers of kidney damage. These include hyperphosphatemia, hyperkalemia, hypernatremia, hyponatremia, and hypocalcemia. Consequently, hyperphosphatemia and vitamin D deficiency/hypocalcemia may lead to secondary hyperparathyroidism. Electrolyte imbalances in the body can be detrimental and cause serious complications if untreated; therefore, they must be managed accordingly to improve health outcomes. The purpose of this coverage policy is to review the coverage criteria of HPSJ’s formulary agents available to treat electrolyte disorders secondary to CKD (Table 1).

TABLE 1: Oral Electrolyte Disorder Agents Formulary Positioning: (Current as of 11/2016)

<table>
<thead>
<tr>
<th>Therapeutic Class</th>
<th>Generic Name (Brand Name)</th>
<th>Available Strengths</th>
<th>Formulary Limits</th>
<th>Average Cost(^*) per 30 days</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HYPERPHOSPHATEMIA</strong></td>
<td>Calcium Acetate (Phoslo, Calphron, Eliphos, Phoslyra)</td>
<td>Tablet: 667 mg</td>
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<td>$93.93</td>
<td>Calcium Acetate capsules/gelcaps are reserved for documented intolerance to tablets.</td>
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<tr>
<td></td>
<td></td>
<td>Capsule: 667 mg</td>
<td>PA</td>
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<tr>
<td></td>
<td></td>
<td>Oral Solution: 667 mg/5mL</td>
<td>NF</td>
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<tr>
<td></td>
<td>Sevelamer Carbonate (Renvela)</td>
<td>Tablet: 800 mg</td>
<td>PA</td>
<td>$609.30</td>
<td>Second line after Phoslo (Calcium Acetate), unless on dialysis, corrected serum calcium &gt; 10.2 mg/dl, or evidence of soft tissue calcification. Powder packets are reserved for a documented inability to swallow Sevelamer tablets.</td>
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<tr>
<td></td>
<td></td>
<td>Powder packet: 0.8 g, 2.4 g</td>
<td>PA</td>
<td>$1,828.81</td>
<td></td>
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<tr>
<td></td>
<td>Sevelamer Hydrochloride (Renagel)</td>
<td>Tablet: 400 mg, 800 mg</td>
<td>PA</td>
<td>$762.03</td>
<td>Second line after Phoslo (Calcium Acetate), unless on dialysis, corrected serum calcium &gt; 10.2 mg/dl, or evidence of soft tissue calcification. Must have tried Renvela and have documented intolerance.</td>
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<tr>
<td></td>
<td>Lanthanum Carbonate (Fosrenol)</td>
<td>Chewable tablet: 500 mg, 750 mg, 1000 mg</td>
<td>PA, QL</td>
<td>$784.92</td>
<td>Third line therapy for patients with treatment failure of Calcium Acetate and Sevelamer. Fosrenol 500 mg and 750 mg tablets are limited to 3 tablets per day of each strength.</td>
</tr>
<tr>
<td></td>
<td>Ferric Citrate (Auryxia)</td>
<td>Tablet: 210 mg</td>
<td>NF</td>
<td>$1,089.59</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sucroferric Oxyhydroxide (Velphoro)</td>
<td>Tablet: 500 mg</td>
<td>NF</td>
<td>$1,183.86</td>
<td></td>
</tr>
<tr>
<td>Therapeutic Class</td>
<td>Generic Name (Brand Name)</td>
<td>Available Strengths</td>
<td>Formulary Limits</td>
<td>Average Cost per 30 days</td>
<td>Notes</td>
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<tr>
<td><strong>Hyperparathyroidism</strong></td>
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<tr>
<td>Vitamin D Analogs</td>
<td>Calcitriol (Calcijex, Rocaltrol)</td>
<td>Capsule: 0.25 mcg, 0.5 mcg; Oral Solution: 1 mcg/mL</td>
<td>--</td>
<td>$24.96</td>
<td>Calcitriol 0.5mcg capsules are NON-FORMULARY.</td>
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<td></td>
<td>Paricalcitol (Zemplar)</td>
<td>Capsule: 1 mcg, 2 mcg, 4 mcg</td>
<td>PA</td>
<td>$517.95</td>
<td>Reserved for patients who have failed Calcitriol.</td>
</tr>
<tr>
<td></td>
<td>Doxercalciferol (Hectorol)</td>
<td>Capsule: 0.5 mcg, 1 mcg, 2.5 mcg</td>
<td>NF</td>
<td>$1,228.50</td>
<td></td>
</tr>
<tr>
<td>Calcimimetics</td>
<td>Cinacalcet (Sensipar)</td>
<td>Tablet: 30 mg, 60 mg, 90 mg</td>
<td>PA, QL, SP</td>
<td>30 mg: $896.40; 60 mg: $1,792.80</td>
<td>Step therapy to patients with secondary hyperparathyroidism with BiPTH &gt; 200 pg/ml despite compliant use of phosphate binders or with CKD-5D. Sensipar 30 mg and 60 mg tablets are limited to two tablets per day of each strength.</td>
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<tr>
<td><strong>Hyperkalemia</strong></td>
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<tr>
<td>Cation-Exchange Resins</td>
<td>Sodium Polystyrene Sulfonate (Kayexalate, Kalexate, Kionex)</td>
<td>Oral suspension: 15 g/60 mL; Rectal enema: 30 g/120 mL</td>
<td>--</td>
<td>$813.38</td>
<td>$2,829.60</td>
</tr>
<tr>
<td></td>
<td>Patiromer (Veltassa)</td>
<td>Powder packet: 8.4 g, 16.8 g, 25.2 g</td>
<td>PA</td>
<td>$798.00</td>
<td>For hyperkalemia in patients at risk for colonic necrosis, hypernatremia, or have heart failure.</td>
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<tr>
<td><strong>Hyponatremia</strong></td>
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<tr>
<td>ADH Receptor Antagonists</td>
<td>Tolvaptan (Samsca)</td>
<td>Tablet: 15 mg, 30 mg</td>
<td>NF</td>
<td>$13,121.84</td>
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</tbody>
</table>

