RIBAX

(Rivaroxaban)

Tablets U.S.P.

2.5mg
10mg
15mg
20mg
Tablets

ریبکس

(ریواروکسابن)

ٹیبلٹس یو۔ایس۔پی۔

۲.۵ ملی گرام
۱۰ ملی گرام
۱۵ ملی گرام
۲۰ ملی گرام

QUALITATIVE AND QUANTITATIVE COMPOSITION

Ribax 20mg tablets U.S.P.:

Each film-coated tablet contains: Rivaroxaban……20mg

Ribax 15mg tablets U.S.P.:

Each film-coated tablet contains: Rivaroxaban……15mg

Ribax 10mg tablets U.S.P.:

Each film-coated tablet contains: Rivaroxaban……10mg

Ribax 2.5mg tablets U.S.P.:

Each film-coated tablet contains: Rivaroxaban……2.5mg

WARNING:

PREMATURE DISCONTINUATION OF RIVAROXABAN INCREASES THE RISK OF THROMBOTIC EVENTS,

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

SPINAL/EPIDURAL HEMATOMA

Epidural or spinal hematomas have occurred in patients treated with Rivaroxaban who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Monitor patients frequently for signs and symptoms of neurological impairment and if observed, treat urgently. Consider the benefits and risks before neuraxial intervention in patients who are or who need to be anticoagulated.

DESCRIPTION

Rivaroxaban, FXa inhibitor, is a pure (S)-enantiomer. It is an odorless, non-hygroscopic, white to yellowish powder. Rivaroxaban is only slightly soluble in organic solvents(e.g., acetone, polyethylene glycol 400) and is practically insoluble in water and aqueous media.

CLINICAL PHARMACOLOGY

Mechanism of Action: Rivaroxaban is a selective inhibitor of FXa. It does not require a cofactor (such as Anti-thrombin III) for activity. Rivaroxaban inhibits free FXa and prothrombinase activity. Rivaroxaban has no direct effect on platelet aggregation, but indirectly inhibits platelet aggregation induced by thrombin. By inhibiting FXa, rivaroxaban decreases thrombin generation. **Pharmacodynamics:** Dose-dependent inhibition of FXa activity was observed in humans. Anti-factor Xa activity is also influenced by rivaroxaban. **Pharmacokinetics: Absorption:** The absolute bioavailability of Rivaroxaban is dose-dependent. Co-administration of RIBAX with food increases the bioavailability of the 20 mg dose. RIBAX 15 mg and 20 mg tablets should be taken with food. The maximum concentrations (Cmax) of rivaroxaban appear 2 to 4 hours after tablet intake. **Distribution:** Plasma protein binding of Rivaroxaban in human plasma is approximately 92% to 95%, with albumin being the main binding component. The steady-state volume of distribution in healthy subjects is approximately 50 L. **Metabolism:** Approximately 51% of an orally administered [14 C]-rivaroxaban dose was recovered as inactive metabolites in urine (30%) and feces (21%). **Excretion:** Rivaroxaban is a low-clearance drug, with a systemic clearance of approximately 10 L/hr in healthy volunteers following intravenous administration.

INDICATIONS AND USAGE

Reduction of Risk of Stroke and Systemic Embolism in Non-valvular Atrial Fibrillation: RIBAX is indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. **Treatment of Deep Vein Thrombosis:** RIBAX is indicated for the treatment of deep vein thrombosis (DVT). **Treatment of Pulmonary Embolism:** RIBAX is indicated for the treatment of pulmonary embolism (PE). **Reduction in the Risk of Recurrence of Deep Vein Thrombosis and of Pulmonary Embolism:** RIBAX is indicated for the reduction in the risk of recurrence of deep vein thrombosis and of pulmonary embolism following initial 6 months treatment for DVT and/or PE. **Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery:** RIBAX is indicated for the prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery.

CONTRAINDICATIONS

RIBAX is contraindicated in patients with: Active pathological bleeding. Severe hypersensitivity reaction (e.g., anaphylactic reactions).

INTERACTIONS

General Inhibition and Induction Properties: Combined P-gp and strong CYP3A4 inhibitors increase exposure to Rivaroxaban and may increase the risk of bleeding. Combined P-gp and strong CYP3A4 inducers decrease exposure to Rivaroxaban and may increase the risk of thromboembolic events. **Drugs that Inhibit Cytochrome P450 3A4 Enzymes and Drug Transport Systems. Interaction with Combined P-gp and Strong CYP3A4 Inhibitors:** Avoid concomitant administration of RIBAX with known combined P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole and ritonavir) **Interaction with Combined P-gp and Moderate CYP3A4 Inhibitors in patients with Renal Impairment**: RIBAX should not be used in patients with CrCl 15 to <80 mL/min who are receiving concomitant combined P-gp and moderate CYP3A4 inhibitors (e.g., erythromycin) unless the potential benefit justifies the potential risk. Drugs that Induce Cytochrome P450 3A4 Enzymes and Drug Transport Systems: Avoid concomitant use of RIBAX with drugs that are combined P-gp and strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifampin, St. John's wort). **Anticoagulants and NSAIDs/Aspirin:** Co-administration of enoxaparin, warfarin, aspirin, clopidogrel and chronic NSAID use may increase the risk of bleeding. Avoid concurrent use of RIBAX with other anticoagulants due to increased bleeding risk unless benefit outweighs risk. Promptly evaluate any signs or symptoms of blood loss if patients are treated concomitantly with aspirin, other platelet aggregation inhibitors, or NSAIDs.

