For adult patients with Short Bowel Syndrome (SBS) dependent on parenteral nutrition/intravenous (PN/IV) support who are taking GATTEX®

Weaning PN/IV support:
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 PN/IV support]”

—The 2002 official recommendations of the American Gastroenterological Association (AGA) on Short Bowel Syndrome¹

Indication
GATTEX® (teduglutide [rDNA origin]) for Injection is indicated for the treatment of adult patients with Short Bowel Syndrome (SBS) who are dependent on parenteral support.

Warnings and Precautions
GATTEX has been associated with possible acceleration of neoplastic growth and enhanced growth of colon polyps, gastrointestinal obstruction, gallbladder, biliary tract and pancreatic disease, increased absorption of fluids leading to fluid overload, and increased absorption of oral medications.
GATTEX® significantly reduced weekly PN/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 PN/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 PN/IV support volume from baseline (immediately before randomization) to both Weeks 20 and 24²

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

- aOf the 39 placebo patients who entered STEPS2, 29 completed 24 months of treatment with GATTEX²
- b30 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 PN/IV support volume from baseline²

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

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

Patients in STEPS2 With ≥20% Reduction in PN/IV Support Volume²

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

- 33% of patients (10/30) were completely independent of the need for PN/IV support while on GATTEX treatment for 30 months²

Important Safety Information

Warnings and Precautions

Neoplastic growth

Colorectal polyps were identified during clinical trials. There is a risk for acceleration of neoplastic growth. Colonoscopy of the entire colon with removal of polyps should be done within 6 months prior to starting treatment with GATTEX and is recommended after 1 year. Subsequent colonoscopies should be done as needed, but no less frequently than every 5 years. 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 risk and benefit considerations.

Please see Important Safety Information on page 7 and click for full Prescribing Information and Medication Guide.
The patients’ PN/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 PN/IV support, unless the PN/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
- PN/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. PN/IV support was determined to be stable when:
- Actual PN/IV support usage matched the prescribed PN/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 PN/IV adjustments permitted during stabilization period.
- Patients entered STEPS once they had their PN/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

**Important Safety Information**

**Warnings and Precautions (continued)**

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

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*Please see Important Safety Information on page 7 and click for full Prescribing Information and Medication Guide.*
Important Safety Information

Warnings and Precautions (continued)

**Biliary and pancreatic disease**
Cholecystitis, cholangitis, choledolithiasis, and pancreatitis have been reported in clinical trials. Patients should undergo laboratory assessment (bilirubin, alkaline phosphatase, lipase, amylase) before starting GATTEX®. Subsequent laboratory tests should be done every 6 months. If clinically meaningful changes are seen, further evaluation is recommended including imaging, and continued treatment with GATTEX should be reassessed.

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*Baseline urine output is the urine volume obtained during the stabilization period before initiating treatment.*
Clinical assessments* for PN/IV volume adjustments were performed

In STEPS, initial patient evaluation occurred as early as 2 weeks after stabilization\(^3\)
- PN/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, PN/IV volume adjustments (up to 30% decrease) and clinical assessments were conducted less frequently\(^4\)
- Week 2, Month 1, Month 2, Month 3, and every 3 months thereafter.

Important Safety Information
Warnings and Precautions (continued)

Fluid overload
Fluid overload and congestive heart failure have been observed in clinical trials. There is potential for fluid overload while on GATTEX\(^\circledR\). If fluid overload occurs, especially in patients with underlying cardiovascular disease, parenteral support should be appropriately adjusted and GATTEX treatment reassessed.
Physicians’ clinical judgment and patients’ personal preference drove approaches to weaning

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

Weaning example


Urine volume at current visit

Baseline urine volume = 1.2 L/d

If 0-.999 L/d
- Increase PN/IV support by ≥10% or to previous level

If 1.0-1.199 L/d but less than baseline
- Increase or maintain PN/IV support volume based on nutritional and hydration status

If 1.2-1.319 L/d increase vs baseline
- Maintain PN/IV support

If ≥1.32 L/d increase vs baseline
- Reduce PN/IV support 10% to 30% from baseline
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Increased absorption of concomitant oral medication

Altered mental status in association with GATTEX® has been observed in patients on benzodiazepines in clinical trials. Patients on concomitant oral drugs (e.g., benzodiazepines, phenothiazines) requiring titration or with a narrow therapeutic index may require dose adjustment while on GATTEX®.

Adverse Reactions

The most common adverse reactions (≥10%) across all studies with GATTEX® are abdominal pain, injection site reactions, nausea, headaches, abdominal distension, upper respiratory tract infection. In addition, vomiting and fluid overload were reported in the SBS studies (1 and 3) at rates ≥10%.

Please click for full Prescribing Information and Medication Guide.
Considerations for weaning PN/IV support from STEPS and STEPS2 studies

• During the 6-month trial\(^3\)
  – Clinical evaluations for PN/IV volume adjustments were made at Weeks 2, 4, 8, 12, 20 and 24
  – Additional safety evaluations were performed 1 week after each PN/IV support adjustment
• Patients tracked their PN/IV support volumes, oral fluid intake, urinary output, and shared with the physician\(^3\)
  – Patients were asked to keep intake as constant as possible while taking GATTEX\(^\circledR\)
• Patients discussed individual preferences for weaning\(^3\)
  – Skipping a day vs reducing the volume of PN/IV support
• Full communication occurred across the multidisciplinary team
  – Prescribers of GATTEX\(^\circledR\) and of PN/IV support
  – Other healthcare providers who may need to adjust oral medications
  – Home infusion companies
  – The patient and caregiver

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For more information about getting patients started on GATTEX\(^\circledR\), contact your GATTEX\(^\circledR\) representative or call Shire at 1-866-888-0660.

Please click for full Prescribing Information and Medication Guide.