teduglutide [rDNA origin] (Gattex®)

Policy # 00372
Original Effective Date: 07/17/2013
Current Effective Date: 08/09/2021

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.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider the use of teduglutide (Gattex®)‡ for the treatment of adult patients with short bowel syndrome who are dependent on parenteral support to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for teduglutide (Gattex) will be considered when all of the following criteria are met:

- Patient is 1 year of age or older; AND
- Patient has a documented diagnosis of Short Bowel Syndrome (SBS); AND
- Patient is dependent on parenteral support; AND
- For continuation of therapy, documentation of decreased parenteral support volume from baseline.
  *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the continued use of teduglutide (Gattex) when there is no documentation of decreased parenteral support volume from baseline to be **not medically necessary.****

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When 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 the use of teduglutide (Gattex) when patient selection criteria are not met (with the exception of those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Gattex is a 33 amino acid manufactured glucagon-like peptide-2 (GLP-2) analog manufactured using a strain of Escherichia coli modified by recombinant DNA technology that is indicated for use in the treatment of short bowel syndrome in pediatric patients 1 year of age and older and adults who are dependent on parenteral support. 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 located in intestinal subpopulations of enteroendocrine cells, subepithelial myofibroblasts and enteric neurons of the submucosal and myenteric plexus. 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).

Each single-use vial of Gattex contains 5 mg of teduglutide as a white lyophilized powder for solution for subcutaneous injection. The dose of Gattex for its approved indication is 0.05 mg/kg once daily by subcutaneous injection.

Short Bowel Syndrome

Short bowel syndrome is a malabsorptive condition which arises from extensive resection of the small bowel. Symptoms vary depending on the length and function of the remaining bowel, but some of the most typical symptoms include diarrhea and malabsorption. Individuals with short bowel syndrome are typically treated with small feedings, anti-diarrhea medications, and sometimes total parenteral nutrition (TPN) or intestinal transplantation. Another treatment option for patients with SBS includes somatropin [rDNA origin] (Zorbtive™)‡. Zorbtive is indicated in SBS patients receiving specialized nutritional support and has only been studied for a 4 week period. L-glutamine powder (Nutrastore®)‡ is also indicated for the treatment of SBS in patients receiving concomitant therapy with human growth hormone.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Gattex was approved in December of 2012 for treatment of short bowel syndrome in adults who are dependent on parenteral support. In May of 2019, the pediatric age was changed to include patients 1 year of age and older. Gattex does have a REMS (Risk Evaluation and Mitigation Strategy) program associated with it in order to inform prescribers and patients about the risks of possible acceleration of neoplastic growth and enhancement of colon polyp growth, gastrointestinal obstruction, and biliary and pancreatic disorders associated with Gattex. It is recommended that a colonoscopy with removal of polyps should be done before initiating treatment with Gattex and is also recommended after 1 year of therapy. Lab assessments for biliary and pancreatic disease should be performed prior to initiating Gattex and every 6 months thereafter.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Study 1 looking at Gattex was a randomized, placebo-controlled, parallel-group study in 86 adults with SBS who had been on parenteral support for at least 12 months and at least 3 times per week. The study began with an 8 week optimization period. The primary endpoint of the study was based on a clinical response, defined as a 20% reduction in weekly parenteral nutrition volume from baseline. Subjects were randomized 1:1 to receive either placebo or the approved dose of Gattex (0.05 mg/kg/day). Sixty-three percent (63%) of the subjects randomized to Gattex vs. 30% of placebo-controlled patients were considered responders ($p<0.001$). At week 24, the mean reduction in mean parenteral support was 4.4 L in Gattex treated subjects vs. 2.3 L for placebo treated subjects. Study 2 is an on-going open-label extension of Study 1. The mean reduction in parenteral volume after one year was 5.2 L/week. Six of the participants in Study 2 were weaned off of their parenteral support.

Study 3 was a randomized, placebo-controlled, parallel-group study in 84 adults with SBS who had been on parenteral support for at least 12 months and at least 3 times per week. This study also began with an optimization period and then subjects were randomized to either placebo, the current FDA approved dose of Gattex, or 0.10 mg/kg/day of Gattex. The primary endpoint of this study was a graded categorical score. The higher dose of Gattex did not reach statistical significance in the graded categorical score in this study. Forty-six percent of Gattex treated patients responded (as defined in Study 1) vs. 6% of placebo controlled patients. Patients treated with Gattex experienced a 2.5 L/week reduction in parenteral support versus 0.9 L/week in the placebo group. Two subjects were weaned off of parenteral support by week 24. Study 4 was an open-label extension of Study 3. The mean reduction in parenteral support was 4.9 L/week after one year of treatment with Gattex. Subjects that were weaned off of parenteral support in Study 3 remained off of parenteral support in Study 4 and an additional subject was weaned off during Study 4.

Study 5 was a 24-week, multicenter study conducted in 59 pediatric patients aged 1 year through 17 years with SBS who were dependent on parenteral support. Patients chose whether to receive Gattex or standard of care (SOC). Patients who chose to receive Gattex treatment were subsequently randomized in a double-blind manner to 0.025 mg/kg/day (n=24) or 0.05 mg/kg/day (n=26), while 9 patients enrolled in the SOC arm. At baseline, the mean parenteral support volume was 60 (±29) mL/kg/day (range: 24 to 133 mL/kg/day) [8 (±4) L/week (range: 3 to 19 L/week)] and mean parenteral support infusion time was 7 (±1) days/week (range: 5 to 7 days/week) and 11 (±3) hours/day (range: 7 to 20 hours/day). The results for the Gattex dosage of 0.05 mg/kg subcutaneously once daily are as follows: 69% achieved a reduction in parenteral support volume of at least 20%, 12% achieved enteral autonomy, 38% achieved a reduction in parenteral support infusion of ≥1 day per week, and the mean change in parenteral support volume from baseline was -23 mL/kg/day (mean of 29% reduction).

Study 6 was a prospective, open-label, long-term extension study of pediatric patients who completed Study 5. 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. Of the 15 patients who initially responded in Study 5 and enrolled in Study 6, 13 patients (87%) required additional treatment with Gattex. Efficacy results at the end of the first 24-week treatment period in Study 6 (total treatment for a mean of 40 weeks) were similar to those achieved at the end of 24 weeks treatment in Study 5. One additional patient treated with 0.05 mg/kg in Study 5 eventually achieved enteral autonomy during follow-up in Study 6.

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References

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Policy History

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06/27/2013	Medical Policy Committee review
07/17/2013	Medical Policy Implementation Committee approval. New policy.
07/10/2014	Medical Policy Committee review
07/16/2014	Medical Policy Implementation Committee approval. No change to coverage.
06/25/2015	Medical Policy Committee review
07/15/2015	Medical Policy Implementation Committee approval. No change to coverage.
06/30/2016	Medical Policy Committee review
07/20/2016	Medical Policy Implementation Committee approval. No change to coverage.
07/06/2017	Medical Policy Committee review
07/19/2017	Medical Policy Implementation Committee approval. No change to coverage.
07/05/2018	Medical Policy Committee review
07/11/2018	Medical Policy Implementation Committee approval. No change to coverage.
07/03/2019	Medical Policy Committee review
07/18/2019	Medical Policy Implementation Committee approval. Changed age to 1 year of age and older due to FDA indication update.
07/02/2020	Medical Policy Committee review
07/08/2020	Medical Policy Implementation Committee approval. No change to coverage.
07/01/2021	Medical Policy Committee review
07/14/2021	Medical Policy Implementation Committee approval. No change to coverage.

Next Scheduled Review Date: 07/2022

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*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.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.