Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Xermelo 250 mg

Film-coated tablets

Each film-coated tablet contains:

telotristat ethyl (as etiprate) 250 mg

Inactive ingredients and allergens in this medicine - see section 6 **'Additional information'**. See also **'Important information about some of this medicine's ingredients'** in section 2.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

Xermelo in combination with a somatostatin analogs (SSA) is used to treat adults who have diarrhea associated with a condition called carcinoid syndrome, when their diarrhea is not sufficiently well controlled with somatostatin analog treatment.

Therapeutic group: substances that affect the digestive system and metabolism.

This medicine is used to treat adults with a condition called carcinoid syndrome. In this condition, a tumor, called a 'neuroendocrine tumor', releases a substance called serotonin into your bloodstream. When the tumor releases too much serotonin into your bloodstream you can get diarrhea. This medicine works by reducing the amount of serotonin made by the tumor, and this reduces the diarrhea you have.

Your doctor will prescribe this medicine if your diarrhea is not sufficiently well controlled with injections of other medicines called 'somatostatin analogs' (lanreotide or octreotide). You must keep having injections of these other medicines when taking Xermelo.

2. Before using this medicine

Do not use this medicine if:
- You are sensitive (allergic) to the active ingredient (telotristat ethyl) or to any of the other ingredients in this medicine (see section 6 **'Additional information'**).

Special warnings about using this medicine

Before taking Xermelo, tell your doctor or pharmacist if:
- you have liver problems. This is because this medicine is not recommended for use in patients with severe liver problems. If you have mild or moderate liver

problems, your doctor may decide to decrease your daily dose of Xermelo. Your doctor will also monitor your liver function.
- you have end-stage kidney disease or are on dialysis. This is because this medicine has not been tested in patients with end-stage kidney disease, requiring dialysis.

During treatment with Xermelo, tell your doctor immediately if you notice any of the following signs and symptoms that suggest that your liver may not be working properly:
- unexplained nausea or vomiting, abnormally dark urine, yellow skin or eyes, pain in the upper right belly.

Your doctor will carry out blood tests to check your liver function and will decide whether you should keep taking this medicine.

During treatment with Xermelo, tell your doctor or pharmacist if:
- you feel down, depressed, or if you feel you have no interest or take no pleasure in doing your normal activities.
- you have signs of constipation, as telotristat reduces bowel motility.

Children and adolescents
This medicine is not indicated for patients under 18 years of age. This is because the medicine has not been tested in this age group.

Tests and follow-up
Your doctor may carry out blood tests before you start taking this medicine and while you are taking it. This is to check that your liver is working properly.

Other medicines and Xermelo
If you are taking, have recently taken, or may take other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. This is because Xermelo can affect the way other medicines work, or other medicines can affect the way Xermelo works. Therefore your doctor may change the dose that you take. Tell your doctor about every medicine. This includes:
- medicines for diarrhea. Both Xermelo and these medicines reduce the number of bowel movements. Taking them together can cause severe constipation. Your doctor may need to change the dose of your medicines.
- medicines used to treat epilepsy, such as valproic acid.
- medicines used to treat the neuroendocrine tumor you have, such as sunitinib or everolimus.
- medicines to treat depression, such as bupropion or sertraline.
- medicines used to prevent transplant rejection, such as cyclosporine.
- medicines used to lower cholesterol levels, such as simvastatin.
- oral contraceptives, such as ethinylestradiol.
- medicines used to treat high blood pressure, such as amlodipine.
- medicines used to treat several cancer types, such as irinotecan, capecitabine and flutamide
- medicines used to reduce the risk of blood clot formation, such as prasugrel
- octreotide. If you need treatment with subcutaneous injections of octreotide, you should have your injection at least 30 minutes after taking Xermelo.

Using this medicine and food
Take this medicine with food.

Pregnancy, breastfeeding, and fertility
If you are pregnant or breastfeeding, think you might be pregnant or are planning to become pregnant, ask your doctor or pharmacist for advice before taking this medicine.
Do not take this medicine if you are pregnant or might become pregnant. It is not known how telotristat may affect the baby.
Women must use effective methods of contraception during treatment with this medicine.
Do not breastfeed if you are taking Xermelo, as this medicine may be passed on to your baby.

