Intradialytic Parenteral Nutrition

Policy # 00228
Original Effective Date: 02/20/2008
Current Effective Date: 02/19/2014

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Total Parenteral Nutrition and Enteral Nutrition in the Home is addressed in medical policy 00088.

When Services Are Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:
- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

Based on review of available data, the Company may consider intradialytic parenteral nutrition (IDPN) when it is offered as an alternative to a regularly scheduled regimen of total parenteral nutrition only in those patients who would be considered candidates for total parenteral nutrition (i.e., a severe pathology of the alimentary tract that does not allow absorption of sufficient nutrients to maintain weight and strength commensurate with the patient’s general condition) to be eligible for coverage.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers intradialytic parenteral nutrition in those patients who would not otherwise be considered candidates for total parenteral nutrition to be investigational.*

When Services Are Considered Not Medically Necessary
Based on review of available data, the Company considers intradialytic parenteral nutrition in those patients who would be considered a candidate for total parenteral nutrition, but for whom the intradialytic parenteral nutrition is not offered as an alternative to total parenteral nutrition, but in addition to regularly scheduled total parenteral nutrition infusions to be not medically necessary.**

Background/Overview
Intradialytic parenteral nutrition (IDPN) is the infusion of an intravenous nutritional formula of hyperalimentation, such as amino acids, glucose, and lipids, during dialysis, to treat protein calorie malnutrition in an effort to decrease the associated morbidity and mortality experienced in patients with renal failure.

Protein calorie malnutrition, typically assessed by measurements of serum albumin, occurs in an estimated 25–40% of those undergoing dialysis and is associated with increased morbidity and mortality. For example, the risk of death is increased more than 10-fold in those whose serum albumin levels are less than 2.5 g/dL, and those with a serum albumin near the normal range (i.e., from 3.5 to 3.9 g/dL) have a mortality rate twice as high as those with albumin greater than 4.0 g/dL.
In patients receiving chronic dialysis, the National Kidney Foundation currently recommends a daily protein intake of equal to or greater than 1.2 g/kg in patients undergoing hemodialysis and equal to or greater than 1.3 g/kg in patients undergoing peritoneal dialysis. Intradialytic parenteral nutrition, i.e., infusing hyperalimentation fluids at the time of either hemodialysis or peritoneal dialysis, has been investigated as a technique to treat protein calorie malnutrition in an effort to decrease the associated morbidity and mortality. In hemodialysis, the IDPN infusion is administered through the venous port of the dialysis tubing, typically, 30 minutes after dialysis has begun, and continued throughout the remainder of a dialysis session. In peritoneal dialysis, sometimes referred to as intraperitoneal parenteral nutrition (IPPN) or intraperitoneal nutrition (IP), parenteral nutrition is infused into the peritoneal cavity during peritoneal dialysis.

**FDA or Other Governmental Regulatory Approval**
Centers for Medicare and Medicaid Services (CMS)
The coverage eligibility of intradialytic parenteral nutrition for Medicare beneficiaries is summarized in a Health Care Financing Administration (HCFA) ruling from December 1996, which established that intradialytic nutrition would be considered eligible for coverage only if the patient would otherwise be a candidate for total parenteral nutrition. This ruling reads in part:

“Medicare coverage policies which apply to parenteral and enteral nutrition therapy items and services apply identically to IDPN therapy items and services, because intradialytic parenteral nutrition therapy is a subset of parenteral and enteral nutrition therapy. Coverage of parenteral and enteral nutrition therapy is amplified in Medicare Coverage Issues manual section 65-10. Daily parenteral therapy is ‘considered reasonable and necessary for a patient with severe pathology of the alimentary tract which does not allow absorption of sufficient nutrients to maintain weight and strength commensurate with the patient’s general condition.’ Intradialytic parenteral nutrition therapy is administered to end stage renal disease (ESRD) patients while they are receiving dialysis. End stage renal disease patients sometimes undergo parenteral therapy to replace fluids and nutrients lost during dialysis. End stage renal disease patients must meet all of the parenteral nutrition therapy coverage requirements to receive intradialytic parenteral nutrition therapy. Those patients who do not meet all of the parenteral nutrition therapy coverage requirements are ineligible to receive Medicare coverage of IDPN therapy under the prosthetic device benefit.…”

The HCFA ruling goes on to clarify the benefits for patients who would be considered candidates for total parenteral nutrition (TPN) and when the IDPN is designed to be offered in lieu of a regularly scheduled infusion of TPN.

