

FDA warns about an increased risk of serious pancreatitis with irritable bowel drug Viberzi (eluxadoline) in patients without a gallbladder

### Safety Announcement

**[03-15-2017]** The U.S. Food and Drug Administration (FDA) is warning that Viberzi (eluxadoline), a medicine used to treat irritable bowel syndrome with diarrhea (IBS-D), should not be used in patients who do not have a gallbladder. An FDA review found these patients have an increased risk of developing serious pancreatitis that could result in hospitalization or death. Pancreatitis may be caused by spasm of a certain digestive system muscle in the small intestine. As a result, we are working with the Viberzi manufacturer, Allergan, to address these safety concerns.

**Patients** should talk to your health care professional about how to control your symptoms of irritable bowel syndrome with diarrhea (IBS-D), particularly if you do not have a gallbladder. The gallbladder is an organ that stores bile, one of the body's digestive juices that helps in the digestion of fat. Stop taking Viberzi right away and get emergency medical care if you develop new or worsening stomach-area or abdomen pain, or pain in the upper right side of your stomach-area or abdomen that may move to your back or shoulder. This pain may occur with nausea and vomiting. These may be symptoms of pancreatitis, an inflammation of the pancreas, an organ important in digestion; or spasm of the sphincter of Oddi, a muscular valve in the small intestine that controls the flow of digestive juices to the gut.

**Health care professionals** should not prescribe Viberzi in patients who do not have a gallbladder and should consider alternative treatment options in these patients. Hospitalizations and deaths due to pancreatitis have been reported with Viberzi use in patients who do not have a gallbladder. Symptoms of pancreatitis have occurred with just one or two doses of Viberzi at the recommended dosage for patients who do not have a gallbladder (75 mg) and who do not consume alcohol.

Physicians can consider both over-the-counter (OTC) or FDA-approved prescription medicines to treat symptoms associated with IBS-D such as OTC bismuth subsalicylate (Kaopectate and Pepto-Bismol), OTC loperamide (Imodium), and prescription medicine diphenoxylate/ atropine (Lomotil) for diarrhea. Also consider OTC medicines for gas relief such as simethicone (Gas-X, Mylicon). Other FDA-approved prescription medicines for IBS-D include alosetron hydrochloride (Lotronex) and the antibiotic rifaximin (Xifaxan).

Viberzi is a prescription medicine used to treat irritable bowel syndrome in adults when the main symptom is diarrhea (IBS-D). IBS-D affects the large intestine and causes cramping, stomach-area or abdomen pain, bloating, gas, and diarrhea. The cause of IBS-D is not known. Viberzi works by decreasing bowel contractions, which leads to less diarrhea. In patients with IBS-D, Viberzi can help ease stomach-area or abdomen pain and improve stool consistency.

From May 2015, when Viberzi was first approved, through February 2017, FDA received 120 reports of serious cases of pancreatitis or death.\* Among the 68 patients who reported their gallbladder status, 56 of them did not have a gallbladder and received the currently recommended dosage of Viberzi. Seventy-six patients were hospitalized, of which two patients died. These two patients did not have a gallbladder. Some cases of serious pancreatitis or death also reported sphincter of Oddi spasm (n=6) or abdominal pain (n=16) (see Data Summary).

We urge patients and health care professionals to report side effects involving Viberzi (eluxadoline) or other medicines to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of the page.

\*The cases were reported to the [FDA Adverse Event Reporting System \(FAERS\)](#).

### **Facts about Viberzi (eluxadoline)**

- Viberzi (eluxadoline) is approved for use in adults for the treatment of irritable bowel syndrome with diarrhea (IBS-D). It is a tablet taken by mouth twice a day with food.
- Viberzi works by activating opioid receptors in the gut to decrease bowel contractions, which leads to less diarrhea. It can also help to ease stomach-area or abdomen pain and improve stool consistency.
- Viberzi is a controlled substance (CIV) and may be abused or lead to drug dependence.
- Avoid using alcohol and other diarrhea medicines while taking Viberzi.
- Use Viberzi along with lifestyle changes, such as limiting foods that aggravate your symptoms, eating more slowly and not overeating, and avoiding carbonated drinks, which can lead to gas and cramping. Some information can be found at the [National Institute of Diabetes and Digestive and Kidney Diseases](#) website.
- Common side effects of the medicine include constipation, nausea, and stomach-area or abdomen pain.
- From May 2015 through July 2016, a nationally estimated number of 34,000 patients received a dispensed prescription for Viberzi (eluxadoline) from U.S. outpatient retail pharmacies. In the same time period, approximately 64,000 Viberzi prescriptions were dispensed from U.S. outpatient retail pharmacies.<sup>1,2</sup>

