Overview

This Coverage Policy addresses the use of oral, enteral or parenteral nutritional supplements that may be necessary for some individuals to maintain adequate nutrition.

Coverage Policy

Coverage for oral and enteral nutritional formula may be governed by state mandates. Oral and enteral nutritional formula benefit plan language differs significantly across plans. Refer to the applicable benefit plan document to determine benefit availability and the terms, conditions and limitations of coverage.

Oral and Enteral Infant Nutritional Formula

Infant (i.e., ≤ 12 months of age) nutritional formula is considered medically necessary when specifically formulated for the treatment of an inborn error of metabolism (e.g., disorder of amino acid or organic acid metabolism).

Home Enteral Infusion Pumps

Coverage for Durable Medical Equipment (DME) home enteral infusion pumps is subject to the terms, conditions and limitations of the applicable benefit plan’s Durable Medical Equipment (DME) benefit and
schedule of copayments. Please refer to the applicable benefit plan document to determine benefit availability and the terms, conditions and limitations of coverage. Coverage for a home enteral infusion pump is independent of whether or not coverage exists for the formula being used.

If coverage for home enteral infusion pumps is available, one (1) home enteral infusion pump is considered medically necessary DME when gravity or syringe feedings are not tolerated or a controlled rate of infusion is required.

**Home Parenteral Nutrition**
Home parenteral/home total parenteral nutrition (TPN) is considered medically necessary when nutritional status cannot be adequately maintained on oral or enteral feedings.

**Home Parenteral Infusion Pumps**
Coverage for home parenteral infusion pumps is subject to the terms, conditions and limitations of the applicable benefit plan's Durable Medical Equipment (DME) benefit and schedule of copayments. Please refer to the applicable benefit plan document to determine benefit availability and the terms, conditions and limitations of coverage.

If coverage for home parenteral infusion pumps is available, one (1) home parenteral infusion pump and associated supplies are considered medically necessary DME when criteria for home parenteral nutrition have been met.

**Intradialytic Parenteral Nutrition (IDPN)**
Intradialytic parenteral nutrition (IDPN) is considered medically necessary when BOTH of the following criteria are met:

- The individual is on chronic hemodialysis.
- The individual is a candidate for total parenteral nutrition (i.e., nutritional status cannot be adequately maintained on oral or enteral feedings).

Specialized intradialytic parenteral nutrition solutions are considered clinically equivalent, but not clinically superior, to standard formulations of intradialytic parenteral nutrition.

Coverage for specialized intradialytic parenteral nutrition may depend upon the applicable health benefit plan definition of medical necessity. Many health benefit plans administered by Cigna contain definitions of medical necessity which include a cost comparison component. For example, some benefit plans administered by Cigna define Medically Necessary/Medical Necessity, in pertinent part, as "not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that individual's illness, injury or disease. Because there are various intradialytic parenteral nutrition preparations, where one may be significantly more expensive than the other but not proven to be clinically superior, a more expensive specialized intradialytic parenteral nutritional solution may be considered not medically necessary under these plans.

**Digestive Enzyme Cartridge**
A digestive enzyme cartridge (e.g., Relizorb™) for use with enteral tube feeding is considered experimental, investigational or unproven.

**Not Medically Necessary Items**
Each of the following items is considered not medically necessary for ANY indication:

- standardized or specialized infant formula for conditions other than inborn errors of metabolism, including, but not limited to: food allergies; multiple protein intolerances; lactose intolerances; gluten-free formula for gluten-sensitive enteropathy/celiac disease; milk allergies; sensitivities to intact protein;
protein or fat maldigestion; intolerances to soy formulas or protein hydrolysates; prematurity; or low birth-
weight
• baby food
• banked breast milk provided to a non-hospitalized infant
• dietary additives and food supplements
• food thickeners
• gluten-free food products
• grocery items that can be blenderized and used with an enteral feeding system
• high protein powders and mixes
• lactose-free products; products to aid in lactose digestion
• low carbohydrate diets
• normal grocery items
• nutritional supplement puddings
• oral/enteral formula used to replace fluids and electrolytes
• oral vitamins and minerals
• weight-loss foods and formula; products to aid weight loss

**General Background**

Specialized nutritional support is often required for patients who have chronic disease or for those undergoing long-term rehabilitation who are at risk for malnutrition. Nutritional support can be provided orally, enterally (through a tube into the stomach or small intestine) and intravenously.

Malnutrition is commonly defined in the medical literature as a non-edematous or post-dialysis weight loss of at least 10% of ideal body weight over a three-month period or a serum albumin of less than 3.4 grams/dL. Malnutrition can occur in otherwise healthy individuals when they are deprived of adequate nutrients for an extended period of time.

