

Risk Evaluation and Mitigation Strategy (REMS) Document

GATTEX (teduglutide) REMS Program

I. Administrative Information

Application Number: NDA 203441

Application Holder: Shire-NPS Pharmaceuticals, Inc.

Initial REMS Approval: 12/2012

Most Recent REMS Update: 02/2021

II. REMS Goals

The goals of the GATTEX REMS are to mitigate the risks of possible acceleration of neoplastic growth and enhancement of colon polyp growth, gastrointestinal obstruction, and biliary and pancreatic disorders associated with GATTEX by:

1. Informing patients about the risks listed above associated with the use of GATTEX
2. Informing healthcare providers about the risks listed above associated with GATTEX

III. REMS Requirements

Shire-NPS Pharmaceuticals, Inc. must provide training to healthcare providers who prescribe Gattex.

The training includes the following educational materials: Prescribing Information, Medication Guide, [Dear Healthcare Professional Letter](#), [Prescriber Education Slide Deck](#), [Post-Training Knowledge Assessment Questions](#), and [Patient and Caregiver Counseling Guide](#). The training must be available online via the REMS website www.GATTEXREMS.com, by calling the REMS Program Call Center, during prescriber visits by Shire representatives, at professional society meetings, and at medical educational venues where Shire has a presence. In addition, the [Prescriber Education Slide Deck](#) must be part of training/educational programs provided by medical science liaisons.

Target Audience	Communication Materials-& Dissemination Plans
Healthcare providers who are likely to prescribe GATTEX	REMS Letter: Dear Healthcare Professional Letter with attachment: Prescriber Education Slide Deck <ol style="list-style-type: none">1. Mail or email to prescribers within 60 calendar days of their initial prescription who are identified as untrained, and again 12 and 24 months later.2. Mail or email to healthcare providers who inquire about how to become trained and request hard copies of the training materials.3. Mail or email to healthcare providers who have not written a prescription for GATTEX within 12 months of completing the REMS training.

To support REMS Program operations, Shire-NPS Pharmaceuticals, Inc. must:

1. Establish and maintain a REMS Program website, www.GATTEXREMS.com. The REMS Program website must include the capability to complete prescriber training online, and the option to print the Prescribing Information, Medication Guide, and REMS materials. All product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS Program website. The REMS Program website must not link back to the promotional product website(s).
2. Make the REMS Program website fully operational and all REMS materials available through the REMS website and REMS call center within 60 calendar days of REMS modification.
3. Establish and maintain a REMS Program call center for REMS participants at 1-855-5GATTEX (1-855-542-8839).
4. Establish and maintain a validated, secure database of all healthcare providers who have completed training for the GATTEX REMS Program.
5. Ensure healthcare providers are able to report completion of training by fax at 1-855-359-3393 and online.

IV. REMS Assessment Timetable

Shire-NPS Pharmaceuticals, Inc. must submit REMS Assessments at 12 months from the date of the initial REMS (12/21/2012) and annually thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Shire-NPS Pharmaceuticals, Inc. must submit each assessment so that it will be received by the FDA on or before the due date.

V. REMS Materials

The following materials are part of the GATTEX REMS:

Training and Educational Materials

Prescriber:

1. [Prescriber Education Slide Deck](#)
2. [Dear Healthcare Professional Letter](#)
3. [Post-Training Knowledge Assessment Questions](#)

Patient:

4. [Patient and Caregiver Counseling Guide](#)

Other Materials

5. [REMS website](#)



GATTEX[®] (teduglutide) REMS Prescriber Education Slide Deck

Shire-NPS Pharmaceuticals, Inc.
300 Shire Way, Lexington, MA 02421

A REMS (Risk Evaluation and Mitigation Strategy) is a program required by the FDA to manage known or potential serious risks associated with a drug product. The Prescriber Education Slide Deck is required by the FDA as part of the GATTEX REMS.

MM/YY



Gattex[®]
(teduglutide) for injection

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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.
- Teduglutide is a recombinant analog of GLP-2.

