# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 203441Orig1s000

# REMS

Initial REMS Approved: 12/21/2012

**NDA 203441 GATTEX®**
**(Teduglutide [rDNA origin]) for Injection**

NPS Pharmaceuticals
550 Hills Drive, 3rd Floor
Bedminster, NJ07921

**RISK EVALUATION AND MITIGATION STRATEGY (REMS)**

# I. GOAL

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.

# II. REMS ELEMENTS

## A. Communication Plan

NPS will implement a communication plan to support implementation of the REMS. The communication plan materials will comprise:

1. **A Dear Healthcare Professional letter** to gastroenterologists, colorectal and gastrointestinal tract surgeons. In order to facilitate prescriber training and education, this initial letter will be distributed within 60 days of approval of GATTEX or at the time of product launch, whichever is sooner. The letter will be sent again at 12 and 24 months after product approval. NPS will also identify and send the DHCP letter to all other GATTEX prescribers within 60 days of the date of initial prescription, and again at 12 and 24 months after their initial prescription. This letter will be distributed via direct mail or electronic delivery and will be accessible via the GATTEX REMS website (www.GATTEXREMS.com). A copy of the Full Prescribing Information and a Medication Guide will be included in the Dear Healthcare Professional letter.

2. **A Dear Professional Society letter** to the leadership of the professional organizations listed below requesting that the letter be provided to the members of these professional organizations. The Dear Professional Society letter will be disseminated via direct mail or electronic delivery within 60 days of approval of GATTEX or at the time of

product launch, whichever is sooner. The letter will be sent again at 12 and 24 months after product approval. A copy of the Full Prescribing Information and a Medication Guide will be included in the Dear Professional Society letter.

i. American Society for Parenteral and Enteral Nutrition
ii. American Gastroenterological Association
iii. American College of Gastroenterology
iv. Society for Surgery of the Alimentary Tract
v. American Society of Colon and Rectal Surgery
vi. American Board of Physician Nutrition Specialists (ABPNS)

The Dear Healthcare Professional letter and the Dear Professional Society letter are part of the REMS and are appended.

The Dear Healthcare Professional letter and the Dear Professional Society letter will be provided to MedWatch at the same time they are provided to the healthcare professionals and the professional society leadership.

## B. Elements To Assure Safe Use

1. Healthcare providers who prescribe GATTEX will receive training.

   a. NPS Pharmaceuticals will ensure that training is made available to healthcare providers who prescribe GATTEX. Training will consist of the Prescriber Education Slide Deck.

   b. Each prescriber will be provided with the **Prescriber Education Slide Deck** which will include the following information:

      i. The risks of possible acceleration of neoplastic growth and enhancement of colon polyp growth associated with GATTEX.

      ii. The serious risk of gastrointestinal obstruction associated with GATTEX.

      iii. The serious risk of biliary and pancreatic disorders associated with GATTEX.

      iv. The recommended screening colonoscopy, follow-up colonoscopy, and monitoring laboratory tests

   c. NPS will ensure that the Prescriber Education Slide Deck will be available in hard copy and on the GATTEX REMS website.

   NPS will ensure that prescribers can report that they have completed the Prescriber Education Slide Deck.

   d. NPS will maintain a list of healthcare providers (HCPs) who have completed the Prescriber Education Slide Deck.

e. In order to facilitate patient and/or caregiver education about GATTEX, NPS will ensure that the **Patient and Caregiver Counseling Guide** will be available for prescribers to use to counsel patients considering GATTEX therapy about the possible acceleration of neoplastic growth and enhancement of colon polyp growth, gastrointestinal obstruction, and biliary and pancreatic disorders associated with GATTEX, as well as the recommended screening colonoscopy, follow-up colonoscopy and monitoring laboratory tests.

f. NPS will ensure that all educational materials listed in or appended to the GATTEX REMS will be available through the GATTEX REMS website, www.GATTEXREMS.com.

g. The following materials are part of the GATTEX REMS and are appended:

- *Prescriber Education Slide Deck*
- *Patient and Caregiver Counseling Guide*
- *GATTEX REMS Website Screenshots*

These materials will also be available by calling NPS Pharmaceuticals at 1-855-5GATTEX or 1-855-542-8839.

