United Pharmaceuticals

Vivazac® Plus

Irbesartan / Hydrochlorothiazide

Description:
VIVAZAC® PLUS is a combination of two active substances, Irbesartan and Hydrochlorothiazide.
Irbesartan belongs to a group of medicines known as angiotensin II receptor antagonists. Angiotensin II is a substance produced in the body that binds to receptors in blood vessels causing them to tighten. This results in an increase in blood pressure. Irbesartan prevents the binding of angiotensin II to these receptors, causing the blood vessels to relax and the blood pressure to be low.
Hydrochlorothiazide is a thiazide diuretic that causes increased in urine output and so causes a lowering in blood pressure.
The two active ingredients in **VIVAZAC® PLUS** works together to lower blood pressure further than if either was given alone.
Properties:
Concomitant administration of Hydrochlorothiazide and Irbesartan has no effect on the pharmacokinetics of either medicinal product.
Absorption: Irbesartan and Hydrochlorothiazide are orally active agents and do not require biotransformation for their activity. Following oral administration of **VIVAZAC® PLUS**, the absolute oral bioavailability is 60-80% and 50-80% for Irbesartan and Hydrochlorothiazide, respectively. Food does not affect the bioavailability of **VIVAZAC® PLUS**. Peak plasma concentration occurs at 1-2 hours after oral administration for Irbesartan and 1-2.5 hours for Hydrochlorothiazide.
Distribution: Plasma protein binding of Irbesartan is approximately 96%, with negligible binding to cellular blood components. The volume of distribution for Irbesartan is 53-93 liters.
Hydrochlorothiazide is 68% protein-bound in the plasma, and its apparent volume of distribution is 0.83-1.14 l/kg.
Metabolism: Irbesartan is metabolized by the liver via glucuronide conjugation and oxidation. The major circulating metabolite is Irbesartan glucuronide (approximately 6%). Hydrochlorothiazide is not metabolized.
Elimination: The total body and renal clearance are 157-176 and 3.0-3.5 ml/min, respectively. The terminal elimination half-life of Irbesartan is 11-15 hours. Steady-state plasma concentrations are attained within 3 days after initiation of a once-daily dosing regimen.
After oral administration of Irbesartan, about 20% is recovered in the urine, and the remainder in the feces. Less than 2% of the dose is excreted in the urine as unchanged Irbesartan.
Hydrochlorothiazide is eliminated rapidly by the kidney. At least 61% of the oral dose is eliminated rapidly by the kidneys.
Indications:
VIVAZAC® PLUS is indicated for the treatment of high blood pressure, when treatment with Irbesartan or Hydrochlorothiazide alone did not provide adequate control of your blood pressure.
Dosage and administration:
Always take **VIVAZAC® PLUS** exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.
Dosage:
The usual dose of **VIVAZAC® PLUS** is one tablet a day.
- **VIVAZAC® PLUS** will usually be prescribed by your doctor when your previous treatment for high blood pressure did not provide appropriate blood pressure reduction. Your doctor will instruct you how to switch from the previous treatment to **VIVAZAC® PLUS**.
Method of administration
VIVAZAC® PLUS is for oral use. Swallow the tablets with a sufficient amount of fluid (e.g. one glass of water). You can take **VIVAZAC® PLUS** with or without food.
- Try to take your daily dose at about the same time each day.
- It is important that you continue to take **VIVAZAC® PLUS** until your doctor tells you otherwise.
- The maximal blood pressure lowering effect should be reached 6-8 weeks after the beginning of the treatment.
Children should not take VIVAZAC® PLUS:
VIVAZAC® PLUSshould not be given to children under 18 years of age. If a child swallows some tablets, contact your doctor immediately.
If you forget to take VIVAZAC® PLUS:
If you accidentally miss a daily dose, just take the next dose as normal.
Do not take a double dose to make up for a forgotten dose.
If you have any further questions on the use of this product, ask your doctor or pharmacist.
Contraindications:
Do not take **VIVAZAC® PLUS**
• If you are allergic (hypersensitive) to irbesartan or any of the other ingredients of **VIVAZAC® PLUS**.
• If you are allergic (hypersensitive) to hydrochlorothiazide or any other sulfonamide-derived medicines.
• If you are more than 3 months pregnant. (It is also better to avoid **VIVAZAC® PLUS** in early pregnancy).
• If you have severe liver or kidney problems.
• If you have difficulty in producing urine.
• If your doctor determines that you have persistently high calcium or low potassium levels in your blood.
• The combination aliskiren with an ARB or ACE-inhibitor is strictly contraindicated in those with kidney impairment or diabetes.
• **VIVAZAC® PLUS** should not be given to children and adolescents under 18 years.
Precautions:
Take special care with **VIVAZAC® PLUS**
Tell your doctor if any of the following apply to you:
• If you get excessive vomiting or diarrhoea;
• If you suffer from kidney problems or have a kidney transplant;
• If you suffer from heart problems;
• If you suffer from liver problems;
• If you suffer from diabetes;
• If you suffer from lupus erythematosus (also known as lupus or SLE);
• If you suffer from primary aldosteronism (a condition related to high production of the hormone aldosterone, which causes sodium retention and, in turn, an increase in blood pressure).