### **Additional Information for Patients**

- Patients who do not have a gallbladder should not take Viberzi. Patients who do not have a gallbladder who are taking Viberzi have an increased risk of developing new or worsening stomach-area or abdomen pain due to pancreatitis with or without sphincter of Oddi spasm.
- Hospitalizations related to pancreatitis, including deaths, have been reported with Viberzi in patients who do not have a gallbladder. Hospitalizations related to pancreatitis have also been reported in patients with a gallbladder. Symptoms of pancreatitis can occur after just one or two doses of Viberzi.
- Stop taking Viberzi right away and get emergency medical care if you develop new or worsening stomach-area or abdomen pain, or pain in the upper right side of your stomach-area or abdomen that may move to your back or shoulder, with or without nausea and vomiting.
- While taking Viberzi, talk to your health care professional before you take any over-the-counter (OTC) medicines to treat diarrhea, constipation or other problems with your bowels or colon, and always take the OTC medicine according to the [Drug Facts Labels](#). Taking other diarrhea medicines while you are taking Viberzi can cause severe constipation.
- Before starting treatment with Viberzi, patients should tell their health care professional if they:
  - Have no gallbladder
  - Have or may have had a blockage in your gallbladder or a sphincter of Oddi problem
  - Have had inflammation of your pancreas
  - Have serious liver problems
  - Have a history of chronic constipation
  - Have or may have had a bowel blockage
  - Have a habit of drinking more than three alcoholic beverages a day
- Talk to your health care professional about how to control your symptoms of irritable bowel syndrome with diarrhea (IBS-D), particularly if you do not have a gallbladder.
- Lifestyle changes, such as limiting foods that aggravate your symptoms, eating more slowly and not overeating, and avoiding carbonated drinks which can lead to gas and cramping can help reduce the symptoms of IBS-D. Some information can be found at the [National Institute of Diabetes and Digestive and Kidney Diseases](#) website.
- Always tell your health care professionals about all the medicines you are taking, including OTC medicines.
- Talk to your health care professional if you are currently taking Viberzi and have any questions or concerns about the medicine.
- Read the patient [Medication Guide](#) that comes with each new Viberzi prescription because the information may have changed. The Medication Guide explains the risks associated with the use of the medicine.
- Report side effects from Viberzi to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of this page.

### **Additional Information for Health Care Professionals**

- Patients who do not have a gallbladder should not take Viberzi. Patients who do not have a gallbladder who are taking Viberzi for irritable bowel syndrome with diarrhea (IBS-D) have an increased risk of developing pancreatitis, sphincter of Oddi spasm, and death.
- Pancreatitis with and without sphincter of Oddi spasm can occur even after the first or second dose of Viberzi, independent of gallbladder status.
- Do not use Viberzi in the following patients:
  1. Who do not have a gallbladder
  2. Have or may have had a blockage of the gallbladder or a sphincter of Oddi problem
  3. Have had pancreatitis or other pancreas problems, including a blockage of the pancreas
  4. History of serious liver problems
  5. History of chronic or severe constipation
  6. Have or may have had intestinal obstruction
  7. History of alcohol abuse, alcohol addiction, or drinks more than three alcoholic beverages a day
- Counsel patients on managing stress and making changes in diet and lifestyle to help control symptoms of IBS-D.
- Tell patients to talk with a health care professional before taking any anti-diarrhea medicine, including over-the-counter medicines.
- Consider alternative treatment options before using Viberzi. Do not prescribe Viberzi in patients who do not have a gallbladder. Other FDA-approved prescription drugs used to treat IBS-D include Lotronex (alosetron hydrochloride) and antibiotic Xifaxan (rifaximin).
- Encourage patients to read the patient [Medication Guide](#) that comes with each new Viberzi prescription because the information may have changed. The Medication Guide explains the risks associated with the use of the medicine.
- Report adverse events involving Viberzi to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of this page.

## Data Summary

From May 2015, when Viberzi was first approved, through February 2017, FDA received reports of 120 serious cases of pancreatitis or death in the FDA Adverse Event Reporting System (FAERS) database. Seventy-six of these cases resulted in hospitalization, of which two patients died. Some cases of serious pancreatitis or death also reported sphincter of Oddi spasm (n=6) or abdominal pain (n=16).

Among the 84 cases that reported a time to onset of the adverse event, serious cases of pancreatitis or death occurred after one or two doses of Viberzi (n=48). Serious cases of pancreatitis also occurred subsequently with prolonged use (n=36).

Among the 68 cases that reported gallbladder status, 56 cases of pancreatitis or death occurred in patients who do not have a gallbladder. The majority of patients (n=44/56)

received the currently recommended dosage of Viberzi (75 mg) for patients who do not have a gallbladder. Of the 56 cases in patients who do not have a gallbladder, 21 reported that the patient did not abuse alcohol and 35 did not report the patient's alcohol use status.

As of February 2017, two deaths considered to be associated with Viberzi have been reported to FDA. Both deaths occurred in patients who did not have a gallbladder. One death was associated with pancreatitis and one death was associated with sphincter of Oddi spasm. The case of death from pancreatitis was characterized by acute, severe abdominal pain, nausea, and vomiting within 60 minutes of taking a single dose of Viberzi. The case of death associated with sphincter of Oddi spasm reported severe abdominal pain and vomiting shortly after taking the first dose of Viberzi. Both patients were hospitalized for treatment. Notably, the patient who experienced pancreatitis died within 3 days of taking the initial Viberzi dose.

### **References**

1. IMS Health, Total Patient Tracker (TPT), May 2015-July 2016. Extracted August 2016.
2. IMS Health, National Prescription Audit (NPA). May 2015-July 2016. Extracted August 2016.

### **Related Information**

[Irritable Bowel Syndrome Treatments Aren't One-Size-Fits-All](#)

[National Institute of Diabetes and Digestive and Kidney Diseases](#)

[The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective](#)

[Think It Through: Managing the Benefits and Risks of Medicines](#)