## C. Timetable for Submission of Assessments

NPS will submit REMS assessments to FDA at 12 months from the date of initial approval of the REMS 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 days before the submission date for that assessment. NPS will submit each assessment so that it is received by the FDA on or before the due date.

Gattex®
(Teduglutide [rDNA origin]) for Injection

**[Date]**

**IMPORTANT DRUG WARNING**

Subject: Risk of possible acceleration of neoplastic growth and enhancement of colon polyp growth, GI obstruction, and biliary and pancreatic disorders with GATTEX® (teduglutide)

Dear Healthcare Professional:

The purpose of this letter is to inform you that GATTEX® (Teduglutide [rDNA origin]) for Injection has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of adult patients with Short Bowel Syndrome (SBS) who are dependent on parenteral support.

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 of GATTEX

### Possible acceleration of neoplastic growth and enhancement of colon polyp growth

- *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 with active gastrointestinal malignancy (GI tract, hepatobiliary, pancreatic), GATTEX therapy should be discontinued. In patients with active non-gastrointestinal malignancy, the clinical decision to continue GATTEX should be made based on risk-benefit considerations.

- *Colorectal Polyps*

Colorectal polyps were identified during the clinical trials. Colonoscopy of the entire colon with removal of polyps must 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.

- *Small Bowel Neoplasia*

Based on benign tumor findings in the rat carcinogenicity study, 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.

### Gastrointestinal obstruction

- Intestinal obstruction has been reported in clinical trials. 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.

**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 must 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. If clinically meaningful changes are seen, further evaluation including imaging of the gallbladder and/or biliary tract is recommended; and the need for continued GATTEX treatment should be reassessed

- *Pancreatic Disease*

Pancreatitis has been reported in clinical studies. For identification of onset or worsening of pancreatic disease, patients must 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. If clinically meaningful changes are seen, further evaluation such as imaging of the pancreas is recommended; and the need for continued GATTEX treatment should be reassessed.

## Appropriate Patient Selection, Counseling, and Monitoring

Prescribers should select the appropriate patients to receive GATTEX in accordance with the approved prescribing information, discuss the benefits and risks of GATTEX with patients, and monitor patients as specified in the approved prescribing information. A Patient and Caregiver Counseling Guide is available for your 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

It is important that healthcare providers understand the serious risks associated with GATTEX. As part of the REMS, healthcare providers should access www.GATTEXREMS.com to review the Prescriber Education Slide Deck and complete a Post-training Knowledge Assessment. The Prescriber Education Slide Deck and the Post-training Knowledge Assessment can also be obtained in hard copy by contacting 1-855-5GATTEX (1-855-542-8839).

## Reporting Adverse Events

To report all suspected adverse events associated with the use of GATTEX, contact

- NPS Pharmaceuticals, toll-free GATTEX Support Line at 1-855-5GATTEX (1-855-542-8839) or Event/Product Complaint Line at 1-855-215-5550,
- FDA MedWatch program at 1-800-FDA-1088 (1-800-332-1088), or via the FDA website at www.fda.gov/medwatch./report.htm

A copy of the letter is available at www. GATTEXREMS.com and through NPS Medical Information (1-855-5GATTEX or 1-855-542-8839). For more information regarding GATTEX, please contact the toll-free GATTEX Support Line at 1-855-5GATTEX (1-855-542-8839) or visit the product website at www.GATTEX.com.

This letter is not a complete description of the risks associated with GATTEX. Please see the enclosed full Prescribing Information for GATTEX for additional safety information.

Gattex
(Teduglutide [rDNA origin]) for Injection

Sincerely,

Roger Garceau, M.D.
Chief Medical Officer
NPS Pharmaceuticals

Enclosures:

- GATTEX Full Prescribing Information
- Medication Guide

**[Date]**

**IMPORTANT DRUG WARNING**

Subject: Risk of possible acceleration of neoplastic growth and enhancement of colon polyp growth, GI obstruction, and biliary and pancreatic disorders with GATTEX® (teduglutide)

Dear Professional Society Leader:

The purpose of this letter is to inform you that GATTEX® (Teduglutide [rDNA origin]) for Injection has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of adult patients with Short Bowel Syndrome (SBS) who are dependent on parenteral support.

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. The REMS includes a healthcare provider education and training.