**Oral and Enteral Nutrition**

Nutritional support provided via the gastrointestinal tract can be taken by mouth or provided enterally. Oral nutrition refers to nutrition taken through the mouth. Enteral nutrition is commonly defined as the provision of nutritional requirements through a tube in the stomach or small intestine. The major types of enteral nutrition formulas include the following (Makola, 2005):

1. Elemental/amino acid-based: contains free amino acids, glucose polymers, and are low fat with only about 2% to 3% of calories derived from long chain triglycerides (LCT)
2. Semi-elemental: contains peptides of varying chain length, simple sugars, glucose polymers or starch and fat, primarily as medium chain triglycerides (MCT)
3. Standard or polymeric: contains intact proteins, complex carbohydrates and mainly LCTs
4. Specialized/disease-specific and immune-enhancing: contains biologically active substances or nutrients such as glutamine, arginine, nucleotides or essential fatty acids

For certain metabolic and malabsorption disorders, an infant or child may require an elemental formal because of the inability to digest whole proteins found in standard formula. Individuals may require enteral nutritional therapy to provide sufficient nutrients to maintain weight and strength commensurate with their overall health status if their nutritional needs cannot be met through dietary adjustments and/or oral supplements. In general, patients may require enteral nutritional therapy when they have one of the following:

• a functional impairment or disease of the structures that normally permit food to reach the small bowel
• a disease of the small bowel that impairs digestion and/or absorption of an oral diet

For most facility inpatient stays, room and board, including food, are covered. Room and board charges are generally inclusive of the bed, related room charges, and food, including special diets such as cardiac, diabetic,
clear liquids, etc., along with general services and activities needed for the care of an inpatient. Some services such as enteral and intravenous feedings may be reimbursed separately.

**Enteral Infusion Pumps**
Enteral feedings are delivered by syringe, gravity, or via an electric infusion pump. Feedings can be delivered on an intermittent or continuous basis. Pump-controlled infusions may be recommended for jejunal feedings and for gastrostomy feedings to decrease gastroesophageal reflux. Medically necessary indications for the use of a pump include:

- The individual's medical condition is such that gravity or syringe feeding is not clinically appropriate (e.g., there is a risk of aspiration or reflux).
- The individual's medical condition requires that the nutritional formula administration rate is such that a pump is required to titrate infusion for patient safety (i.e., less than 100 cc per hour).
- The individual has severe diarrhea, dumping syndrome, fluctuating blood glucose levels, or a condition that results in circulatory overload.

**U.S. Food and Drug Administration (FDA):** According to the FDA, an infusion pump is a medical device that delivers fluids in a controlled manner to a patient in a clinical setting or at home. There are multiple types of infusion pumps which include large volume, syringe and enteral pumps. Many pumps have safety features such as alarms that are intended to activate in the event of a problem. These infusion pumps are approved through the FDA 510(k) process as Class II devices.

**Inborn Errors of Metabolism**
Oral or enteral nutritional formula may be required for infants, defined by the Centers for Disease Control and Prevention (CDC) as zero to one year of age (CDC, 2019), with inborn errors of metabolism. The broad category of “metabolic diseases” includes inborn errors of amino acid metabolism, such as phenylketonuria, maternal phenylketonuria, maple syrup urine disease, homocystinuria, methylmalonacidemia, propionicacidemia, isovalericacidemia, and other disorders of leucine metabolism; glutaricaciduria type I and tyrosinemia types I and II; and urea cycle disorders. These are all disorders treatable by dietary modifications, which can prevent complications like severe intellectual disability and death (Greer: American Academy of Pediatrics Committee on Nutrition, 2003). In these disorders, the metabolic pathway is disrupted and excessive accumulation of an amino acid or other product results. If the appropriate dietary restriction of one or more applicable amino acids is introduced early in life, complications can be prevented or limited. Specialized medical food, including low protein and amino acid modified food, may be required as the infant outgrows the need for formula. While conditions such as mitochondrial disorders are considered metabolic diseases, there is typically no specific treatment for these disorders. As such, specific nutritional replacement therapy does not treat the condition or prevent neurologic injury and subsequent developmental issues in infants and children.

**Malabsorption Syndromes**
Individuals with malabsorption syndromes may benefit from enteral nutritional support. Malabsorption syndrome refers to the disordered or inadequate absorption of nutrients from the intestinal tract, especially the small intestine. Enteral nutritional support may be indicated when the formula comprises the primary source of nutrition (i.e., 60% or more of caloric nutritional intake). Malabsorption syndromes may be associated with or due to a number of diseases, including (Garcia-Careaga, 2004):

- infections
- tropical sprue
- celiac disease
- pancreatic insufficiency
- pancreatitis
- cystic fibrosis
- post-gastrectomy malabsorption
- Crohn's disease
- ulcerative colitis (when there are documented objective signs and symptoms of malabsorption such as serum albumin levels)
• short-bowel syndrome
• radiation enteritis
• parenchymal liver disease
• cholestatic liver disease
• post-intestinal resection malabsorption
• eosinophilic gastrointestinal disorders
• Whipple’s disease
• giardiasis
• lymphangiectasia

Malabsorption can also be due to the use of specific drugs that cause inadequate digestion or bind or precipitate bile salts such as neomycin, cholestyramine and orlistat.

Conditions that are not considered malabsorption syndromes include, but are not limited to:

• food allergies
• cow’s milk allergies
• lactose intolerance
• sensitivities to intact protein
• protein or fat malabsorption
• multiple protein intolerances

**Digestive Enzyme Cartridges**
A digestive enzyme cartridge (e.g., Relizorb™) is a medical device designed to mimic the normal function of pancreatic lipase for use in adults on enteral tube feeding who have trouble breaking down and absorbing fats. It is a point-of-care device designed to fit in line with enteral feeding circuits. The device is designed to hydrolyze (break down) fats present in enteral formulas from triglycerides into fatty acids and monoglycerides to allow for their absorption and utilization by the body. This breakdown of fats is intended to mimic the function of the enzyme lipase in patients who do not excrete sufficient levels of pancreatic lipase.