PA = Prior Authorization; QL = Quantity limit; SP = Specialty Pharmacy; NF = Non-Formulary
*Based on standard rates and standard dosing

**EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION**

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed and approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HSPJ Medical Review Guidelines (UM06).

**Vitamin D Analogs**

**Calcitriol (Calcijex, Rocaltrol); Paricalcitol (Zemplar)**

**Calcitriol 0.25mcg capsules (Calcijex, Rocaltrol)**

- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A
- **Other notes:**
  - Calcitriol 0.5mcg capsules are non-formulary.
Paracalcitol (Zemplar)

- **Coverage Criteria:** Reserved for patients who have failed Calcitriol.
- **Limits:** None
- **Required Information for Approval:** Medication fill history showing patient has tried Calcitriol at any point.
- **Other notes:** None

Calcimimetics

Cinacalcet (Sensipar)

- **Coverage Criteria:** Reserved for patients with secondary hyperparathyroidism with BiPTH > 200 pg/ml despite compliant use of phosphate binders or with CKD-5D.
- **Limits:** PA required.
- **Required Information for Approval:** Medication fill history showing continuous fills of phosphate binders OR CKD-5D AND clinic notes or laboratory data showing patient has BiPTH > 200 pg/mL.
- **Other notes:**
  - Restricted to specialty pharmacy.
  - Sensipar 30 mg tablets are limited to 2 tablets per day.
  - Sensipar 60 mg tablets are limited to 2 tablets per day.

Phosphate Binders

Calcium Acetate (Phoslo, Phoslyra, Calphron, Eliphos); Sevelamer Carbonate (Renvela); Sevelamer HCl (Renagel); Lanthanum Carbonate (Fosrenol)

Calcium Acetate (Phoslo, Phoslyra, Calphron, Eliphos)

- **Coverage Criteria:**
  - Calcium Acetate Capsules/Gelcaps: Reserved for treatment failure to calcium acetate tablets and have documented inability to swallow tablets.
- **Limits:** PA required for Calcium Acetate Capsules/Gelcaps.
- **Required Information for Approval:** N/A
- **Other Notes:**
  - First-line treatment for hyperphosphatemia.
  - Concurrent use of Vitamin D helps with absorption of calcium.
  - Phoslyra is non-formulary.

Sevelamer Carbonate (Renvela), Sevelamer HCl (Renagel)

- **Coverage Criteria:**
  - **Renvela Tablets:** Second line treatment for hyperphosphatemia after Calcium Acetate, unless on dialysis, corrected serum calcium > 10.2 mg/dl, or evidence of soft tissue calcification.
  - **Renvela Packets:**Must have documented inability to swallow Sevelamer Tablets.
  - **Renagel tablets:** Must have tried Renvela and have documented intolerance to Renvela.
- **Limits:** PA required.
- **Required Information for Approval:** Medication fill history showing patient has tried Calcium Acetate or Sevelamer Carbonate in the past, clinic notes stating patient is on dialysis or has soft tissue calcification, or laboratory data showing patient's corrected serum calcium > 10.2 mg/dL.
- **Other Notes:** None

Lanthanum Carbonate (Fosrenol)

- **Coverage Criteria:** Third line therapy for patients with treatment failure of Calcium Acetate and Sevelamer.
- **Limits:** PA required.
- **Required Information for Approval:** Medication fill history showing patient has tried Calcium Acetate and Sevelamer in the past.
- **Other Notes:**
  - Fosrenol 500mg tablets are limited to 3 tablets per day.
  - Fosrenol 750mg tablets are limited to 3 tablets per day.
Cation-Exchange Resins

Sodium Polystyrene Sulfonate (Kayexalate, Kalexate, Kionex); Patiromer (Veltassa)

**Sodium Polystyrene Sulfonate (Kayexalate, Kalexate, Kionex)**

- **Coverage Criteria:**
  - SPS Solution: None
  - SPS Rectal Enemas: Reserved for patients with vomiting not successfully treated by oral anti-nausea medications, or have upper GI problems, including paralytic ileus.