**We are sending your organization this communication to distribute to members of your organization who may be appropriate prescribers of Gattex.**

## Serious Risks of Gattex

### Possible acceleration of neoplastic growth and enhancement of colon polyp growth

- *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 with active gastrointestinal malignancy (GI tract, hepatobiliary, pancreatic), GATTEX therapy should be discontinued. In patients with active non-gastrointestinal malignancy, the clinical decision to continue GATTEX should be made based on risk-benefit considerations.

- *Colorectal Polyps*

Colorectal polyps were identified during the clinical trials. Colonoscopy of the entire colon with removal of polyps must 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.

- *Small Bowel Neoplasia*

Based on benign tumor findings in the rat carcinogenicity study, 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.

### Gastrointestinal obstruction

- Intestinal obstruction has been reported in clinical trials. 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.

**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 must 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. If clinically meaningful changes are seen, further evaluation including imaging of the gallbladder and/or biliary tract is recommended; and the need for continued GATTEX treatment should be reassessed

- *Pancreatic Disease*

Pancreatitis has been reported in clinical studies. For identification of onset or worsening of pancreatic disease, patients must 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. If clinically meaningful changes are seen, further evaluation such as imaging of the pancreas is recommended; and the need for continued GATTEX treatment should be reassessed.

## Appropriate Patient Selection, Counseling, and Monitoring

Prescribers should select the appropriate patients to receive GATTEX in accordance with the approved prescribing information, discuss the benefits and risks of GATTEX with patients, monitor patients as specified in the approved prescribing information and report adverse events to NPS Pharmaceuticals.

## GATTEX Healthcare Provider Training

It is important that healthcare providers understand the serious risks associated with GATTEX. As part of the REMS, healthcare providers should access www.GATTEXREMS.com to review the Prescriber Education Slide Deck and complete a Post-training Knowledge Assessment. The Prescriber Education Slide Deck and the Post-training Knowledge Assessment can also be obtained in hard copy by contacting 1-855-5GATTEX (1-855-542-8839).

## Reporting Adverse Events

To report all suspected adverse events associated with the use of GATTEX, contact

- NPS Pharmaceuticals, toll-free GATTEX Support Line at 1-855-5GATTEX (1-855-542-8839) or Event/Product Complaint Line at 1-855-215-5550,
- FDA MedWatch program at 1-800-FDA-1088 (1-800-332-1088) or via the FDA website at www.fda.gov/medwatch./report.htm

A copy of the letter is available at www. GATTEXREMS.com or via NPS Medical Information (1-855-5GATTEX).

Should your members require additional information about GATTEX, please direct them to contact the toll-free GATTEX Support Line at 1-855-5GATTEX (1-855-542-8839) or visit the product website at www.GATTEX.com.

This letter is not a complete description of the risks associated with GATTEX. Please see the enclosed full Prescribing Information for GATTEX for additional safety information.

Gattex
(Teduglutide [rDNA origin]) for Injection

Sincerely,

Roger Garceau, M.D.
Chief Medical Officer
NPS Pharmaceuticals

Enclosures:

- GATTEX full Prescribing Information
- Medication Guide

# GATTEX® (Teduglutide [rDNA origin]) for Injection
## For subcutaneous use only

NPS Pharmaceuticals, Inc.
550 Hills Drive, Bedminster, NJ 07921

Reference ID: 3235717

# Table of Contents



Gattex® (Teduglutide [rDNA origin]) for Injection



Reference ID: 3235717

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

GLP-2, glucagon-like peptide-2

# Overview
## Important Adverse Reactions of Special Interest

- Possible safety risks with GATTEX
  - Possible acceleration of neoplastic growth and enhanced growth of colorectal polyps
  - Gastrointestinal 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 with narrow therapeutic index

Gattex®
(Teduglutide [rDNA origin]) for Injection



Reference ID: 3235717

# 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 can not be excluded that GATTEX promotes growth of existing neoplasms in the GI tract
- 3 patients on GATTEX were reported with neoplasms*:
  - 2 cases of lung cancer with smoking history
  - 1 case of GI metastatic adenocarcinoma (unknown origin) following abdominal radiation for Hodgkin's disease

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

* As of October 30th, 2011

Gattex® (Teduglutide [rDNA origin]) for Injection

# 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.*
- *Based on benign tumor findings in the rat carcinogenicity study, 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.*
- *In patients with active gastrointestinal malignancy (GI tract, hepatobiliary, pancreatic), GATTEX therapy should be discontinued.*
- *In patients with active non-gastrointestinal malignancy, the clinical decision to continue GATTEX should be made based on risk-benefit considerations.*
- *In patients at increased risk for malignancy, the clinical decision to use GATTEX should be considered only if the benefits outweigh the risks.*

