Gattex (teduglutide)
Policy Number: C5774-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
05/2014	04/2019	04/2020
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL**
	RxPA	Q2 2019

PRODUCTS AFFECTED:
Gattex (teduglutide)

DRUG CLASS:
Glucagon-Like Peptide-2 (GLP-2) Analogs

ROUTE OF ADMINISTRATION:
Subcutaneous

PLACE OF SERVICE:
Specialty Pharmacy

AVAILABLE DOSAGE FORMS:
Gattex-single-use vial kit (containing 5mg of teduglutide) and a kit containing 30 single-use vials

FDA-APPROVED USES:
For the treatment of adult and pediatric patients 1 year of age and older with short bowel syndrome who are dependent on parenteral support.

COMPENDIAL APPROVED OFF-LABELED USES: None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS: short bowel syndrome

REQUIRED MEDICAL INFORMATION:

A. SHORT BOWEL SYNDROME:
1. Diagnosis of short bowel syndrome defined by clinical documentation of less than 200cm of remnant functional intestine. Documentation of confirmed diagnosis required (which may include, but not be limited to, test reports, chart notes from provider's office, or hospital admission notes)
   AND
2. An initial nutritional assessment has been completed by a registered dietitian who has determined that oral/enteral nutrition is not sufficient to meet nutritional goals. Prescriber to submit completed nutritional assessment.
   AND
3. Dependence on parenteral nutrition documented by BOTH of the following: Dependent on parenteral nutrition (PN) and/or intravenous (IV) fluids at least 12 consecutive months continuously AND Three (3) or more days per week of parenteral nutrition support (fluids, electrolytes and/or nutrients)

AND

4. Member has a body mass index of 15 kg/m2 or more
   AND
5. For members with his/her large intestine intact: A colonoscopy must be completed within 6 months before starting Gattex. Clinical documentation of colonoscopy within six months prior to initiation of teduglutide to confirm absence of gastrointestinal malignancy.
   AND
6. The following laboratory results must be assessed within 6 months before starting Gattex and every 6 months for the duration of therapy: Alkaline phosphatase, Amylase, Bilirubin and Lipase
   AND
7. The following must NOT be applicable to member: History of colorectal or other GI malignancy, Received biologic treatment for Crohn's disease or immunosuppressant drugs within 3 months before starting Gattex , Used a biologic drug within 6 months before starting Gattex, Gastrointestinal malignancy OR intestinal or stomal obstruction
   AND
8. Documented clinically significant failure/intolerance/contraindication to BOTH of the following therapy: an antimotility agent (e.g. loperamide [Imodium], diphenoxylate/atropine [Lomotil]), and an antisecretory agent (i.e. PPI, H2 blocker, octreotide [Sandostatin])

DURATION OF APPROVAL: Initial authorization: up to 4 months (16 weeks), Continuation of therapy: 6 months

QUANTITY: Thirty (30) vials per 30 days. A maximum supply of 30 days will be dispensed at a time

PRESCRIBER REQUIREMENTS: Prescribed by or in consultation with a Board-certified gastroenterologist who is a certified REMS provider

AGE RESTRICTIONS: 1 year of age or older

GENDER:
Male and female

CONTINUATION OF THERAPY:

A. SHORT BOWEL SYNDROME:
   1. Member continues to meet initial criteria
      AND
   2. Adherence to therapy at least 85% of the time as verified by Prescriber and member's medication fill history (review Rx history for compliance)
      AND
   3. Positive response or demonstrated efficacy to therapy as evidenced by an improvement as measured by a standardized disease activity tool: Documentation of a 20% or more decrease in parenteral support (i.e. parenteral nutrition and/or intravenous fluids) decreased in volume (ml) from baseline weekly requirement (prior to initiation of Gattex therapy) OR Documentation of reduction in the numbers of days of required parenteral nutrition support OR With continued treatment, Prescriber has a reasonable expectation that this member can be removed from parenteral support within the next 6 months

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION: All other uses of the mentioned drugs that are not an FDA-approved indication or included in 'Coverage Criteria' section above are considered experimental/investigational and is not a covered benefit. The following list is not all-

inclusive and is subject to change based on research and medical literature: Chemotherapy-induced enteritis, Gastro-intestinal mucositis, Gastro-intestinal stromal tumors, inflammatory bowel disease (Crohn's disease and ulcerative colitis), Necrotizing enterocolitis, Post-operative ileus OR Radiation-induced enteritis