USE IN SPECIFIC POPULATION

Pregnancy(Category C): Use RIBAX with caution in pregnant patients because of the potential for pregnancy related hemorrhage and/or emergent delivery with an anticoagulant that is not readily reversible. The anticoagulant effect of RIBAX cannot be reliably monitored with standard laboratory testing. **Labor and Delivery:** Safety and effectiveness of RIBAX during labor and delivery have not been studied in clinical trials. However, in animal studies maternal bleeding and maternal and fetal death occurred at the rivaroxaban dose of 40 mg/kg. **Nursing Mothers:** Many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Rivaroxaban, use with caution or discontinue. **Pediatric Use:** Safety and effectiveness in pediatric patients have not been established. **Geriatric Use:** Both thrombotic and bleeding event rates were higher in these older patients. **Females of Reproductive Potential:** Females of reproductive potential requiring anticoagulation should discuss pregnancy planning with their physician. **Renal Impairment:** Rivaroxaban exposure increased by approximately 44 to 64% in subjects with renal impairment, increase in pharmacodynamic effects were also observed. **Treatment of DVT and/or PE, and Reduction in the Risk of Recurrence of DVT and of PE:** Avoid the use of RIBAX in patients with CrCl <30 mL/min. **Prophylaxis of DVT Following Hip or Knee Replacement Surgery:** Avoid the use

of RIBAX in patients with CrCl <30 mL/min. **Hepatic Impairment:** The safety or PK of Rivaroxaban in patients with severe hepatic impairment (Child-Pugh C) has not been evaluated. Avoid the use of Rivaroxaban in patients with moderate (Child-Pugh B) and severe (Child-Pugh C) hepatic impairment or with any hepatic disease associated with coagulopathy.

OVERDOSAGE

Overdose of Rivaroxaban may lead to hemorrhage. Discontinue RIBAX and initiate appropriate therapy if bleeding complications associated with over dosage occur.

PRECAUTIONS

Increased risk of thrombotic events after premature discontinuation.
risk of bleeding, reversal of anticoagulant effect, spinal/epidural anesthesia or puncture, use in patients with renal impairment, non-valvular atrial fibrillation, use in patients with hepatic impairment, use with p-gp and strong cyp3a4 inhibitors or inducers, risk of pregnancy-related hemorrhage, patients with prosthetic heart valves.

ADVERSE REACTIONS

Increased risk of stroke after discontinuation in non-valvular atrial fibrillation.
Bleeding risk. Spinal/epidural hematoma. Other effects include, nausea, vomiting, diarrhea, constipation, dyspepsia, abdominal pain, hypotension, pain in extremities, pruritus and rash. Less commonly dry mouth, thrombocythaemia, tachycardia, syncope, malaise, rarely jaundice & oedema.

SIDE EFFECTS

Back pain , bleeding gums , bloody stools bowel or bladder dysfunction , burning, itching, numbness, tingling feelings coughing up blood difficulty with breathing or swallowing dizziness, headache .

DOSAGE AND ADMINISTRATION

Take 15 mg and 20 mg tablets with food.
Non-valvular Atrial Fibrillation: For patients with CrCl >50 mL/min: 20 mg orally, once daily with the evening meal. For patients with CrCl 15 - 50 mL/min: 15 mg orally, once daily with the evening meal. **Treatment of DVT, PE, and Reduction in the Risk of Recurrence of DVT and of PE:** 15 mg orally twice daily with food for the first 21 days for the initial treatment of acute DVT or PE. After the initial treatment period, 20 mg orally once daily with food for the remaining treatment and the long-term reduction in the risk of recurrence of DVT and PE. **Prophylaxis of DVT Following Hip or Knee Replacement Surgery:** 10 mg orally, once daily with or without food. **Discontinuation for Surgery and other Interventions:** If anticoagulation must be discontinued to reduce the risk of bleeding with surgical or other procedures, RIBAX should be stopped at least 24 hours before the procedure to reduce the risk of bleeding. **Switching to and from RIBAX Switching from Warfarin to RIBAX:** When switching patients from warfarin to RIBAX, discontinue warfarin and start RIBAX as soon as the International Normalized Ratio (INR) is below 3.0 to avoid periods of inadequate anticoagulation. **Switching from RIBAX to Warfarin:** No clinical trial data is available to guide converting patients from RIBAX to warfarin. Rivaroxaban affects INR, so INR measurements made during co-administration with warfarin may not be useful for determining the appropriate dose of warfarin. One approach is to discontinue RIBAX and begin both a parenteral anticoagulant and warfarin at the time the next dose of RIBAX would have been taken. **Switching from RIBAX to Anticoagulants other than Warfarin:** For patients currently taking RIBAX and transitioning to an anticoagulant with rapid onset, discontinue RIBAX and give the first dose of the other anticoagulant (oral or parenteral) at the time that the next RIBAX dose would have been taken. **Switching from Anticoagulants other than Warfarin to RIBAX:** For patients currently receiving an anticoagulant other than warfarin, start RIBAX 0 to 2 hours prior to the next scheduled evening administration of the drug (e.g., low molecular weight heparin or non-warfarin oral anticoagulant) and omit