**U.S. Food and Drug Administration (FDA):** According to the FDA, Relizorb is an enzyme packed cartridge that hydrolyzes fats in enteral formula. It is 510k approved as a Class II medical device indicated for use in pediatric patients (ages 5 years and above) and adult patients to hydrolyze fats in enteral formula (FDA, 2016).

**Literature Review:** A prospective, single-arm, multicenter, open-label study (ASSURE trial) conducted by Stevens et al. (2018) evaluated the safety, tolerability and improvement of fatty acids (FA) in red blood cells (RBC) when using a Relizorb cartridge during enteral nutrition (EN) feedings in patients (n=39) with cystic fibrosis (CF). Patients were included in the study if they were ≥4 years with a confirmed diagnosis of CF, a documented history of exocrine pancreatic insufficiency (EPI), taking enteral formula a minimum of four times per week, using pancreatic enzyme replacement therapy (PERT), and consuming an unrestricted fat diet. The primary outcome measured the change in the omega-3 index, which is a measure of the percentage of total DHA (docosahexaenoic acid) plus EPA (eicosapentaenoic acid) relative to the total fatty acid (FA) composition present in RBC membranes. Secondary efficacy outcomes included changes in plasma and erythrocyte membrane composition (%) of total EPA, total DHA, and omega-6 to omega-3 FAs (a key marker of inflammation) as well as plasma concentrations of total DHA+EPA. Changes in weight gain and standardized body weight and body mass index (BMI) were also examined. Safety and tolerability outcomes included the frequency and severity of adverse events (AEs) and unanticipated adverse device effects (UADEs), incidence of GI symptoms, clinical and laboratory findings, vital signs, and use of concomitant medications. All outcomes were measured at observation initiation (day –14), before Relizorb initiation (day 0), and at 30-day intervals during the Relizorb treatment period (days 30, 60, and 90). Thirty-six patients completed the 90-day study, there were not any adverse events related to Relizorb use. Fat absorption increased significantly from a baseline value of 4.4%, to 8.4% at 60 days and 9.4% at 90 days (p<0.001 for each increase from baseline to 60 and 90 days). The secondary efficacy outcomes changed significantly from baseline to each post-baseline visit. The composition (%) of erythrocyte membrane total DHA and total EPA, and plasma concentrations of total DHA+EPA values increased. The omega-6 to omega-3 FA ratios decreased in both erythrocyte membranes and
plasma. Body mass index (BMI) did not change significantly over the course of the study period. Author noted limitations included the small patient population, short term follow-up and the open label study design. Furthermore, other than EN, dietary intake was not recorded limiting the ability to assess whether oral caloric intake was adequate to lead to weight gain.

Freedman et al. (2017) conducted a multicenter, randomized, double-blind, crossover trial (n=33) to evaluate the safety, tolerability, and fat absorption of a new in-line digestive cartridge (Relizorb) that hydrolyzes fat in enteral formula provided to patients with cystic fibrosis (CF). The trial included subjects that had a diagnosis of CF, history of exocrine pancreatic insufficiency (EPI), received enteral nutrition at least four times a week through a feeding tube, used pancreatic enzyme replacement therapy (PERT), and stable health status. The study was divided into three periods A, B and C. In period A, all subjects received standard enteral formula (Peptamen 1.5) for seven days. Subjects were then randomized into two groups during period B. One group had digestive cartridges and the second group had placebo/sham cartridges. After a seven day washout period, there was a crossover and subjects received enteral nutrition through the opposite cartridge. In period C, all subjects received impact peptide (high fat and long chain triglycerides) given overnight with Relizorb digestive cartridge for seven days. The outcomes measured changes in plasma fatty acid concentrations of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) for 24 hours along with the safety and tolerability of the cartridge. When Relizorb was compared with placebo were the total and peak concentration of DHA+EPA were significantly higher with digestive cartridge use (p<0.001). There were no gastrointestinal (GI) adverse effects reported that were temporally associated with digestive or placebo cartridges. Three, 11, and four non-GI adverse effects occurred in periods A, B, and C, respectively and were not considered to be treatment related. Adverse effects such as such as abdominal pain, bloating, constipation and diarrhea, were lower with digestive cartridge use compared with period A. In addition, > 50% of subjects reported a decrease in severity of most GI events with digestive cartridge use in period C compared with period A. Author noted limitations of the study were the small sample size and the use of only one feeding cartridge to measure fat absorption and seven days to measure safety. Additional randomized controlled trials with larger patient populations and long-term follow-up are needed to support the outcomes of this study.

Hayes published an updated Search and Summary in 2018 on the digestive enzyme cartridge, Relizorb (Alcresta Therapeutics Inc.) for enzyme hydrolysis in patients receiving enteral nutrition. The review included five abstracts (two randomized controlled trials, a case study and two review articles). Hayes concluded that there is insufficient published evidence to assess the safety and/or impact on health outcomes or patient management for the use of Relizorb in patients receiving enteral nutrition (Hayes, 2018).

