PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

This medicine is dispensed with a doctor's prescription only

Orilissa® 150 mg
Orilissa® 200 mg

The active ingredient and its quantity:
Each tablet contains:
Orilissa 150 mg, Film-coated tablets
Elagolix (as sodium) 150 mg
Orilissa 200 mg, Film-coated tablets
Elagolix (as sodium) 200 mg
For the list of inactive ingredients, please see section 6 "Further Information" in this leaflet.

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed to treat your ailment/for you. Do not pass it to others. It may harm them even if it seems to you that their ailment/medical condition is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Orilissa is indicated for the management of moderate to severe pain associated with endometriosis.
Therapeutic group: anti-gonadotropin-releasing hormone.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:
- you are sensitive (allergic) to elagolix or to any of the additional ingredients contained in the medicine (listed in section 6). (for detailed information of hypersensitivity reactions see section 4 "Side Effects").
- you are pregnant.
- you have osteoporosis.
- you have severe liver disease.
- you are taking medicines called organic anion transporting polypeptide (OATP)1B1 inhibitors that are known or expected to significantly increase the blood levels of elagolix (the active ingredient in Orilissa).
  Ask your doctor or pharmacist if you are not sure if you are taking one of these medicines.

Special Warnings Regarding Use of the Medicine
Orilissa may cause serious side effects, including:
- **Decreased Bone Mineral Density**
  - While you are taking Orilissa, your estrogen levels will be low. Low estrogen levels can lead to bone mineral density loss.
  - If you have bone density decrease on Orilissa treatment, your bone density may improve after you stop taking Orilissa but complete recovery may not occur. It is unknown if these bone changes could increase your risk for broken bones in the future. For this reason, your doctor may limit the length of time you take Orilissa.
    Your doctor may advise you to take vitamin D and calcium supplements to prevent that.
- **Changes in Menstrual Bleeding Pattern and Reduced Ability to Recognize Pregnancy**
  - During Orilissa treatment you may experience a reduction in the amount, intensity and duration of your period, which may make it harder for you to realize if you become pregnant in a timely manner (for detailed information, please refer to sub-section "pregnancy and breastfeeding").
- **Interaction with hormonal contraceptives**
  - Orilissa does not prevent pregnancy. Using Orilissa 200 mg twice a day with a birth control medicine that contains ethynylestradiol may lead to increased risk of side effects caused by ethynylestradiol. Some of these side effects can include heart attack, stroke, or blood clots. You will need to use effective methods of birth control that do not contain hormones such as condoms or spermicides while taking Orilissa and for 28 days after you stop taking Orilissa (see sub-section "pregnancy and breastfeeding").
- **Potential for Reduced Effectiveness of Orilissa when Used with Birth Control Medicines that Contain Estrogen**
  - Birth control medicines that contain estrogen may make Orilissa less effective. It is not known how well Orilissa will work while you are taking progestin-only birth control (for detailed information, please refer to sub-section "pregnancy and breastfeeding").
  - Talk to your doctor about which birth control to use during treatment with Orilissa. Your doctor may change the birth control you were on before you start taking Orilissa (for detailed information, please refer to sub-section "pregnancy and breastfeeding").
- **Suicidal Thoughts, Suicidal Behavior, and Worsening of Mood Disorders**
  - In clinical trials, some women experienced suicidal thoughts and behavior, including one suicide.
  - If you experience new or worsening depression, anxiety or other mood changes talk to your doctor right away, especially if the side effects are new, worse, or bother you. If you have suicidal thoughts or behavior seek for immediate medical attention (for detailed information, please refer to section 4 "side effects").
- **Changes in Liver Function Tests**
  - In clinical trials, increases to some liver function tests occurred with Orilissa. Your Physician will use the lowest effective dose of Orilissa and instruct you to promptly seek medical attention in case of symptoms and signs that may reflect liver injury (for detailed information, please refer to section 4 "side effects").

Before you take Orilissa, tell your doctor, pharmacist, if you:
- have or have had broken bones or other condition that may cause bone problems.
- have or have had depression, mood problems or suicidal thoughts or behavior.
- have liver function problems.
- think you may be pregnant. You should avoid becoming pregnant while taking Orilissa.
- are breastfeeding or plan to breastfeed. Talk to your doctor about the best way to feed your baby if you take Orilissa.