GLP-2, glucagon-like peptide-2


Gattex[®]
(teduglutide) for injection

Overview

Important Adverse Reactions of Special Interest

- Safety risks with GATTEX
 - Possible acceleration of neoplastic growth
 - Enhanced growth of colorectal polyps
 - Intestinal obstruction
 - Gallbladder, biliary tract and pancreatic disease
 - Increased absorption of fluids leading to fluid overload in patients with cardiovascular disease
 - Increased absorption of oral medications

Possible Acceleration of Neoplastic Growth

- GLP-2 receptors are localized mainly in the GI tract.¹
- GATTEX promotes growth of intestinal epithelial cells in the GI tract.
- It cannot be excluded that GATTEX promotes growth of existing neoplasms in the GI tract.
- 3 adult patients on GATTEX were reported to have neoplasms:*
 - 2 cases of lung cancer with extensive smoking history
 - 1 case of GI metastatic adenocarcinoma (unknown origin) following abdominal radiation for Hodgkin's disease
- No GATTEX-treated pediatric patients were reported to have neoplasms in the pediatric clinical studies.**

1. Munroe DG et al. Proc Natl Acad Sci. 1999; 96:1569-1573.

* As of 24 January 2013; ** As of 24 July 2018

Possible Acceleration of Neoplastic Growth

GATTEX Label – Warnings and Precautions

Possible Acceleration of Neoplastic Growth

- Based on the pharmacologic activity and findings in animals, GATTEX has the potential to cause hyperplastic changes including neoplasia.
- In patients at increased risk for malignancy, the clinical decision to use GATTEX should be considered only if the benefits outweigh the risks.
- In patients who develop active gastrointestinal malignancy (GI tract, hepatobiliary, pancreatic) while on GATTEX, discontinue GATTEX treatment.
- In patients who develop active non-gastrointestinal malignancy while on GATTEX, the clinical decision to continue GATTEX should be made based on risk-benefit considerations.
- Based on tumor findings in the rat and mouse carcinogenicity studies, patients should be monitored clinically for small bowel neoplasia. If a benign neoplasm is found, it should be removed. In case of small bowel cancer, GATTEX therapy should be discontinued.

**Gattex**[®]
(teduglutide) for injection

Enhanced Growth of Colorectal Polyps

- GATTEX's mechanism of action and nonclinical data are consistent with a potential to enhance growth of polyps.
- In the adult clinical studies, 14 patients with SBS were diagnosed with polyps of the GI tract after initiation of study treatment.
 - 2 patients in the SBS-placebo-controlled studies: 2 colorectal villous adenomas
 - 1 patient (1/59; 2%) on placebo with an inflammatory stomal polyp after 3 months
 - 1 patient (1/109; 1%) on GATTEX 0.05 mg/kg/day with a hyperplastic sigmoidal polyp after 5 months
 - 12 GATTEX-treated patients (12/173; 6.9%) in the extension studies:***
 - 2 colorectal villous adenomas
 - 2 hyperplastic polyps
 - 4 colorectal tubular adenoma
 - 1 serrated adenoma
 - 1 rectal inflammatory polyp
 - 1 colorectal polyp biopsy not done
 - 1 small duodenal polyp
- In the pediatric clinical studies (up to 69 weeks of exposure) there was one case of cecal polyp that was not biopsied and was not seen on repeat colonoscopy.**

* As of 24 January 2013; ** As of 24 July 2018

Enhanced Growth of Colorectal Polyps

GATTEX Label – Warnings and Precautions

Colorectal Polyps in adults

- Colonoscopy of the entire colon with removal of polyps should be done within 6 months prior to starting treatment with GATTEX.
- A follow-up colonoscopy (or alternate imaging) is recommended at the end of 1 year of GATTEX.
- Subsequent colonoscopies should be done every 5 years or more often as needed. If a polyp is found, adherence to current polyp follow-up guidelines is recommended.
- In case of diagnosis of colorectal cancer, GATTEX therapy should be discontinued.

Enhanced Growth of Colorectal Polyps

GATTEX Label – Warnings and Precautions

Colorectal Polyps in children and adolescents

- Fecal occult blood testing prior to initiating treatment with GATTEX should be done.
- Colonoscopy/sigmoidoscopy is required if there is unexplained blood in the stool.
- Subsequent fecal occult blood testing annually in children and adolescents should be performed 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.

