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

The medicine is dispensed with a doctor's prescription only

Akynzeo® 300 mg/0.5 mg

Capsules

Active ingredients:
Each capsule contains 300 mg netupitant and 0.5 mg palonosetron as hydrochloride salt.
For the list of the additional ingredients, see section 6. See also 'Important information about some of the medicine's ingredients' in section 2.

Read the entire leaflet carefully before using the medicine.
This leaflet contains concise information about the medicine. If you have any further questions, please refer to the doctor or pharmacist.
This medicine was prescribed for treating your condition. 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 the medicine intended for?

The medicine is intended for prevention of nausea and vomiting as an acute or delayed result of chemotherapy.
Therapeutic group:
Anti-nausea and vomiting agents: Netupitant – blocks substance P from binding to neurokinin 1 (NK-1) receptor, Palonosetron – blocking serotonin (5-HT_3) receptor.

By blocking the activity of substance P and serotonin, the medicine prevents stimulation of the vomiting center and as a result, also the feeling of nausea.

2. Before using the medicine

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredients or to any of the additional ingredients the medicine contains (for the list of the additional ingredients, see section 6).
- You are pregnant.

Special warnings regarding the use of the medicine:

Before treatment with the medicine tell the doctor if:

- You suffer from liver problems.
- You suffer from bowel obstruction or have suffered in the past from constipation.
- You or someone in your family suffer or have suffered in the past from a heart problem called: QT interval prolongation, or if you suffer from any other heart problem.
- You suffer from imbalance of salts (electrolytes) in your blood (e.g. potassium or magnesium).

Use in Children:
There is no information on the safety and efficacy of the use of this medicine in children and adolescents under 18 years of age.

Drug interactions:

If you are taking, or have recently taken any other medicines, including non-prescription medicines and nutritional supplements, please tell the doctor or pharmacist. Especially inform the doctor or pharmacist if you are taking the following medicines (it should be noted that the following list indicates the active ingredients in the medicines. If you are not sure whether you are using one of these medicines, please check with the doctor or pharmacist):

- Certain medicines for the treatment of depression and anxiety from the SSRIs or SNRIs groups such as: fluoxetine, paroxetine, sertraline, fluvoxamine, citalopram, escitalopram, venlafaxine, duloxetine.

Also, inform the doctor if you are being treated with one of the following medicines, because the doctor may change their dosage:

- Medicines that affect the heartbeat, such as amiodarone, nicardipine, quinidine, moxifloxacin, haloperidol, chlorpromazine, quetiapine, thioridazine, domperidone.
- Medicines with a narrow therapeutic range that are metabolized primarily by CYP34A, such as: cyclosporine, tacrolimus, sirolimus, everolimus, alfentanil, fentanyl, diergotamine, ergotamine or quinidine.
- Certain chemotherapy medicines such as docetaxel, etoposide, irinotecan.
- Rifampicin, erythromycin, dexamethasone, ketoconazole.
- Midazolam.
- Zidovudine, valproic acid, morphine, digoxin, dabigatran, colchicine.

Use of the medicine and food:
The medicine can be taken independently of mealtimes.

Pregnancy and breastfeeding:
If you are pregnant, think you are pregnant, are planning a pregnancy or if you are breastfeeding, consult the doctor before taking the medicine.

- Before starting the treatment, a pregnancy test should be performed to ensure you are not pregnant.
- Use contraceptives, as recommended by the doctor, during the treatment and for up to a month after completion.
- Do not use the medicine if you are pregnant, or if you might become pregnant and are not using contraceptives.
- Do not breastfeed while using the medicine and up to a month after you stop using it.

Driving and use of machinery:
The use of this medicine may cause dizziness and/or tiredness. If you experience these symptoms, do not drive or operate machinery.

Important information about some of the medicine's ingredients:

- The capsules contain sucrose and sorbitol (types of sugar), sodium and may contain traces of soy.
- If you suffer from intolerance to some sugars, inform the doctor before taking the medicine. Each capsule contains 7 mg sorbitol and 20 mg sucrose.
- Each capsule contains less than 1 mmol sodium (23 mg), i.e. it is considered “sodium-free”.
- The capsules may contain traces of lecithin derived from soy. If you are allergic to peanuts or soy and you notice any sign of an allergic reaction, refer to a doctor immediately. Symptoms of an allergic reaction may include: urticaria (raised and itchy skin rash), skin rash, itching, breathing or swallowing difficulties, swelling of the mouth, face, lips, tongue or throat; sharp drop in blood pressure.

3. How to use the medicine?

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine.
The dosage and the manner of treatment will be determined by the doctor only.
The standard dosage is usually: one capsule, about an hour before the chemotherapy. Swallow the capsule whole.
Do not take another capsule in the days after the chemotherapy, unless you are about to undergo another chemotherapy cycle.
Do not exceed the recommended dose.
The medicine can be taken independently of mealtimes.