administration of the other anticoagulant. For patients with CrCl 15 to 50 mL/min, the recommended dose is 15 mg once daily with the evening meal. **Missed Dose:** If a dose of RIBAX is not taken at the scheduled time, administer the dose as soon as possible on the same day as follows: For patients receiving 15 mg twice daily: The patient should take RIBAX immediately to ensure intake of 30 mg RIBAX per day. In this particular instance, two 15 mg tablets may be taken at once. The patient should continue with the regular 15 mg twice daily intake as recommended on the following day. For patients receiving 20 mg, 15 mg once daily: The patient should take the missed RIBAX dose immediately. **Administration Options:** For patients who are unable to swallow whole tablets, 15mg or 20mg RIBAX tablets may be crushed and mixed with applesauce immediately prior to use and administered orally. After the administration of a crushed RIBAX 15 mg or 20 mg tablet, the dose should be immediately followed by food. **Administration via nasogastric (NG) tube or gastric feeding tube:** After confirming gastric placement of the tube, 15mg or 20mg RIBAX tablets may be crushed and suspended in 50 mL of water and administered via an NG tube or gastric feeding tube. Since Rivaroxaban absorption is dependent on the site of drug release, avoid administration of RIBAX distal to the stomach which can result in reduced absorption and thereby, reduced drug exposure.

DOSAGE: As directed by the physician.

INSTRUCTIONS: Store at 25°C,
excursions permitted to 15°C - 30°C.
Protect from sunlight and moisture.
Keep all medicines out of the reach of children.

PRESENTATION

RIBAX (Rivaroxaban) tablets 20mg are available in Alu-Alu blister pack of 1x14's tablets. RIBAX (Rivaroxaban) tablets 15mg are available in Alu-Alu blister pack of 1x14's tablets. RIBAX (Rivaroxaban) tablets 10mg are available in Alu-Alu blister pack of 1x10's tablets. RIBAX (Rivaroxaban) tablets 2.5mg are available in Alu-Alu blister pack of 1x14's tablets.

علامات/طریقہ استعمال: نون والولیر ایٹریل فبریلشن کے مریضوں میں
اسٹروک اور سسٹیمک ایمبولیسم کے خطرے میں کمی کے لئے استعمال کیا جاتا ہے۔
گہری رگ میں منجمد خون کے علاج کیلئے۔
پلمونری ایمبولیسم کے علاج کیلئے۔
گھٹنے اور کولہے کی متبادل سرجری میں خون کے منجمد ہونے سے بچاؤ کے لئے استعمال کیا جاتا ہے۔ ۱۵ اور ۲۰ ملی گرام ٹیبلٹس کھانے کے ساتھ لی جائے۔
نون والولیر ایٹریل فبریلشن: کریٹینین کلیئرنس ۱۵-۵۰ ملی گرام/منٹ میں ۱۵ ملی گرام دن میں ایک دفعہ رات کے کھانے کے ساتھ لی جائے۔
جبکہ ۵۰ ملی گرام/منٹ سے زیادہ کریٹینین کلیئرنس میں ۲۰ ملی گرام دن میں ایک مرتبہ رات کے کھانے کے ساتھ لی جائے۔
مضر اثرات: خون کے منجمد ہونے کے دورانیہ میں اضافہ ہوسکتا ہے۔
کمر درد، مسوڑوں سے خون آنا، پاخانے میں خون آنا، مثانے میں خرابی، جلن، کھجلی، سن ہونا، کھانسی میں خون آنا، سانس لینے اور نگلنے میں تکلیف، چکر اور سر درد۔
احتیاط: جگر اور گردے کے مریض احتیاط سے استعمال کریں۔
دل کے مریض احتیاط سے استعمال کریں۔
خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات: ۲۵ ڈگری سینٹی گریڈ پر رکھیں، محفوظ رکھنے کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔
سورج کی روشنی اور نمی سے محفوظ رکھیں۔ تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

For detailed information:

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ISO 9001:2015 ISO 14001:2015 ISO 45001:2018

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