Intestinal Obstruction

- 12 adult patients were reported to have one or more episodes of serious intestinal obstruction/stenosis events*
 - 6 in SBS placebo-controlled studies
 - 3/77 (3.9%) on GATTEX, 0.05 mg/kg/day
 - 3/32 (9.4%) on GATTEX, 0.10 mg/kg/day**
 - None in placebo-group
 - Onset 1 day to 6 months
 - 2/6 patients had recurrence of intestinal obstruction in the extension studies
 - 6 additional patients in the extension studies (all on GATTEX, 0.05 mg/kg/day)
 - Onset 6 days to 19 months
 - Of all 8 patients with an episode of intestinal obstruction/stenosis in the extension studies, 2 patients required endoscopic dilatation and 1 required surgical intervention

* As of 24 January 2013; ** Note that as per the GATTEX Prescribing Information, the recommended dosage of GATTEX for both adult and pediatric patients is 0.05 mg/kg/day



Intestinal Obstruction

- 1 pediatric patient was reported to have a serious reaction of obstruction that was assessed as related to teduglutide in the pediatric clinical studies.**
 - GATTEX was temporarily withheld, the obstruction resolved without additional intervention, and there was no recurrence once GATTEX was restarted.

** As of 24 July 2018

Intestinal Obstruction

GATTEX Label – Warnings and Precautions

Intestinal Obstruction

- Intestinal obstruction has been reported in clinical studies and postmarketing.
- In patients who develop intestinal or stomal obstruction, GATTEX should be temporarily discontinued while the patient is clinically managed.
- GATTEX may be restarted when the obstructive presentation resolves, if clinically indicated.

Gallbladder and Biliary Tract Disease

- 13/173 (7.5%) of GATTEX-treated adult patients were reported to have biliary events, including cholecystitis and gallstones/sludge in pooled Phase III SBS studies*
 - 5 adult patients had a history of biliary disease
 - None of these events resulted in study withdrawal
- No GATTEX-treated pediatric patients were reported to have biliary events related to teduglutide in the pediatric clinical studies.**

* As of 24 January 2013; **As of 24 July 2018

Gallbladder and Biliary Tract Disease

GATTEX Label – Warnings and Precautions

Gallbladder and Biliary Tract Disease

- Cholecystitis, cholangitis, and cholelithiasis have been reported in clinical studies and postmarketing.
- Patients should undergo laboratory assessment of bilirubin and alkaline phosphatase within 6 months prior to starting GATTEX.
- Subsequent laboratory assessments are recommended at least every 6 months while on GATTEX. If clinically meaningful changes are seen, further evaluation including imaging of the gallbladder and/or biliary tract is recommended. Reassess the need for continued GATTEX treatment.

Pancreatic Disease

- 3/173 (1.7%) of GATTEX-treated adult patients were reported to have pancreatitis in pooled Phase III SBS studies.*
 - All 3 patients had a history of pancreatitis
 - None of these events resulted in study withdrawal
- No GATTEX-treated patients were reported to have pancreatic adverse events related to teduglutide in the pediatric clinical studies.**

* As of 24 January 2013; **As of 24 July 2018

Pancreatic Disease

GATTEX Label – Warnings and Precautions

Pancreatic Disease

- Pancreatitis has been reported in adult clinical studies.
- Patients should undergo laboratory assessment of lipase and amylase within 6 months prior to starting GATTEX.
- Subsequent laboratory assessments are recommended at least every 6 months while on GATTEX; if clinically meaningful changes are seen, further evaluation such as imaging of the pancreas is recommended; reassess the need for continued GATTEX treatment.

Post-marketing Data Source: Intestinal Obstruction, Biliary and Pancreatic Disease

- All post marketing data are reviewed on an ongoing basis. No new safety findings have been uncovered regarding intestinal obstruction, biliary or pancreatic disease.
- As of 30 August 2018, estimated cumulative worldwide patient exposure to teduglutide was 4,740 patient-years.

Risk	Number of Cumulative Post-Marketing Cases*
Intestinal Obstruction	314
Gallbladder and Biliary Tract Disease	122
Pancreatic disease	431

*Post-marketing data are reported on a voluntary basis from a population of uncertain size, and it is not always possible to obtain reliable estimate of AE frequency, or to establish a causal relationship of AEs to drug exposure.