If you have accidentally taken a higher dosage or if a child has accidentally swallowed the medicine, refer immediately to a doctor or a hospital emergency room and bring the medicine package with you. Symptoms of an overdose may include: headache, dizziness, constipation, anxiety, palpitations (feeling heartbeats), euphoria, pain in the legs.

If you forgot to take the medicine tell the doctor.

If you stop taking the medicine: the medicine is taken to help prevent nausea and vomiting as a result of chemotherapy. If you do not want to use it, consult with the doctor. If you decide not to use this medicine (or a similar medicine), the chemotherapy may cause you nausea and vomiting.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.
If you have further questions concerning the use of the medicine, refer to the doctor or pharmacist.

4. Side effects

As with any medicine, the use of Akynzeo may cause side effects in some users. Do not be alarmed while reading the list of side effects, you may not suffer from any of them.

Stop the treatment and refer to a doctor or a hospital emergency room immediately, if the following serious side effects appear:

- Severe allergic reaction. Symptoms of a severe allergic reaction include: urticaria/hives (raised and itchy skin rash), skin rash, itching, breathing or swallowing difficulties, swelling of the mouth, face, lips, tongue or throat; sharp drop in blood pressure (*very rare side effects, appear in less than 1 user out of 10,000*).

Additional side effects:

Common side effects (appear in 1-10 users out of 100):

- Headache, constipation, tiredness.

Uncommon side effects (appear in 1-10 users out of 1,000):

- Hair loss, lack of energy (weakness), decreased appetite, high blood pressure, urticaria, heart muscle problems, ECG problems (QT and PR interval prolongation, conduction disorders, tachycardia, atrioventricular block first degree), vertigo (spinning sensation), dizziness, insomnia, abdominal problems including: discomfort, feeling bloated, nausea, pains, indigestion, belching, wind or diarrhea.
- Changes seen in blood tests: high levels of certain enzymes (including alkaline phosphatase in the blood and transaminases in the liver); high creatinine levels (kidney function test); low neutrophils levels (type of white blood cells that fight infections); high levels of white blood cells.

Rare side effects (appear in 1-10 users out of 10,000):

- Back pain, joint pain, pains in limbs; feeling hot, reddening of the face and/or other skin areas (flushing); skin rash and itching, feeling drowsiness/sleepiness, sleep problems, ringing in the ears, vomiting, low blood pressure, chest pain (not related to the heart), numbness, blurred vision; sudden nervous breakdown, mood changes, bladder infection and inflammation, hemorrhoids, conjunctivitis (type of eye infection), low potassium levels (as seen in blood tests), change or disturbance in heart rhythm, heart valve problems, decrease in blood flow to the heart muscle; tongue coating, swallowing difficulties, dry mouth, hiccups, aftertaste after taking the medicine.
- Additional changes seen in blood tests: high levels of creatine phosphokinase/creatine phosphokinase MB (indicating a sudden decrease in blood flow to the heart); high troponin levels (indicating heart function problems), high bilirubin levels (indicating liver function problems), high myoglobin levels (indicating muscle injury), high levels of urea in the blood (indicating kidney problems), high levels of lymphocytes (type of white blood cells that help the body fight diseases), increase in neutrophil count, low white blood cell levels.
- Additional ECG problems (ST segment depression, ST-T segment abnormal, bundle branch block right/left, atrioventricular block second-degree).

Side effects of unknown frequency (effects whose frequency has not yet been determined):

- Serotonin syndrome. Symptoms may include: agitation, tremor, sweating, muscle spasms (including involuntary movements), excessive muscle tone, fever.

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

Side effects may be reported to the Ministry of Health by clicking on the link "Report on side effects following medicinal treatment" on the homepage of the Ministry of Health website (www.health.gov.il) which leads to an online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Avoid poisoning! This medicine, and any other medicine, must be stored in a closed place out of the reach and sight of children and/or babies, 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) 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 ingredients, the capsules also contain:
Microcrystalline cellulose, sucrose lauric acid esters, povidone K-30, croscarmellose sodium, purified water, silicon dioxide/silica colloidal hydrated, sodium stearyl fumarate, magnesium stearate (vegetable grade), glycerol monocaprylocaprate (type I), glycerin (anhydrous), polyglyceryl oleate, butylated hydroxyanisole, gelatin (type 195), sorbitol (A810, 50/50 w/glycerin), titanium dioxide (E171), yellow iron oxide (E172), red iron oxide (E172), shellac glaze (partially esterified), iron oxide black (E172), propylene glycol.

- The capsules contain sucrose, sorbitol, sodium and might also contain traces of soy. See also section 2, 'Important information about some of the medicine's ingredients'.

- Each capsule contains 7 mg sorbitol and 20 mg sucrose.

What does the medicine look like and what does the package contain?
The package contains one or four white-caramel colored capsules with 'HE1' printed on them.

Registration Holder: Rafa Laboratories Ltd., PO Box 405, Jerusalem 9100301.
Manufacturer: Helsinn Birex Pharmaceuticals Ltd., Dublin, Ireland.
Medicine registration number in the National Medicines Registry of the Ministry of Health: 155-79-34343

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