PDL NEW DRUG REVIEW

Proprietary Name: Gattex®
Common Name: teduglutide
PDL Category: Inflammatory Bowel Agents

Comparable Products	Preferred Drug List Status
Zorbtive	Non-Preferred with Conditions

Summary

Indications and Usage: Treatment of adults with Short Bowel Syndrome (SBS) who are dependent on parenteral support. This is a pregnancy category B medication. The safety and efficacy of use in children under the age of 18 have not been established.

Drug Interactions: Clinical drug interaction studies were not performed; however, based on the pharmacodynamic effect of teduglutide, there may be a potential for the increased absorption of oral medications if given concomitantly. This should be kept in mind when using products that require dose titration or have a narrow therapeutic index.

Dosage Forms: Powder for injection in a single-use glass vial containing 5mg teduglutide as lyophilized powder. Once reconstituted with 0.5ml Sterile Water for Injection, a maximum of 0.38ml of the reconstituted sterile solution contains 3.8mg of teduglutide.

Recommended Dosage: A daily dose of 0.05mg/kg body weight to be given subcutaneously (SC) once daily is recommended. Gattex® should not be given IV or IM. It is recommended that the sites of injection be rotated, with the sites including the thighs, arms, and quadrants of the abdomen. It is recommended that the dose be reduced by 50% in those with moderate and severe renal impairment, as well as end-stage renal disease. While dose adjustment is not required in those with mild and moderate hepatic impairment, use in those with severe hepatic impairment has not been formally studied.

It is recommended that a colonoscopy of the entire colon be performed within 6 months prior to starting Gattex® treatment. Any polyps found should be removed. A follow-up colonoscopy should be performed after 1 year of treatment. At this point, if no polyps are found then subsequent colonoscopies are recommended to be done no less than every 5 years.

It is also recommended that laboratory assessments be performed within 6 months prior to initiating Gattex® treatment. These should include bilirubin, alkaline phosphatase, lipase, and amylase. Ensuing lab assessments should be done every 6 months.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions = reported % incidence for drug minus reported % incidence for placebo.* The most common adverse events reported with Gattex® include abdominal pain (10.6%), upper respiratory tract infection (12.4%), nausea (4.4%), abdominal distension (17.8%), vomiting (1.5%), fluid overload (4.9%), flatulence (2.3%), hypersensitivity (2.7%), appetite disorders (3.1%), sleep disturbances (5.2%), cough (5.2%), and skin hemorrhage (3.5%).

In those with a stoma, GI stoma complications were reported by 41.9% of the Gattex® group vs 13.6% of the placebo group.

Gattex® has the potential to cause hyperplastic changes, including neoplasia. It is recommended that the benefits and risk of Gattex® treatment be weighed in those with increased risk for malignancy. In those with active GI malignancy, therapy should be discontinued.

In the SBS clinical studies, 6 subjects were seen to have GI polyps after starting treatment. One was from the placebo group, and the other 5 were from the Gattex® group. It is therefore recommended that baseline and follow-up colonoscopies be performed.

As biliary and pancreatic disease have been reported in clinical studies, it is recommended that lab assessments of bilirubin, alkaline phosphatase, lipase, and amylase be performed within 6 months prior to starting therapy and at least every 6 months while on therapy.

Contraindications: There are currently no contraindications listed in the prescribing information.

Manufacturer: By: Hospira, Inc; Distributed by: NPS Pharmaceuticals

Analysis: Teduglutide, the active ingredient of Gattex®, is an analog of naturally occurring human glucagon-like peptide-2 (GLP-2). It is a 33 amino acid GLP-2 analog that is made using a strain of *E. coli* modified by recombinant DNA technology. GLP-2 is secreted by L-cells of the distal intestine and is known to increase intestinal and portal blood flow, as well as inhibit gastric acid secretion. Teduglutide binds to the GLP-2 receptors and activates them, which causes a local release of mediators such as insulin-like growth factor (IGF)-1, nitric oxide, and keratinocyte growth factor (KGF).

Four studies were performed to assess the safety and efficacy teduglutide for the treatment of adults with SBS who are dependent on parenteral nutrition/intravenous (PN/IV) support. Study 1 was a placebo-controlled trial while study 2 was an open-label extension of study 1. Study 1 was a randomized, double-blind, placebo-controlled study and had a primary endpoint based on a clinical response, which was defined as a subject achieving at least 20% reduction in weekly PN/IV volume from baseline to weeks 20 and 24. Results suggested that 63% of the Gattex® group were considered responders as compared with 30% of the placebo group, which was statistically significantly different ($p=0.002$). The mean reduction in weekly PN/IV volume was 4.4 l with Gattex® as compared with 2.3L with placebo, which was also statistically significantly different ($p<0.001$). 97% of those in study 1 entered into study 2. Of those who responded in study 1, 100% sustained their response to Gattex® in study 2. Additionally, after another 28 weeks of treatment, 72% achieved response with Gattex® treatment.

Study 3 (N=84) was also a randomized, double-blind, placebo-controlled study including adults with SBS dependent upon PN/IV support, with study 4 being a blinded, uncontrolled extension of study 3. In this trial, subjects were randomized to Gattex® 0.05mg/kg, Gattex® 0.10mg/kg, or placebo. The primary outcome was a graded categorical score that, and the high dose did not achieve statistical significance. Response (defined as ≥20% reduction in PN/IV fluid from baseline to weeks 20 and 24) was seen in 46% of the Gattex® 0.05mg/kg group vs 6% of the placebo group. At 24 weeks, both Gattex® groups (0.05mg/kg and 0.1mg/kg) had a 2.5L/week reduction in parenteral support requirements vs 0.9L/week for the placebo group. Of those who responded in study 3, 75% sustained a response to Gattex® after one year of treatment. At the end of the study, response was achieved by 68% of the subjects.

Gattex® is the first in its class with this mechanism of action; however, Zorbtive®, a growth hormone, and NutreStore® are also approved for SBS. Comparator trials with Gattex® were not found. It is recommended that Gattex® remain non-preferred and require prior authorization to verify diagnosis and laboratory assessments.

PDL Placement:

- ☐ **Preferred**
- ☒ **Non-Preferred**
- ☐ **Preferred with Conditions**

References

[1] Gattex® [package insert]. Bedminster, NJ: NPS Pharmaceuticals; 2012.