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

This medicine is dispensed with a doctor's prescription only

Akeega® 50/500
Akeega® 100/500

Film-coated tablets

Active ingredients
Akeega 50/500
Each film-coated tablet contains:
niraparib (as tosylate monohydrate) 50 mg,
abiraterone acetate 500 mg

Akeega 100/500
Each film-coated tablet contains:
niraparib (as tosylate monohydrate) 100 mg,
abiraterone acetate 500 mg

Inactive ingredients and allergens in this medicine: see section 2 under 'Important information about some of this medicine's ingredients', and section 6 'Additional information'.

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?

Akeega is indicated with prednisone or prednisolone for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC) and BRCA 1/2 mutations (germline and/or somatic) in whom chemotherapy is not clinically indicated.

Therapeutic group: cancer medicines

Niraparib is a type of cancer medicine called a PARP inhibitor. PARP inhibitors block an enzyme called poly [adenosine diphosphate-ribose] polymerase (PARP). PARP helps cells repair damaged DNA. When PARP is blocked, cancer cells cannot repair their DNA, resulting in tumour cell death and helping to control the cancer.

Abiraterone stops your body from making testosterone; this can slow the growth of prostate cancer.

When you take this medicine, your doctor will also prescribe another medicine called prednisone or prednisolone. This is to lower your chances of getting high blood pressure, having too much water in your body (fluid retention), or having reduced blood levels of a chemical known as potassium.

2. Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to niraparib or abiraterone acetate (the active ingredients), or to any of the other ingredients in this medicine (see section 6).
- You are a woman, and in particular a pregnant woman; Akeega is intended for use in men only.
- You have severe liver damage.
- In combination with Ra-223 treatment (which is used to treat prostate cancer). This is because of a possible increase in the risk of bone fractures or death.

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

Special warnings about using this medicine
Talk to you doctor or pharmacist before or during treatment with this medicine if:

- You have low blood cell counts. Signs and symptoms you need to look out for include fatigue, fever or infection, and abnormal bruising or bleeding. Akeega may also lower your blood cell counts. Your doctor will test your blood regularly throughout your treatment.
- You have high blood pressure or heart failure or low blood potassium level (low blood potassium may increase the risk of heart rhythm problems), have had other heart or blood vessel problems, have an irregular or rapid heart rate, shortness of breath, gain weight rapidly, or swelling in the feet, ankles, or legs. Your doctor will measure your blood pressure regularly throughout your treatment.
- You experience headaches, vision changes, confusion, or seizure. These may be signs of a rare neurological side effect named posterior reversible encephalopathy syndrome (PRES) that has been associated with use of niraparib, an active ingredient of Akeega.
- You experience high fever, fatigue and other signs and symptoms of severe infection.
- You have blood clots in the lungs, or have had them in the past.
- You have liver problems.
- You have low or high levels of sugar in the blood.
- You experience muscle weakness and/or muscle pain.

If you develop low blood cell counts for a long period of time while taking Akeega, this may be a sign of more serious problems with the bone marrow, such as ‘myelodysplastic syndrome’ (MDS) or ‘acute myeloid leukaemia’ (AML). Your doctor may want to test your bone marrow to check for these problems.

Before taking Akeega, also talk to your doctor or pharmacist about:

- the effect Akeega may have on your bones.
- taking prednisone or prednisolone (another medicine you must take with Akeega).

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking this medicine.

Children and adolescents
This medicine is not intended for use in children and adolescents.

Tests and follow-up
- Akeega may affect your liver, but you may not notice any symptoms of liver problems. When you are taking this medicine, your doctor will therefore check your blood periodically to look for any effects on your liver.
- Your doctor will perform blood count tests before starting treatment and regularly throughout the treatment.
- Your doctor will measure your blood pressure regularly throughout the treatment.
- Your doctor may perform additional tests as required.

Interactions with other medicines
If you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:
- medicines that prevent the body from producing testosterone, since they may increase the risk of heart rhythm problems:
    - medicines for treatment of heart rhythm problems (e.g. quinidine, disopyramide, procainamide, amiodarone, dofetilide, ibutilide and sotalol).
    - a medicine known to increase the risk of heart rhythm problems (e.g., methadone), used for pain relief and as part of drug addiction detoxification; moxifloxacin, an antibiotic; antipsychotics, used for serious mental illnesses.
- medicines affecting the CYP3A4 enzyme, such as phenytoin, carbamazepine, rifampicin, rifabutin, rifapentine, phenobarbital, St. John's wort (hypericum perforatum), ketoconazole.
- medicines metabolised by the CYP2D6 enzyme, such as metoprolol, propranolol, desipramine, venlafaxine, haloperidol, risperidone, propafenone, flecainide, codeine, oxycodone, dextromethorphan and tramadol.
- medicines metabolised by the CYP2C8 enzyme, such as pioglitazone and repaglinide.
- cytotoxic medicines.
- vaccines (live-attenuated).
- immunosuppressants.
- a medicine named spironolactone.

