Oral Phosphate Binders

BACKGROUND

Phosphorus is the second most abundant element in the human body, most commonly occurring as part of the *phosphate* molecule (phosphorous bound with oxygen). This element plays an essential role in several body functions, including energy production and the development of teeth and bones.

While necessary to conduct these vital processes, phosphate blood levels must also be kept within normal limits (≤4.5 mg/dL) to prevent health issues. As the responsibility of regulating phosphate levels falls to the kidneys, individuals with **chronic kidney disease (CKD)** may be unable to sufficiently filter phosphate out of the body.

Hyperphosphatemia – the condition of elevated phosphate levels – can lead to complications such as **secondary hyperparathyroidism**, **metabolic bone disease**, and **vascular calcification**.

Secondary hyperparathyroidism occurs when high phosphate levels and low vitamin D/calcium levels prompt overproduction of parathyroid hormone (PTH; functions to counteract those imbalances). The subsequent effects can weaken bones and predispose individuals to osteoporosis. Extraskeletal calcification, such as calcium buildup within blood vessels, is a significant complication of hyperphosphatemia and secondary hyperparathyroidism. This effect directly increases the risk of cardiovascular mortality in those with advanced CKD.

For these reasons**, oral phosphate binders** are designed to balance blood phosphate levels in affected individuals. These products are administered with meals, to act on phosphate as it is ingested and lower the amounts absorbed into the blood stream. These agents generally bind to freely circulating phosphate molecules and form insoluble complexes to be excreted.

CHOOSING A PHOSPHATE BINDER

Selecting an appropriate oral phosphate binder should be resident-specific. Products are available in various oral dosage forms, require different dosing quantities (with some products demonstrating onerous pill burden), exhibit unique ancillary benefits and adverse effects, and have varied price points. Select products may be more suitable for certain residents based on their clinical profile and patient preferences.

Oral phosphate binders can be broken down into five general categories:

1. **Calcium-Based**
2. **Non-Absorbable Polymers**
3. **Lanthanum-Based**
4. **Iron-Based**
5. **Miscellaneous**

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1. Calcium-Based Phosphate Binders

Example: **Calcium Acetate (PhosLo®)**

- Generally inexpensive and widely available.
- Due to inherent calcium load, a good choice for residents presenting with concomitant hypocalcemia.
- Conversely, not ideal for residents with high serum calcium or otherwise at risk for hypercalcemia (e.g., receiving vitamin D analogs).
    - Calcium acetate is available as 667 mg capsules and tablets, each containing 169 mg elemental calcium.
    - Generally, residents should not exceed 6,003 mg/day of calcium acetate (1,500 mg/day elemental calcium) and limit total elemental calcium intake from all sources (i.e., dietary and phosphate binders) to ≤2,000 mg/day.
- Requisite large doses may cause pill burden and swallowing concerns.
    - Standard dosing: 1,334 mg calcium acetate (2 tabs/caps) with each meal. Increase or decrease dose (e.g., by 667 mg per meal) at 2 week intervals as needed to obtain targeted serum phosphorus concentrations; usual dosage range: 1,334 to 2,001 mg calcium acetate (2-3 tabs/caps) with each meal.

2. Non-Absorbable Polymers

Example: **Sevelamer Carbonate (Renvela®), Sevelamer Hydrochloride**

- Non-calcium formulations demonstrate lower risk of hypercalcemia and vascular calcification.
- These polymer options may have ancillary benefits such as cholesterol lowering, uric acid lowering, and anti-inflammatory effects.
- Sevelamer preparations are associated with a higher incidence of adverse GI effects such as nausea, diarrhea or constipation, and flatulence.
- When choosing sevelamer products, providers should consider the salt formulation as it can affect the overall acidity of the body.
    - Sevelamer carbonate is preferred in patients with nondialysis-dependent chronic kidney disease or metabolic acidosis (due to risk of metabolic acidosis with sevelamer hydrochloride).
    - Sevelamer carbonate and sevelamer hydrochloride are dosed the same on a milligram-to-milligram basis; when switching between products, use the same dose.
- Pill size may present issue for individuals with swallowing concerns.
    - Available as 800 mg oral packets, 800 mg oral tablets, and 400 mg oral tablets (sevelamer hydrochloride only).
    - Initial oral dosing is based on serum phosphorous levels:
        - >5.5 to <7.5 mg/dL: 800 mg 3 times daily with meals.
        - 7.5 to <9 mg/dL: 1,200 to 1,600 mg 3 times daily with meals.
        - ≥9 mg/dL: 1,600 mg 3 times daily with meals.
- Generally, more expensive than calcium-based phosphate binders.