Sources: spontaneous cases, solicited cases , cases from Registry TED-R13-002



Fluid Overload

- 23/173 (13.3%) of adult patients treated with GATTEX were reported to have fluid overload in pooled Phase III SBS studies.*
- Fluid overload should be considered when administering GATTEX in patients with underlying heart disease.
- No GATTEX-treated patients were reported to have serious events of fluid overload in the pediatric clinical studies.** There was 1 patient who had a non-serious related adverse event of peripheral edema in the 0.025 mg/kg/day group.†

* As of 24 January 2013; **As of 24 July 2018

† Note that as per the GATTEX Prescribing Information, the recommended dosage of GATTEX for both adult and pediatric patients is 0.05 mg/kg/day


Gattex®
(teduglutide) for injection

Fluid Overload

GATTEX Label – Warnings and Precautions

Cardiovascular Disease

- Due to increased intestinal fluid absorption, patients with cardiovascular disease, such as cardiac insufficiency and hypertension, should be monitored with regard to fluid overload, especially during initiation of therapy.
- Parenteral nutrition/intravenous (PN/IV) fluid volume should be reassessed relative to signs of fluid overload.
- In case of a significant deterioration of the cardiovascular disease, the need for continued GATTEX treatment should be reassessed.

PN/IV Volume Adjustment in Adults

To minimize the risk of fluid overload, the following adjustment algorithm is recommended.

48-Hour Urine Output**	PN/IV* Action
<ul style="list-style-type: none"> • <1.0 L/day or target based on stabilized urine output 	<ul style="list-style-type: none"> • Increase PN/IV* by $\geq 10\%$ (week 2) or to previous level
<ul style="list-style-type: none"> • ≥ 1.0 L/day but < baseline 	<ul style="list-style-type: none"> • If patient is dehydrated or inadequately nourished, increase PN/IV* • If not dehydrated maintain PN/IV*
<ul style="list-style-type: none"> • 0% to <10% increase over baseline 	<ul style="list-style-type: none"> • Maintain PN/IV*
<ul style="list-style-type: none"> • $\geq 10\%$ increase over baseline 	<ul style="list-style-type: none"> • Reduce PN/IV* by $\geq 10\%$ of stabilized baseline level up to a clinically appropriate amount (maximum of 30%)

* PN/IV=parenteral nutrition and/or intravenous fluids

** Baseline urine output is volume obtained during stabilization period before treatment is initiated

†Data presented are based on the STEPS clinical trial and are not contained within the Gattex label

Jeppesen PB, et al. Gastroenterology. 2012;143:1473-81

PN/IV Volume Adjustment in Children and Adolescents

To minimize the risk of fluid overload or dehydration, the following nutritional support adjustment algorithm is suggested:

- Clinic visits every 1-2 weeks during the first 6 weeks of treatment
- Evaluate hydration status at every clinic visit, which may include:
 - Weight trajectory
 - Urine sodium (target > 20 meq/L)
 - Urine output (target 25-50 ml/kg/day)
 - Physical exam findings of hydration status
- Adjust PN/IV volume in increments/decrements of 10%-30% to avoid fluid overload or dehydration
- At every clinic visit, evaluate growth trajectory, enteral intake, and severity of diarrhea
- If growth trajectory is adequate and diarrhea is manageable, consider reducing PN calories and increasing enteral nutrition

Increased Absorption of Concomitant Oral Medications

- Based on the pharmacodynamic effect of GATTEX, there is a potential for increased absorption of concomitant oral medications
- Considerations should be given for dosage adjustment of concomitant oral medications requiring titration or that have a narrow therapeutic index

Increased Absorption of Concomitant Oral Medication

GATTEX Label – Warnings and Precautions

Risks resulting from increased absorption of concomitant oral medications

- Altered mental status in association with GATTEX has been observed in patients on benzodiazepines in adult clinical studies.
- Patients on concomitant oral medications (e.g., benzodiazepines, phenothiazines) requiring titration or with a narrow therapeutic index may require a reduction in dosage of the concomitant drug while on GATTEX.