- **Limits:**
  - SPS Solution: None
  - SPS Rectal Enemas: PA required.

- **Required Information for Approval:** For approval of rectal enemas, documentation of past anti-nausea medications tried and/or history of upper GI problems.

- **Other Notes:** None

**Patiromer (Veltassa)**

- **Coverage Criteria:** Reserved for patients at risk of colonic necrosis (impaction, chronic constipation, inflammatory bowel disease, ischemic colitis, vascular intestinal atherosclerosis, bowel obstruction), OR Hypernatremia, OR Diagnosis of Heart Failure; AND Potassium >5.5 mEq/L.

- **Limits:** PA required.

- **Required Information for Approval:** Clinic notes documenting risk for colonic necrosis (impaction, chronic constipation, inflammatory bowel disease, ischemic colitis, vascular intestinal atherosclerosis, bowel obstruction), labs documenting Hypernatremia, or diagnosis of heart failure with labs showing potassium (K+) > 5.5 mEq/L.

- **Other Notes:** None

**CLINICAL JUSTIFICATION**

**HYPERPHOSPHATEMIA AND HYPERPARATHYROIDISM**

HPSJ’s coverage policy for electrolyte disorders secondary to CKD, specifically hyperphosphatemia and hyperparathyroidism, is based on recommendations by the National Kidney Foundation (NKF) Kidney Disease Outcome and Quality Initiative (K/DOQI) and Kidney Disease, Improving Global Outcomes (KDIGO). Hyperphosphatemia and hyperparathyroidism are two common complications that arise from CKD, so it is crucial to treat them accordingly. Serum phosphorus, calcium, vitamin D, and parathyroid (PTH) concentrations are all correlated to each other, so treatment of disorders of each parameter requires evaluation of the other parameters. KDIGO guidelines recommend the evaluation and treatment for hyperphosphatemia, hypocalcemia, and vitamin D deficiency in patients with intact parathyroid (PTH) levels above the upper limit normal. The guidelines recommend calcium- and non-calcium-containing phosphate binders for the treatment of hyperphosphatemia, and vitamin D analogs and calcimimetics for the treatment of secondary hyperparathyroidism. Excretion of serum phosphorus is reduced with decreased kidney function and causes phosphorus retention, leading to hyperphosphatemia. High serum phosphate concentrations are associated with increased risk of death and cardiovascular disease (CVD) in patients with CKD. For every 1 mg/dL increase in serum phosphate concentration, the risk of death increases by 18%, and coronary artery, thoracic, aortic valve, and mitral valve calcification increased by 21%, 33%, 25%, and 62%, respectively. Dietary phosphate restriction has questionable efficacy in treating and preventing hyperphosphatemia, as studies have shown that restrictive dietary phosphate is associated with poorer nutritional status. As such, phosphate binders remain the mainstay of therapy for hyperphosphatemia in patients with CKD.
HYPERKALEMIA

The current treatments available to treat hyperkalemia include reduction of dietary potassium intake, modification of contributing medications, and use of cation-exchange resins (e.g., Sodium Polystyrene Sulfonate (SPS) and Patiromer). SPS has historically been used in the treatment of hyperkalemia, but its use is limited by (1) questionable efficacy in reducing serum potassium levels, (2) poor gastrointestinal (GI) tolerability, and (3) rare occurrences of colonic necrosis. Newer agents, such as Patiromer, have shown adequate efficacy in clinical trials in lowering elevated potassium levels as well.

HYPONATREMIA

The American Academy of Family Physicians (AAFP) recommends treatment with 3% saline for severe symptomatic hyponatremia. Vaptans may also be used for hospitalized patients with clinically significant euvoletic and hypervolemic hyponatremia, but the AAFP recommends against their routine use. In the United States, the only available vaptans are oral Tolvaptan (Samsca®) and intravenous Conivaptan (Vaprisol®). But HPSJ will keep vaptan agents as non-formulary as it is not recommended for use in hyponatremia.

REFERENCES

6. Velphoro (sucroferric oxyhydroxide) tablets [prescribing information]. Waltham, MA: Fresenius Medical Care North America; September 2014.
17. Kayexalate (sodium polystyrene sulfonate) [prescribing information]. Laval, Quebec: Sanofi-Aventis Canada Inc; July 2014.
### REVIEW & EDIT HISTORY

<table>
<thead>
<tr>
<th>Document Changes</th>
<th>Reference</th>
<th>Date</th>
<th>P&amp;T Chairman</th>
</tr>
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<tbody>
<tr>
<td>Creation of Policy</td>
<td>Phosphate Binder 5-18-10.doc</td>
<td>05/2010</td>
<td>Allen Shek, PharmD</td>
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<tr>
<td>Update to Policy</td>
<td>HPSJ Coverage Policy – Renal – Complications Secondary to CKD  2016-12.docx</td>
<td>12/2016</td>
<td>Johnathan Yeh, PharmD</td>
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</table>

*Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy.*