

CONTRAINDICATIONS

- Apixaban is contraindicated for use by patients with severe hypersensitivity to the drug.
- Apixaban is contraindicated in any patient with active pathological bleeding, as apixaban use increases the risk of bleeding and can cause serious and potentially fatal bleeding.
- The use of apixaban in patients with prosthetic heart valves has not been studied; use in this population is not recommended.

STORAGE CONDITIONS AND OTHER INFORMATION

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the carton and on the blister after EXP. Ask your pharmacist how to throw away medicines you no longer use.

PRESENTATION:

Actapix 2.5mg tablet is available in blister pack of 30's.
Actapix 5mg tablet is available in blister pack of 30's.

ہدایات:

- خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
- دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر روشنی سے بچا کر خشک جگہ پر رکھیں۔
- صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کریں۔
- بچوں کی پہنچ سے دور رکھیں۔

Manufactured by:

Kaizen Pharmaceuticals (Pvt.) Ltd.,
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Bin Qasim, Karachi-75020, Pakistan.

Art no: 627/1

Actapix®

(APIXABAN)

Actapix Tablet 2.5mg

Each film coated tablet contains:
Apixaban 2.5 mg.

Actapix Tablet 5mg

Each film coated tablet contains:
Apixaban 5 mg.

ایکٹا پکس
(ایپکزابان)

۲۰۵ ملی گرام اور ۵ ملی گرام

WARNING: PREMATURE DISCONTINUATION OF APIXABAN INCREASES THE RISK OF THROMBOTIC EVENTS

Premature discontinuation of any oral anticoagulant, including APIXABAN, increases the risk of thrombotic events. To reduce this risk, consider coverage with another anticoagulant if APIXABAN is discontinued for a reason other than pathological bleeding or completion of a course of therapy.

CLINICAL PHARMACOLOGY:

Pharmacodynamics:

The pharmacodynamic effects of apixaban are reflective of the mechanism of action (FXa inhibition). As a result of FXa inhibition, apixaban prolongs clotting tests such as prothrombin time (PT), INR and activated partial thromboplastin time (aPTT). Changes observed in these clotting tests at the expected therapeutic dose are small and subject to a high degree of variability. They are not recommended to assess the pharmacodynamic effects of apixaban. In the thrombin generation assay, apixaban reduced endogenous thrombin potential, a measure of thrombin generation in human plasma.

Apixaban also demonstrates anti-FXa activity as evident by reduction in Factor Xa enzyme activity in multiple commercial anti-FXa kits, however results differ across kits. Data from clinical trials are only available for the Rotachrom® Heparin chromogenic assay. Anti-FXa activity exhibits a close direct linear relationship with apixaban plasma concentration, reaching maximum values at the time of apixaban peak plasma concentrations. The relationship between apixaban plasma concentration and anti-FXa activity is approximately linear over a wide dose range of apixaban.

Pharmacokinetics:

Absorption/Bioavailability:

The absolute bioavailability of apixaban is approximately 50% for doses up to 10 mg. Apixaban is rapidly absorbed with maximum concentrations (C_{max}) appearing 3 to 4 hours after tablet intake. Intake with food does not affect apixaban AUC or C_{max} at the 10 mg dose. Apixaban can be taken with or without food.

Distribution and Protein Binding:

Plasma protein binding in humans is approximately 87%. The volume of distribution (V_{ss}) is approximately 21 liters.

Metabolism:

In humans Apixaban dose is 25% recovered as metabolites with the majority recovered in faeces.

O-demethylation and hydroxylation at the 3-oxopiperidiny moiety are the major sites of biotransformation. Apixaban is metabolised mainly via CYP3A4/5 with minor contributions from CYP1A2, 2C8, 2C9, 2C19, and 2J2. Unchanged apixaban is the major drug-related component in human plasma with no active circulating metabolites present. Apixaban is a substrate of transport proteins, P-gp and breast cancer resistance protein (BCRP).

Elimination:

Apixaban has multiple routes of elimination. Of the administered apixaban dose in humans, approximately 25% was recovered as metabolites, with the majority recovered in faeces. Renal excretion of apixaban accounts for approximately 27% of total clearance.

Effects of this medicine

Actapix contains the active substance Apixaban and belongs to a group of medicines called anticoagulants. This medicine helps to prevent blood clots from forming by blocking Factor Xa, which is an important component of blood clotting. Actapix is used in adults: – to prevent a blood clot from forming in the heart in patients with an irregular heart beat (atrial fibrillation) and at least one additional risk factor. Blood clots may break off and travel to the brain and lead to a stroke or to other organs and prevent normal blood flow to that organ (also known as a systemic embolism). A stroke can be life-threatening and requires immediate medical attention. – to treat blood clots in the veins of your legs (deep vein thrombosis) and in the blood vessels of your lungs (pulmonary embolism), and to prevent blood clots from re-occurring in the blood vessels of your legs and/or lungs.

POSODOLOGY:

Prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation (NVAf).