Especially tell your doctor if you take:
- birth control that contains hormones. Your doctor may advise you to change your method of birth control.

Children and adolescents
The safety and efficacy of the medicine Orilissa was not tested in children.

Tests and monitoring
Before you start treatment with Orilissa, your doctor may instruct you to do pregnancy test (for detailed information, please refer to sub-section "pregnancy and breastfeeding").
Your doctor may instruct you to do an X-ray test called a DXA scan to check your bone mineral density (if you have certain conditions or take other medicines that can cause decrease in bone mineral density, or if you have broken a bone with minimal or no injury).
During treatment with Orilissa, your doctor may instruct you to conduct a blood test to check your liver function.

Drug-Drug Interactions
If you are taking, or if you have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Especially if you taking:
- medicines to treat arrhythmia (e.g. digoxin) and medicines known as substrates of P-glycoprotein (P-gp).
- medicines to treat tuberculosis (e.g. rifampin), medicines for lowering fat in the blood (e.g. gemfibrozil) or medicines that prevent organ rejection after a transplant (e.g. cyclosporin) and are known as strong inhibitors of OATP1B1 (for detailed information please refer to sub-section "do not use the medicine if").
- medicines to treat anxiety or trouble sleeping (e.g. oral midazolam) or other benzodiazepines that are known substrates of CYP3A.
- medicines to lower blood cholesterol (e.g. rosuvastatin).
- medicines to treat stomach ulcers or known as proton pump inhibitors (e.g. omeprazole) and are known as substrates of CYP2C19.
- medicines to treat fungal infections (e.g. ketoconazole) and medicines known as strong inhibitors of CYP3A.
- birth control that contains hormones (e.g., combined hormonal contraceptives such as oral ethynylestradiol/levonorgestrel).

Taking Orilissa with food
Orilissa can be taken with or without food.

Pregnancy and breastfeeding
Effects on pregnancy
- **Do not take** Orilissa if you are trying to become or are pregnant. It may increase the risk of fetal abnormalities and miscarriage.
- **If you think you are pregnant,** stop taking Orilissa right away and call your doctor.
- Orilissa may change your menstrual periods (irregular bleeding or spotting, a decrease in menstrual bleeding, or no bleeding at all), making it hard to know if you are pregnant. Watch for other signs of pregnancy such as breast tenderness, weight gain and nausea.
- Orilissa does not prevent pregnancy. You need to use effective methods of birth control while taking Orilissa and for 28 days after you stop taking Orilissa. Examples of effective methods can include condoms or spermicides, which do not contain hormones.
- Birth control medicines that contain estrogen may make Orilissa less effective. There is no information regarding the combination of Orilissa with progestin-only birth control.
- Talk to your doctor about which birth control to use during treatment with Orilissa. Your doctor may change the birth control you were on before you start taking Orilissa.
- Your doctor will instruct you to do pregnancy test before you start treatment with Orilissa or will have you start taking Orilissa within 7 days after you start your period.

Breastfeeding
Before you take Orilissa, tell your doctor if you are breastfeeding or plan to breastfeed. It is not known if Orilissa passes into your breastmilk. Talk to your doctor about the best way to feed your baby if you take Orilissa.

Driving and using machines
Orilissa is unlikely to affect the ability to drive and use machines.

Important information regarding some of the excipients of Orilissa
Orilissa 150 mg:
Each tablet contains 34.4 mg sodium (main component of cooking/table salt). This is equivalent to 1.72% of the recommended maximum daily dietry intake of sodium for an adult.
Orilissa 200 mg:
Each tablet contains 45.9 mg sodium (main component of cooking/table salt). This is equivalent to 2.30% of the recommended maximum daily dietry intake of sodium for an adult.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use this medicine according to the doctor's instructions.
Check with the doctor or pharmacist if you are not sure regarding the dosage and treatment regimen of the medicine.
The dosage and treatment regimen will be determined by the doctor only. The usual dosage is:
- Orilissa 150 mg, take it 1 time each day. The maximum treatment duration for this strength is 2 years.
- Orilissa 200 mg, take it 2 times each day. The maximum treatment duration for this strength is 6 months.