**IMPORTANT DRUG WARNING
FDA-Required REMS Safety Information**

Risks associated with GATTEX:

- Possible acceleration of neoplastic growth and enhancement of colon polyp growth
- GI obstruction
- Biliary and pancreatic disorders

Dear Healthcare Professional:

The purpose of this letter is to remind you about the serious risks associated with GATTEX[®] (teduglutide) for Injection and the need for ongoing monitoring for these risks.

The FDA has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary to ensure that the benefits of GATTEX outweigh the potential risks.

Serious Risks:

Acceleration of neoplastic growth and enhancement of colon polyp growth

- *Possible Acceleration of Neoplastic Growth*

Based on the pharmacologic activity and findings in animals, GATTEX has the potential to cause hyperplastic changes including neoplasia.

- *Possible Small Bowel Neoplasia*

Based on benign tumor findings in the mouse and rat carcinogenicity studies, patients should be monitored clinically for small bowel neoplasia. If a benign neoplasm is found, it should be removed. In case of small bowel cancer, GATTEX therapy should be discontinued.

- *Colorectal Polyps*

Colorectal polyps were identified during the clinical studies. In adults, colonoscopy of the entire colon with removal of polyps should be done within 6 months prior to starting treatment with GATTEX. A follow-up colonoscopy (or alternate imaging) is recommended at the end of 1 year of GATTEX. Subsequent colonoscopies should be done every 5 years or more often as needed. In children and adolescents, fecal occult blood testing should be performed 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.

Gastrointestinal obstruction

Intestinal obstruction has been reported in clinical studies. In patients who develop intestinal or stomal obstruction, GATTEX should be temporarily discontinued while the patient is clinically managed and restarted when the obstructive presentation resolves, if clinically indicated.

Biliary and pancreatic disorders

- *Gallbladder and Biliary Tract Disease*

Cholecystitis, cholangitis, and cholelithiasis, have been reported in clinical studies. For identification of the onset or worsening of gallbladder/biliary disease, patients should undergo laboratory assessment of bilirubin and alkaline phosphatase within 6 months prior to starting GATTEX, and at least every 6 months while on GATTEX; or more frequently if needed.

- *Pancreatic Disease*

Pancreatitis has been reported in clinical studies. For identification of onset or worsening of pancreatic disease, patients should undergo laboratory assessment of lipase and amylase within 6 months prior to starting GATTEX, and at least every 6 months while on GATTEX; or more frequently if needed.

Appropriate Patient Selection, Counseling, and Monitoring

Prescribers should select the appropriate patients to receive GATTEX in accordance with the approved Prescribing Information (PI), discuss the benefits and risks of GATTEX with patients or caregivers, and monitor patients as specified in the approved (PI). The *Patient and Caregiver Counseling Guide* is available for use in discussing GATTEX with patients. The guide can be accessed via www.GATTEXREMS.com or by contacting 1-855-5GATTEX (1-855-542-8839).

GATTEX Healthcare Provider Training

As part of the REMS, healthcare providers who intend to prescribe GATTEX, should access www.GATTEXREMS.com to review the *Prescriber Education Slide Deck* and complete the *Post-Training Knowledge Assessment Questions*. Training can be completed either online or through a paper-based process:

- 1) **Online:** visit www.GATTEXREMS.com to review the REMS materials and follow the instructions to complete the Post-Training Knowledge Assessment Questions online.
- 2) **Paper-based:** review the REMS materials and fax the completed Post-Training Knowledge Assessment Questions to 1-855-359-3393.

Indication

GATTEX 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.



Reporting Adverse Events

Report all suspected adverse events associated with the use of GATTEX, at 1-855-5GATTEX (1-855-542-8839); or to the FDA MedWatch program at 1-800-FDA-1088 (1-800-332-1088), or via the website at <https://www.fda.gov/Safety/MedWatch/default.htm>

Please see the enclosed PI for GATTEX for additional safety information.

