Gattex® (teduglutide) Prior Authorization Program Summary

This prior authorization program applies to Commercial, GlenPlus, Blue Partner, NetResults A series, SourceRx and Health Insurance Marketplace formularies.

OBJECTIVE
The intent of the Gattex (teduglutide) Prior Authorization (PA) program is to appropriately select patients for treatment according to product labeling and/or clinical studies and/or clinical practice guidelines. Dosing is restricted to FDA labeled dosing for the patient's diagnosis.

TARGET AGENTS
Gattex® (teduglutide)

Agent(s)	GPI	Multisource Code
Gattex® (teduglutide)		
5 mg single use vial kit	52533070006420	M, N, O, or Y

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Initial Evaluation
Gattex will be approved when ALL of the following are met:

1. ONE of the following:
   A. The patient has a diagnosis of short bowel syndrome (SBS) and BOTH of the following:
      i. The patient is currently receiving parenteral nutrition/intravenous fluids (PN/IV) at least 3 days per week
      AND
      ii. BOTH of the following:
         1. The patient has had a colonoscopy within the last 6 months
         AND
         2. If polyps were present at this colonoscopy, the polyps were removed

   OR
   B. The patient has another FDA approved indication
   AND
2. The prescriber is a specialist in the area of the patient's diagnosis (e.g., gastroenterologist) or has consulted with a specialist in the area of the patient's diagnosis.
   AND
3. The patient does not have any FDA labeled contraindications to therapy
   AND
4. The dose is within the FDA-labeled dose for the requested diagnosis

Length of Approval: 6 months

Renewal Evaluation
Gattex will be approved when ALL of the following are met:

1. The patient has been previously approved for the requested agent through the Prime Therapeutics PA process

AND

2. The prescriber is a specialist in the area of the patient's diagnosis (e.g., gastroenterologist) or has consulted with a specialist in the area of the patient's diagnosis
   AND
3. If the patient is using parenteral nutrition/intravenous fluids (PN/IV), the patient has had at least a 20% reduction from baseline in PN/IV fluids
   AND
4. The patient does not have any FDA labeled contraindications to therapy
   AND
5. The dose is within the FDA-labeled dose for the requested diagnosis

Length of Approval: 12 months

Agent	Contraindication(s)
Gattex (teduglutide)	None

This pharmacy policy is not an authorization, certification, explanation of benefits or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All pharmacy policies are based on (i) information in FDA approved package inserts (and black box warning, alerts, or other information disseminated by the FDA as applicable); (ii) research of current medical and pharmacy literature; and/or (iii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

The purpose of pharmacy policies are to provide a guide to coverage. Pharmacy policies are not intended to dictate to physicians how to practice medicine. Physicians should exercise their medical judgment in providing the care they feel is most appropriate for their patients.

Neither this policy, nor the successful adjudication of a pharmacy claim, is guarantee of payment.

FDA APPROVED INDICATIONS AND DOSAGE

Agent	Indication	Dosage & Administration
Gattex® (teduglutide)	Short Bowel Syndrome (SBS) in adult patients who are dependent of parenteral support	**SBS:** 0.05 mg/kg subcutaneously once daily 0.025 mg/kg subcutaneously once daily in patients with moderate to severe renal impairment

CLINICAL RATIONALE

Short Bowel Syndrome (SBS) is a result of either surgical resection or congenital defects. Patients with SBS have an inability to maintain protein, fluid, electrolyte, and micronutrient balance. These patients are prone to malnutrition, diarrhea, dehydration, and an inability to maintain weight. Patients often require long-term parenteral nutrition (PN) or intravenous fluids (IV). These therapies come with significant complications and require frequent monitoring of liver function, vitamin, mineral, and trace element levels.[2,4]

Clinical care of SBS patients mainly focuses on optimizing intestinal function through oral rehydration, anti-diarrheal agents, anti-secretory agents, growth hormone, glutamine and dietary intervention. There are surgical procedures (e.g. bowel lengthening or intestinal transplant) utilized in the management of SBS but these procedures are associated with significant morbidity and mortality and are only considered for select patients.