Your doctor will let you know how long you should take Orilissa.
Do not exceed the recommended dose.
How to take Orilissa
- Take the tablets with or without food at about the same time each day.
- Swallow the tablets whole. There is no information regarding chewing, crushing and breaking the tablets.

If you accidentally have taken a higher dosage
If you took an overdose or if a child accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room, and bring the package of the medicine with you.
If you forget to take Orilissa
- 150 mg (1 time each day), take it as soon as you remember as long as it is on the same day. Do not take more than 1 tablet each day.
- 200 mg (2 times each day), take it as soon as you remember as long as it is on the same day. Do not take more than 2 tablets each day.

If you stop using Orilissa
You should adhere the treatment as instructed by the doctor.
Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.
Do not take medicines in the dark! Check the label and dose each time you take medicine. Wear glasses if you need them.
If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Orilissa may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.
Serious side effects that were reported and were not proven that are caused by taking Orilissa:
- appendicitis
- back pain

Serious side effects:
- **suicidal thoughts, suicidal behavior, and worsening of mood.** Orilissa may cause suicidal thoughts or actions. Talk to your doctor right away or get medical help immediately if you have any of these symptoms, especially if they are new, worse, or bother you:
  - thoughts about suicide or dying
  - attempts to commit suicide
  - depression or worsening depression
  - anxiety or worsening anxiety
  - other unusual changes in behavior or mood

You, your family or caregiver should pay attention to any changes, especially sudden changes in your mood, behaviors, thoughts, or feelings.
- **abnormal liver tests.** Talk to your doctor right away if you have any of these signs and symptoms of liver problems:
  - yellowing of the skin or the whites of the eyes (jaundice)
  - dark amber-colored urine
  - feeling tired (fatigue or exhaustion)
  - nausea and vomiting
  - generalized swelling
  - right upper stomach area (abdomen) pain
  - bruising easily

Very common side effects (effects that occur in more than 1 in 10 users):
- hot flashes
- headache
- nausea

Common side effects (effects that occur in 1-10 out of 100 users):
- difficulty sleeping
- absence of periods
- anxiety
- joint pain
- depression and mood changes
- decreased libido
- diarrhea
- abdominal pain
- weight gain
- dizziness
- constipation
- irritability

Side effects with unknown frequency:
- decrease in bone mineral density
- changes in the menstrual periods including in the menstrual bleeding pattern
- changes in blood lipid parameters
- hypersensitivity reactions (including anaphylaxis, angioedema, and urticaria) – signs of serious allergic reactions which may include swelling of the lips, face, or difficulty breathing, skin itching, redness or swelling
- thinning of uterine lining

If a side effect has occurred, if any of the side effects worsen or if you experience a side effect not mentioned in the leaflet, consult the doctor.
Reporting side effects
Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects due to Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) printed on the carton package.
- Store at 2 to 30°C.

6. FURTHER INFORMATION

What Orilissa contains?
Orilissa 150 mg:
In addition to the active ingredient, the medicine also contains:
Mannitol, sodium carbonate monohydrate, pregelatinized starch, povidone, polyvinyl alcohol, magnesium stearate, polyethylene glycol, talc, titanium dioxide, carmine high tint.
Orilissa 200 mg:
In addition to the active ingredient, the medicine also contains:
Mannitol, sodium carbonate monohydrate, pregelatinized starch, povidone, polyvinyl alcohol, magnesium stearate, polyethylene glycol, talc, titanium dioxide, iron oxide red.
What Orilissa looks like and the contents of the package?
- Orilissa 150 mg, film-coated tablet is a light pink, oblong, debossed with "EL 150" on one side.
- Orilissa 200 mg, film-coated tablet is light orange, oblong, debossed with "EL 200" on one side.

Orilissa is dispensed in the following packs:

Packaging Presentation	Number of Tablets
150 mg	4 X 7 (28) tablets
200 mg	4 X 14 (56) tablets

- License holder and its address: AbbVie Biopharmaceuticals Ltd., 4 Haharash St., Hod Hasharon, Israel.
- Manufacturer name and its address: AbbVie Inc., 1N Waukegan Road, North Chicago, IL 60064 USA.
- Revised in November 2021, according to MoH guidelines.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health:
  Orilissa 150 mg: 164-66-35928.
  Orilissa 200 mg: 164-67-35953.