For adults with Short Bowel Syndrome (SBS) dependent on parenteral support/intravenous (PS/IV) support who are taking GATTEX®

Weaning PS/IV in adults:
An overview of the weaning protocol from STEPS and STEPS2

“Attempts should be made, when appropriate, to wean patients who have sufficient absorptive capacity [off PS/IV support]”
— The 2002 official recommendations of the American Gastroenterological Association (AGA) on Short Bowel Syndrome

Indication
GATTEX® (teduglutide) for injection is indicated for the treatment of adults and pediatric patients 1 year of age and older with Short Bowel Syndrome (SBS) who are dependent on parenteral support.

Important Safety Information
Warnings and Precautions
GATTEX has been associated with acceleration of neoplastic growth, intestinal obstruction, biliary and pancreatic disease, fluid imbalance and fluid overload, and increased absorption of concomitant oral medication.
GATTEX® significantly reduced weekly PS/IV support volume (STEPS)²

More than twice as many patients taking GATTEX had a clinical response in 6 months (STEPS)²

- 63% (27/43) for GATTEX vs 30% (13/43) for placebo compared to baseline (P=0.002)
- STEPS (Study 1 in Prescribing Information)
  - STEPS was a 6-month, randomized, double-blind, placebo-controlled, multicenter clinical trial of adult SBS patients dependent on PS/IV support ≥3 times/week for ≥12 months²
  - The primary efficacy endpoint was based on a clinical response defined as a ≥20% reduction in weekly PS/IV support volume from baseline (immediately before randomization) to both Weeks 20 and 24²

GATTEX showed a long-term clinical response (STEPS²)²

- *Of the 39 placebo patients who entered STEPS2, 29 completed 24 months of treatment with GATTEX²
- 30 GATTEX patients completed a total duration of 30 months (STEPS followed by STEPS²)²
- STEPS2 (Study 2 in Prescribing Information)
  - 97% (76/78) of patients who completed STEPS elected to enroll in STEPS2 (n=37, GATTEX; n=39, placebo). STEPS2 was a 24-month, open-label extension study. All patients (n=88), including 12 who were never in STEPS, received GATTEX in STEPS2. Clinical response was defined as a ≥20% reduction in weekly PS/IV support volume from baseline²

GATTEX increased the day(s) off of PS/IV support from baseline²

- 54% of patients on GATTEX (21/39) achieved at least a one day per week reduction in PS/IV support vs 23% on placebo (9/39) in the 6-month study (STEPS)²,³,⁴

  *After randomization of the intent-to-treat population (n=86), 1 patient was randomized in error, 4 patients in the GATTEX arm and 3 patients in the placebo arm discontinued treatment, leaving 78 evaluable patients.

GATTEX helped patients achieve complete independence from PS/IV support²

- No patients were completely independent of the need for PS/IV support at 6 months in STEPS³

Important Safety Information

Warnings and Precautions

Acceleration of neoplastic growth

Colorectal polyps were identified during clinical trials. There is a risk for acceleration of neoplastic growth. In adults, within 6 months prior to starting treatment with GATTEX, colonoscopy of the entire colon with removal of polyps should be performed and follow-up colonoscopy (or alternate imaging) is recommended at the end of 1 year of GATTEX. Subsequent colonoscopies should be performed every 5 years or more often as needed.
Patient flow during STEPS and through STEPS2

The patients’ PS/IV support was optimized and stabilized prior to randomization

**Optimization**

Patients were assessed at planned intervals (Weeks 2, 4, 6, and 8, ±3 days) for hydration and nutrition.

- 48-hour oral fluid intake and urine output were measured immediately before each visit
  - Measurements included 1-day on and 1-day off PS/IV support, unless the PS/IV support was infused daily
- Blood and urine samples were collected at each visit to evaluate hydration and nutrition
  - A targeted urine output of 1.0 to 2.0 L/d was used to determine if patients required optimization or could enter the stabilization period
- PS/IV support was adjusted in targeted increments of ≥10% of the volume at the previous visit

**Stabilization**

During the stabilization period, oral fluid intake and urine volume could not deviate ±25% from the optimized levels. PS/IV support was determined to be stable when:

- Actual PS/IV support usage matched the prescribed PS/IV support
- 48-hour oral fluid intake and urine output volumes were within ±25% of baseline
- Urine output volume of 2-4 L/48 hours

No further PS/IV adjustments permitted during stabilization period.

- Patients entered STEPS once they had their PS/IV fluid optimized and stabilized
- Patients who failed to remain stable for ≥4 consecutive weeks immediately before randomization underwent repeat optimization. If patients failed to stabilize after 2 attempts, they did not proceed into the study

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**Important Safety Information**

**Warnings and Precautions (continued)**

**Acceleration of neoplastic growth (continued)**

In children and adolescents, perform fecal occult blood testing prior to initiating treatment with GATTEX. Colonoscopy/sigmoidoscopy is required if there is unexplained blood in the stool. Perform subsequent fecal occult blood testing annually in children and adolescents while they are receiving GATTEX. Colonoscopy/sigmoidoscopy is recommended for all children and adolescents after 1 year of treatment, every 5 years thereafter while on continuous treatment with GATTEX, and if they have new or unexplained gastrointestinal bleeding.