“However, parenteral and enteral nutrition, including IDPN therapy, services and items which are otherwise covered under section 1861(s)(8) can be denied under section 1862(a)(1) for lack of medical necessity: … Example, if a Medicare beneficiary with ESRD, a dialysis patient who meets all of the requirements for coverage of parenteral nutrition therapy, receives IDPN therapy during dialysis and also receives parenteral nutrition therapy on the other days of the week when the patient is not on dialysis, it may be determined that the patient is receiving an excessive number of lipids. A claim for Medicare payment that is denied because the patient, who qualifies for parenteral nutrition therapy coverage, is receiving an excessive number of lipids would be denied as not reasonable and necessary under section 1862(a)(1)(A) of the Act… Therefore the precise statutory basis for the coverage or denial of parenteral and enteral nutrition therapy, including
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IDPN therapy, services and items is crucial and determinative as to whether or not limitation on liability protections can be applied."

Rationale/Source
Systematic Reviews
While IDPN has been available for many years, there has never been a consensus regarding either its efficacy or patient selection criteria. In 1993, the Office of Health Technology Assessment, the technology assessment arm of Medicare, published a review concluding that studies of IDPN reported equivocal results and the data did not validate its efficacy. Subsequently, in 1999, Foulks reported on an evidenced-based evaluation of IDPN. The analysis concluded that the overall quality of the literature was poor; only 3 randomized controlled trials (RCTs) were identified, and 1 was a feasibility study only; the other 2 had methodologic flaws or used types of IDPN that were not routinely used or were not available in the United States. The remaining literature consists of case series, which obviously cannot control for the many variables in the renal dialysis population that may contribute to increased morbidity and mortality. According to Foulks’ analysis, the majority of case series had methodologic flaws including heterogeneity in study design, patient selection criteria, types of IDPN used, and adequacy of dialysis. Dukkipati and colleagues conducted a systematic review of IDPN for the treatment of malnutrition in hemodialysis patients in 2010. The authors identified only 3 RCTs and found the data were insufficient to conduct a meta-analysis and to demonstrate net benefits in health outcomes with the use of IDPN. The authors concluded further clinical trials on IDPN are needed, and those trials should measure survival, quality of life, and nutritional status.

Randomized Controlled Trials
An RCT of 186 malnourished hemodialysis patients from 38 treatment centers in France studied the effects of adding IDPN to oral supplementation compared to oral supplementation alone (1 year of treatment with 2-year follow up). Based on intention-to-treat analysis, no differences were found in 2-year survival, hospitalizations, Karnofsky score, body mass index (BMI), or serum albumin and prealbumin levels between treatment groups. The study was powered to detect a 10% reduction in mortality with 78% power (5% α error). Meeting the stated nutritional goals (orally or parenterally) may have improved outcomes; an editorialist suggests that both groups had approximately 15% improved survival compared to historical controls.

Nonrandomized Comparative Studies
The largest study is a retrospective case series comparing the morbidity of 1,679 IDPN-treated patients with that of 22,517 nontreated patients. This study found that dialysis patients with a serum albumin level of less than 3.4 g/dL who were treated with IDPN had significant increases in albumin and creatinine over time. In addition, these patients experienced a significant decrease in the odds ratio for death at 1 year compared to those who were not treated with IDPN. Interestingly, the odds ratio for death increased for IDPN-treated patients who had an albumin level of greater than 3.4 mg/dL. Pupim and colleagues performed a detailed analysis of protein metabolism in 7 patients receiving IDPN during hemodialysis. These patients would not have been considered candidates for IDPN on the basis of their nutritional status. While the administration of IDPN was associated with a sharp increase in protein anabolism, the effect was only transient. An accompanying editorial points out that in patients with renal disease, malnutrition is a multifaceted problem
that is not related to insufficient or improper food or diet and probably cannot be corrected by simply supplying more or a different balance of nutrition.

