Ivagen™ 5mg, 7.5mg Tablets

(IVABRADINE)

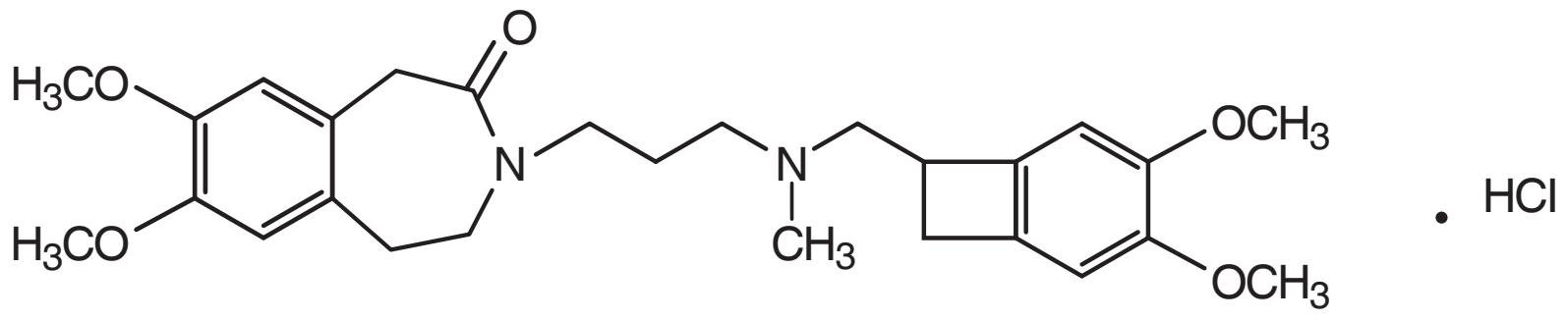
آئِواجِن ۵ ملی گرام ۷.۵ ملی گرام ٹیبلٹس

(آئِوابراڈِن)

DESCRIPTION:

Ivagen is a type of medicine called a selective If current inhibitor. It helps to lower the heart rate which can be helpful in treating both angina & heart failure.

Chemical Structure



CHEMICAL NAME: 3-(3-{[((7S)-3,4 Dimethoxybicyclo[4,2,0]octa-1,3,5-trien-7-yl) methyl]methylamino}propyl)-1,3,4,5-tetrahydro-7,8-dimethoxy-2H-3-benzaze pin-2-one, hydrochloride. **Molecular formula:** C27H36N2O5, HCl. **Molecular weight:** 505.06

COMPOSITION

Ivagen 5mg Tablets:
Each film-coated tablet contains:
Ivabradine Hydrochloride eq. to Ivabradine.....5mg
Genix Specifications

Ivagen 7.5mg Tablets:
Each film-coated tablet contains:
Ivabradine Hydrochloride eq. to Ivabradine.....7.5mg
Genix Specifications

MODE OF ACTION

IVAGEN is a heart rate lowering agent. It acts by selective and specific inhibition of the cardiac pacemaker I*Kf* current, an important ionic current that usually controls spontaneous diastolic depolarization in the sinus node and thereby regulates heart rate. The cardiac effects of IVAGEN are specific to the sinus node and IVAGEN has no effect on intra-atrial, atrioventricular or intraventricular conduction times, myocardial contractility or ventricular repolarisation. An elevated heart rate increases myocardial oxygen demand and limits tissue perfusion, the latter by reducing the duration of diastole, during which most myocardial perfusion occurs. Therefore, a pure reduction in heart rate can reduce myocardial ischaemia and prevent angina pectoris.

THERAPEUTIC INDICATIONS

Treatment of coronary artery disease: Symptomatic treatment of chronic stable angina pectoris in coronary artery disease adults with normal sinus rhythm. **IVAGEN is indicated:** In adults unable to tolerate or with a contra-indication to the use of beta-blockers or in combination with beta-blockers in patients inadequately controlled with an optimal beta-blocker dose and whose heart rate is > 60 bpm. **Treatment of chronic heart failure**: IVAGEN is indicated in chronic heart failure NYHA II to IV class with systolic dysfunction, in patients in sinus rhythm and whose heart rate is ≥ 75 bpm, in combination with standard therapy including beta-blocker therapy or when beta-blocker therapy is contraindicated or not tolerated.

PHARMACOKINETIC PROPERTIES

Absorption and bioavailability: IVAGEN is rapidly and almost completely absorbed after oral administration with a peak plasma level reached in about 1 hour under fasting condition. The absolute bioavailability of the film-coated tablets is around 40%, due to first-pass effect in the gut and liver. Food delayed