In case of intestinal malignancy (GI tract, hepatobiliary, pancreatic), discontinue GATTEX. The clinical decision to continue GATTEX in patients with non-gastrointestinal malignancy should be made based on benefit-risk considerations.
Weaning protocol for STEPS and STEPS2[^3][^4]

48-hour urine output

- **<1.0 L/d or target, based on stabilized urine output**
  - PS/IV support increased by ≥10% or to the previous level

- **≥1.0 L/d but less than baseline
d**
  - If dehydrated or inadequately nourished, PS/IV support increased; if not, PS/IV support was maintained

- **<10% increase vs baseline**
  - PS/IV support maintained

- **≥10% increase vs baseline**
  - PS/IV support reduced by ≥10% up to a clinically appropriate amount (30% maximum)

**STEPS/STEPS2 study continuation until next clinical assessment**[^*]

**If well-tolerated, PS/IV support volume was maintained**

**If not well-tolerated, PS/IV support was resumed at the previously well-tolerated level**

**Interim safety evaluation done 1 week later:**
- Repeat 48-hour urine collection
- Clinical evaluation
  - Clinical signs and symptoms of dehydration
  - Weight changes
  - Review of recorded oral fluid intake
  - Blood samples (hematocrit, creatinine, blood urea nitrogen)
  - Urine sodium

[^*]: Baseline urine output is the urine volume obtained during the stabilization period before initiating treatment

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**Important Safety Information**

**Warnings and Precautions (continued)**

**Intestinal obstruction**

Intestinal obstruction has been reported in clinical trials and postmarketing. In patients who develop intestinal or stomal obstruction, GATTEX should be temporarily discontinued pending further clinical evaluation and management.

**Biliary and pancreatic disease**

Cholecystitis, cholangitis, cholelithiasis, and pancreatitis have been reported in clinical trials and postmarketing. Laboratory assessment (bilirubin, alkaline phosphatase, lipase, amylase) should be obtained within 6 months prior to starting GATTEX. Subsequent laboratory tests should be done every 6 months or more often as needed. If clinically meaningful changes are seen, further evaluation is recommended including imaging, and continued treatment with GATTEX should be reassessed.
Clinical assessments* for PS/IV volume adjustments were performed

In STEPS, initial patient evaluation occurred as early as 2 weeks after stabilization³

• PS/IV support volume adjustments (up to 30% decrease) and clinical assessments were made at
  Weeks 2, 4, 8, 12, 20, and 24

In the long-term (24-month) study STEPS2, PS/IV volume adjustments (up to 30% decrease) and clinical assessments were conducted less frequently⁴

• Week 2, Month 1, Month 2, Month 3, and every 3 months thereafter

Important Safety Information

Warnings and Precautions (continued)

*Fluid imbalance and fluid overload*

Fluid overload and congestive heart failure have been observed in clinical trials. If fluid overload occurs, especially in patients with underlying cardiovascular disease, parenteral support should be adjusted and GATTEX treatment reassessed. If significant cardiac deterioration develops while on GATTEX, continued GATTEX treatment should be reassessed.

Discontinuation of treatment with GATTEX may also result in fluid and electrolyte imbalance. Fluid and electrolyte status should be monitored in patients who discontinue treatment with GATTEX.
Physicians’ clinical judgment and patients’ personal preference drove approaches to weaning

With the goal of reducing PS/IV support volume in mind, decisions addressed whether to:
- Stop a day of PS/IV support
- Reduce the percentage volume for the days that PS/IV support was administered
- Change the proportion of the PS/IV constituents
- Completely wean off PS/IV support, if possible

Hypothetical weaning example

Important Safety Information
Warnings and Precautions (continued)

*Increased absorption of concomitant oral medication*
In clinical trials, one patient receiving prazepam concomitantly with GATTEX experienced dramatic deterioration in mental status progressing to coma during first week of GATTEX therapy. Patients receiving concomitant oral drugs requiring titration or with a narrow therapeutic index should be monitored for adverse reactions due to potential increased absorption of the concomitant drug. The concomitant drug may require a reduction in dosage.
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**Adverse Reactions**

The most common adverse reactions (≥ 10%) with GATTEX are abdominal pain, nausea, upper respiratory tract infection, abdominal distension, injection site reaction, vomiting, fluid overload, and hypersensitivity.

**Use in Specific Populations**

Breastfeeding is not recommended during treatment with GATTEX.

Please click here for full Prescribing Information.
Considerations for weaning PS/IV support from STEPS and STEPS2 studies

- During the 6-month trial:
  - Clinical evaluations for PS/IV volume adjustments were made at Weeks 2, 4, 8, 12, 20 and 24
  - Additional safety evaluations were performed 1 week after each PS/IV support adjustment
- Patients tracked their PS/IV support volumes, oral fluid intake, urinary output, and shared with the physician:
  - Patients were asked to keep intake as constant as possible while taking GATTEX®
- Patients discussed individual preferences for weaning:
  - Skipping a day vs reducing the volume of PS/IV support
- Full communication occurred across the multidisciplinary team:
  - Prescribers of GATTEX® and of PS/IV support
  - Other healthcare providers who may need to adjust oral medications
  - Home infusion companies
  - The patient and caregiver

Important Safety Information (continued)

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