Parenteral Nutrition
Parenteral nutrition refers to the intravenous provision of micro- or macro-nutrients to prevent or correct nutritional deficiency. It is typically reserved for situations when there is inadequate or insufficient absorption of nutrients through the gastrointestinal tract. Peripheral parenteral nutrition (PPN) is typically used for a short time (up to two weeks) because of limited patient tolerance and few suitable peripheral veins. In patients whose disease produces temporary or permanent loss of the absorptive surface of the small intestine, longer term parenteral nutrition may be required. Long-term total parenteral nutrition (TPN) is necessary when parenteral feedings are indicated for longer than two weeks, peripheral access is limited, nutrient needs are large or fluid restriction is required. TPN is delivered through a central catheter that is burrowed through a subcutaneous tunnel on the anterior chest. Home parenteral nutrition may be indicated in patients who require long-term TPN. Indications for home parenteral nutrition include: bowel infarction, pathological conditions resulting in short bowel syndrome, inflammatory bowel disease with multiple fistulas, malabsorption-associated radiation enteritis, scleroderma, carcinoma of the bowel, an abdominal cavity that results in chronic obstruction, intestinal dysfunction, or diarrhea and malabsorption associated with aggressive chemotherapy or abdominal irradiation.

In general, it is clinically appropriate to initiate parenteral nutrition when all of the following are met:

- Weight and strength maintenance commensurate with the patient’s overall health status cannot be achieved by modifying the nutrient composition of the enteral diet (e.g., lactose-free diet) or by utilizing pharmacologic means to treat the etiology of the malabsorption.
- The patient is malnourished (i.e., 10% weight loss over three months or less and serum albumin less than or equal to 3.4 gm/dL).
• The patient has a disease or clinical condition that has not responded to altering the manner of delivery of appropriate nutrients (e.g., slow infusion of nutrients through a tube with the tip located in the stomach or jejunum).

In addition to the above criteria, additional specific indications for parenteral nutrition include any of the following:

• The patient has undergone (within the past three months) massive small bowel resection leaving less than or equal to five feet of small bowel beyond the ligament of Treitz.
• The patient has a short bowel syndrome severe enough that the patient has a net gastrointestinal fluid and electrolyte malabsorption such that on an oral intake of 2.5–3 liters/day the enteral losses exceed 50% of the oral/enteral intake, and the urine output is less than one liter/day.
• The patient requires bowel rest for at least three months and is receiving intravenously 20–35 cal/kg/day for treatment of symptomatic pancreatitis with/without pancreatic pseudocyst, severe exacerbation of regional enteritis, or a proximal enterocutaneous fistula where tube feeding distal to the fistula is not possible.
• The patient has complete mechanical small bowel obstruction where surgery is not an option.
• The patient is significantly malnourished (i.e., 10% weight loss over three months or less and serum albumin less than or equal to 3.4 gm/dl) and has very severe fat malabsorption (i.e., fecal fat exceeds 50% of oral/enteral intake on a diet of at least 50 gm of fat/day as measured by a standard 72-hour fecal fat test).

The use of parenteral nutrition is not without risk and should only be considered when adequate nutritional intake cannot be achieved through oral or enteral nutrition. Parenteral nutrition can cause serious complications related to the presence of intravenous lines and metabolic imbalances from inappropriate nutrient formulations. Central venous catheter insertion can result in damage to local structures including: pneumothorax, brachial plexus injury, subclavian and carotid artery puncture, hemothorax, thoracic duct injury, and chylothorax. Air embolism and thrombosis of the catheter or veins can also occur. Fluid overload, hypertriglyceridemia, hypercalcemia, hypoglycemia, hyperglycemia and nutrient deficiencies can all result from administering the inappropriate combination and proportion of nutrients (Howard, et al., 2003; Klein and Rubin, 2002; Koretz, et al., 2001).

**Intradialytic Parenteral Nutrition (IDPN)**

IDPN, which includes intraperitoneal nutrition (IPN), is a form of parenteral nutrition infused during dialysis. IDPN has been proposed as a treatment option for protein calorie malnutrition in an effort to decrease the associated morbidity and mortality experienced by some patients on maintenance hemodialysis or peritoneal dialysis. This type of parenteral nutrition has the advantage of providing calories and protein during hemodialysis without the need for a central venous catheter. The serum albumin level is considered to be a key measure for assessing nutritional status (Koppel, 2001; National Kidney Foundation (NKF)/Kidney Disease Outcomes Quality Initiative [KDOQI], 2000).

The nutritional components of typical IDPN solutions are as follows (Dukkipati, et al., 2010):

**Standard IDPN Composition** (final concentrations are 11% amino acids, 11.1% dextrose, 4.6% lipids): Protein: 97 g; Carbohydrate: 98 g; Fat: 41 g; Non-protein kcal: 743; Total volume: 880 ml

**Carbohydrate-Control IDPN Composition** (final concentrations are 11.6% amino acids, 8.9% dextrose, 4.6% lipids): Protein: 96 g; Carbohydrate: 73.5 g; Fat: 38 g; Non-protein kcal: 630; Total volume: 825 ml

IDPN is generally indicated when the malnourished patient suffers from a permanently (i.e., greater than three months) impaired gastrointestinal tract and there is insufficient absorption of nutrients to maintain adequate strength and weight. It may also be indicated in malnourished patients with a functioning gastrointestinal tract but who are metabolically challenged, resulting in the inability to meet protein and energy requirements (1.2 gm protein/kg/day) with food intake or enteral feedings. The clinical record should demonstrate that the patient
cannot be maintained on oral or enteral feedings and that due to severe pathology of the gastrointestinal tract or metabolic challenges, the patient must be infused with nutrients. Infusions should be vital to the nutritional stability of the patient and not supplemental to a deficient diet caused by dialysis.

Indications for IDPN include both of the following:

- patients who cannot tolerate or have not responded adequately to oral or enteral supplements
- patients who have clinical signs of malnutrition such as serum albumin concentrations of < 3.4 gm/dL, a 10% loss of ideal body weight, a dietary protein intake of < 0.8 gm/kg, and a dietary intake of < 25 kcal/kg (Lazarus, 1999).