Enclosures:

- *Prescriber Education Slide Deck*
- *Post-Training Knowledge Assessment Questions*
- *GATTEX Prescribing Information*
- *Medication Guide*

Assessment Question:

Possible Acceleration of Neoplastic Growth

- **Based on the pharmacologic activity and findings in animals, GATTEX has the potential to cause hyperplastic changes including neoplasia. In patients at increased risk for malignancy or those with active non-gastrointestinal malignancy, the clinical decision to continue GATTEX should be made based on risk-benefit considerations. GATTEX should be discontinued in patients with active gastrointestinal malignancy (GI tract, hepatobiliary, pancreatic).**
 - A. True
 - B. False



Assessment Question: Intestinal Obstruction

- **Intestinal obstruction has been reported in clinical studies. Which of the following statements regarding obstruction is true:**
 - A. Patients with symptoms suggestive of these conditions should be permanently discontinued from GATTEX.
 - B. In patients who develop intestinal or stomal obstruction, GATTEX should be temporarily discontinued while the patient is clinically managed. GATTEX may be restarted when the obstructive presentation resolves, if clinically indicated.
 - C. GATTEX should be discontinued if mucosal hypertrophy at a stoma is observed.

Assessment Question:

Gallbladder, Biliary Tract, and Pancreatic Disease

- **Biliary disease (cholecystitis, cholangitis, cholelithiasis) and pancreatic disease (pancreatitis) have been reported in clinical studies. What is the recommended schedule for assessments for bilirubin, alkaline phosphatase, lipase and amylase?**
 - A. Within 6 months following initiation of GATTEX, and every 6 months thereafter.
 - B. Within 6 months prior to starting GATTEX, and subsequently at least every 6 months while on GATTEX, or more frequently if needed. Imaging is recommended if there are clinically meaningful changes in biliary or pancreatic functional markers.
 - C. At the time GATTEX is started (within 2 weeks), and then annually. Imaging is recommended for a possible obstruction if there are clinically meaningful elevations biliary or pancreatic functional markers.

Assessment Question:

Enhanced Growth of Colorectal Polyps

- **Colorectal polyps were identified during the clinical studies in adults. In adults, colonoscopy should be done according to which of the following schedules:**
 - A. Colonoscopy (or alternate imaging) of the entire colon with removal of polyps at the end of 1 year of GATTEX therapy, and subsequently every 5 years.
 - B. Colonoscopy (or alternate imaging) of the entire colon with removal of polyps within 6 months prior to starting GATTEX, subsequently every 5 years.
 - C. Colonoscopy (or alternate imaging) of the entire colon with removal of polyps within 6 months prior to starting GATTEX. A follow-up colonoscopy (or alternate imaging) is recommended at the end of 1 year of treatment. If no polyp is found, subsequent colonoscopies should be done every 5 years or more often as needed. If a polyp is found, adherence to current polyp follow-up guidelines is recommended.

Assessment Question: Enhanced Growth of Colorectal Polyps

- **In children and adolescents, colonoscopy should be done according to which of the following schedules:**
 - A. Colonoscopy (or alternate imaging) of the entire colon with removal of polyps within 6 months prior to starting GATTEX, and subsequently every 5 years.
 - B. Perform fecal blood testing prior to initiating treatment. Colonoscopy/sigmoidoscopy is required if there is unexplained blood in the stool. Perform subsequent fecal occult blood testing annually while 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.
 - C. No colonoscopy is required for children and adolescents. Only fecal occult blood testing is required prior to initiating treatment with GATTEX and annually thereafter.

Assessment Question:

Fluid Overload

- **Fluid overload and congestive heart failure have been observed in clinical studies, which were deemed to be related to enhanced fluid absorption associated with GATTEX. What is the recommended management for patients regarding fluid overload?**
 - A. Patients should be monitored with regard to fluid overload, especially during initiation of therapy.
 - B. If fluid overload occurs, parenteral support should be adjusted and the need for continued GATTEX treatment should be reassessed.
 - C. If significant cardiac deterioration develops while on GATTEX, the need for continued GATTEX treatment should be reassessed.
 - D. All of the above.