OTHER SPECIAL CONSIDERATIONS: None

BACKGROUND:
Teduglutide is an analog of naturally occurring human glucagon-like peptide-2 (GLP-2), a peptide secreted by L-cells of the distal intestine. Endogenous GLP-2 is a 33-amino peptide gastrointestinal, trophic hormone involved in the structural and functional repair and regeneration of intestinal cells. Gattex (teduglutide [rDNA origin]) differs from GLP-2 through the substitution of one amino acid. However, endogenous GLP-2 is rapidly degraded by dipeptidyl peptidase-IV (DDP-IV) resulting in a half-life of only 7 minutes. Teduglutide is created in Escherichia coli, and differs from human GLP-2 by the substitution of glycine for alanine at position 2. As a result, teduglutide is resistant to DDPIV degradation, thereby increasing the half-life and allowing for once daily subcutaneous administration. Teduglutide improves bowel function by enhancing absorption of nutrients and fluids, and decreases dependence on parenteral nutrition.

Gattex (teduglutide) is indicated for the treatment of adult patients with Short Bowel Syndrome (SBS) who are dependent on parenteral support. Gattex received Orphan Drug designation on June 29, 2000 and subsequently submitted a new drug application (NDA) to the Food and Drug Administration (FDA) on 30 November 2011, seeking approval for the treatment of adult patients with Short Bowel Syndrome (SBS) to improve intestinal absorption of fluid and nutrients. Gattex (teduglutide) is the first in its class with this mechanism of action.

Short Bowel Syndrome
Short bowel syndrome (SBS) is often defined as that symptom complex which occurs in adults who have less than 200 centimeters of combined jejunum-ileum following small bowel resection.A,8-10 SBS is a disorder clinically defined by malabsorption, diarrhea, steatorrhea, fluid and electrolyte disturbances, and malnutrition. Short bowel syndrome may be a congenital or acquired condition. Infants may be born with congenital jejunal or ileal atresia. Otherwise, short bowel syndrome results from surgical resection of bowel. The final common etiologic factor in all causes of short-bowel syndrome is the functional or anatomic loss of extensive segments of small intestine so that absorptive capacity is severely compromised. Although resection of the colon alone typically does not result in short-bowel syndrome, the condition's presence can be a critical factor in the management of patients who lose significant amounts of small intestine. Due to the reduction in surface area, sub-optimized GI function occurs directly leading to reduced absorption of macronutrients, water, and electrolytes, leaving many at risk for malnutrition, diarrhea, dehydration, and weight loss. The extent of nutrition and fluid needs in SBS patients is dependent upon multiple factors including the amount of residual intestine and colon, presence of an ileal segment, and degree of spontaneous intestinal adaptation following resection.

Conventional treatments include dietary manipulations, oral rehydration solutions, antidiarrheal and antisecretory treatments. Pharmacologic management of SBS may include use of anti-motility agents (e.g. loperamide and diphenoxylate), or antisecretory agents that reduce gastric acid

secretion (e.g., H2 receptor antagonists, proton pump inhibitors, somatostatin analog).8-10
Recombinant growth hormone (somatropin, ZORBTIVE™) is approved for the treatment of SBS (for up to 4 weeks) in patients receiving specialized nutritional support, based on reductions in caloric content and frequency of administration of parenteral nutrition with treatment compared to placebo. Glutamine (NUTRESTORE™) is also approved for the treatment of SBS (for up to 16 weeks) in patients receiving specialized nutritional support when used in conjunction with a recombinant human growth hormone that is approved for this indication. Comparator trials with Gattex (teduglutide) were not found.
Based on a Cochrane systematic review of treatment with human growth hormone with or without glutamine in patients with SBS, it was noted that treatment increased weight and energy absorption. The authors noted the limitation that the benefits returned to baseline after discontinuation of therapy and conclusive evidence is not available to recommend this treatment. Further studies that evaluate human growth hormone treatment during the immediate phase of bowel adaptation are needed.

The current AGA guidelines (2003) did not recommend glutamine or growth hormone for the management of SBS since these agents do not lead to morphological changes in the intestine but may cause significant peripheral edema.B GLP-2 analogs [Gattex (teduglutide)] were not addressed since it was investigational at the time of the writing of these guidelines**.**

APPENDIX: None

REFERENCES:

1. Gattex [package insert]. Lexington, MA: Shire-NPS Pharmaceuticals, Inc.; July 2016.

2. Jeppesen P, Pertkiewicz M, Messing B, et al. Teduglutide reduces need for parenteral support among patients with short bowel syndrome with intestinal failure. Gastroenterology.2012; 143:1473-1481.