Using this medicine and food
This medicine must not be taken with food (see section 3, 'How to use this medicine'), as this may increase your risk of side effects.

Pregnancy, breastfeeding, and fertility
Pregnancy
Akeega is not intended for use in women.
- This medicine may cause harm to the unborn child if it is taken by women who are pregnant.
- Women who are pregnant or who may become pregnant should wear gloves if they need to touch or handle Akeega.

Contraception for men using Akeega (and their female partners):
- If you are having sex with a woman who can become pregnant, use a condom and another effective birth control method. Use contraception during treatment and for 4 months after stopping treatment. Talk to your doctor if you have any questions about contraception.

- If you are having sex with a pregnant woman, use a condom to protect the unborn child.

Fertility
No clinical studies investigating the effect of Akeega on fertility have been conducted. In animal studies, reduced male fertility was observed upon treatment with niraparib or abiraterone acetate, but this effect was reversible following treatment cessation.

Driving and using machines
Taking Akeega may make you feel weak, unfocused, tired or dizzy. This may influence your ability to drive and use machines. Use caution is required when driving or using machines.

Important information about some of this medicine's ingredients
Akeega contains lactose and sodium.
- Akeega contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.
- This medicine contains less than 1 mmol (23 mg) sodium per 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.

The recommended starting dosage is two tablets of Akeega 100/500 once a day. Akeega 50/500 tablets are used for dosage adjustment.

Do not exceed the recommended dose.

Method of administration
- Take this medicine by mouth.
- Do not take Akeega with food.
- Take Akeega tablets as a single dose once daily on an empty stomach at least one hour before or at least two hours after eating (see section 2, 'Using this medicine and food').
- Swallow the tablets whole with water. Do not break, crush, or chew the tablets. This will ensure that the medicine works as well as possible.
- Akeega is taken with a medicine called prednisone or prednisolone.
    - Take prednisone or prednisolone exactly according to your doctor's instructions.
    - You need to take prednisone or prednisolone every day while you are taking Akeega.
    - The amount of prednisone or prednisolone you take may need to be changed in case of a medical emergency. Your doctor will tell you if you need to change the amount of prednisone or prednisolone you take. Do not stop taking prednisone or prednisolone unless your doctor tells you to.

Your doctor may also prescribe other medicines while you are taking Akeega.

If you have accidentally taken a higher dose
If you have taken more tablets than you should, contact your doctor. You may be at an increased risk of side effects.
If a child or an adolescent has swallowed Akeega, immediately take them to the hospital and bring the medicine package with you to show to the emergency room doctor.

If you forget to take the medicine
If you forget to take Akeega or prednisone or prednisolone, take your usual dose as soon as you remember on the same day, and return to the usual intake schedule on the next day.
If you forget to take Akeega or prednisone or prednisolone for more than one day - talk to your doctor straight away.
Do not take a double dose to make up for a forgotten dose.

Adhere to the treatment as recommended by your doctor.

If you stop taking this medicine
Do not stop taking Akeega or prednisone or prednisolone unless your doctor tells you to.

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>

As with any medicine, using Akeega 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
Stop taking Akeega and seek medical attention immediately if you notice any of the following symptoms:

Very common side effects - affect more than 1 in 10 users:
- Bruising or bleeding for longer than usual if you hurt yourself - these may be signs of a low blood platelet count (thrombocytopenia).
- Being short of breath, feeling very tired, having pale skin or fast heartbeat - these may be signs of a low red blood cell count (anaemia).
- Fever or infection - low white blood cell count (neutropenia) can increase your risk for infection. Signs may include fever, chills, feeling weak or confused, cough, pain or burning feeling when passing urine. Some infections can be serious and may lead to death.
- Muscle weakness, muscle twitching or a pounding heartbeat (palpitations). These may be signs that the w level of potassium in your blood is low (hypokalaemia).
- Increased level of the enzyme alkaline phosphatase in the blood.

Side effects of unknown frequency (the frequency of these effects has not been established yet) - not reported with the use of Akeega, but reported with the use of niraparib or abiraterone acetate (components of Akeega)
- Allergic reaction (including a severe allergic reaction that may be life-threatening). Signs include: raised and itchy rash (hives) and

swelling - sometimes of the face or mouth (angioedema), causing difficulty in breathing, and collapse or loss of consciousness.
- A sudden increase in blood pressure, which may be a medical emergency that could lead to organ damage or can be life-threatening.