Assessment Question:

Increased Absorption of Concomitant Oral Medication

- **GATTEX may increase absorption of concomitant oral medications. Altered mental status in association with GATTEX has been observed in patients on benzodiazepines in clinical studies. Which of the following statements is true?**
 - A. Patient on concomitant oral drugs requiring titration or with a narrow therapeutic index may require dose adjustment while on GATTEX.
 - B. Oral medications requiring titration or that have a narrow therapeutic index should be discontinued prior to starting GATTEX.
 - C. No dose adjustment considerations are needed, but patients on oral medications should be monitored carefully.

GATTEX REMS: What You Need to Know About GATTEX[®] Treatment: A Patient & Caregiver Counseling Guide

Patients and Caregivers:

Your doctor or nurse will go over this Patient & Caregiver Counseling Guide with you. Make sure you ask any questions that you may have about GATTEX. Keep this guide for important safety information about the serious risks and reactions of GATTEX.

Healthcare Providers:

Review this Patient & Caregiver Counseling Guide with your patient or caregiver(s) each time and provide your patient with a copy to take home.



What is GATTEX®?

GATTEX is a prescription medicine used in adults and children 1 year of age and older with Short Bowel Syndrome (SBS) who need additional nutrition or fluids from intravenous (IV) feeding (parenteral support). It is not known if GATTEX is safe and effective in children under 1 year of age.

What Are the Most Serious Risks Related to GATTEX Treatment?

GATTEX can make abnormal cells that are already in your body grow faster.

There is a potential risk that abnormal cells could become cancer. If you, or the patient you care for, get cancer of the bowel (intestines), liver, gallbladder, or pancreas while using GATTEX, your doctor should stop GATTEX treatment. If you, or the patient you care for, get other types of cancers, you and your doctor should discuss the risks and benefits of using GATTEX.

GATTEX may cause polyps in the colon (large intestine).

Polyps are growths on the inside of the colon.

BEFORE you start GATTEX, your doctor will:	AFTER you start GATTEX, your doctor will:
<ul style="list-style-type: none">✓ In adults, check your colon for polyps within 6 months before starting GATTEX and remove all polyps.✓ In children and adolescents, check for blood in the stool.	<ul style="list-style-type: none">✓ Check your colon for new polyps at the end of 1 year of using GATTEX. If no polyp is found, your doctor should check you for polyps as needed and at least every 5 years.✓ Remove any new polyps. If cancer is found in a polyp, you must stop GATTEX treatment.

GATTEX may prevent food, fluids, and gas from moving through your bowels (intestines)

in a normal way. Tell your doctor if you, or the patient you care for, have any of these symptoms that could be a sign of blockage of the bowel:

- Trouble having a bowel movement or passing gas
- Stomach area (abdomen) pain or swelling
- Nausea
- Vomiting
- Swelling and blockage of your stoma opening, if you have a stoma

GATTEX can cause swelling (inflammation) or blockage of your gallbladder or pancreas.

Your doctor will do tests to check your gallbladder and pancreas within 6 months before starting GATTEX and at least every 6 months while you, or the patient you care for, are using GATTEX.

Tell your doctor right away if you get:

- Stomach area (abdomen) pain and tenderness
- Chills
- Fever
- Change in your stools
- Nausea
- Vomiting
- Dark urine
- Yellowing of your skin or the whites of eyes

What Can I Do to Help Lower the Risks of GATTEX?

Tell your doctor if you, or the patient you care for, have:

- Cancer or a history of cancer
- Had polyps anywhere in your bowel (intestines) or rectum
- Heart problems
- High blood pressure
- Problems with your gallbladder, pancreas, kidneys
- Any other medical condition
- Are pregnant or planning to become pregnant. It is not known if GATTEX will harm your unborn baby. Tell your doctor right away if you become pregnant while using GATTEX.
- Are breastfeeding or plan to breastfeed. It is not known if GATTEX passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby while using GATTEX. Breastfeeding is not recommended during treatment with GATTEX.
- Are taking medicines, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Using GATTEX with certain other medicines may cause side effects.

Where Can I Get More Information on GATTEX?

For more information about the GATTEX REMS, visit GATTEXREMS.com. Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

Please read the Medication Guide in full and ask your doctor if you have any questions. A copy of the Medication Guide can be obtained by visiting www.GATTEXREMS.com or by calling 1-855-5GATTEX (1-855-542-8839) to obtain a hard copy.





