

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

This medicine is dispensed with a doctor's prescription only

**XPOVIO®**

**Tables 20 mg, 40 mg, 50 mg or 60 mg**

**Name of active ingredient and quantity in a dosage unit:**

Selinexor 20 mg, 40 mg, 50 mg or 60 mg

For a list of inactive ingredients and allergens in this medicine see section 6, 'Additional information' in this leaflet.

**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 for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

**1. What is this medicine intended for?**

- XPOVIO in combination with bortezomib and dexamethasone is intended to treat adult patients with multiple myeloma who have received at least one prior therapy.
- XPOVIO in combination with dexamethasone is intended to treat adults with relapsed or refractory multiple myeloma (RRMM), who have received at least 3 prior therapies, and whose disease was refractory to at least one proteasome inhibitor (PI) therapy, one immunomodulatory agent (IMiD), and an anti-CD38 monoclonal antibody (mAb).
- XPOVIO is intended to treat adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including diffuse large B-cell lymphoma arising from follicular lymphoma, after at least 2 lines of systemic therapy.

**Therapeutic group:** used to treat certain types of cancer by inhibiting XPO1.

XPOVIO inhibits the transporter exportin 1 (XPO1). XPO1 inhibition leads to accumulation of tumor-suppressor proteins in the nucleus, reduction in cancer proteins in cells, and death of cancer cells.

**2. Before using this medicine**

**Do not use this medicine if:**

- You are sensitive (allergic) to the active ingredient or to any of the other ingredients in this medicine (see section 6).

**Special warnings about using this medicine**

- Reduced number of neutrophils (neutropenia) - XPOVIO can cause a decrease in neutrophil levels. See the section 'Side effects' in this leaflet. Your doctor will monitor your neutrophil levels and may change your dose of XPOVIO or stop your treatment temporarily.
- Toxicity in the digestive system - See the section 'Side effects' in this leaflet.
- Decrease in sodium level - XPOVIO can cause a decrease in sodium levels (hyponatremia). Your doctor will monitor your serum sodium levels while you are taking XPOVIO. Your doctor may change your dose of XPOVIO, stop your treatment temporarily, or completely stop your treatment depending on your side effects. See the section 'Side effects' in this leaflet.

- Neurological toxicity - XPOVIO can cause neurological side effects. See the sections 'Driving and using machines' and 'Side effects' in this leaflet.

**Before using XPOVIO, tell your doctor if:**

- you have or have recently had an infection - XPOVIO can cause infections. See the section 'Side effects' in this leaflet.
- you have or have had bleeding - low platelet counts (thrombocytopenia) are common when using XPOVIO and can sometimes cause severe bleeding and even death. See the section 'Side effects' in this leaflet. Your platelet counts must be monitored while you are taking XPOVIO. If necessary, your treatment may be stopped either temporarily or permanently and/or your dose will be reduced, or you will be given supportive care. Your doctor may order a platelet transfusion or other treatments for your low platelet counts. **Tell your doctor right away if you have any bleeding or easy bruising during treatment with XPOVIO.**
- you are pregnant or are planning to have a baby. XPOVIO can harm your unborn baby. Please see the information under 'Pregnancy, breastfeeding, and fertility'.

**Children and adolescents:**

This medicine is not intended for children and adolescents under 18 years old. There is no information about how safe or effective this medicine is in children and adolescents under 18 years old.

**Tests and follow-up:**

- Your doctor may order blood tests, weight and nutritional state monitoring, and a blood volume test before and during treatment with XPOVIO. These tests will be more frequent during the first three months of treatment with XPOVIO, and later as needed. Your doctor may change your dose of XPOVIO, stop your treatment temporarily, or completely stop your treatment depending on your side effects.
- For information about tests and follow-up related to use at childbearing age (in men and women), please see the information under 'Pregnancy, breastfeeding, and fertility'.

**Drug interactions:**

**If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.**

**Using this medicine and food:**

You can take XPOVIO either with food or between meals.

It is important for you to eat enough calories to help prevent weight loss during treatment with XPOVIO. It is also important for you to drink enough fluids to prevent dehydration during treatment with XPOVIO.

**Pregnancy, breastfeeding, and fertility:**

Pregnancy

If you are pregnant, think you may be pregnant, or are planning to have a baby, consult your doctor before starting XPOVIO.

If you are a woman of childbearing potential, your doctor will order a pregnancy test before you start taking XPOVIO.

Consult your doctor right away if you become pregnant or think you might be pregnant during treatment with XPOVIO. There is no information about using XPOVIO in pregnant women. XPOVIO can harm your unborn baby.

#### Birth control

- **Women:** Women of child-bearing potential should use effective birth control during treatment with XPOVIO and for one week after their last dose of XPOVIO.
- **Men:** Men of child-bearing potential should use effective birth control during treatment with XPOVIO and for one week after their last dose of XPOVIO.

#### Breastfeeding

If you are breastfeeding, consult your doctor before starting XPOVIO.

Due to the possibility of serious side effects in a breastfed child, women should not breastfeed during treatment with XPOVIO and for one week after their last dose of XPOVIO.

