xxxxxxxx-5343

VALSARTAN

TORVAL-80
TORVAL-160

80 mg and 160 mg Film-Coated Tablet
Angiotensin II Antagonist

FORMULATION:
Each film-coated tablet contains:
Valsartan ..... 80 mg and 160 mg
PRODUCT DESCRIPTION
Valsartan (Torval-80) 80 mg is a brick red coloured oval shaped, biconvex film coated tablet with breakline on both sides.
Valsartan (Torval-160) 160 mg is a yellow coloured oval shaped, biconvex film coated tablet with breakline on both sides.
CLINICAL PHARMACOLOGY
Mechanism of Action
Angiotensin II is formed from angiotensin I in a reaction catalyzed by angiotensin-converting enzyme (ACE, kininase II). Angiotensin II is the principal pressor agent of the renin angiotensin system, with effects that include vasoconstriction, stimulation of synthesis and release of aldosterone, cardiac stimulation, and renal reabsorption of sodium. Valsartan blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT1 receptor in many tissues, such as vascular smooth muscle and the adrenal gland. Its action is therefore independent of the pathways for angiotensin II synthesis. There is also an AT2 receptor found in many tissues, but AT2 is not known to be associated with cardiovascular homeostasis. Valsartan has much greater affinity (about 20,000-fold) for the AT1 receptor than for the AT2 receptor. The increased plasma levels of angiotensin II following AT1 receptor blockade with Valsartan may stimulate the unblocked AT2 receptor. The primary metabolite of Valsartan is essentially inactive with an affinity for the AT1 receptor about one 200th that of Valsartan itself. Blockade of the renin-angiotensin system with ACE inhibitors, which inhibit the biosynthesis of angiotensin II from angiotensin I, is widely used in the treatment of hypertension. ACE inhibitors also inhibit the degradation of bradykinin, a reaction also catalyzed by ACE. Because Valsartan does not inhibit ACE (kininase II), it does not affect the response to bradykinin. Whether this difference has clinical relevance is not yet known. Valsartan does not bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation. Blockade of the angiotensin II receptor inhibits the negative regulatory feedback of angiotensin II on renin secretion, but the resulting increased plasma renin activity and angiotensin II circulating levels do not overcome the effect of Valsartan on blood pressure.
Pharmacokinetics
Valsartan is rapidly absorbed following oral administration, with a bioavailability of about 23%. Peak plasma concentrations of valsartan occur 2 to 4 hours after an oral dose. It is between 94 and 97% bound to plasma proteins. Valsartan is not significantly metabolised and is excreted mainly via the bile as unchanged drug. The terminal elimination half-life is about 5 to 9 hours. Following an oral dose about 83% is excreted in the feces and 13% in urine.
INDICATIONS
Used in the management of hypertension, to reduce cardiovascular mortality in patients with left ventricular dysfunction after myocardial infarction, and in the management of heart failure.
DOSAGE AND ADMINISTRATION
Hypertension: The recommended initial dose is 80mg once daily. This may be increased, if necessary, to 160mg once daily, although doses of up to 320mg once daily have been used. A lower initial dose of 40mg once daily may be used in elderly patients over 75 years, and in those with intravascular volume depletion; similar dosage reductions have been suggested in renal or hepatic impairment.
Heart Failure: The recommended starting dose is 40mg twice daily. The dose should be increased, as tolerated, to 160mg twice daily.
Hepatic and Renal Impairment: Initial dose of 40mg daily in patients with moderate to severe renal impairment (creatinine clearance less than 20mL/minute). A 40mg initial dose is also recommended in patients with mild to moderate hepatic impairment with a maximum dose of 80mg daily.
Myocardial Infarction: Initially 20 mg twice daily increased over several weeks to 160 mg twice daily if tolerated (consider lower dose in mild to moderate hepatic impairment).
Or as prescribed by the physician.
CONTRAINDICATIONS
It is contraindicated in patients who are hypersensitive to any of its component.
WARNINGS
Fetal/Neonatal Morbidity and Mortality
Drugs that act directly on the renin-angiotensin system can cause fetal and neonatal morbidity and death when administered to pregnant women. When pregnancy is detected, Valsartan should be discontinued as soon as possible. The use of drugs that act directly on the renin-angiotensin system during the second and third trimesters of pregnancy has been associated with fetal and neonatal injury, including hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death. Oligohydramnios has also been reported, presumably resulting from decreased fetal renal function; oligohydramnios in this setting has been associated with fetal limb contractures, craniofacial deformation, and hypoplastic lung development. Prematurity, intrauterine growth retardation, and patent ductus arteriosus have also been reported, although it is not clear whether these occurrences were due to exposure to the drug.