Gattex®
(Teduglutide [rDNA origin]) for Injection

# Possible Enhanced Growth of Colorectal Polyps

- 4/173 (2.3%) GATTEX-treated patients developed GI polyps in pooled Phase III SBS studies*
  - 2 villous adenomas
  - 2 hyperplastic
- GATTEX mechanism of action and nonclinical data are consistent with a potential to enhance growth of polyps

* As of October 30th, 2011

Gattex® (Teduglutide [rDNA origin]) for Injection

# Possible Enhanced Growth of Colorectal Polyps
# GATTEX Label – Warnings and Precautions

*Colorectal Polyps*

- *Colonoscopy of the entire colon with removal of polyps must 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.*

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# Gastrointestinal Obstruction

- 12 patients experienced one or more episodes of intestinal obstruction/stenosis*
  - 6 in SBS placebo-controlled studies
    - 3/77 (3.9%) on GATTEX, 0.05 mg/kg/day
    - 3/32 (9.4%) on GATTEX, 0.05 mg/kg/day
    - None in placebo-group
    - Onset 1 day to 6 months
  - 6 in the extension studies (all on GATTEX, 0.05 mg/kg/day)
    - Onset 6 days to 7 months
  - Of all of these patients, 1 patient required endoscopic dilatation; and none required surgical intervention

* As of October 30th, 2011

Gattex® (Teduglutide [rDNA origin]) for Injection

# Gastrointestinal Obstruction
# GATTEX Label – Warnings and Precautions

*Intestinal Obstruction*

- *Intestinal obstruction has been reported in clinical trials.*
- *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.*

Gattex® (Teduglutide [rDNA origin]) for Injection

# Gallbladder and Biliary Tract Disease

- 11/173 (6.4%) of GATTEX-treated patients reported biliary events, including cholecystitis and gallstones/sludge in pooled Phase III SBS studies*
  - 5 patients had a history of biliary disease
  - None of these events resulted in study withdrawal

* As of October 30th, 2011

Gattex® (Teduglutide [rDNA origin]) for Injection

# 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 .*
- *Patients must undergo initial (within 6 months prior) laboratory assessment of bilirubin and alkaline phosphatase.*
- *Subsequent laboratory assessments are recommended every 6 months; if a clinically meaningful elevation is seen imaging of the biliary tract is recommended to identify possible obstruction.*

Gattex® (Teduglutide [rDNA origin]) for Injection

# Pancreatic Disease

- 3/173 (1.7%) of GATTEX-treated patients developed pancreatitis in pooled Phase III SBS studies*
  - All 3 patients had a history of pancreatitis
  - None of these events resulted in study withdrawal

* As of October 30th, 2011

Gattex® (Teduglutide [rDNA origin]) for Injection

# Pancreatic Disease
# GATTEX Label – Warnings and Precautions

*Pancreatic Disease*

- *Pancreatitis has been reported in clinical studies.*
- *Patients must undergo initial (within 6 months prior) laboratory assessment of lipase and amylase.*
- *Subsequent laboratory assessments are recommended every 6 months; if a clinically meaningful elevation is seen imaging of the pancreas is recommended to identify possible obstruction.*

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Reference ID: 3235717

# Fluid Overload

- 23/173 (13.3%) of patients treated with GATTEX reported fluid overload in pooled Phase III SBS studies*
- Fluid overload should be considered when administering GATTEX in patients with underlying heart disease

* As of October 30th, 2011

Gattex® (Teduglutide [rDNA origin]) 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.*

Gattex® (Teduglutide [rDNA origin]) for Injection

# PN/IV Volume Adjustment

- In order to reduce risk for fluid overload the following PN/IV volume adjustment algorithm is suggested
  - Determine pre-treatment urine output (ideally 1 to 2 L/day)
  - Determine urine output  2 to 4 weeks after starting treatment
  - Reduce weekly PN/IV volume by 10% to 30% if urine output increased at least 10% compared with pre-treatment volume
  - Evaluate if the patient tolerated the PN/IV reduction 1 to 2 weeks later
  - Continue monitoring urine output on a regular basis and adjust PN/IV volume accordingly with the goal of reducing or achieving complete independence from PN/IV support and maintaining clinical nutrition status

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# Increased Absorption of Concomitant Oral Medication

- 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 medication requiring titration or that have a narrow therapeutic index

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# Increased Absorption of Concomitant Oral Medication
# GATTEX Label – Warnings and Precautions

*Risks Resulting from 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, etc.) requiring titration or with a narrow therapeutic index may require dose adjustment while on GATTEX.*

Gattex®
(Teduglutide [rDNA origin]) for Injection

# GATTEX® Patient and Caregiver Counseling Guide

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.