A case series was published of 22 hemodialysis patients with acute illnesses (major surgery, infection) treated with IDPN for 1.5 to 48 months as nutritional supplementation (not support). IDPN was discontinued when the following were met: weight ceased to decline, stabilized, or increased; protein catabolic rate was greater than 1.0 g/kg/d; and serum albumin levels were greater than 3.8 g/dL. IDPN was well-tolerated and associated with improvements from baseline of several nutritional parameters. Without a comparison group, it is impossible to conclude that the effects were due to IDPN, and therefore this study does not affect the policy statement regarding patients who would otherwise not be candidates for TPN.

Predictors of IDPN response on hypoalbuminemia were examined in a study of 196 hypoalbuminemic patients receiving maintenance hemodialysis who underwent IDPN. The study suggested that IDPN treatment can improve hypoalbuminemia in patients receiving maintenance hemodialysis and that the likelihood and magnitude of response to IDPN in these patients is associated with the baseline severity of hypoalbuminemia. The authors suggest that this association may be useful in risk stratification of malnourished dialysis patients and recommend that their findings be confirmed through further controlled trials. Also of potential future interest, Pupim et al. reported that in a small series (n=8) of chronic hemodialysis patients, intradialytic oral nutrition or IDPN both led to highly positive whole-body net balance during hemodialysis.

Two other uncontrolled studies also suggest an improved outcome associated with IDPN. Due to the numerous biases inherent in any uncontrolled trial, these studies cannot validate whether IDPN is associated with an improved mortality. The observed treatment effect could be related to a selection bias in which very ill patients, i.e., those expected to die, were not offered IDPN. In addition, IDPN administration may be associated with an increased attentiveness to dialysis parameters, counseling, and nutritional advice, etc. These studies suggest that being selected for IDPN may be associated with an improved mortality rate, but analysis of the direct contribution of IDPN will require controlled trials. No studies were identified addressing IDPN in peritoneal dialysis patients.

Ongoing Clinical Trials
A May 24, 2013 search of online site ClinicalTrials.gov identified only one multicenter German study on IDPN, NCT00501956, which has been completed. In this study, 140 malnourished hemodialysis patients were randomized to receive hemodialysis without IDPN or hemodialysis with 16 weeks of IDPN during each dialysis session followed by 12 weeks without IDPN. The study completion date was December 2010; the results have not been published.

In addition, results from one comparative study that addressed changes of serum prealbumin levels of IDPN in malnourished hemodialysis patients have been published in abstract form in 2012. No full-length publication is available for this study. Statistical calculation was undertaken for 32 patients per study group. IDPN was reported to lead to a significant increase of prealbumin during the 16-week course of treatment (26.31 mg/L), compared to the non-interventional control group (1.84 mg/L, p=.02). Due to the small sample size, the results would benefit from further study.
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size, there was a lack of statistical power to evaluate responsiveness of the secondary endpoints in this study (e.g., albumin, transferrin, quality of life).

Summary
IDPN is the infusion of an intravenous nutritional formula of hyperalimentation, such as amino acids, glucose, and lipids, during dialysis, to treat protein calorie malnutrition in an effort to decrease the associated morbidity and mortality experienced in patients with renal failure.

Evidence of efficacy of IDPN treatment is limited. Available evidence demonstrates improvements in intermediate outcomes such as increases in serum albumin and catabolic rate. However, long-term data on survival, quality of life, and other nutritional status outcomes are unavailable. Therefore, IDPN may only be considered medically necessary when it is offered as an alternative to a regularly scheduled regimen of TPN in patients who would be considered candidates for TPN. IDPN is considered not medically necessary when added to regularly scheduled infusions of TPN and may be harmful due to the excess administration of lipids. Finally, due to the limited availability of data on IDPN in patients who would not otherwise be considered TPN candidates, the impact on net health outcome is not known and therefore, is considered investigational in these patients.

References
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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

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02/13/2008 Medical Director review
02/20/2008 Medical Policy Committee approval.
02/04/2009 Medical Director review
02/19/2009 Medical Policy Committee approval. No change to coverage eligibility.
02/04/2010 Medical Policy Committee approval
02/17/2010 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/03/2011 Medical Policy Committee review

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02/16/2011 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/02/2012 Medical Policy Committee review
02/15/2012 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/07/2013 Medical Policy Committee review
02/20/2013 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/06/2014 Medical Policy Committee review
02/19/2014 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 02/2015

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
   1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
   2. credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
   3. reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. in accordance with nationally accepted standards of medical practice;
B. clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and 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 patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community. Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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