

28<sup>th</sup> September 2017

**Eluxadoline (Truberzi ▼): Risk of pancreatitis and sphincter of Oddi spasm**

Dear Healthcare professional,

Allergan Pharmaceuticals International Limited in agreement with the European Medicines Agency and MHRA would like to inform you of the following:

***Summary***

- **Truberzi should be initiated and supervised by a specialist physician experienced in diagnosis and management of gastrointestinal disorders.**
- **An increased risk of pancreatitis, sometimes fatal, and sphincter of Oddi spasm amongst patients taking Truberzi (eluxadoline) tablets has been identified; most cases of serious pancreatitis occurred in patients without a gallbladder.**
- **Eluxadoline is contraindicated in patients without a gallbladder and patients with known or suspected biliary tree and/or pancreatic duct obstruction (e.g. gallstones, tumour, periampullary duodenal diverticulum) or sphincter of Oddi disease or dysfunction.**

***Background on the safety concern***

Truberzi (eluxadoline) is a mu- and kappa-opioid receptor agonist and delta-opioid receptor antagonist approved for the treatment of irritable bowel syndrome with diarrhoea (IBS-D) in adults.

Serious risks with eluxadoline include pancreatitis and sphincter of Oddi spasm.

- Pancreatitis and sphincter of Oddi spasm have been reported in patients treated with eluxadoline, including serious cases resulting in hospitalisation and fatalities, primarily in patients without a gallbladder.
- Most of the reported cases of serious pancreatitis and sphincter of Oddi spasm occurred within a week of starting treatment with eluxadoline and some patients developed symptoms after one to two doses, but cases of pancreatitis after a longer duration of treatment have also been reported.

The Truberzi Product Information has been updated to provide additional warnings and precautions associated with pancreatitis, further clarification of the contraindications intended to reduce the risk of pancreatitis, as well as to add a restriction that therapy with eluxadoline should be initiated and supervised by a physician experienced in diagnosis and management of gastrointestinal disorders.

### ***Recommendations for risk minimization***

Among the contraindications with eluxadoline, doctors are reminded not to prescribe the medicine to patients in the following situations:

- Alcohol abuse
- Known or suspected biliary tree and/or pancreatic duct obstruction (e.g. gallstones, tumour, periampullary duodenal diverticulum) or sphincter of Oddi disease or dysfunction
- Patients without a gallbladder (e.g., due to cholecystectomy or agenesis)
- A history of pancreatitis or known or suspected structural diseases of the pancreas, including pancreatic duct obstruction

Physicians should:

- Confirm the patient's full medical history before prescribing eluxadoline
- Inform patients about symptoms suggestive of pancreatitis and sphincter of Oddi spasm and instruct them to stop treatment and seek medical attention if they experience these
- Instruct patients to avoid alcohol use
- Monitor patients for new or worsening abdominal pain
- Discontinue eluxadoline if symptoms of pancreatitis occur

### ***Call for reporting***

Healthcare providers and patients are encouraged to report suspected adverse drug reactions in patients taking Truberzi to Allergan and the MHRA via the Yellow Card Scheme. Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle ▼

It is easiest and quickest to report ADRs online via the Yellow Cards website -

<https://yellowcard.mhra.gov.uk/>

Alternatively, prepaid Yellow Cards for reporting are available:

- o by writing to FREEPOST YELLOW CARD (no other address details necessary)
- o by emailing [yellowcard@mhra.gsi.gov.uk](mailto:yellowcard@mhra.gsi.gov.uk)
- o at the back of the British National Formulary (BNF)
- o by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- o or by downloading and printing a form

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.

### ***Company contact point***


Adverse events: [UK\\_Medinfo@allergan.com](mailto:UK_Medinfo@allergan.com)

You may also contact our medical information department at:

Allergan Ltd, Marlow International, The Parkway, Marlow, SL7 1YL, United Kingdom  
Tel: +44 1628 494026  
Email: UK\_Medinfo@allergan.com

if you have any questions about the information contained in this letter or the safe and effective use of Truberzi.

Yours faithfully,

A handwritten signature in black ink, appearing to read "R Leaback". The signature is fluid and cursive, with a long horizontal stroke at the end.

Richard Leaback  
Country Medical Director