**Literature Review:** While there is compelling evidence demonstrating the role that malnutrition plays in morbidity and mortality in the chronic dialysis patient, the evidence is less clear on treatment options and the impact specific treatments, including IDPN, have on health outcomes. Thabet et al. (2017) reported the results of a prospective randomized control study that evaluated the efficacy of intradialytic parenteral nutrition (IDPN) therapy in malnourished patients (n=40) with refractory anemia. The study included patients 22 to 56 years of age who were on regular hemodialysis (HD) three times a week for at least six months. The patients had been prescribed a maintenance dose of 300 IU/Kg/week of erythropoietin and were malnourished according to a BMI < 23, a positive malnutrition inflammation score (MIS) and baseline serum albumin less than 3.5g/dl. The patients were randomized into two groups. Group I (n=20) received IDPN during each HD session for six months and Group II (n=20) did not receive IDPN. The primary outcome was the improvement of refractory anemia in patients that received IDPN. Additional outcomes included MIS, body weight and serum albumin levels. No patients were lost to follow-up. A gradual increase in hemoglobin level, serum albumin and BMI alongside a gradual decrease in MIS score were observed in patients who received IDPN therapy after three and six months of treatment when compared to their baseline. There was a significant elevation of the hemoglobin level and serum albumin in the IDPN group when compared with the other group after three months of treatment (p=0.001) and (p=0.003) respectively, while the MIS score was significantly decreased (p=0.001). The BMI was significantly increased after six months of treatment in the IDPN group (p=0.001). The intradialytic infusion of IDPN solutions was well tolerated. Side effects such as flushing, headache and fever were not seen in any of the patients. However, the authors noted that 18 of the 20 patients in the IDPN group were nauseated occasionally, but this side effect was tolerated by the patients.

Marsen et al. (2017) conducted a prospective, multicenter RCT (n=107) of maintenance hemodialysis patients with protein-energy wasting (PEW) to evaluate the impact of IDPN on biochemical and clinical parameters of nutritional status. Patients randomized to the intervention group (n=53) received standardized nutritional counseling plus IDPN three times weekly for 16 weeks followed by a treatment-free period of 12 weeks. The control group (n=54) received standardized nutritional counseling only. Patient selection criteria included moderate to severe malnutrition, maintenance hemodialysis therapy (three times per week) for more than six months, and presence of two of the following three criteria: albumin <35 g/L, prealbumin <250 mg/L, or phase angle alpha <4.5° assessed by bioelectrical impedance analysis. The primary outcome measure was the change in serum prealbumin from baseline to end of the study period (V6/week 16). Secondary outcomes included increase in parameters of protein metabolism (albumin, transferrin, PCR), and improvement in health-related quality of life (SF-12). The trial was completed by 32/53 (60.4%) patients in the intervention group and 47/54 (87.0%) patients in the control group. The proportion of patients who achieved a relevant (> 15%) increase in prealbumin level at week four was twice as high in the intervention group compared to the control group (41.0% vs. 20.5%; p=0.0415). The increase was sustained at 12 weeks. Analyses showed no statistically significant or clinically important differences in the measured secondary study outcomes for either treatment. The overall occurrence of adverse events, primarily gastrointestinal disorders, was higher in patients receiving IDPN compared to patients in the control group. The study is limited by the short-term follow-up period and loss to follow-up. However the results suggest that IDPN administration may improve prealbumin levels in malnourished hemodialysis patients in the short-term.

A systematic review by Sigrist et al. (2010) found the evidence from available randomized controlled trials (RCTs) (n=3 studies) insufficient to demonstrate either a net benefit or a net harm associated with the use of IDPN in malnourished hemodialysis patients. Another systematic review (n=3 RCTs) by Foulks (1999) found...
considerable heterogeneity in study design, patients selected for therapy, types of IDPN used and outcome criteria. Therefore a clear recommendation could not be made regarding the use of IDPN.

Cano et al. (2007) conducted an RCT (n=166) of malnourished hemodialysis patients who received oral nutritional supplements with or without 12 months of IDPN. Multivariate analysis showed that an increase in prealbumin of > 30 mg/L within three months, a marker of nutritional improvement, independently predicted a 54% decrease in two-year mortality, as well as reduced hospitalizations and improved general well-being. Both groups demonstrated improvement in body mass index and the nutritional parameters serum albumin and prealbumin (p<0.05). Study results demonstrated no survival advantage for the IDPN group.

Additional evidence in the published peer-reviewed medical literature evaluating the safety and effectiveness of IDPN consists of nonrandomized comparative trials, cohort studies, and case series (Korzets, et al., 2008; Joannidis, et al., 2008; Cherry, et al., 2002; Pupim, et al., 2002; Capelli, et al., 1994; Chertow, et al., 1994). Some studies have had small sample sizes and short duration of follow-up. Outcomes have included improvement in dry weight, serum albumin levels, and survival rates. The largest study to date, Chertow et al. (1994), was a multicenter retrospective case series comparing the morbidity of IDPN patients (n=1679) with untreated controls (n=22,517). Dialysis patients with a serum albumin of < 3.4 gm/dL who were treated with IDPN experienced increased albumin and creatinine levels, as demonstrated on time trend analyses. A reduction in the odds of death at one year with the effect stronger at lower levels of creatinine compared to controls was also reported.