The recommended dose of apixaban is 5 mg taken orally twice daily. The recommended dose of apixaban is 2.5 mg taken orally twice daily in patients with NVAf and at least two of the following characteristics: age $\geq$ 80 years, body weight $\leq$ 60 kg, or serum creatinine $\geq$ 1.5 mg/dL (133 micromole/L). Therapy should be continued long-term.

Usual dose:

Dose of apixaban is 5 mg taken orally twice daily.

- Swallow the tablet with a drink of water.
- Try to take the tablets at the same times every day to have the best treatment effect.
- If you have difficulty swallowing the tablet whole, talk to your doctor about other ways to take Actapix. The tablet may be crushed and mixed with water, or 5% dextrose in water, or apple juice or apple puree, immediately before you take it.

Instructions for crushing:

- Crush the tablets with a pestle and mortar.
- Transfer all the powder carefully into a suitable container then mix the powder with a little e.g., 30 mL (2 tablespoons), water or one of the other liquids mentioned above to make a mixture.
- Swallow the mixture.
- Rinse the pestle and mortar you used for crushing the tablet and the container, with a little water or one of the other liquids (e.g., 30 mL), and swallow the rinse. If necessary, your doctor may also give you the crushed Actapix tablet mixed in 60 mL of water or 5% dextrose in water, through a nasogastric tube.

Overdose:

Overdose of apixaban may result in a higher risk of bleeding. In the event of haemorrhagic complications, treatment must be discontinued and the source of bleeding investigated. The initiation of appropriate treatment, e.g., surgical haemostasis, the transfusion of fresh frozen plasma or the administration of a reversal agent for factor Xa inhibitors should be considered.

Missed Dose:

If you are not sure what to do or have missed more than one dose, ask your doctor, pharmacist or nurse.

Take the dose as soon as you remember and:

- Take the next dose of Actapix at the usual time then continue as normal.

PRECAUTIONS WHILE TAKING THIS MEDICINE

Talk to your doctor, pharmacist or nurse before you take this medicine if you have any of the following: – an increased risk of bleeding, such as:

- Bleeding disorders, including conditions resulting in reduced platelet activity
- Very high blood pressure, not controlled by medical treatment.
- You are older than 75 years.
- You weigh 60 kg or less – a severe kidney disease or if you are on dialysis.
- A liver problem or a history of liver problems Actapix will be used with caution in patients with signs of altered liver function.

Take special care with Actapix

If you know that you have a disease called antiphospholipid syndrome

(a disorder of the immune system that causes an increased risk of blood clots), tell your doctor who will decide if the treatment may need to be changed.

Children and adolescents

Actapix is not recommended in children and adolescents under 18 years of age.

Women of Childbearing Potential

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor, pharmacist or nurse for advice before taking this medicine.

Pregnant Women

- The effects of Actapix on pregnancy and the unborn child are not known.
- You should not take Actapix if you are pregnant.
- Contact your doctor immediately if you become pregnant while taking Actapix.
- It is not known if Actapix passes into human breast milk.

Effects on ability to drive and use machines

Actapix has no or negligible influence on the ability to drive and use machines.

SIDE EFFECTS:

If you get any side effects, talk to your doctor, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

Bleeding including:

- From your nose
- From your gums
- Blood in the urine
- Bruising and swelling
- In your stomach, your bowel, from your rectum
- In your mouth
- From the vagina
- Anaemia which may cause tiredness or paleness
- Reduced number of platelets in your blood (which can affect clotting)
- Nausea (feeling sick)
- Skin rash
- Blood tests may show: – an increase in gamma-glutamyltransferase (GGT) or alanine aminotransferase (ALT).

SPECIAL WARNINGS:

Increased risk of bleeding, such as:

- Bleeding disorders, including conditions resulting in reduced platelet activity.
- Very high blood pressure, not controlled by medical treatment.
- You are older than 75 years.
- You weigh 60 kg or less.

DRUG INTERACTIONS:

Keep a list of all the products you use (including prescription/nonprescription drugs and herbal products) and share it with your doctor and pharmacist. Some products that may interact with this drug include:

- Mifepristone, other drugs that can cause bleeding/bruising (including antiplatelet drugs such as clopidogrel, "blood thinners" such as warfarin, enoxaparin), certain antidepressants (including SSRIs such as fluoxetine, SNRIs such as desvenlafaxine/venlafaxine).

Other medications can affect the removal of apixaban from your body, which may affect how apixaban works. Examples include certain azole antifungals (such as itraconazole, ketoconazole, posaconazole), conivaptan, HIV protease inhibitors (such as lopinavir, ritonavir), rifamycins (such as rifabutin), St. John's wort, drugs used to treat seizures (such as carbamazepine, phenytoin), among others. Check all prescription and nonprescription medicine labels carefully since many medications contain pain relievers/fever reducers (aspirin, NSAIDs such as ibuprofen, naproxen) that may increase your risk for bleeding if taken together with this medication.