Short term outcomes for patients maintained on PN/IV are pretty good. The need for long-term parenteral nutrition depends on the length of the small bowel resected, the site of resection, and the presence of colon in continuity with the small bowel.[4] However over time patients can lose venous access or develop septic complications. The use of pharmacologic therapies to decrease the need for PN/IV has shown good results in this patient population.

EFFICACY[1]
Gattex is an analog of naturally occurring human glucagon-like peptide-2 (GLP-2). GLP-2 is a peptide secreted by L-cells of the distal intestine. GLP-2 is known to increase intestinal and portal blood flow, and inhibit gastric acid secretion. Gattex binds to the glucagon-like peptide-2 receptors. Activation of these receptors results in the local release of multiple mediators including insulin-like growth factor (IGF)-1, nitric oxide, and keratinocyte growth factor (KGF).

The safety and efficacy of teduglutide was evaluated in 4 clinical studies; 2 placebo controlled and 2 extension studies. Study 1 with the open-label extension Study 2 was in adults with SBS who were dependent on PN/IV for at least 12 months and required PN at least 3 times per week. Patients were randomized to placebo (n=43) or teduglutide (n=43) at 0.05 mg/kg/day for 24 weeks. Clinical assessments and volume adjustments (up to 30% decrease) were done at weeks 2, 4, 8, 12, 20, and 24. The primary efficacy endpoint was based on clinical response, defined as at least a 20% reduction in weekly PN/IV volume from baseline to both Weeks 20 and 24. In this trial 63% (27/43) of treated patients and 30% (13/43) of placebo treated patients were considered responders (p=0.002). The mean reduction at Week 24 in PN/IV volume was 4.4 L for teduglutide treated (pre-treatment baseline of 12.9 L/week) versus 2.3 L for placebo treated (pre-treatment baseline of 13.2 L/week) patients from baseline. In the extension Study 2, of the responders from Study 1 who entered Study 2 100% (25/25) sustained their response to teduglutide after one year of continuous treatment. A 20% or > reduction of PN was achieved in 72% (31/43) patients after an additional 28 weeks of therapy. The study results for Study 3 and 4 were similar.

SAFETY[1]
Gattex has no labeled contraindications but does have warnings concerning neoplastic growth, intestinal obstruction, biliary and pancreatic disease, and fluid overload.

Gattex has the potential to cause hyperplastic changes including neoplasia. There is risk of acceleration of neoplastic growths including small bowel neoplasia and colorectal polyps due to the pharmacologic activity and findings in animals. Due this risk, a colonoscopy of the entire colon should be done within 6 months prior to starting therapy. If polyps are present, they should be removed at least 6 months prior to starting treatment with Gattex. A follow-up colonoscopy (or alternate imaging) is recommended at the end of 1 year of Gattex therapy and at least every 5 years thereafter while on therapy.

Intestinal obstruction has been reported with Gattex in clinical trials. In patients who develop intestinal or stromal obstruction, Gattex should be temporarily discontinued while the patient is clinically managed. Gattex may be restarted when the obstructive presentation resolves.

Cholecystitis, cholangitis, cholelithiasis, and pancreatitis have been reported in clinical studies with Gattex treatment. Patients should undergo laboratory assessment of bilirubin, alkaline phosphatase, lipase, and amylase within 6 months prior to starting Gattex and at least every 6 months while on Gattex.

Fluid overload and congestive heart failure have been observed in clinical trials, which were felt to be related to enhanced fluid absorption associated with Gattex. If fluid overload occurs, parenteral support should be adjusted and Gattex treatment should be reassessed.

Gattex has the potential to increase absorption of concomitant oral medications. Agents that require titration or have a narrow therapeutic index require careful monitoring and possible dose adjustments.

REFERENCES

1. Gattex prescribing information. NPS Pharmaceuticals, Bedminster NJ. July 2016.
2. Cagir, Burt. Short-Bowel Syndrome Treatment & Management. Medscape. December 2017. Available at: http://emedicine.medscape.com/article/193391-treatment. Accessed March 2018.
3. FDA Summary Review. Gattex. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Label_ApprovalHistory#apphist. Accessed 2/6/13.
4. DeBaise Jk. UpToDate Management of short bowel syndrome in adults. Last updated January 2018.