Although study results have been variable, in general the available evidence is supportive of the use of IDPN in a subset of maintenance hemodialysis patients who are unable to meet daily nutritional requirements with oral or enteral intake.

Specialized Intradialytic Nutrition Solutions: Specialized solutions of IDPN (e.g., Proplete® [Pentec Health, Inc. Boothwyn, PA]) have purportedly been formulated to meet the needs of the hemodialysis patients who are protein malnourished or take in enough calories but inadequate amounts of protein. According to the manufacturer, Proplete contains no lipids and less carbohydrates compared to traditional IDPN. Specialized formulations of IDPN have not been proven to be clinically superior to a standard formulation of total parenteral nutrition.

Literature Review: Currently there are no available clinical studies in the published peer-reviewed medical literature clinical studies demonstrating the superiority of specialized preparations of IDPN. It has not been shown that use of specialized solutions result in better outcomes (e.g., improvement in dry weight, serum albumin levels) for dialysis patients compared to standard preparations.

Professional Societies/Organizations
American Gastroenterological Association (AGA): The AGA published medical position statements on enteral (1995) and parenteral (2001) nutrition. Enteral nutrition is considered for patients who cannot or will not eat, who have a functioning gastrointestinal tract and a safe method of access. Enteral support should be initiated after 1–2 weeks without nutrition. Enteral feeding is preferable over parenteral therapy, provided there are no contraindications, access can be obtained safely and oral intake is not possible. Mechanical obstruction is the only contraindication to enteral feeding. For short-term needs, a nasogastric or nasoenteric tube is used, whereas a gastrostomy or jejunostomy tube is used for long-term needs. In general, parenteral nutrition is indicated to prevent the adverse effects of malnutrition in patients who are unable to obtain adequate nutrients by oral or enteral routes. The decision to use parenteral nutrition requires an understanding of the patient’s clinical condition and anticipated outcome, judgment as to the patient’s ability to tolerate undernutrition, knowledge of the clinical efficacy of parenteral nutrition and an appreciation of the patient’s desires and needs.

National Kidney Foundation (NKF): The NKF clinical practice guideline for nutrition in children with chronic kidney disease stated that a trial of IDPN to augment inadequate nutritional intake is suggested for malnourished children (BMI-for-height-age < 5th percentile) receiving maintenance hemodialysis who are unable to meet their nutritional requirements through oral and tube feeding (NKF/Kidney Disease Outcomes Quality Initiative [KDOQI], 2009).
National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI): The NKF KDOQI (2000) listed indications for nutritional support in individuals who are undergoing maintenance dialysis and are unable to meet their protein and energy needs. According to the NKF, the period of inadequate intake after which nutritional support should be instituted ranges from days to two weeks depending on the severity of the patient’s condition, degree of malnutrition, and degree of inadequacy of their intake. A complete nutritional assessment should be done, and any reversible or treatable condition or medication that would interfere with appetite or cause malnutrition should be eliminated or treated. Oral diet may be supplemented with energy and protein supplements. If oral nutrition is inadequate, tube feedings should be offered. If tube feedings are not used or are contraindicated, IDPN should be considered in combination with oral intake. TPN should be considered if IDPN and oral intake do not meet the protein and energy needs.

Centers for Medicare & Medicaid Services (CMS)
- National Coverage Determination (NCD) for Enteral and Parenteral Nutritional Therapy (180.2), effective date 7/11/1984. The NCD is broader in scope than the Coverage Policy. Refer to the CMS NCD table of contents link in the reference section.
- Local Coverage Determination (LCD): Multiple LCDs found. Refer to the LCD table of contents link in the reference section.

Use Outside of the US
A 2006 guideline developed by the National Institute for Health and Clinical Excellence (NICE) states that nutrition support should be considered in people who are malnourished, as defined by any of the following:
- a body mass index (BMI) of less than 18.5 kg/m²
- unintentional weight loss greater than 10% within the last 3–6 months
- a BMI of less than 20 kg/m² and unintentional weight loss greater than 5% within the last 3–6 months

Nutrition support should also be considered for those at risk for malnutrition including individuals who have a poor absorptive capacity, have high nutrient losses, and/or have increased nutritional needs from causes such as catabolism. The guideline further stated that if there is either partial or complete intestinal failure (e.g., obstruction, ileus, extensive surgical resection, malabsorption), or if the gastrointestinal tract cannot be accessed, some or all of a patient’s nutritional needs may be met using an intravenous infusion of parenteral nutrition (PN) (NICE, 2006; updated 2017).

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Generally excluded from coverage regardless of indication or use:

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>B4149</td>
<td>Enteral formula, manufactured blenderized natural foods with intact nutrients, includes proteins, fats, carbohydrates, vitamins and minerals, may include fiber, administered through an enteral feeding tube, 100 calories = 1 unit</td>
</tr>
<tr>
<td>B4150</td>
<td>Enteral formula, nutritionally complete with intact nutrients, includes proteins, fats, carbohydrates, vitamins and minerals, may include fiber, administered through an enteral feeding tube, 100 calories = 1 unit</td>
</tr>
<tr>
<td>B4152</td>
<td>Enteral formula, nutritionally complete, calorically dense (equal to or greater than 1.5 Kcal/ml) with intact nutrients, includes proteins, fats, carbohydrates, vitamins and minerals, may include fiber, administered through an enteral feeding tube, 100 calories = 1 unit</td>
</tr>
<tr>
<td>B4153</td>
<td>Enteral formula, nutritionally complete, hydrolyzed proteins (amino acids and peptide chain), includes fats, carbohydrates, vitamins and minerals, may include fiber, administered through an enteral feeding tube, 100 calories = 1 unit</td>
</tr>
</tbody>
</table>
### Enteral Formula