There is no information regarding the presence of the medicine or its metabolites in breast milk, or their effects on the breastfed child or milk production.

#### Fertility

XPOVIO can impair fertility in women and in men. Consult your doctor if you have any further questions or concerns about fertility.

#### **Driving and using machines:**

Do not drive or operate dangerous machines while using XPOVIO, because it can cause tiredness, confusion, and dizziness.

#### **Important information about some of this medicine's ingredients:**

This medicine contains less than 1 mmol sodium (23 mg) per 100 mg dose, 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 - considering your medical condition and your side effects.

The recommended dose is usually:

- **In combination with dexamethasone for multiple myeloma:** 80 mg in combination with 20 mg of dexamethasone. Repeat the treatment twice a week: on the first and third day of every week.
- **In combination with bortezomib and dexamethasone for multiple myeloma:** as prescribed by your doctor for you.
- **For diffuse large B-cell lymphoma:** 60 mg. Repeat the treatment twice a week: on the first and third day of every week.

**Do not exceed the recommended dose.**

**Before and during treatment, your doctor will prescribe medicines to help prevent nausea and vomiting side effects. Tell your doctor if the prescribed medicine does not help control your nausea and vomiting.**

**It is important for you to eat and drink enough to prevent weight loss. Talk to your doctor if you notice that you are losing weight.**

**Treatment duration:**

Your doctor will decide how long you need to take this medicine based on your medical condition, how well the treatment is working, and your side effects.

**How to take this medicine:**

- Swallow the tablets whole with water.
- Do not break, chew, crush, or divide the tablets. This is because mild skin reactions were observed on contact with the contents of the tablets.
- Take the tablets at the same time of day every time.

**If you have accidentally taken a higher dose:** 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 or if you take your dose late,** take the next dose at the next regularly scheduled day and time for taking your medicine.

**If you vomit after taking this medicine,** do not take an extra dose. Take the next dose at the next regularly scheduled day and time for taking your medicine.

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop taking this medicine without consulting your doctor.

**Do not take medicines in the dark! Check the label and dose every time 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. Side effects**

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

**Serious side effects:**

**Very common side effects (affect more than one in ten users):**

- Low platelet counts in your blood - This side effect is very common when using XPOVIO and can sometimes cause severe bleeding and even death. Your doctor may order a platelet transfusion.  
**Tell your doctor right away if you have any of the following signs of reduced number of platelets:**  
**- tendency to bleeding or easy bruising.**
- Low white blood cell counts - Low white blood cell counts are common with XPOVIO and can sometimes be severe. You may have an increased risk of getting bacterial infections while you are using XPOVIO. Your doctor may prescribe antibiotics if you have signs or symptoms of infection, or certain medicines to help increase your blood count, if needed.
- Infections - Infections are very common with XPOVIO. These infections can be serious and can even cause death. You may get upper or lower respiratory tract infections, such as pneumonia, and an infection throughout your body

(sepsis). **Tell your doctor right away if you have a cough, chills or fever, during treatment with XPOVIO.**

- **Nausea and vomiting** - Nausea and vomiting are common with XPOVIO and can sometimes be severe. These side effects may affect your ability to eat and drink and may also make you lose body fluids and essential salts (electrolytes) causing dehydration. You may need to receive IV fluids or other treatments to help prevent dehydration. Your doctor will prescribe anti-nausea medicines for you to take before you start and during treatment with XPOVIO. Please see the information under 'How to use this medicine?'
- **Diarrhea** - Diarrhea is common with XPOVIO and can sometimes be severe. You can lose too much body fluids and essential salts (electrolytes). You may need to receive IV fluids or other treatments to help prevent dehydration. Your doctor will prescribe anti-diarrhea medicine for you as needed.
- **Loss of appetite and/or weight loss** - These side effects are very common with XPOVIO and can sometimes be severe. Tell your doctor straight away if you notice loss of appetite and/or if you notice that you are losing weight. Your doctor may change your dose of XPOVIO. Your doctor may also prescribe medicines to increase your appetite or prescribe nutritional support.
- **Decreased sodium levels** - This side effect is very common when using XPOVIO and can sometimes be severe. Low sodium levels in your blood can happen if you have nausea, vomiting, or diarrhea, and you become dehydrated. Also loss of appetite can cause decreased sodium. Your doctor will order blood tests before you start taking XPOVIO to check your blood sodium level. You may also be asked to do blood tests during your treatment with XPOVIO and also after your treatment has ended. These tests will be more frequent during the first two months of treatment with XPOVIO. Your doctor may change your dose of XPOVIO, depending on your blood sodium level. Your doctor may also prescribe a change in your diet, IV fluids and/or other medicines to raise the level of sodium in your blood.
- **Neurologic effects** - XPOVIO can cause neurologic side effects that can sometimes be severe and life-threatening. XPOVIO can cause: dizziness, fainting, decreased alertness, and changes in your mental status including confusion and decreased awareness of things around you (delirium). In some people, XPOVIO may also cause problems with thinking (cognitive problems), and seeing or hearing things that are not really there (hallucinations). XPOVIO can also make you very sleepy or drowsy. **Consult your doctor right away if you get any of these symptoms.** Your doctor may change your dose of XPOVIO or stop your treatment depending on your side effects.
- **New or worsening cataract, a cloudy or loss of transparency of the lens in the eye** - New or worsening cataract are common with XPOVIO. If a cataract forms, your vision may decrease, and you may need eye surgery to remove the cataract and restore your vision. Tell your doctor right away if you have symptoms of a cataract such as double vision, blurred vision, sensitivity to light or glare.

