Inpatient Intestinal Rehabilitation Therapy
Archived Medical Policy

Archived medical policies are no longer subject to periodic review, are maintained for reference, and may be returned to active status if the need is identified.

Policy # 00074
Original Effective Date: 06/05/2002
Archived Date: 06/20/2012

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.

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 inpatient intestinal rehabilitation, consisting of metabolic evaluation, patient counseling and education, nutritional counseling, physical therapy and treatment with growth hormone and glutamine in patients with short bowel syndrome who are dependent on TPN to be investigational.*

Background/Overview
Massive loss of intestinal surface area results in intestinal failure (short bowel syndrome is one type), characterized by malabsorption of fluids, electrolytes and other nutrients. Common causes of short bowel syndrome include resection related to volvulus, thrombosis of the superior mesenteric artery, Crohn’s disease or trauma. While some adaptation (characterized by elongation and dilation of remnant bowel) of remaining intestinal surface can improve nutrient absorption, patients with less than 60cm of functional jejunum or ileum typically require permanent total parenteral nutrition (TPN). While intestinal transplantation is one alternative, there has been research interest in methods to increase intestinal adaptation as a nonsurgical alternative. Specifically, intestinal adaptation is thought to be related to exposure of the remaining mucosa to luminal nutrients, the presence of enteric hormone and pancreatic-biliary secretion and the trophic effects of various extrinsic growth factors and hormone. For example, the amino acid glutamine, administered either enterally or parenterally, is known to induce a trophic or regenerative effect on the bowel. Growth hormone is also thought to have a trophic effect on the bowel.

Specialized inpatient programs were developed to offer intensive counseling and tailored regimens of diet modification, glutamine and growth hormone therapy to patients with short bowel syndrome. The goal of these programs is to either eliminate or reduce the need for TPN. These programs offer an inpatient program of 2 to 4 weeks, during which time the patient undergoes detailed metabolic evaluations to determine the feasibility of an oral diet, intestinal adaptation therapy with dietary modification (diet high in complex carbohydrates and low in fat), glutamine and growth hormone and a gradual weaning of total parenteral nutrition, if possible. Patients are also under extensive counseling and education and participate in a physical rehabilitation program. At completion of the program, the patients are discharged on only the diet and the supplemental glutamine.
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**FDA or Other Governmental Regulatory Approval**

U.S. Food and Drug Administration (FDA)  
In December 2003, the FDA approved the use of Zorbtive (Serono), a recombinant human growth hormone, for treatment of short bowel syndrome.

The FDA has noted growth hormone for patients with short bowel syndrome should be limited to patients receiving specialized nutritional support in conjunction with optimal management of short bowel syndrome. Specialized nutritional support may consist of a high-carbohydrate, low-fat diet adjusted for individual patient requirements. Optimal management may include dietary adjustments, enteral feedings, parenteral nutrition, fluid and micronutrient supplements. Zorbtive is administered daily at 0.1mg/kg subcutaneously up to 8mg/day. Administration of Zorbtive for longer than four weeks has not been adequately studied per the FDA indications.

**Rationale/Source**

The published data are almost exclusively derived from researchers working at the Nutritional Restart Center near Boston. Most reports consist of small case series, many with presumably overlapping patients. One case series consists of 45 patients with short bowel syndrome maintained on long-term parenteral nutrition. These patients were treated with growth hormone, glutamine and a modified diet for four weeks and then followed up for an average of 1.8 years. After four weeks of therapy, 58% no longer required TPN. At follow-up, the percentage of patients not receiving TPN fell to 40%. A review article published in the same year included 67 adults receiving TPN, and presumably includes overlapping patients. At completion of the 4-week program, the TPN requirement for each patient was noted as either off (52%), reduced (38%), or no change (10%). Over an unspecified follow-up period, there was some attrition of the treatment effect.

The relative contributions of the pharmacologic, dietary and counseling/education aspects of the overall program cannot be determined. Specifically, some researchers have questioned whether the treatment effect was primarily due to meticulous dietary counseling as opposed to any effect from glutamine or growth hormone. For example, Scolapio conducted a randomized 6-week double-blind, placebo-controlled trial of eight patients who alternatively received growth hormone, glutamine supplementation and a high carbohydrate, low-fat diet alternating with the placebo treatment. Active treatment was associated with an increased body weight and lean body mass, decreased percent body fat without an increase in fluid, or macronutrient absorption. All patients receiving active treatment developed peripheral edema, suggesting that an increase in extracellular fluid may have been responsible for the positive findings. In addition, after discontinuation of growth hormone, the weight returned to baseline. In another blinded crossover study of eight patients, Szkudlarek and colleagues examined the effect of growth hormone and glutamine supplementation on intestinal function. Unlike the above study, the patients did not receive a high carbohydrate, low-fat diet. Growth hormone with glutamine was not associated with improved intestinal absorption of energy, carbohydrate, sodium, potassium, calcium or magnesium.
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An additional research question is the contribution of an intensive inpatient program, compared to similar elements of the program offered in an outpatient setting. This issue has not been addressed in the published literature.