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GATTEX REMS (Risk Evaluation and Mitigation Strategy)

A REMS (Risk Evaluation and Mitigation Strategy) is a program required by the Food and Drug Administration (FDA) to manage known or potential serious risks associated with a drug product.

The purpose of the GATTEX REMS is to inform healthcare providers, patients and caregivers about the following risks:

- Possible acceleration of neoplastic growth and Enhancement of colon polyp growth
- Gastrointestinal obstruction
- Biliary and pancreatic disorders

Prescribers who intend to treat patients with GATTEX should review the educational materials and complete the Post-Training Knowledge Assessment Questions.

Retraining is also available for prescribers who have not written a prescription for GATTEX within 12 months of completing assessment questions.

FOLLOW THE TWO STEP PROCESS BELOW FOR INITIAL TRAINING OR RETRAINING:



Review the Prescriber Education Slide Deck



Complete your Post-Training Knowledge Assessment Questions



FOR HEALTHCARE PROVIDERS

- + [Dear Healthcare Professional Letter](#)
- + [Prescriber Education Slide Deck](#)
- + [Post-Training Knowledge Assessment Questions](#)
- + [Patient & Caregiver Counseling Guide](#)
- + [Prescribing Information](#)
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Interested in taking a GATTEX REMS Healthcare Provider Survey? Click Below

[Get started](#)





GATTEX REMS (Risk Evaluation and Mitigation Strategy)

GATTEX® (teduglutide) REMS Prescriber Education Slide Deck

Shire-NPS Pharmaceuticals, Inc.
300 Shire Way, Lexington, MA 02421

A REMS (Risk Evaluation and Mitigation Strategy) is a program required by the FDA to manage known or potential serious risks associated with a drug product. The Prescriber Education Slide Deck is required by the FDA as part of the GATTEX REMS.

05/2019



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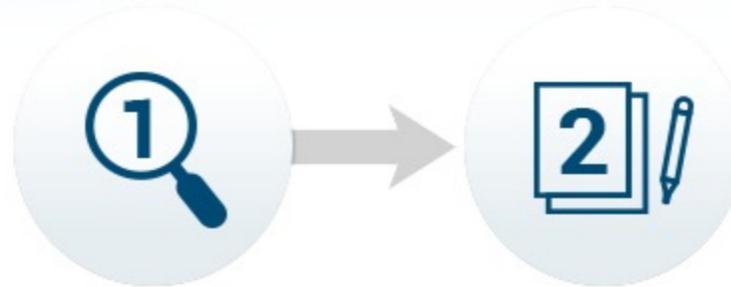


GATTEX REMS (Risk Evaluation and Mitigation Strategy)

**You have completed the
Prescriber Education Slide Deck.**

[Continue](#)

Next step: Complete your Post-Training Knowledge Assessment Questions.



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Prescriber Training - Welcome

You have selected to take the Post-Training Knowledge Assessment Questions.

Before completing your Post-Training Knowledge Assessment Questions, you should review the Prescriber Education Slide Deck.

If you have already reviewed the Prescriber Education Slide Deck, please begin the Post-Training Knowledge Assessment Questions.

If this is your first time taking the Post-Training Knowledge Assessment Questions, please select "First-Time Prescriber". If you are taking Retraining, please select "Prescriber Retraining".

First-Time
Prescriber

Prescriber
Retraining

Prescriber Training - Identification

NPI:

First Name:

Last Name:

Submit

Prescriber Retraining

Our records indicate that you have previously taken the GATTEX assessment. Please select "Prescriber Retraining" if you would like to complete retraining. For additional assistance, please call the GATTEX REMS Coordination Center at 1-855-5GATTEX (1-855-542-8839). Thank you.



Prescriber Training - Identification

NPI:

First Name:

Last Name:

Submit

First-Time Prescriber

Our records indicate that you have not previously taken the GATTEX assessment. Please select "First-Time Prescriber". For additional assistance, please call the GATTEX REMS Coordination Center at 1-855-5GATTEX (1-855-542-8839). Thank you.

**You have successfully completed
Prescriber Retraining, and your
responses have been recorded. Thank
you.**

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

JOYCE A KORVICK
02/11/2021 10:30:57 AM