

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

The medicine is dispensed
with a doctor's prescription only

Zytiga[®] 250 mg

Tablets

Active ingredient and its quantity

Abiraterone acetate 250 mg, equivalent to 223 mg of abiraterone.

Inactive ingredients and allergens in the preparation – see section 2 “Important information about some of the ingredients of the medicine” and section 6 “Further Information”.

Read the 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 for the treatment of your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Zytiga 250 mg is a prescription medicine containing an active ingredient called abiraterone acetate. Zytiga 250 mg is a CYP17 enzyme inhibitor, given in combination with prednisone for the treatment of:

- metastatic castration-resistant prostate cancer.
- adult males with newly diagnosed high-risk metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT).

Therapeutic group:

Specific inhibitor of the enzyme CYP17.

2. BEFORE USING THE MEDICINE

Do not use the medicine:

- If you are sensitive (allergic) to abiraterone acetate or to any of the additional ingredients contained in the medicine. For a list of the additional ingredients, see section 6 “Further Information”.
- If you are a woman, and especially a pregnant woman. Zytiga 250 mg is intended for use in males only.
- If you suffer from severe liver damage.
- In combination with Ra-223 (used to treat prostate cancer).

Do not take the medicine if any of the above apply to your condition. If you are not sure, consult with your doctor or pharmacist before taking the medicine.

Special warnings regarding use of the medicine

Before treatment with Zytiga 250 mg, talk to the doctor:

- If you suffer from liver problems
 - If you suffer from high blood pressure, heart failure, or low blood potassium levels (low blood potassium levels may increase the risk of heart rhythm problems)
 - If you suffer from other heart problems or blood vessel problems
 - If you suffer from an irregular heart rate or a rapid heart rate
 - If you suffer from shortness of breath
 - If you have gained weight rapidly
 - If you have swelling in the feet, ankles or legs
 - If you have taken in the past a medicine called ketoconazole to treat prostate cancer
 - On the need to take this medicine with a medicine called prednisone
 - About possible effects on your bones
 - If you have high blood sugar levels.
- Tell your doctor if you are aware of any heart or blood vessel problems, including heart rhythm problems (arrhythmia), or you are being treated with medication for these conditions.
 - Tell your doctor if you have yellowish skin or eyes, darkening of the urine, severe nausea or vomiting. All these could be symptoms of liver problems. Rarely, failure of liver function (called acute liver failure) may occur and could lead to death.
 - You may suffer from a decrease in red blood cells, reduced sex drive (libido), muscle weakness and muscle pain.
 - Zytiga 250 mg must not be taken in combination with Ra-223 due to an increased risk of bone fractures or death.

If you plan to take Ra-223 following treatment with Zytiga 250 mg and prednisone, you must wait 5 days before starting treatment with Ra-223.

If you are not sure if the mentioned effects apply to you, talk to your doctor or pharmacist before taking the medicine.

Children and adolescents

The medicine is not intended for use in children or adolescents. If a child or adolescent accidentally swallowed the medicine, proceed to the hospital immediately with the medicine leaflet in order to show it to the doctor.

Tests and follow-up

Zytiga 250 mg could affect your liver, and you may not have any symptoms. Your doctor will occasionally perform blood tests during treatment with Zytiga 250 mg to check liver function.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or

pharmacist.

Zytiga 250 mg may increase the effect of a number of medicines, including heart medicines, tranquilisers, some medicines for treatment of diabetes, nutritional supplements such as St. John's wort and other medicines. It is possible that the doctor may decide to change the dosage of these medicines. In addition, some medicines may increase or decrease the effect of Zytiga 250 mg. This effect may cause side effects to occur or, alternatively, impair the effectiveness of Zytiga 250 mg.

Other medicines taken with Zytiga 250 mg

Androgen deprivation medication may increase the risk of heart rhythm problems. Inform the doctor if you are receiving:

- medicines to treat heart rhythm problems (e.g., quinidine, procainamide, amiodarone and sotalol).
- medicines known to increase the risk of heart rhythm problems (e.g., methadone – for pain relief and detoxification from drug addiction, moxifloxacin – an antibiotic, antipsychotics – for serious mental illnesses).

It is advisable to prepare a list of all the medicines you are taking in order to inform your doctor or pharmacist.

Use of the medicine and food

Do not take Zytiga 250 mg with food. Taking Zytiga 250 mg with food may cause more of the medicine to be absorbed by the body than is needed and this may cause side effects. Take Zytiga 250 mg as a single dose once daily on an empty stomach. Zytiga 250 mg must be taken at least two hours after a meal and food must not be eaten for at least one hour after taking Zytiga 250 mg.

Pregnancy, breastfeeding and fertility

Zytiga 250 mg is not intended for use in women.

This medicine may harm the fetus if taken during pregnancy.

Women who are pregnant or may become pregnant should wear gloves if they come into contact with Zytiga 250 mg.

A man who has sexual intercourse with a woman who could become pregnant should use a condom and another effective contraceptive measure.

A man who has sexual intercourse with a pregnant woman should use a condom to protect the fetus.

Driving and operating machinery

Zytiga 250 mg is not expected to affect the ability to drive or operate machinery.

Important information about some of the ingredients of the medicine

Zytiga 250 mg contains lactose. If you know that you have intolerance to certain sugars, refer to your doctor before starting to take Zytiga 250 mg.