#### **Additional side effects:**

*Side effects that occurred in patients with multiple myeloma treated with XPOVIO in combination with bortezomib and dexamethasone:*

#### **Very common** (may affect more than 1 in 10 patients):

- fatigue
- fever

- nausea
- vomiting
- peripheral neuropathy
- dizziness
- upper respiratory tract infections
- weight loss
- diminished appetite
- cataract
- blurred vision
- decrease in platelet counts – thrombocytopenia
- decrease in lymphocyte counts – lymphopenia
- decrease in blood phosphate level – hypophosphatemia
- anemia
- decrease in blood sodium level – hyponatremia
- decrease in the neutrophil count – neutropenia

*Side effects that occurred in patients with multiple myeloma treated with XPOVIO in combination with dexamethasone:*

**Very common** (may affect more than 1 in 10 patients):

- upper respiratory infections
- lung inflammation (pneumonia)
- reduced platelet count (thrombocytopenia)
- anemia
- vomiting
- reduced number of neutrophils (neutropenia)
- reduced number of white blood cells (leucopenia)
- reduced number of lymphocytes (lymphopenia)
- loss of appetite
- weight loss
- decreased blood sodium (hyponatremia)
- increased blood sugar (hyperglycemia)
- dehydration
- increased blood creatinine (hypercreatininemia)
- decreased blood potassium (hypokalemia)
- changes in mental state
- insomnia
- dizziness
- changes in sense of taste
- headache
- blurred vision
- shortness of breath
- cough
- nosebleed
- nausea
- diarrhea
- constipation
- fatigue
- fever

*Side effects that occurred in patients with large B-cell lymphoma treated with XPOVIO:*

**Very common** (may affect more than 1 in 10 patients):

- upper respiratory infections
- lung inflammation (pneumonia)
- urinary tract infection
- loss of appetite
- weight loss
- dizziness
- changes in sense of taste
- changes in mental state
- peripheral neuropathy, sensory
- blurred vision
- lower blood pressure
- bleeding
- cough
- shortness of breath
- nausea
- diarrhea
- constipation
- vomiting
- stomach ache
- muscle and skeletal pain
- fatigue
- fever
- Edema (swelling)
- reduced platelet count
- decreased hemoglobin
- reduced lymphocyte count
- reduced neutrophil count
- decreased sodium levels
- increased glucose levels
- increased creatinine levels
- reduced phosphate levels
- decreased potassium levels
- increased potassium levels
- increased creatinine kinase levels
- increased ALT level
- decreased albumin levels
- increased AST level
- increased bilirubin level

**Common** (may affect up to 1 in 10 patients):

- infection
- herpes virus infection
- neutropenia with fever
- dehydration
- headache
- loss of consciousness
- cataract
- heart failure
- falls

**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](http://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>

You may also report by email to the registration holder's patient safety unit at [drugsafety@neopharmgroup.com](mailto:drugsafety@neopharmgroup.com)

### **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 package. The expiry date refers to the last day of that month.

### **Storage conditions**

Do not store above 30°C.

Do not throw away any medicine via wastewater or household waste. Ask your doctor or pharmacist how to throw away 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:**

microcrystalline cellulose (Avicel® PH-101), microcrystalline cellulose (Avicel® PH-102), croscarmellose sodium, povidone K30, sodium lauryl phosphate, colloidal silicone dioxide, magnesium stearate.

Tablet shell contains:

Opadry® II blue, Oprady® 200 clear.

#### **What the medicine looks like and contents of the pack:**

20 mg film-coated tablets are blue, round, and bi-convex, and are marked "K20" on one side of the tablet.

40 mg film-coated tablets are blue, oval, and are marked "X40" on both sides of the tablet.

50 mg film-coated tablets are blue, oval, and are marked "X50" on both sides of the tablet.

60 mg film-coated tablets are blue, oval, and are marked "X60" on both sides of the tablet. The tablets are packaged in aluminum blister cards, available in packs of 4, 8, 12, 16, 20, 24, or 32 tablets per pack.

Not all pack sizes may be marketed.

#### **Registration holder's name and address:**

Promedico Ltd., 6 Hashiloach Street, POB 3340, Petah Tikva, 4917001

#### **Manufacturer's name and address:**

Karyopharm Therapeutics, Newton, USA

#### **Registration number of the medicine in the Ministry of Health's National Drug Registry:**

XPOVIO 20mg 167-04-36451-99

XPOVIO 40mg 178-17-37897-99  
XPOVIO 50mg 178-18-37898-99  
XPOVIO 60mg 178-19-37899-99

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