**Healthcare providers:** Please review this guide with your patient and/or your patient's caregiver.

**Patients:** Please read the enclosed Medication Guide in full and ask your doctor if you have any questions.

Reference ID: 3235717

## Understanding the Risks With GATTEX®

**GATTEX may cause serious side effects, including:**

- **Making abnormal cells grow faster.** GATTEX can make abnormal cells that are already in your body grow faster. There is a higher chance the abnormal cells could become cancer. If you get cancer of the bowel (intestines), liver, gallbladder, or pancreas while using GATTEX, your healthcare provider should stop GATTEX.
- If you get other types of cancers, you and your healthcare provider should discuss the risks and benefits of using GATTEX.

**Polyps in the colon (large intestine).** Polyps are growths on the inside of the colon.
**Before you start using GATTEX, your healthcare provider will:**

- Have your colon checked for polyps within 6 months before starting GATTEX
- Have any polyps removed

**To keep using GATTEX, your healthcare provider should:**

- Have your colon checked for new polyps at the end of 1 year of using GATTEX. If no polyp is found, your healthcare provider should check you for polyps as needed and at least every 5 years.
- Have any new polyps removed

If cancer is found in a polyp, your healthcare provider should stop GATTEX.

**Blockage of the bowel (intestines).** A bowel blockage keeps food, fluids, and gas from moving through the bowels in the normal way. Tell your healthcare provider if you have any of these symptoms of a bowel blockage:

- 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

If blockage is found, your healthcare provider may temporarily stop GATTEX.

**Swelling (inflammation) or blockage of your gallbladder or pancreas.**

Your healthcare provider will do tests to check your gallbladder and pancreas within 6 months before starting GATTEX and at least every 6 months while you are using GATTEX.

Tell your healthcare provider 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



## Monitor Your Treatment With GATTEX

**GATTEX may cause serious side effects, including:**

- **Fluid overload.** Your healthcare provider will check you for too much fluid in your body. Too much fluid in your body may lead to heart failure, especially if you have heart problems. Tell your healthcare provider if you get swelling in your feet and ankles, you gain weight very quickly (water weight), or you have trouble breathing.
- See “Understanding the risks with GATTEX” on page 2 of this guide

**The most common side effects of GATTEX include:**

- Stomach area (abdomen) pain or swelling
- Cold or flu-like symptoms
- Nausea
- Vomiting
- Holding too much fluid in the body (swelling of face, ankles, hands or feet)

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

**Please read the enclosed Medication Guide.**

Gattex®
(Teduglutide [rDNA origin]) for Injection

## The GATTEX® Discussion

**Before you use GATTEX, tell your healthcare provider if you:**

- Have cancer or a history of cancer
- Have or had polyps anywhere in your bowel (intestines) or rectum
- Have heart problems
- Have high blood pressure
- Have problems with your gallbladder, pancreas, kidneys
- Have any other medical condition
- Are pregnant or planning to become pregnant. It is not known if GATTEX will harm your unborn baby. Tell your healthcare provider 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. You and your healthcare provider should decide if you will use GATTEX or breastfeed. You should not do both.

**Tell your healthcare providers about all the oral medicines you take,** including prescription and over-the-counter medicines, vitamins, and herbal supplements. Using GATTEX with certain other oral medicines may affect each other causing side effects.