Zytiga 250 mg contains 27.2 mg sodium (the main component of table/cooking salt) in 4 tablets, which is the daily dosage. This should be taken into account in patients who are on a controlled sodium diet. This is equivalent to 1.36% of the

recommended maximum daily dietary intake of sodium for an adult.

3. HOW SHOULD THE MEDICINE BE USED?

Always use the preparation according to the doctor's instructions.

Check with the doctor or pharmacist if you are uncertain regarding the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the doctor only.

Zytiga 250 mg should be taken with prednisone in accordance with the instructions you received from the doctor.

The usual dosage is generally 4 tablets of Zytiga 250 mg daily (1,000 mg per day). For metastatic castration-resistant prostate cancer (CRPC), take Zytiga 250 mg together with 5 mg prednisone twice daily.

For metastatic hormone-sensitive prostate cancer (mHSPC), take Zytiga 250 mg together with 5 mg prednisone daily.

Do not exceed the recommended dose.

It is possible that the doctor may change the dosage as needed.

Taking the medicine:

- Swallow the Zytiga 250 mg tablets whole.
- Do not halve the tablets since there is no score line.
- Do not pulverize, crush or chew the tablets.
- Swallow Zytiga 250 mg tablets with water.
- Take Zytiga 250 mg on an empty stomach. Do not take Zytiga 250 mg with food. Taking Zytiga 250 mg with food may cause more of the medicine to be absorbed by the body than is needed and this may cause side effects. Zytiga 250 mg must be taken at least two hours after a meal and food must not be eaten for at least one hour after taking Zytiga 250 mg.
- Zytiga 250 mg is taken together with a medicine called prednisone. Take the prednisone according to the doctor's instructions.
- Take prednisone every day while using Zytiga 250 mg.
- It may be necessary to change the dosage of prednisone if there is a change in your medical condition. The doctor will instruct you on whether you need to change the amount of prednisone you are taking. Do not stop taking prednisone unless the doctor instructs you to stop.

Instructions for opening the bottle:

The plastic bottle comes with a child-proof cap. Open the cap according to the following instructions:

- Press the plastic cap downwards while turning it counter-clockwise
- Remove the cap

Child-proof caps have significantly lowered the annual number of cases of poisoning due to medicines. However, if you have difficulty opening the package, you can ask the pharmacist to remove the cap's safety mechanism and replace it with a regular, easy-to-open cap.

If you took a higher dosage than recommended, or if a child has accidentally swallowed the medicine, immediately refer to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take a dose of Zytiga 250 mg or prednisone, take the next dose the following day at the usual time.

If you forgot to take more than one dose of Zytiga 250 mg or prednisone, consult the doctor immediately.

Adhere to the treatment regimen as recommended by the doctor.

Even if there is an improvement in your health, do not stop taking Zytiga 250 mg or prednisone without first consulting the doctor.

Do not take medicines in the dark! Check the label and the 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 Zytiga 250 mg 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.

Stop taking the medicine and refer to the doctor immediately if you experience any of the following effects:

Muscle weakness, muscle twitches or a pounding heart beat (palpitations). These may be signs of low blood potassium levels.

Additional side effects:

Very common side effects – effects that occur in more than one user in ten:

- Fluid in your legs or feet
- Low blood potassium level
- Increase in liver function values
- High blood pressure
- Urinary tract infection
- Diarrhea

Common side effects – effects that occur in 1-10 users in 100:

- High blood fat level
- Chest pain
- Irregular heart beat (atrial fibrillation)
- Heart failure
- Rapid heart rate
- Severe infection called sepsis
- Bone fractures
- Indigestion
- Blood in urine

- Rash

Uncommon side effects – effects that occur in 1-10 users in 1,000:

- Adrenal gland problems (related to a problem in the balance of salts and fluids)
- Abnormal heart rhythm (arrhythmia)
- Muscle weakness and/or muscle pain

Rare side effects – effects that occur in 1-10 users in 10,000:

- Lung irritation (allergic alveolitis)
- Failure of liver function (called acute liver failure)

Side effects whose frequency is unknown:

Heart attack, changes in ECG (QT interval prolongation), severe allergic reactions with difficulty in swallowing or breathing, swelling of the face, lips, tongue or throat, or an itchy rash.

Loss of bone mass may occur in men treated for prostate cancer with Zytiga 250 mg. Zytiga 250 mg in combination with prednisone may increase loss of bone mass.

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage

(www.health.gov.il) that directs you 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 safe place out of the reach and sight of children and/or infants 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) appearing on the package. The expiry date refers to the last day of that month.
- Store the medicine below 30 degrees Celsius.
- Shelf life after first opening: 30 days.
- Store Zytiga 250 mg tablets in the original package.
- Do not discard any unused medicine into the household waste bin or into the local wastewater system. Ask the pharmacist how to dispose of medicines you no longer need. These measures will help to protect the environment.

6. FURTHER INFORMATION

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

Lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, povidone, sodium lauryl sulfate, magnesium stearate and silica, colloidal

anhydrous.

- What the medicine looks like and the contents of the package:

Zytiga 250 mg tablets are white to off-white in color, oval-shaped, with “AA250” imprinted on one side.

- The tablets are provided in a plastic bottle with a plastic, child-proof cap.
- Each bottle contains 120 tablets. Each carton contains one bottle.

Manufacturer: Janssen Cilag SpA, Italy, Via C. Janssen, 04100, Borgo, San Michele, Latina.

Registration Holder: J-C Health Care Ltd., Kibbutz Shefayim 6099000, Israel.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 148-03-33481

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