You must tell your doctor if you think you are (or might become) pregnant. **VIVAZAC® PLUS** is not recommended in early pregnancy, and must not be taken if you are more than 3 months pregnant, as it may cause serious harm to your baby if used at that stage.
You should also tell your doctor:
• If you are on a low-salt diet;
• If you have signs such as abnormal thirst, dry mouth, general weakness, drowsiness, muscle pain or cramps, nausea, vomiting, or an abnormally fast heart beat which may indicate an excessive effect of hydrochlorothiazide (contained in **VIVAZAC® PLUS**);
• If you experience an increased sensitivity of the skin to the sun with symptoms of sunburn (such as redness, itching, swelling, blistering) occurring more quickly than normal;
• If you are going to have an operation (surgery) or be given anaesthetics.
• The hydrochlorothiazide contained in this medicine could produce a positive result in an anti-doping test.
• Combination of Irbesartan (an ARB drug) with an ACE inhibitor (such as benazepril, captopril, cilazapril, delapril, enalapril, fosinopril, imidapril, lisinopril, moexipril, perindopril, quinapril, ramipril, spirapil, trandolapril, zofenopril) was associated with an increased risk of hyperkalaemia, kidney damage, low blood pressure.
• Combination of Irbesartan (an ARB drug) with an ACE inhibitor is not recommended and, in particular, patients with diabetes-related kidney problem should not be given an ARB with an ACE-inhibitor.
• In a small number of patients (mostly with heart failure) there may still be a medical need to combine medicines of two classes (ARB drug swith ACE inhibitors). When this is considered absolutely necessary, it will be carried out under specialist supervision with close monitoring of kidney function, fluid and salt balance and blood pressure.
Important information about some of the ingredients of VIVAZAC® PLUS:
VIVAZAC® PLUS contains lactose. If you have been told by your doctor that you have intolerance to some sugars (e.g. lactose), contact your doctor before taking this medicine.
- Effect on ability to drive and use machines: No studies on the effects on the ability to drive and use machines have been performed. **VIVAZAC® PLUS** is unlikely to affect your ability to drive or use machines. However occasionally dizziness or weariness may occur during treatment of high blood pressure. If you experience these; talk to your doctor before attempting to drive or use machines.
Use during pregnancy and lactation:
Pregnancy
You must tell your doctor if you think you are (or might become) pregnant. Your doctor will normally advise you to stop taking **VIVAZAC® PLUS** before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of **VIVAZAC® PLUS**.
VIVAZAC® PLUS is not recommended in early pregnancy, and must not be taken when more than 3 months pregnant, as it may cause serious harm to your baby if used after the third month of pregnancy.
Lactation
Tell your doctor if you are breast-feeding or about to start breast-feeding. **VIVAZAC® PLUS** is not recommended for mothers who are breast-feeding, and your doctor may choose another treatment for you if you wish to breast-feed, especially if your baby is newborn, or was born prematurely.
Drug interactions:
Please tell your doctor or pharmacist if you are taking or have recently have taken any other medicines, including medicines obtained without a prescription.
Diuretic agents such as the hydrochlorothiazide contained in **VIVAZAC® PLUS** may have an effect on other medicines. Preparations containing lithium should not be taken with **VIVAZAC® PLUS** without close supervision by your doctor.
You may need to have blood checks if you take:
• Potassium supplements.
• Salt substitutes containing potassium.
• Potassium sparing medicines or other diuretics (water tablets).
• Some laxatives.
• Medicines for the treatment of gout.
• Therapeutic vitamin D supplements.
• Medicines to control heart rhythm.
• Medicines for diabetes; oral agent or Insulins.
• Carbamazepine (a medicine for the treatment of epilepsy).
It is also important to tell the doctor if you are taking other medicines to reduce your blood pressure, steroids, medicines to treat cancer, pain killers or arthritis medicines, or colestyramine and colestipol resins for lowering blood cholesterol.
Taking VIVAZAC® PLUS with food and drink:
VIVAZAC® PLUS can be taken with or without food.
Due to the Hydrochlorothiazide contained in **VIVAZAC® PLUS**, if you drink alcohol while on treatment with this medicine , you may have an increased feeling of dizziness on standing up specially when getting up from a sitting position.
Side effects:
Like all medicines **VIVAZAC® PLUS** can cause side effects although not everybody gets them. Some of these effects may be serious and may require medical attention.
Rare cases of allergic skin reactions (rash, urticaria), as well as localized swelling of the face, lips and \ or tongue have been reported in patients taking Irbesartan.
If you get any of these symptoms or get shortness of breath, stop taking **VIVAZAC® PLUS** and contact your doctor immediately.
Side effects reported for patients treated with **VIVAZAC® PLUS** were:
Common side effects (affect 1 to 10 users in 100)
• Nausea/vomiting,
• Abnormal urination,
• Fatigue,
• Dizziness (including when getting up from a lying or sitting position).
