SERUM PHOSPHORUS TESTING

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INSTRUCTIONS FOR USE
This Medical Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the enrollee specific document must be referenced. The terms of an enrollee's document (e.g., Certificate of Coverage (COC) or Summary Plan Description (SPD)) may differ greatly. In the event of a conflict, the enrollee's specific benefit document supersedes this Medical Policy. All reviewers must first identify enrollee eligibility, any federal or state regulatory requirements and the plan benefit coverage prior to use of this Medical Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

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BACKGROUND

Phosphorus is an element that plays an important role in many physiologic systems. Phosphate is a component of cell membranes and biological macromolecules including nucleotides, proteins, lipids and carbohydrates. It is key to the activity of coenzymes, the metabolism of carbohydrates, the maintenance of acid-base balance, and the release of oxygen from hemoglobin. Phosphorylated compounds such as adenosine triphosphate are necessary for biochemical energy generation. Eighty-five percent of phosphorus resides in bone (mostly as hydroxyapatite), 14% is present in cells and less than 1% is represented in plasma. Organic and inorganic phosphate is present in plasma, although serum phosphate assays generally measure inorganic phosphate. Phosphate is resorbed from bone and also absorbed from the diet in the small intestine; it is filtered by the glomerulus. The majority of this phosphate is then reabsorbed by the renal tubule, mainly by the proximal convoluted tubule by a transporter that is inhibited by metabolic acidosis. Acid-base balance, hormones and vitamin D modulate intestinal absorption and renal reabsorption of phosphorus. Parathyroid hormone (PTH)

inhibits renal reabsorption of phosphorus, and growth hormone decreases renal excretion. Vitamin D increases renal reabsorption. Normal renal function is key to the maintenance of serum phosphorus levels.

The reference range for adults is 2.5-4.5 mg/dL, but levels are higher in children.[1] Cut-off levels for clinical interventions are serum phosphorus levels less than 1.5 g/dL[1] and greater than 5 mg/dL.[2] Given the number of systems that must function normally for proper absorption and excretion of phosphorus, hypophosphatemia and hyperphosphatemia are both commonly encountered in clinical medicine and have a multitude of causes.

Symptoms and signs of hypophosphatemia include confusion, paresthesia, seizure, coma, cardiac dysrhythmia, congestive heart failure, respiratory failure, hypoxia, and myalgia. Severe hypophosphatemia can decrease acid excretion in the kidney and thereby result in metabolic acidosis. Hemolytic anemia can result when phosphate levels are inadequate to maintain red blood cell elasticity.

Symptoms of hyperphosphatemia include nausea and vomiting, seizures, mental status changes, dysrhythmias, weakness, muscle cramps due to attendant hypocalcemia, tetany, decreased visual acuity, and prolongation of the Q-T interval. Severe hyperphosphatemia can lead to an elevated serum anion gap and should be considered in its differential diagnosis.[3]

Conditions and medications that cause an intracellular shift of phosphate, decreased intestinal absorption, or decreased renal reabsorption cause hypophosphatemia. Most cases of hypophosphatemia result from a defect in renal tubular reabsorption of phosphorus. Excessive PTH and renal tubular disorders cause a low serum phosphate with the presence of phosphate in the urine. With intracellular shifts of phosphorus that occur secondary to respiratory alkalosis or insulin administration, phosphate is virtually undetectable in the urine. Severe burns, gram-negative sepsis and overdose of aspirin lead to a respiratory alkalosis that causes hypophosphatemia due to increased glycolysis. Administration of glucose and carbohydrates causes an intracellular shift of phosphorus.

Refeeding syndrome can be fatal. This syndrome was first observed in World War II prisoners who were fed after deprivation of sustenance; patients with cancer, chronic alcoholism, and eating disorders are at risk for the syndrome when refeeding is commenced. It can occur regardless of whether the refeeding is oral, enteral, or parenteral. The condition is characterized by severe electrolyte and fluid shifts. Hypophosphatemia is the cardinal sign of refeeding syndrome. The metabolic abnormalities that occur can cause respiratory and cardiac failure. Prevention of refeeding syndrome entails checking key electrolyte levels, including phosphate, before refeeding and then supplementing phosphate at 0.3-0.6 mmol/kg/day while monitoring the serum level for the first 2 weeks.[4]

Medications can cause hypophosphatemia. Glucose, antacids, steroids and diuretics commonly cause low serum phosphorus levels. Glucose shifts extracellular phosphate into cells. Antacids can decrease intestinal absorption of phosphate and steroids can increase urinary excretion. Diuretics can inhibit carbonic anhydrase, directly inhibit distal renal tubular absorption of phosphate, or affect phosphate balance through changes in potassium and magnesium homeostasis. Other drugs affecting phosphate levels include insulin, acetaminophen, and parenteral iron.[5]

Poor dietary intake of phosphorus due to alcoholism or anorexia nervosa causes hypophosphatemia. Any number of intestinal pathologies including celiac disease, tropical sprue and inflammatory bowel disease that decrease absorption of phosphate can lower serum levels.