An updated search of the medical literature found that there is no consistent definition or components of intestinal rehabilitation nor is there long-term health outcomes measured for intestinal rehabilitation. Studies continued to assess the relative contributions of growth hormone, glutamine, glucagon-like peptide-2 and diet but did not assess the optimal treatment settings or components of intestinal rehabilitation according to patient characteristics.

One study involved 12 adults with short bowel syndrome who were dependent on a home-based, high carbohydrate parenteral nutrition diet. Patients were randomized in a double-blind placebo-controlled crossover study. Patients received daily low-dose growth hormone and placebo for 2- to 3-week periods separated by a 1-week washout period. Treatment with growth hormone increased intestinal absorption of energy, nitrogen, carbohydrates and fats. The increased food absorption represented 37% +/- 16% of total parenteral energy delivery. Body weight, lean mass and D-xylose absorption increased. However, the study did not assess long-term health outcomes beyond the immediate study period.

One study assigned 59 patients with life-threatening complications of intestinal failure to three treatment options. Sixty-eight percent of patients were considered appropriate candidates for intestinal transplants, 10% were managed with rehabilitation and 17% were maintained on optimized parenteral nutrition. All patients managed with rehabilitation were weaned from parenteral nutrition within six months.

Wu and colleagues assessed bowel rehabilitation combined with trophic therapy and found that 33 of 38 patients maintained well body weight and serum albumin concentrations after an average follow-up of 5.9 +/- 4.3 years for the 33 survival patients. Nutrient absorption in eight patients treated with growth hormone and glutamine seemed to increase, but the effects occurred only during the treatment period and were not sustained.

The FDA label for Zorbive indicates growth hormone has been shown in human clinical trials to enhance the transmucosal transport of water, electrolytes and nutrients. The FDA approval for Zorbive was based on the results of a randomized, controlled, Phase III clinical trial in which patients dependent on intravenous parenteral nutrition who received Zorbive (either with or without glutamine) over a four-week period had significantly greater reductions in the weekly total volume of intravenous parenteral nutrition required for nutritional support. However, the effects beyond four weeks were not evaluated nor was the treatment location (inpatient vs. outpatient) identified.

An updated search was conducted for the period of 2005 through May 2006. No clinical trial publications were identified that would alter the conclusions reached above. Therefore, the coverage statement is...
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unchanged. Byrne and colleagues followed up 41 patients with short bowel syndrome dependent on parenteral nutrition for three months after participating in a 4-week inpatient intestinal rehabilitation program in which patients were randomized in a double-blind, controlled trial to evaluate growth hormone, glutamine and optimal diet. Parenteral nutrition volume, calories and infusions were most reduced in patients who received growth hormone plus glutamine and diet. This group was also the only treatment group to maintain reductions in parenteral nutrition significantly after three months. However, how reductions in parenteral nutrition translated into health outcomes was not reported.

2007–2008 Update
The policy was updated with a literature search in May 2008. None of the articles identified lead to a change in the coverage statement. While published series report the benefits of a multidisciplinary intestinal rehabilitation program, the specific role and benefits, if any, of an inpatient intestinal rehabilitation program remain uncertain. In reporting on outcomes of children referred to an intestinal rehabilitation program over a 4-year period, Torres and colleagues comment that with an aggressive medical and surgical approach, some patients with intestinal failure and advanced liver disease can avoid transplantation, and that early referral to specialized centers is recommended before the development of advanced liver disease.

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Policy History
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05/18/2002 Medical Policy Committee review
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06/24/2002 Format revision. No substance change to policy.
06/01/2004 Medical Director review
06/15/2004 Medical Policy Committee review
06/28/2004 Managed Care Advisory Council approval
06/07/2006 Medical Director review
06/21/2006 Medical Policy Committee approval. Format revision including addition of FDA and or other governmental regulatory approval and rationale/source.
06/04/2008 Medical Director review
06/18/2008 Medical Policy Committee approval. Coverage eligibility unchanged.
06/04/2009 Medical Director review

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06/03/2010 Medical Policy Committee review
06/16/2010 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/02/2011 Medical Policy Committee review
06/14/2012 Medical Policy Committee review
06/20/2012 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Archived

Next Scheduled Review Date: Archived.

*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.

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