• Blood tests may show raised levels of an enzyme that measures the muscle and heart function (creatine kinase) or raised levels of substances that measure kidney function (blood urea nitrogen, creatinine).
If any of these side effects causes you problems, talk to your doctor.
Uncommon side effects (affect 1 to 10 users in 1,000)
• Diarrhoea,
• Low blood pressure,
• Fainting,
• Heart rate increased,
• Flushing,
• Swelling,
• Sexual dysfunction (problems with sexual performance),
• Blood tests may show lowered levels of potassium and sodium in your blood.
If any of these side effects causes you problems, talk to your doctor.
Undesirable effects where the frequency is not known are: headache, ringing in the ears, cough, taste disturbance, indigestion, pain in joints and muscles, liver function abnormal and impaired kidney function, increased level of potassium in your blood and allergic reactions such as rash, hives, swelling of the face, lips, mouth, tongue or throat. Uncommon cases of jaundice (yellowing of the skin and/or whites of the eyes) have also been reported.
As for any combination of two active substances, side effects associated with each individual component cannot be excluded.
Side effects associated with irbesartan alone
In addition to the side effects listed above, chest pain has also been reported.
Side effects associated with hydrochlorothiazide alone
Loss of appetite; stomach irritation; stomach cramps; constipation; jaundice (yellowing of the skin and/or whites of the eyes); inflammation of the pancreas characterised by severe upper stomach pain, often with nausea and vomiting; sleep disorders; depression; blurred vision; lack of white blood cells, which can result in frequent infections, fever; decrease in the number of platelets (a blood cell essential for the clotting of the blood), decreased number of red blood cells (anaemia) characterised by tiredness, headaches, being short of breath when exercising, dizziness and looking pale; kidney disease; lung problems including pneumonia or build-up of fluid in the lungs; increased sensitivity of the skin to the sun; inflammation of blood vessels; a skin disease characterized by the peeling of the skin all over the body; cutaneous lupus erythematosus, which is identified by a rash that may appear on the face, neck, and scalp; allergic reactions; weakness and muscle spasm; altered heart rate; reduced blood pressure after a change in body position; swelling of the salivary glands; high sugar levels in the blood; sugar in the urine; increases in some kinds of blood fat; high uric acid levels in the blood, which may cause gout.
It is known that side effects associated with hydrochlorothiazide may increase with higher doses of hydrochlorothiazide.
If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.
Overdosage:
Symptoms and signs:
The most likely manifestations of irbesartan overdose are expected to be hypotension and tachycardia; bradycardia might also occur.
Overdose with hydrochlorothiazide is associated with electrolyte depletion (hypokalaemia, hypochloremia, hyponatraemia) and dehydration resulting from excessive diuresis. The most common signs and symptoms of overdose are nausea and somnolence. Hypokalaemia may result in muscle spasms and/or accentuate cardiac arrhythmias associated with the concomitant use of digitalis glycosides or certain anti-arrhythmic medicinal products.
Treatment:
No specific information is available on the treatment of overdose with **VIVAZAC® PLUS**. The patient should be closely monitored, and the treatment should be symptomatic and supportive. Management depends on the time since ingestion and the severity of the symptoms. Suggested measures include induction of emesis and/or gastric lavage. Activated charcoal may be useful in the treatment of overdose. Serum electrolytes and creatinine should be monitored frequently. If hypotension occurs, the patient should be placed in a supine position, with salt and volume replacements given quickly.
Irbesartan is not removed by haemodialysis. The degree to which Hydrochlorothiazide is removed by haemodialysis has not been established.
Storage Conditions:
Store up to 30˚C, Protect from Moisture.
Presentation:
VIVAZAC® PLUS 150/12.5: Each film coated tablet contains 150 mg Irbesartan and 12.5 mg Hydrochlorothiazide in packs of 30 tablets.
VIVAZAC® PLUS 300/12.5: Each film coated tablet contains 300 mg Irbesartan and 12.5 mg Hydrochlorothiazide in packs of 30 tablets.
VIVAZAC® PLUS 300/25: Each film coated tablet contains 300 mg Irbesartan and 25 mg Hydrochlorothiazide in packs of 30 tablets.
Hospital packs are also available.
Excipients:
Lactose, Croscarmellose sodium, Starch, Hypromellose, Microcrystalline Cellulose, Colloidal silicon dioxide, Magnesium Stearate, Opadry White O-YL 28900, Yellow Iron Oxide & Red Iron Oxide.

This is a medicament
· Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
· Follow strictly the doctor´s prescription, the method of use and the instructions of the pharmacist who sold the medicament.
· The doctor and the pharmacist are experts in medicine, its benefits and risks.
· Do not by yourself interrupt the period of treatment prescribed for you.
· Do not repeat the same prescription without consulting your doctor.
· Keep medicament out of the reach of children.
COUNCIL OF ARAB HEALTH MINISTERS
UNION OF ARAB PHARMACISTS

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June, 2014
M3-14-0654