Renal failure is the most common cause of hyperphosphatemia. Nonetheless, severe hyperphosphatemia does not occur until advanced stages of chronic renal failure. Other causes of hyperphosphatemia include iatrogenic sources and tumor lysis syndrome. Tumor lysis syndrome is characterized by potentially fatal metabolic perturbations that occur spontaneously in cancer or following cancer therapies. It is most commonly seen in patients receiving chemotherapy for leukemias and lymphomas.[6] Manifestations include hyperkalemia, hyperphosphatemia, hyperuricemia and hypocalcemia. Destruction of tumor cells, which contain higher levels of phosphate than normal cells, releases intracellular phosphate. Correction of electrolyte imbalances and prevention of acute renal failure are the cornerstones of therapy.
Elevations in serum phosphorus also occur after severe exertion, and this finding was corroborated by a study that measured biochemical and hematologic laboratory parameters before and after the Boston Marathon.[7] In this setting, the increase in serum phosphorus is attributed to rhabdomyolysis and hemolysis.

The evaluation of a serum phosphorus level is important in critically ill patients along with suspected victims of child abuse, chronic kidney disease patients, and individuals who will receive therapies that increase serum phosphorus levels. During the physical evaluation of a child suspected of being physically abused, caregivers look for signs of normal growth and development, and a serum phosphorus level may be one of the laboratory tests used to rule out bone mineralization disorders due to malnutrition, such as rickets.[8]

In patients with chronic kidney disease undergoing dialysis, vascular calcification and subsequent cardiac events complicate hyperphosphatemia. Hyperphosphatemia is associated with increased risk of death in patients with chronic kidney disease according to a recent meta-analysis.[9] Once serum levels top 6.5 mg/dL, mortality increases 18-39% compared to patients without elevated levels.[2] Marked hyperphosphatemia generally does not occur until the glomerular filtration rate falls to below 25 ml/min.[2]

Patients with chronic kidney disease abnormally metabolize minerals, and patients with stage 3 and higher chronic kidney disease cannot excrete phosphate appropriately. This hyperphosphatemia and the attendant hypocalcemia can cause hyperparathyroidism. Subsequently, bone disorders are found in the majority of patients with stage 3 and higher chronic kidney disease. The diagnosis of chronic kidney disease-mineral and bone disorder (CKD-MBD) requires the measurement of serum phosphorus, calcium, and PTH.

Guidelines from the Kidney Disease Improving Global Outcomes CKD-MBD Work Group recommend monitoring serum phosphorus levels at CKD stage 2 in children and at CKD stage 3 in adults. The interval for monitoring levels should be based on clinical information but the guidelines state that reasonable intervals would be every 6-12 months for stage 3, every 3-6 months for stage 4, and every 1-3 months for stage 5.[10] Disease stage determines the choice of phosphate-binding agents versus dialysis to treat hyperphosphatemia.

In a study of patients with chronic, stable asthma, electrolyte disturbances were observed in 43%, most commonly hypomagnesemia and hypophosphatemia. Because β_2-agonists can cause hypophosphatemia, this population of patients with stable asthma and hypophosphatemia are at higher risk for complications from treatment of acute exacerbations of asthma with nebulized or IV β_2-agonists.[11]

POLICY

For the following CPT code(s) in Table 1, the patient should have a diagnosis (ICD-10-CM) code(s) listed in the attached files below.

Table 1. HCPCS Codes (Alphanumeric, CPT© AMA)

HCPCS Code	Description
84100	Phosphorus inorganic (phosphate)

ICD-10 Diagnosis Codes (Proven)

CMP-035 Serum Phosphorus ICD10_v1

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POLICY HISTORY/REVISION HISTORY

Date	Action/Description
12/07/2017	Annual Policy Review Completed – no changes.
01/21/2017	Updated ICD10 codes as per CMS recommendations. Removed ICD9 code file.
12/03/2015	Annual Policy Review Completed – no changes.
10/01/2015	Removed ICD9 table. Embedded ICD9/ ICD10 PDF files.