- **B4158**: Enteral formula, for pediatrics, nutritionally complete with intact nutrients, includes proteins, fats, carbohydrates, vitamins and minerals, may include fiber and/or iron, administered through an enteral feeding tube, 100 calories = 1 unit

- **B4159**: Enteral formula, for pediatrics, nutritionally complete soy based with intact nutrients, includes proteins, fats, carbohydrates, vitamins and minerals, may include fiber and/or iron, administered through an enteral feeding tube, 100 calories = 1 unit

- **B4160**: Enteral formula, for pediatrics, nutritionally complete calorically dense (equal to or greater than 0.7 Kcal/ml) with intact nutrients, includes proteins, fats, carbohydrates, vitamins and minerals, may include fiber, administered through an enteral feeding tube, 100 calories = 1 unit

- **B4161**: Enteral formula, for pediatrics, hydrolyzed/amino acids and peptide chain proteins, includes fats, carbohydrates, vitamins and minerals, may include fiber, administered through an enteral feeding tube, 100 calories = 1 unit

- **S9433**: Medical food nutritionally complete, administered orally, providing 100% of nutritional intake

### Oral and Enteral Infant Nutritional Formula

Considered Medically Necessary when infant (i.e., ≤ 12 months of age) nutritional formula is specifically formulated for the treatment of an inborn error of metabolism (e.g., disorder of amino acid or organic acid metabolism):

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>B4154†</td>
<td>Enteral formula, nutritionally complete, for special metabolic needs, excludes inherited disease of metabolism, includes altered composition of proteins, fats, carbohydrates, vitamins and/or minerals, may include fiber, administered through an enteral feeding tube, 100 calories = 1 unit</td>
</tr>
<tr>
<td>B4155†</td>
<td>Enteral formula, nutritionally incomplete/modular nutrients, includes specific nutrients, carbohydrates (e.g. glucose polymers), proteins/amino acids (e.g. glutamine, arginine), fat (e.g. medium chain triglycerides) or combination, administered through an enteral feeding tube, 100 calories = 1 unit</td>
</tr>
<tr>
<td>B4157</td>
<td>Enteral formula, nutritionally complete, for special metabolic needs for inherited disease of metabolism, includes proteins, fats, carbohydrates, vitamins and minerals, may include fiber, administered through an enteral feeding tube, 100 calories = 1 unit</td>
</tr>
<tr>
<td>B4162</td>
<td>Enteral formula, for pediatrics, special metabolic needs for inherited disease of metabolism, includes proteins, fats, carbohydrates, vitamins and minerals, may include fiber, administered through an enteral feeding tube, 100 calories = 1 unit</td>
</tr>
<tr>
<td>S9435***</td>
<td>Medical foods for inborn errors of metabolism</td>
</tr>
</tbody>
</table>

†Note: Generally excluded from coverage when used to treat conditions other than infant inborn errors of metabolism

††Note: Considered Medically Necessary if used to report infant nutritional formula for the treatment of inborn errors of metabolism