Your other healthcare providers may need to change the dose of any oral medicines you take while using GATTEX. Tell the healthcare provider who gives you GATTEX if you will be taking a new oral medicine.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

**Remember:**

- Tell your doctor if you have any side effect that bothers you or that does not go away
- You may report side effects to the FDA at 1-800-FDA-1088 (332-1088)
- You can also call the toll-free GATTEX Information Line at 1-855-5GATTEX (542-8839)

**For more information about GATTEX, visit www.GATTEXREMS.com.**

**Please read the enclosed Medication Guide.**

To learn more, visit www.GATTEXREMS.com.

nps pharmaceuticals

Gattex® (Teduglutide)

Gattex®
(Teduglutide [rDNA origin]) for Injection

# RISK EVALUATION AND MITIGATION STRATEGY (REMS)

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure that the benefits of a drug outweigh its risks. The FDA has required a REMS for GATTEX.

The purpose of the GATTEX REMS is to inform healthcare providers and patients 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 education and training materials before prescribing Gattex.

## FOR HEALTHCARE PROVIDERS

+ Dear Healthcare Professional Letter
+ Dear Professional Society Letter
+ Prescriber Education Slide Deck
+ Post-training Knowledge Assessment
+ Patient & Caregiver Counseling Guide
+ Full Prescribing Information
+ Medication Guide

## FOLLOW THE TWO STEP PROCESS BELOW:

1. Review the Prescriber Education Slide Deck
2. Take your Post-training Knowledge Assessment




Reference ID: 3235717

Gattex®
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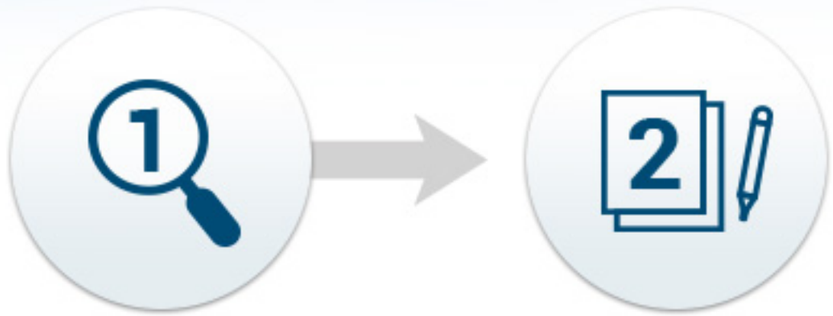
# RISK EVALUATION AND MITIGATION STRATEGY (REMS)

## You have completed the Prescriber Education Slide Deck.

Next step: Take your Post-training Knowledge Assessment. Continue

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+ Return to Prescriber Education Slide Deck

Gattex®
(Teduglutide [rDNA origin]) for Injection

You have selected to take the Knowledge Assessment for GATTEX.

Before completing your Post-training Knowledge Assessment, 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

Next

Notes:
This is the first screen that a user will come to when they select the link from the GATTEXREMS.com

Gattex®
(Teduglutide [rDNA origin]) for Injection

NPI:

First Name:

Last Name:

Next

Notes:
Based on the NPI, First Name and Last Name provided, we will check the GATTEX REMS Database and then the NPI database. If there is no match, we will display a message to have the person call 1-855-TEAMNPS for assistance.

Gattex®
(Teduglutide [rDNA origin]) for Injection

You are about to begin the GATTEX Knowledge Assessment.

You will need approximately 10 minutes to complete the assessment. After 20 minutes of inactivity, your session will expire and you will be logged out of the Knowledge Assessment.

You will need to complete the assessment in its entirety from start to finish in order to have your information saved.
Please click the start button to begin the Post-training Knowledge Assessment.

Start

Notes:
This is the screen prior to getting to the knowledge assessment.

Gattex®
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Date: <Completion date>
NPI Number: <NPI Number>
HCP Name: <First Name> <Last Name>

Certificate Completion #: <Certificate Completion Number>

This certificate confirms that you have completed the GATTEX Knowledge Assessment

Please print a copy of this certificate for your records.
Once you have printed the certificate, please close the window

Print Certificate

Notes:
After the last question in the Knowledge Assessment, the user will be presented with the following Web page.
Anything list between the characters "<>" will be pulled from a database
When the user clicks Print Certificate, another window will open with the text to be printed.

Date: <Completion date>
NPI Number: <NPI Number>
HCP Name: <First Name> <Last Name>

Certificate Completion #: <Certificate Completion Number>

This certificate confirms that you have completed the GATTEX Knowledge Assessment

Please print a copy of this certificate for your records.
Once you have printed the certificate, please close the window

Notes:
Window after the user clicks Print Certificate.

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

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/s/

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VICTORIA KUSIAK
12/21/2012