



File Name	Orladeyo_israel_PIL_ENG-D14-F		
Product	orladeyo_	Job No.	SO22001095
Language	English	Artwork	Patient Leaflet

Document History

Ver.	Date	Change description	By
	29-Nov-22 16:09	Last save	

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

This medicine is dispensed with a doctor's prescription only

Orladeyo® 110 mg, hard gelatin capsules

Orladeyo® 150 mg, hard gelatin capsules

The active substance and its quantity per dosage unit:

Each Orladeyo capsule contains berotralstat (as dihydrochloride) 110 mg or 150 mg.

For a list of inactive ingredients and allergens in the preparation: 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?

Orladeyo is intended to prevent attacks of Hereditary Angioedema (HAE) in adults and children aged 12 and older.

Restriction of use: Orladeyo is not intended for the treatment of an acute attack of Hereditary Angioedema.

Therapeutic group:

Orladeyo belongs to the group of haematological drugs used to treat hereditary angioedema.

ATC code: B06AC06

Berotralstat, the active ingredient in Orladeyo, blocks the activity of kallikrein enzymes in plasma, resulting in low levels of bradykinin. This prevents the swelling and pain that can be caused by attacks of hereditary angioedema.

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).

Before treatment with Orladeyo, inform your doctor if:

- You have liver problems or are undergoing kidney dialysis.

Special warnings regarding the use of this medicine

- It is not known if Orladeyo is safe and effective to treat an acute Hereditary Angioedema attack. Do not take additional doses of Orladeyo to treat an acute attack of hereditary angioedema.
- Taking more than one Orladeyo capsule a day can cause serious side effects, including **heart rhythm disorders**. Patients who take more than one capsule of Orladeyo per day may experience a heart rhythm disorder called "QT prolongation". This disorder can cause an abnormal heart rhythm. Do not take more than one capsule of Orladeyo a day.

Children and adolescents

Orladeyo is not intended for children under 12 years of age. There is no information regarding the safety and effectiveness of the use of Orladeyo in children under 12 years of age.

Drug interactions

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

Taking Orladeyo with certain other medicines may affect how the other medicines work, and other medicines may affect how Orladeyo works.

In particular inform your doctor if you are taking:

- P-gp or BCRP inhibitors, such as cyclosporine (to prevent transplant rejection) - these medicines may increase the blood levels of Orladeyo.
- P-gp or BCRP inducers, e.g. rifampin (antibiotics), hypericum perforatum (St. John's wort) - these medicines may reduce the blood levels of Orladeyo and are therefore not recommended to be taken together with Orladeyo.
- Certain medicines with a narrow therapeutic range that are predominantly metabolised by the CYP2D6 enzyme, e.g. pimozone, thioridazine (against psychosis), or by the CYP3A4 enzyme, e.g. fentanyl (for pain relief), cyclosporine (to prevent transplant rejection) - Orladeyo may increase their blood levels.
- Medicines that are metabolized by P-gp, e.g. digoxin (for the treatment of cardiac arrhythmias) - Orladeyo may increase their blood levels.

Using Orladeyo and food

Orladeyo should be taken with food.

Pregnancy, breastfeeding, and fertility

Pregnancy

It is not known whether Orladeyo can harm your unborn baby. Tell your doctor if you are pregnant or planning to become pregnant.

Breastfeeding

It is not known whether Orladeyo passes into your breastmilk or affects milk production. Tell your doctor if you are breastfeeding or plan to breastfeed.

The doctor will help you decide on the best way to feed your baby during treatment with Orladeyo.

Driving and using machines

Orladeyo does not affect your ability to drive or use machines.

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 dosage of Orladeyo is usually 1 capsule, by mouth, 1 time every day with food.

Do not exceed the recommended dose.

The capsule must be swallowed whole. **Do not chew** the capsule.

The duration of the treatment will be determined by your doctor according to your medical condition, the effectiveness of the treatment and the side effects.

If you have accidentally taken a higher dose: in case you have taken a higher dose, you should contact a doctor immediately

Taking more than one Orladeyo capsule a day can cause serious side effects, including heart rhythm problems

If you forget to take the medicine: if you forgot to take this medicine at the scheduled time, take the missed dose as soon as possible, but no more than one capsule a day.

Adhere to the treatment as recommended by the doctor.

Even if there is an improvement in your health, you should not stop taking the medicine without consulting your doctor.

Do not take medicine 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 regarding the use of this medicine, consult your doctor or pharmacist.

4. Side effects

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

Orladeyo may cause serious side effects, including:

Heart rhythm problems can occur if you take more than one capsule of Orladeyo a day.

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

- Abdominal pain (abdominal discomfort, upper abdominal pain and abdominal tenderness)
- Vomiting
- Diarrhoea (frequent bowel movements)
- Back pain
- Heartburn

Common side effects (side effects that may affect 1-10 in 100 users):

- An increase in the level of liver enzymes in the blood
- Headache
- Fatigue
- Flatulence

Uncommon side effects (side effects that may affect 1-10 in 1,000 users):

- Rash (passes quickly, itches)

Gastrointestinal side effects (including abdominal pain, vomiting and diarrhoea) usually appeared at the start of treatment with Orladeyo, decreased during treatment and usually went away without treatment.

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 of 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>

In addition, you can report by sending an e-mail to the patient safety unit of the registration holder: 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 Orladeyo 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:

Store below 25°C.

6. Additional information

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

Pregelatinised starch, crospovidone, magnesium stearate, colloidal silicon dioxide

What the medicine looks like and contents of the pack:

Orladeyo 150 mg: two-part hard capsules: a white body with a black imprint "150" and a light blue cap with a black imprint "BCX", containing a white or almost white or off-white powder.

Orladeyo110 mg: light blue capsules with a white imprint "110" on body and a white imprint "BCX" on cap, containing a white or almost white or off-white powder.

The capsules are supplied in a carton containing 28 capsules.

The capsules are packed in four child-resistant shell packs, each containing a 7-capsule blister card.

Registration holder's name and address:

Neopharm (Israel) 1996 Ltd.,
6 HaShiloach St., Petah Tikva 4917001.

Manufacturer's name and address:

BioCryst Pharmaceuticals Incorporation,
4505 Emperor Blvd., Suite 200, Durham, North Carolina 27703, United States.

Approved in July 2022.

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

Orladeyo 110 mg: 170-35-37012-99

Orladeyo 150 mg: 170-34-36972-99