Driving and using machines
Xermelo may have a small effect on your ability to drive or use any tools or machines. If you feel tired, you should wait until you feel better before driving or using any tools or machines.

Important information about some of this medicine's ingredients
Xermelo contains lactose
Xermelo contains lactose (a type of sugar). If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicine.

Xermelo contains sodium
This medicine contains less than 23 mg sodium per tablet, that is to say essentially "sodium-free".

3. How to use this medicine?
Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

Only your doctor will determine your dose and how you should take this medicine. The recommended dose is usually one tablet (250 mg) three times a day. The maximum dose of Xermelo is 750 mg in 24 hours.

Your doctor will decide how long you should take Xermelo.
If you have liver problems, your doctor may decide to reduce your daily dose of Xermelo.
Take this medicine with food.
You should keep having injections of somatostatin analogs (lanreotide or octreotide) during the treatment with Xermelo.

How to take this medicine
There is no information about crushing, splitting, or chewing the tablets.

Do not exceed the recommended dose.

If you have accidentally taken a higher dose
You may feel nausea, or vomit, or have diarrhea or stomach ache. If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to take the medicine
If you forget to take your medicine at the scheduled time, skip the missed dose and take your next dose at the usual time.
Do not take a double dose to make up for a forgotten dose.

Adhere to the treatment as recommended by your doctor.
Do not stop taking this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose <u>every time</u> you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. <u>Side effects</u>

Like with all medicines, using Xermelo may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Consult your doctor immediately if you notice any of the following side effects:

- nausea and vomiting, abnormally dark urine, yellow skin or eyes, pain in the upper right belly.
  These may be signs that your liver is not working properly. This might also be shown by changes in your blood test results, such as an increase of liver enzymes: gamma-glutamyl transferase (very common, may affect more than 1 in 10 people), transaminases and blood alkaline phosphatase (common, may affect up to 1 in 10 people).

Other side effects
Tell your doctor, pharmacist, or nurse if you notice any of the following side effects:

<u>Very common side effects (affect more than one in ten users)</u>

- stomach ache
- feeling tired or weak
- feeling nausea

<u>Common side effects (affect 1-10 in 100 users)</u>

- wind
- fever
- headache
- constipation
- swollen stomach
- decreased appetite
- swelling (build-up of fluid in the body)
- depression, you may experience decreased self-esteem, lack of motivation, sadness or low mood

<u>Uncommon side effects (affect 1-10 in 1,000 users)</u>

- Impacted stools (bowel obstruction, faecaloma), you may experience constipation, watery diarrhea, pale skin (anemia), nausea, vomiting, weight loss, back pain or stomach pains particularly after eating or a reduction in passing water (urination).
  Tell your doctor immediately if you experience any of the following side effects:

- Breathing problems, rapid heartbeat, fever, incontinence (uncontrollable urination), confusion, dizziness or agitation.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects
You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use the medicine after the expiry date (exp. date) which is stated on the carton and blister tray. The expiry date refers to the last day of that month.

Storage conditions
Store below 30°C.

Do not throw away medicines via wastewater or household waste. Ask your pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:

Tablet content
lactose anhydrous, croscarmellose sodium, hydroxypropylcellulose, magnesium stearate, colloidal silicon dioxide.
Coating
Opadry II 85F18422 White components:
polyvinyl alcohol (partially hydrolyzed) (E1203), titanium dioxide (E171), macrogol/PEG (E1521), talc (E553b).

What the medicine looks like and contents of the pack
The tablets are white to off-white, film-coated and oval shaped, with 'T-E' debossed on one side and '250' debossed on the other.

The tablets are packaged in blister trays. The blister trays are packaged in a carton. Each carton contains 90 film-coated tablets.

Registration holder's name and address
Medison Pharma Ltd., 10 Hashiloah St., POB 7090, Petah Tikva.

Manufacturer's name and address
Ipsen Pharma, 65 quai Georges Gorse, 92100 Boulogne-Billancourt, France.

Revised in July 2021 according to MOH guidelines.

Registration number of the medicine in the Ministry of Health's National Drug Registry
161-97-35443-00