09-J1000-91

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Reviewed: 04/09/14

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Subject: Teduglutide (rDNA origin) (Gattex®) Injection

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DESCRIPTION:

Short bowel syndrome (SBS) is defined as loss of intestinal absorptive capacity and results from surgical resection, congenital defect, or disease.1 The management of SBS is focused on maintaining fluid, electrolyte, and nutrient balances; after bowel resection, most individuals require continuous parenteral support to maintain nutritional status during intestinal rehabilitation, a process where enteral feeds are gradually advanced, parenteral support is weaned, and medical treatments promote adaptation, maximize absorptive capacity, and prevent complications of enteral and parenteral nutrition therapy.1 The goal of intestinal rehabilitation is complete weaning from long-term parenteral support. A subset of individuals with more severe forms of SBS may develop intestinal failure and become unable to maintain protein-energy, fluid, electrolyte, or micronutrient balance. These individuals are likely to be remain dependent on parenteral nutritional support (intravenous fluids with or without parenteral nutrition) to avoid starvation.1

Teduglutide (Gattex™) was approved by the U.S. Food and Drug Administration (FDA) on December 21, 2012 for the treatment of adult patients with short bowel syndrome (SBS) who are dependent on parenteral support.[2] In 2019, the FDA extended this approval to include children as young as 1 year old. Prior to FDA approval, teduglutide received orphan drug status for the treatment of SBS.[3] Teduglutide is an analog of naturally occurring human glucagon-like peptide-2 (GLP-2) and works by activating GLP-2 receptors in intestinal tissue.[2,4,5] Exogenous GLP-2 administration inhibits gastric acid secretion and gastric emptying, stimulates intestinal blood flow, increases intestinal barrier function, and enhances nutrient and fluid absorption.[6]

The safety and efficacy of teduglutide were evaluated in the STEPS trial, a 24-week, randomized, double-blind, placebo-controlled trial of 86 subjects with intestinal failure due to SBS.[7] Subjects had been dependent on parenteral support for a median of four years. Prior to randomization, subjects entered a 16-week parenteral support optimization and stabilization period designed to establish the minimal level of parenteral support. After optimization and stabilization, subjects were randomized to receive 24 weeks of teduglutide 0.05 mg/kg or placebo daily.[7]

The primary endpoint was the proportion of responders at week 20 who maintained response at week 24; response was defined as a 20% or greater reduction in volume of parenteral support.[7] Adjustments to parenteral volume were made at week 2, 4, 8 12, 16, and 20 based on urine output as described in Table 1. At week 24, 63% of subjects receiving teduglutide and 30% of subjects receiving placebo were responders (p=0.002).[7] The mean percent reduction in parenteral support volume was 32% (4.4 L/week) in the teduglutide group and 21% (2.3 L/week) in the placebo group (p=0.03). The number of adverse events, serious adverse events, treatment-emergent adverse events, or discontinuations due to serious adverse events was comparable between treatment groups. No subject in either group was weaned completely off parenteral support. The observed improvement in the placebo group was attributed to appropriate day-to-day fluid management and strict adherence to a weaning protocol.

Table 1. STEPS Trial: Parenteral volume adjustment based on 48-hour urine output

Urine output	**Change in parenteral support volume**
< 1.0 L/day	Increase by ≥ 10% or to previous level
≥ 1.0 L/day but less than baseline	Increase if dehydrated, inadequately nourished
0 to < 10% increase from baseline	No change
≥ 10% increase from baseline	Reduce by ≥ 10% to a clinically appropriate amount

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of teduglutide (Gattex) injection **meets the definition of medical necessity** for members meeting the following criteria:

1. Diagnosis of short bowel syndrome
2. Currently dependent on parenteral support (e.g., parenteral nutrition, intravenous fluids) for a period of at least 12 continuous months
3. Documentation of baseline parenteral support volume (liters/week)
4. **NO** active gastrointestinal malignancy
5. **NO** biliary disease
6. **NO** pancreatic disease
7. Dose does not exceed 0.05 mg/kg once daily
8. Age 1 years or older

Duration of approval: 6 months

Continuation of teduglutide (Gattex) injection **meets the definition of medical necessity** for members meeting the following criteria:

1. Member has met Florida Blue's initial criteria for coverage
2. Minimum 20% reduction in parenteral support volume (liters/week) from baseline

Duration of approval: 6 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

0.05 mg/kg once daily by subcutaneous injection; rotate injection sites among the four quadrants of the abdomen, thighs, or arms

Dose Adjustments

Renal Impairment

- CrCl < 50 mL/min: Reduce daily dose by 50%

Drug Availability

Teduglutide is available as a 5 mg single-use injection.

PRECAUTIONS:

Precautions/Warnings

- Acceleration of neoplastic growth – In those at increased risk for malignancy, the clinical decision to use teduglutide should be considered only if the benefits outweigh the risks; in those with active gastrointestinal malignancy (GI tract, hepatobiliary, pancreatic), teduglutide should be discontinued
- Colorectal polyps – Colonoscopy of the entire colon with removal of polyps should be done within six months prior to starting treatment
- Biliary and pancreatic disease – Pancreatitis, cholecystitis, cholangitis, and cholelithiasis have been reported in clinical trials of teduglutide; for identification of onset or worsening symptoms, laboratory assessment of lipase, amylase, bilirubin, and alkaline phosphatase should occur within six months prior to starting treatment, and at least every six months while receiving teduglutide

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding:

J3490	Unclassified drugs

ICD-10 Diagnosis Codes That Support Medical Necessity:

K91.2	Postsurgical malabsorption, not elsewhere classified

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

DEFINITIONS:

None applicable.

RELATED GUIDELINES:

Hyperalimentation, 09-A4000-04

OTHER:

None applicable.

REFERENCES:

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2. Teduglutide. Clinical Pharmacology [Internet Database]. Gold Standard, Inc., 2019 [cited 5/20/19]. Available from: http://www.clinicalpharmacology-ip.com/.
3. Orphan Drug Designations and Approval [Internet Database]. U.S. Food and Drug Administration, 2019 [cited 5/20/19]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
4. Teduglutide. In: DRUGDEX® System [Internet Database]. Greenwood Village, Colo: Thomson Micromedex. Updated periodically [cited 5/20/19]. Available from: http://www.thomsonhc.com/.
5. NPS Pharmaceuticals. Gattex (teduglutide) injection. 2019 [cited 5/20/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=66b69c1e-b25c-44d3-b5ff-1c1de9a516fa/.
6. Jeppesen PB, Gilroy R, Pertkiewicz M, et al. Randomised placebo-controlled trial of teduglutide in reducing parenteral nutrition and/or intravenous fluid requirement in patients with short bowel syndrome. Gut. 2011; 60:902-14.

7. Jeppesen PB, Pertikiewicz M, Messing B, et al. Teduglutide reduces need for parenteral support among patients with short bowel syndrome with intestinal failure. Gastroenterology. 2012; 143:1473-81.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 04/09/14.

GUIDELINE UPDATE INFORMATION:

06/15/13	New Medical Coverage Guideline.
05/15/14	Review and revision to guideline; consisting of reformatting position statement, updating references.
11/01/15	Revision: ICD-9 Codes deleted.
7/15/19	Revision to guideline; consisting of updating position statement