Gattex (teduglutide) Prior Authorization Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
11/1/2023	4/1/2016

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Gattex® (teduglutide) Single use vial kit	Short Bowel Syndrome (SBS) in adults and pediatric patients 1 year of age and older who are dependent on parenteral support		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Short Bowel Syndrome	Short Bowel Syndrome (SBS) occurs when, after surgery or congenitally, a patient is left with less than 200 cm of functional small intestine. Absorption is related to the amount of residual intestine; patients at greatest nutritional risk generally have a duodenostomy or a jejunoileal anastomosis with less than 35 cm of residual small intestine, jejunocolic or ileocolic anastomosis with less than 60 cm of residual small intestine, or an end jejunostomy with less than 115 cm of residual small intestine.(2) The removal or loss of a segment of the small intestine does not necessarily result in SBS. Often, additional factors play a role in the eventual development of the disorder. These factors include: • The specific segment of the intestines that is lost • The remaining length of the small intestines • Whether the colon is intact • Whether the valve at the junction of the small and large intestines (ileocecal valve) is intact • The presence of any underlying disease • The age and overall health of the individual Also, with appropriate rehabilitation, the remaining healthy small intestine will undergo a process of adaption with time, and the intestinal lining may grow larger (hypertrophy) and ultimately absorb more, which may lessen an individual's particular symptoms.(3) The most important aspects of medical management of SBS are to provide adequate macro- and micronutrients and fluid to prevent energy malnutrition, specific nutrient

	deficiencies and dehydration, and correction and prevention of acid-base disturbances.(2) Treatment includes glucose-polymer-based oral rehydration solutions (ORS) to decrease dehydration and total parenteral nutrition (TPN) in patients with residual jejunum ending in a jejunostomy. For patients with residual colon in continuity, ORS may still be of value provided sufficient sodium is present in the diet. For patients with no remaining jejunum, who have residual ileum, the presence of glucose in the ORS is not critical because ileal water absorption is not affected by the presence of glucose.(2,4) High-dose H_2 antagonists and proton pump inhibitors reduce gastric fluid secretion, and fluid losses during the first 6 months post-enterectomy. Fluid losses usually require long-term control with anti-motility agents, such as loperamide hydrochloride or diphenoxylate (4-16 mg per day). If these are ineffective, especially in patients without colon in continuity or in patients with minimal residual jejunum or duodenum, use of codeine sulfate (15-60 mg two to three times a day) or tincture of opium may be necessary.(2,4)
Efficacy (1)	Gattex (teduglutide) 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 in adults. Study 1, with the open-label extension into 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 equal to 43) or teduglutide (n equal to 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 greater than 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. Gattex was also studied in a 24-week, multicenter study in 59 patients aged 1 year through 17 years with short bowel syndrome who were dependent on parenteral support. Patients chose whether to receive Gattex or standard of care. Patients who chose to receive Gattex were subsequently randomized in a double-blind manner to 0.025 mg/kg/day or 0.05 mg/kg/day. 69% of patients had a reduction in parenteral support of at least 20%, 12% achieved enteral autonomy, and 38% had a reduction in parenteral support by greater than 1 day/week. A sixth study was a prospective, open-label, long-term extension study of pediatric patients who completed the pediatric study. In the extension study, patients received additional treatment with Gattex 0.05 mg/kg subcutaneously once daily if they deteriorated or stopped improving after discontinuation of prior Gattex treatment. Efficacy results were similar to those achieved at the end of 24 weeks in the original pediatric study.
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 to this risk, a colonoscopy of the entire colon should be done within 6 months prior to starting therapy in adult patients. If polyps are present, they should be removed at least 6 months prior to starting treatment with Gattex. In pediatric patients a fecal occult blood test should be performed within 6 months prior to starting therapy. If there is unexplained blood in the stool a colonoscopy/sigmoidoscopy should be performed. 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 for all patients. 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

Number	Reference
1	Gattex prescribing information. NPS Pharmaceuticals, Bedminster NJ. January 2022.
2	American Gastroenterological Association medical position statement: Short bowel syndrome and intestinal transplantation. Gastroenterology, Volume 124, Issue 4, 1105-1110. Last updated April 2003.
3	National Organization for Rare Disorders (NORD). Rare Disease Database. Short Bowel Syndrome.
4	Nightingale J, Woodward JM. Guidelines for management of patients with a short bowel. Gut. 2006 Aug; 55 (suppl 4): iv1-iv12.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Gattex	teduglutide (rdna) for inj kit	5 MG	M ; N ; O ; Y	N		

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Gattex	teduglutide (rdna) for inj kit	5 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
			Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** 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 ALL of the following: 1. The patient has less than 200 cm of functional small intestine **AND** 2. ONE of the following: A. The patient has tried and had an inadequate response to maximal use of TWO anti-diarrheal agents (e.g., loperamide, diphenoxylate) used concomitantly with oral rehydration solution **OR** B. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** C. The prescriber has provided documentation that anti-diarrheal agents (e.g. loperamide, diphenoxylate) used concomitantly with oral rehydration solution cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 3. The patient is currently receiving parenteral nutrition/intravenous fluids (PN/IV) at least 3 days per week **AND** 4. ONE of the following: A. The patient is a pediatric patient at least 1 year of age AND BOTH of the following: 1. A fecal occult blood test has been performed within 6 months prior to initiating treatment with the requested agent **AND** 2. ONE of the following: A. There was no unexplained blood in the stool **OR** B. There was unexplained blood in the stool AND a colonoscopy or a sigmoidoscopy was performed **OR** B. The patient is an adult AND BOTH of the following: 1. The patient has had a colonoscopy within 6 months of initiating treatment with the requested agent **AND** 2. If polyps were present at this colonoscopy, the polyps were removed **OR** B. The patient has another FDA approved indication for the requested agent **AND** 2. If the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND**

Module	Clinical Criteria for Approval
	3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., gastroenterologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 5. The requested quantity (dose) does not exceed the maximum FDA labeled dose for the requested indication **Length of Approval:** 6 months **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. If the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., gastroenterologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. If the patient is using parenteral nutrition/intravenous fluids (PN/IV), the patient has had at least a 20% reduction in PN/IV fluids from baseline prior to therapy with the requested agent **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 6. The requested quantity (dose) does not exceed the maximum FDA labeled dose for the requested indication **Length of Approval:** 12 months