### ICD-10-CM Diagnosis Codes

<table>
<thead>
<tr>
<th>Diagnosis Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>D81.810</td>
<td>Biotinidase deficiency</td>
</tr>
<tr>
<td>D81.818</td>
<td>Other biotin-dependent carboxylase deficiency</td>
</tr>
<tr>
<td>E70.0</td>
<td>Classical phenylketonuria</td>
</tr>
<tr>
<td>E70.1</td>
<td>Other hyperphenylalaninemas</td>
</tr>
<tr>
<td>E70.20-E70.29</td>
<td>Disorder of tyrosine metabolism</td>
</tr>
<tr>
<td>E70.40- E70.49</td>
<td>Disorders of histidine metabolism</td>
</tr>
<tr>
<td>E70.5</td>
<td>Disorders of tryptophan metabolism</td>
</tr>
<tr>
<td>E70.8</td>
<td>Other disorders of aromatic amino-acid metabolism</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>----------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>E70.9</td>
<td>Disorder of aromatic amino-acid metabolism, unspecified</td>
</tr>
<tr>
<td>E71.0</td>
<td>Maple-syrup-urine disease</td>
</tr>
<tr>
<td>E71.110-</td>
<td>Branch chain organic acidurias</td>
</tr>
<tr>
<td>E71.118</td>
<td></td>
</tr>
<tr>
<td>E71.120-</td>
<td>Disorders of propionate metabolism</td>
</tr>
<tr>
<td>E71.128</td>
<td></td>
</tr>
<tr>
<td>E71.19</td>
<td>Other disorders of branched-chain amino-acid metabolism</td>
</tr>
<tr>
<td>E71.2</td>
<td>Disorder of branched-chain amino-acid metabolism, unspecified</td>
</tr>
<tr>
<td>E71.30</td>
<td>Disorder of fatty-acid metabolism, unspecified</td>
</tr>
<tr>
<td>E71.310-</td>
<td>Disorders of fatty-acid oxidation</td>
</tr>
<tr>
<td>E71.318</td>
<td></td>
</tr>
<tr>
<td>E71.32</td>
<td>Disorders of ketone metabolism</td>
</tr>
<tr>
<td>E71.39</td>
<td>Other disorders of fatty-acid metabolism</td>
</tr>
<tr>
<td>E71.40</td>
<td>Disorders of carnitine metabolism, unspecified</td>
</tr>
<tr>
<td>E71.41</td>
<td>Primary carnitine deficiency</td>
</tr>
<tr>
<td>E71.42</td>
<td>Carnitine deficiency due to inborn errors of metabolism</td>
</tr>
<tr>
<td>E71.448</td>
<td>Other secondary carnitine deficiency</td>
</tr>
<tr>
<td>E71.50</td>
<td>Peroxisomal disorder, unspecified</td>
</tr>
<tr>
<td>E71.520</td>
<td>Childhood cerebral X-linked adrenoleukodystrophy</td>
</tr>
<tr>
<td>E71.53</td>
<td>Other group 2 peroxisomal disorders</td>
</tr>
<tr>
<td>E71.541</td>
<td>Zellweger-like syndrome</td>
</tr>
<tr>
<td>E71.542</td>
<td>Other group 3 peroxisomal disorders</td>
</tr>
<tr>
<td>E71.548</td>
<td>Other peroxisomal disorders</td>
</tr>
<tr>
<td>E72.00-E72.09</td>
<td>Disorders of amino-acid transport</td>
</tr>
<tr>
<td>E72.10-E72.19</td>
<td>Disorders of sulfur-bearing amino-acid metabolism</td>
</tr>
<tr>
<td>E72.20-E72.29</td>
<td>Disorder of urea cycle metabolism</td>
</tr>
<tr>
<td>E72.3</td>
<td>Disorders of lysine and hydroxyllysine metabolism</td>
</tr>
<tr>
<td>E72.4</td>
<td>Disorders of ornithine metabolism</td>
</tr>
<tr>
<td>E72.50-E72.59</td>
<td>Disorder of glycine metabolism</td>
</tr>
<tr>
<td>E72.89</td>
<td>Other specified disorders of amino-acid metabolism</td>
</tr>
<tr>
<td>E72.9</td>
<td>Disorder of amino-acid metabolism, unspecified</td>
</tr>
<tr>
<td>E74.01</td>
<td>von Gierke disease</td>
</tr>
<tr>
<td>E74.02</td>
<td>Pompe disease</td>
</tr>
<tr>
<td>E74.03</td>
<td>Cori disease</td>
</tr>
<tr>
<td>E74.04</td>
<td>McArdle disease</td>
</tr>
<tr>
<td>E74.09</td>
<td>Other glycogen storage disease</td>
</tr>
<tr>
<td>E74.21</td>
<td>Galactosemia</td>
</tr>
<tr>
<td>E74.29</td>
<td>Other disorders of galactose metabolism</td>
</tr>
<tr>
<td>E74.4</td>
<td>Disorders of pyruvate metabolism and gluconeogenesis</td>
</tr>
<tr>
<td>E75.21</td>
<td>Fabry (-Anderson) disease</td>
</tr>
<tr>
<td>E75.22</td>
<td>Gaucher disease</td>
</tr>
<tr>
<td>E75.23</td>
<td>Krabbe disease</td>
</tr>
<tr>
<td>E75.26</td>
<td>Sulfatase deficiency</td>
</tr>
<tr>
<td>E88.41</td>
<td>MELAS syndrome</td>
</tr>
<tr>
<td>E88.42</td>
<td>MERRF syndrome</td>
</tr>
</tbody>
</table>

**Home Parenteral/Home Total Parenteral Nutrition (TPN) and Intradialytic Parenteral Nutrition (IDPN)**

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

<table>
<thead>
<tr>
<th>HPCPS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>B4164</td>
<td>Parenteral nutrition solution; carbohydrates (dextrose), 50% or less (500 ml=1 unit)-home mix</td>
</tr>
<tr>
<td>B4168</td>
<td>Parenteral nutrition solution; amino acid, 3.5% (500 ml=1 unit)-home mix</td>
</tr>
</tbody>
</table>
### Home Enteral/Parenteral Infusion Pumps

**Considered Medically Necessary when criteria in the applicable policy statements listed above are met:**

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>B9002</td>
<td>Enteral nutrition infusion pump, any type</td>
</tr>
</tbody>
</table>

### Digestive Enzyme Cartridge

**Considered Experimental/Investigational/Unproven:**

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>B4105</td>
<td>In-line cartridge containing digestive enzyme(s) for enteral feeding, each</td>
</tr>
<tr>
<td>Q9994</td>
<td>In-line cartridge containing digestive enzyme(s) for enteral feeding, each (code deleted 12/31/2018)</td>
</tr>
</tbody>
</table>

### Additional Items

**Not Medically Necessary:**

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>B4100</td>
<td>Food thickener, administered orally, per ounce</td>
</tr>
</tbody>
</table>
B4102 | Enteral formula, for adults, used to replace fluids and electrolytes (e.g. clear liquids), 500 ml=1 unit

B4103 | Enteral formula, for pediatrics, used to replace fluids and electrolytes (e.g. clear liquids), 500 ml=1 unit

B4104 | Additive for enteral formula (e.g. fiber)

S9434 | Modified solid food supplements for inborn errors of metabolism

T2101† | Human breast milk processing, storage and distribution only

*Note: Considered Not Medically Necessary when provided to a non-hospitalized infant

<table>
<thead>
<tr>
<th>ICD-10-CM Diagnosis</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Codes</td>
<td></td>
</tr>
</tbody>
</table>


References


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