Other side effects

Very common side effects - affect more than 1 in 10 users:
- urinary tract infection
- low number of white blood cells (leukopenia), seen in blood tests
- decreased appetite
- difficulty sleeping (insomnia)
- feeling dizzy
- shortness of breath
- constipation
- nausea
- vomiting
- back pain
- joint pain
- feeling very tired
- feeling weak
- weight loss
- bone fractures

Common side effects - affect up to 1 in 10 users:
- infectious pneumoniae
- lung infection (bronchitis)
- infection of the nose and throat (nasopharyngitis)
- low number of a type of white blood cell (lymphopenia), seen in blood tests
- high level of a type of fat (hypertriglyceridemia) in the blood
- depression
- feeling anxious
- headache
- fast heartbeat
- fast or uneven heartbeat (palpitations)
- irregular heartbeat (atrial fibrillation)
- heart failure, causing shortness of breath and swollen legs
- heart attack
- cough
- blood clot in the lungs, causing chest pain and shortness of breath
- inflamed lung tissue
- stomach pain
- indigestion
- diarrhoea
- bloating
- sores in the mouth
- dry mouth
- inflamed liver (hepatitis) based on blood tests
- skin rash
- muscle aches
- blood in the urine
- swollen hands, ankles, or feet
- increased level of creatinine in the blood
- increased level of the enzyme aspartate aminotransferase in the blood
- increased level of the enzyme alanine aminotransferase in the blood

Uncommon side effects - affect up to 1 in 100 users:
- severe infection (sepsis) that spreads from the urinary tract throughout the body
- inflamed eye (conjunctivitis)
- feeling confused
- difficulty thinking, remembering information, or solving problems (cognitive impairment)
- change in the sense of taste
- chest discomfort, often brought on by physical activity
- abnormal ECG (electrocardiogram), which could be a sign of heart problems
- nose bleeds
- inflammation of the protective linings in the body cavities, such as the nose, mouth, or digestive system
- sudden liver failure
- increased sensitivity of the skin to sunlight
- increased level of gamma-glutamyltransferase in the blood

Side effects of unknown frequency (the frequency of these effects has not been established yet) – not reported with the use of Akeega, but reported with the use of niraparib or abiraterone acetate (components of Akeega)
- low numbers of all types of blood cells (pancytopenia)
- brain condition with symptoms including seizures (fits), headache, confusion, and changes in vision (posterior reversible encephalopathy syndrome or PRES), which is a medical emergency that could lead to organ damage or can be life-threatening
- adrenal gland problems (related to salt and water problems) where too little hormone is produced, which may cause problems like weakness, tiredness, loss of appetite, nausea, dehydration and skin changes
- inflamed lungs caused by an allergic reaction (allergic alveolitis)
- muscle disease (myopathy), which may cause muscle weakness, stiffness or spasms
- breakdown of muscle tissue (rhabdomyolysis), which may cause muscle cramps or pains, tiredness and dark urine

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.

You can report side effects to the Ministry of Health by following the 'Reporting Side Effects of Drug Treatment' link on the Ministry of Health home page (www.health.gov.il), which opens an online form for reporting side effects, or 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 your doctor.

Do not use the medicine after the expiry date (exp. date) which is stated on the container (blister foil, inner wallet, outer wallet and carton). The expiry date refers to the last day of that month.

Storage conditions: Store below 30°C. Store in the original package.

Do not throw away medicines via wastewater or household waste. Ask the 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 ingredients, this medicine also contains:

Akeega 50/500
Tablet core
Silicified microcrystalline cellulose, lactose monohydrate, crospovidone, sodium lauryl sulfate, hypromellose, magnesium stearate, colloidal anhydrous silica

Tablet coating
Polyvinyl alcohol, talc, titanium dioxide, iron oxide yellow, glycerol monocaprylocaprate type 1, sodium lauryl sulphate, iron oxide red, iron oxide black

Akeega 100/500
Tablet core
Silicified microcrystalline cellulose, lactose monohydrate, crospovidone, sodium lauryl sulfate, hypromellose, magnesium stearate, colloidal anhydrous silica

Tablet coating
Polyvinyl alcohol, talc, titanium dioxide, iron oxide yellow, glycerol monocaprylocaprate type 1, sodium lauryl sulphate, iron oxide red

What the medicine looks like and contents of the pack:

Akeega 50/500
Film-coated yellowish orange to yellowish brown oval tablets, debossed with 'N 50 A' on one side and plain on the other side.

Akeega 100/500
Film-coated orange oval tablets, debossed with 'N 100 A' on one side and plain on the other side.

Each box contains 56 film-coated tablets in two cardboard wallet packs containing 28 film-coated tablets each, packed in aluminium blisters.

Registration holder's name and address: J-C Health Care Ltd., Kibbutz Shefayim, 6099000.

Manufacturer's name and address:
Patheon France, 40 Boulevard De Champaret, Bourgon Jallieu, 38300, France

Registration numbers of the medicine in the Ministry of Health National Drug Registry:
Akeega 50/500: 175-82-37788-99
Akeega 100/500: 175-83-37789-99

Approved in May 2024.
Based on EU SmPC as a reference leaflet.