Diostar®
valsartan

Pharmacological Information
Diostar® (valsartan) is an orally active, potent, and specific angiotensin II receptor antagonist. It acts selectively on the AT_1 receptor subtype, which is responsible for the known actions of angiotensin II.
Diostar® does not inhibit ACE, also known as kininase II, which converts angiotensin I to angiotensin II and degrades bradykinin. Since there is no effect on ACE and no potentiation of bradykinin or substance P, angiotensin II antagonists are unlikely to be associated with cough. **Diostar®** does not bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation. Administration of **Diostar®** to patients with hypertension results in reduction of blood pressure without affecting pulse rate. In most patients, after administration of a single oral dose, onset of antihypertensive activity occurs within 2 hours, and the peak reduction of blood pressure is achieved within 4-6 hours. The antihypertensive effect persists over 24 hours after dosing. During repeated dosing, the maximum reduction in blood pressure with any dose is generally attained within 2-4 weeks and is sustained during long-term therapy.
Abrupt withdrawal of **Diostar®** has not been associated with rebound hypertension or other adverse clinical events. In hypertensive patients **Diostar®** has no notable effects on total cholesterol, fasting triglycerides' fasting serum glucose, or uric acid.

Pharmacokinetics
Absorption of **Diostar®** after oral administration is rapid, although the amount absorbed varies widely. Mean absolute bioavailability for valsartan is 23%. The pharmacokinetics of **Diostar®** are linear in the dose range tested. There is no change in the kinetics of **Diostar®** on repeated administration, and little accumulation when dosed once daily. Plasma concentrations were observed to be similar in males and females. Valsartan is highly bound to serum protein (94-97%), mainly serum albumin. Steady state volume of distribution is low (about 17 L). Plasma clearance is relatively slow (about 2 L/h) when compared with hepatic blood flow (about 30 L/h). Of the absorbed dose of valsartan, 70% is excreted in the faeces and 30% in the urine, mainly as unchanged compound.

Indications
- Treatment of hypertension.
- Treatment of heart failure (NYHA class II-IV) in patients receiving usual therapy such as diuretics, digitalis and either ACE inhibitors or beta-blockers but not both.

Dosage and administration
Diostar® can be given either with or without food.

- **Hypertension:** The recommended dose of **Diostar®** is 80mg once daily, irrespective of race, age, or gender. The anti hypertensive effect is substantially present within 2 weeks and maximal effects are seen after 4 weeks. In patients whose blood pressure is not adequately controlled, the daily dose may be increased to 160mg. **Diostar®** may also be administered with other antihypertensive agents.

- **Heart failure:** The recommended starting dose of **Diostar®** is 40mg twice daily. Up titration to 80mg and 160mg twice daily should be done to the highest dose, as tolerated by the patient. The maximum daily dose administered in clinical trials is 320 mg in divided doses.

Pregnancy and lactation
- Valsartan should not be used during pregnancy. If pregnancy is detected during therapy, Valsartan should be discontinued as soon as possible.
- It is not known whether Valsartan is excreted in human milk. Valsartan was excreted in the milk of lactating rats. Thus, it is not advisable to use Valsartan in nursing mothers.

Use in Children
- The safety and efficacy of Valsartan have not been established in children.

Impaired renal function
No dosage adjustment is required for patients with renal impairment. However, in severe cases (creatinine clearance < 10 mL/min.) no data are available, and therefore caution is advised. No studies have been performed in patients undergoing dialysis. However, Valsartan is highly bound to plasma protein and is unlikely to be removed by dialysis.

Hepatic impairment
No dosage adjustment is required for patients with hepatic insufficiency. Particular caution should be exercised when administering Valsartan to patients with biliary obstructive disorders.

Adverse Reactions
- **Adverse Reactions <1%:**
  Dizziness, drowsiness, ataxia, fatigue, hypotension, Increased serum potassium, Abdominal pain, dysgeusia, neutropenia, increased LFT s, cough, viral infection.

- **Adverse Reactions >1%:**
  Headache, alopecia, upper respiratory infection, cough, diarrhea, rhinitis, sinusitis, nausea, pharyngitis, edema, arthralgia.

Clinical Laboratory Tests
- No special monitoring of laboratory parameters is necessary for patients with essential hypertension receiving valsartan therapy.

Precautions
- **Sodium- and/or volume-depleted patients:** such as those receiving high doses of diuretics, symptomatic hypotension may occur in rare cases after initiation of therapy with valsartan. Sodium and/or volume depletion should be corrected before starting treatment with valsartan, for example by reducing the diuretic dose. If hypotension occurs, the patient should be placed in the supine position and, if necessary, given an I.V. infusion of normal saline. Treatment can be continued once the blood pressure has stabilized.
- **Renal artery stenosis:** since other drugs that affect the renin-angiotensin-aldosterone system may increase blood urea and serum creatinine in patients with bilateral or unilateral renal artery stenosis, monitoring is recommended as a safety measure.

Effects on ability to drive and use machines
As with other antihypertensive agents, it is advisable to exercise caution when driving or operating machinery.

Drug interactions
Although valsartan is highly bound to plasma proteins, in vitro studies have not shown any interaction at this level with a range of molecules which are also highly protein bound, such as diclofenac, furosemide, and warfarin.
Concomitant use of potassium sparing diuretics, potassium supplements, or salt substitutes containing potassium may lead to increases in serum potassium and in heart failure patients to increases in serum creatinine. If co-medication is considered necessary, caution is advisable.

Contraindications
Diostar® is contraindicated in patients who are hypersensitive to Valsartan or any component of this product.

Overdosage
Although there is no experience of over dosage with Valsartan, the major sign that might be expected is marked hypotension. If the ingestion is recent, vomiting should be induced, otherwise, the usual treatment would be I.V. infusion of normal saline solution.
Valsartan is unlikely to be removed by hemodialysis.

Presentations:
Diostar® 80mg F/C tablet: Valsartan 80mg/tab (Available in 30 tab pack)
Diostar® 160mg F/C tablet: Valsartan 160mg/tab (Available in 30 tab pack)