absorption by approximately 1 hour, and increased plasma exposure by 20 to 30 %. The intake of the tablet during meals is recommended in order to decrease intra-individual variability in exposure. **Distribution:** IVAGEN is approximately 70% plasma protein bound and the volume of distribution at steady-state is close to 100-litre in patients. The maximum plasma concentration following chronic administration at the recommended dose of 5 mg twice daily is 22 ng/ml (CV=29%). The average plasma concentration is 10 ng/ml (CV=38%) at steady-state. **Biotransformation:** IVAGEN is extensively metabolised by the liver and the gut by oxidation through cytochrome P450 3A4 (CYP3A4) only. The major active metabolite is the N-desmethylated derivative (S 18982) with an exposure about 40% of that of the parent compound. The metabolism of this active metabolite also involves CYP3A4. IVAGEN has low affinity for CYP3A4, shows no clinically relevant CYP3A4 induction or inhibition and is therefore unlikely to modify CYP3A4 substrate metabolism or plasma concentrations. Inversely, potent inhibitors and inducers may substantially affect IVAGEN plasma concentrations. **Elimination:** IVAGEN is eliminated with a main half-life of 2 hours (70-75% of the AUC) in plasma and an effective half-life of 11 hours. The total clearance is about 400 ml/min and the renal clearance is about 70 ml/min. Excretion of metabolites occurs to a similar extent via faeces and urine. About 4% of an oral dose is excreted unchanged in urine. Linearity/non linearity The kinetics of IVAGEN is linear over an oral dose range of 0.5 – 24 mg.

DOSAGE

The usual recommended dose is 5 mg twice daily. The dose may be increased after 2 to 4 weeks to 7.5 mg twice daily, if necessary. If the heart rate decreases below 50 bpm at rest or if the patient experiences symptoms related to bradycardia, the dose should be reduced to 2.5 mg twice daily. Treatment should be stopped if the heart rate remains below 50 bpm or if symptoms of bradycardia persist. Adults over the age of 75 years should start treatment with a lower dose i.e. 2.5 mg twice daily.

PATIENTS WITH RENAL IMPAIRMENT

No dose adjustment is required in patients with renal insufficiency and creatinine clearance above 15 ml/min

No data are available in patients with creatinine clearance below 15 ml/min. IVAGEN should therefore be used with precaution in this population.

PATIENTS WITH HEPATIC IMPAIRMENT

No dose adjustment is required in patients with mild hepatic impairment. Caution should be exercised when using IVAGEN in patients with moderate hepatic impairment. IVAGEN is contra-indicated for use in patients with severe hepatic insufficiency, since it has not been studied in this population and a large increase in systemic exposure is anticipated.

CONTRAINDICATIONS

- Hypersensitivity to the active substance or to any of the excipients.
- Resting heart rate below 60 beats per minute prior to treatment
- Cardiogenic shock
- Acute myocardial infarction
- Severe hypotension (< 90/50 mmHg)
- Severe hepatic insufficiency
- Sick sinus syndrome
- Sino-atrial block
- Unstable or acute heart failure
- Pacemaker dependent (heart rate imposed exclusively by the pacemaker)
- Unstable angina
- AV-block of 3rd degree
- Combination with strong cytochrome P450 3A4 inhibitors such as azole antifungals (ketoconazole, itraconazole), macrolide antibiotics (clarithromycin, erythromycin per os, josamycin, telithromycin), HIV protease inhibitors (nelfinavir, ritonavir) and nefazodone.

DRUG INTERACTIONS

If you are taking another drug concomitantly or if you have just finished treatment with another medicine, inform the attending doctor in order to prevent hazards or lack of efficacy arising from drug interactions. This is especially important for medicines belonging to the following groups: Medicines for high blood pressure or angina pectoris (such as: diltiazem, verapamil), QT prolonging medicines to treat either heart rhythm disorders or other conditions (such as: quinidine, sotalol, amiodarone, disopyramide, ibutilide); bepridil (for Angina Pectoris), fluconazole (an antifungal agent), rifampicin (an antibiotic); barbiturates (for epilepsy) phenytoin (for epilepsy); Hypericum perforatum or St John's Wort (herbal treatment for depression); certain types of medicines to treat anxiety and schizophrenia such as pimozide, ziprasidone, sertindole); anti- malarial medicines (such as mefloquine or halofantrine); erythromycin IV (an antibiotic); pentamidine (an antiparasitic medicine); cisapride (against the heart burn)

PREGNANCY AND LACTATION

IVAGEN is contraindicated for use during pregnancy and
Lactation

SPECIAL POPULATIONS

Older people: no pharmacokinetic differences (AUC and Cmax) have been observed between elderly (≥ 65 years) or very elderly patients (≥ 75 years) and the overall population.

SIDE-EFFECTS

In addition to the desired activity of the medicine, adverse reactions may occur during the course of this medicine, for example: luminous visual phenomena (brief moments of increased brightness, most often caused by sudden changes in light intensity), blurred vision, slowing down of the heart rate, headache. Other side effects that may appear, although less frequently are: palpitations. If any of these side effects are bothering some or continue, consult a doctor.

SIDE-EFFECTS WHICH REQUIRE SPECIAL ATTENTION

Less common side effects reported are: disturbances in heart rate, nausea, constipation, diarrhoea, vertigo, dyspnoea, muscle cramps and changes in laboratory parameters (blood tests) - if these side effects appear, consult a doctor.

DOSAGE

As directed by the physician.

INSTRUCTIONS

Store below 30ºC. Protect from heat, light & moisture.
Keep all medicines out of the reach of children.

PRESENTATION

Ivagen (Ivabradine) 5mg tablets are available in Alu-Alu blister pack of 2x14's.
Ivagen (Ivabradine) 7.5mg tablets are available in Alu-Alu blister pack of 2x14's.

خوراک : معالج کی ہدایت کے مطابق استعمال کریں۔
ہدایات : ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، روشنی اور نمی سے محفوظ رکھیں۔تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

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