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3. Lanthanum-Based Phosphate Binders

Example: **Lanthanum Carbonate (Fosrenol®)**

- Benefit of no calcium load.
- Relatively newer and more potent than calcium-containing phosphate binders and non-absorbable polymers.
    - Benefit of lower pill burden.
- Available as 500 mg, 750 mg, 1000 mg oral chewables and 750 mg, 1000 mg oral packs.
- Initial oral dosing: 1,500 mg/day in divided doses taken with or immediately after meals.
    - Dosage adjustment: Increase or decrease dose by 250 or 500 mg per meal at 2- to 3-week intervals as needed to obtain targeted serum phosphorus concentrations; usual dosage range: 1,500 to 3,000 mg/day in divided doses.
- Lanthanum carbonate is associated with fewer GI side effects than sevelamer preparations.

4. Iron-Based Phosphate Binders

Example: **Ferric Citrate (Auryxia®)**, **Sucroferric Oxyhydroxide (Velphoro®)**

- Do not contain calcium and demonstrate a low pill burden.
- Risk of adverse GI effects due to iron content, including abdominal pain and dark-colored stools.
- Best for patients with concomitant iron deficiency (anemia).
- **Ferric Citrate**: 2 tablets (420 mg of elemental iron) 3 times daily with meals initially. May titrate dose by 1 or 2 tablets (210 to 420 mg of elemental iron) per day at ≥1-week intervals as needed to obtain targeted serum phosphorus levels. Maximum dose of 12 tablets per day (2,520 mg of elemental iron).
- **Sucroferric Oxyhydroxide**: 1 tablet (500 mg iron) 3 times daily with meals initially. May titrate dose by 1 tablet (500 mg iron) per day at ≥1-week intervals as needed to obtain targeted serum phosphorus concentrations. Maximum dose: 6 tablets (3,000 mg iron) per day.

5. Miscellaneous

- **Tenapanor (Xphozah®)** is an additional therapy seen in hyperphosphatemia, which is not a phosphate binder itself.
    - This product is a Sodium/Hydrogen Exchanger 3 (NHE3) Inhibitor, which works differently to prevent phosphate absorption within the gastrointestinal tract.
    - Tenapanor is typically reserved as a last line agent due to its adverse effect of diarrhea, which can lead to dehydration, and its numerous drug interactions.
    - Usual oral dose (add-on therapy in patients on dialysis with inadequate response to phosphate binders): 30 mg twice daily (may decrease dose if needed based on serum phosphate concentration and GI tolerability).
- **Aluminum Hydroxide** is an alternative metal-based phosphate binder (like iron-based and lanthanum-based) used off-label for refractory hyperphosphatemia (not used long-term as extended use has been associated with aluminum toxicity).
    - Usual initial oral dose (for short-term use [≤4 weeks] in patients with severe hyperphosphatemia [e.g., serum phosphorus levels >7 mg/dL] despite treatment with other nonaluminum phosphate binders): 300 to 600 mg 3 times daily with meals.

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SUMMARY

Oral phosphate binders aid in phosphate excretion, reducing the risk of hyperphosphatemia-related complications and cardiovascular mortality. These agents are available in multiple formulations, including those that contain calcium, iron, and heavy metals, as well as non-absorbable polymers. Choosing an appropriate phosphate binder for residents with CKD should take into consideration their differing clinical profiles, the resident's comorbid conditions and resident preferences, and any other medications they are prescribed.

References:

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