Hypotension
Excessive hypotension was rarely seen (0.1%) in patients with uncomplicated hypertension treated with Valsartan alone. In patients with an activated renin-angiotensin system, such as volume-and/or salt-depleted patients receiving high doses of diuretics, symptomatic hypotension may occur. This condition should be corrected prior to administration of Valsartan or the treatment should start under close medical supervision.
If excessive hypotension occurs, the patient should be placed in the supine position and, if necessary, given an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further treatment, which usually can be continued without difficulty once the blood pressure has stabilized.
Hypotension in Heart Failure Patients
Caution should be observed when initiating therapy in patients with heart failure. Patients with heart failure given Valsartan commonly have some reduction in blood pressure, but discontinuation of therapy because of continuing symptomatic hypotension usually is not necessary when dosing instructions are followed.
PRECAUTIONS
Valsartan should be used with caution in patients with hepatic impairment, cirrhosis, or biliary obstruction.Valsartan is excreted in urine and in bile and in reduced doses may therefore be required in patients with renal impairment and should be considered in patients with hepatic impairment. Patients with volume depletion (for example those who have received high- dose diuretic therapy) may experience hypotension; volume depletion should be corrected before starting therapy, or a low initial dose should be used. Since hyperkalemia may occur, serum-potassium concentrations should be monitored, especially in the elderly and patients with renal impairment, and the concomitant use of potassium-sparing diuretics should generally be avoided
DRUG INTERACTIONS
No clinically significant pharmacokinetic interactions were observed when Valsartan was coadministered with amlodipine, atenolol, cimetidine, digoxin, furosemide, glyburide, hydrochlorothiazide, or indomethacin. The valsartan-atenolol combination was more antihypertensive than either component, but it did not lower the heart rate more than atenolol alone. Coadministration of Valsartan and warfarin did not change the pharmacokinetics of Valsartan or the time-course of the anticoagulant properties of warfarin. CYP 450 Interactions: The enzyme(s) responsible for Valsartan metabolism have not been identified but do not seem to be CYP 450 isozymes. The inhibitory or induction potential of Valsartan on CYP 450 is also unknown. As with other drugs that block angiotensin II or its effects, concomitant use of potassium sparing diuretics (e.g. spironolactone, triamterene, amiloride), potassium supplements, or salt substitutes containing potassium may lead to increases in serum potassium and in heart failure patients to increases in serum creatinine.
ADVERSE EFFECTS
The most common adverse effects include headache, dizziness, vertigo, fatigue, diarrhea, abdominal pain, muscle cramps, dry cough, hypotension, nausea, pruritus, rash,constipation, dry mouth, impotence. Other reported events seen less frequently include chest pain, syncope, anorexia, vomiting, and angioedema.
"For suspected adverse drug reaction, report to FDA: www.fda.gov.ph or to TORRENT: www.torrentpharma.com".
Patient to seek medical attention immediately at the first sign of any adverse drug reaction shall appear.
OVERDOSAGE
Limited data are available related to overdosage in humans. The most likely manifestations of overdosage would be hypotension and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted. Valsartan is not removed from the plasma by hemodialysis.
CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.
STORAGE
Store at temperatures not exceeding 30^{o}C. Protect from light and moisture.
AVAILABILITY:
Valsartan (Torval-80) 80 mg Film-Coated Tablet - Alu-Alu Blister Pack of 10's (Box of 30's) - DRP-2852
Valsartan (Torval-160) 160 mg Film-Coated Tablet - Alu-Alu Blister Pack of 10's (Box of 30's) - DRP-2854
DATE OF FIRST AUTHORIZATION
March 25, 2011
DATE OF REVISION
July 2016

torrent PHARMA

Manufactured by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.

Imported and Distributed by :
TORRENT PHARMA PHILIPPINES INC.
Units 3 & 4, 34th Floor, Zuellig Building
Makati Avenue Corner Paseo de Roxas
Makati City, PHILIPPINES

PRODUCT NAME :	Torval	**COUNTRY :** Philippines	**LOCATION :** INDRAD		**Supersedes A/W No.:**		
ITEM / PACK :	Insert	**NO. OF COLORS:** 1	**REMARK :**				
DESIGN STYLE :	Front/Back	**PANTONE SHADE NOS.:**	**SUBSTRATE :**				
CODE :	xxxxxxxx-5343		**Activities**	**Department**	**Name**	**Signature**	**Date**
DIMENSIONS (MM) :	150 x 180		Prepared By	**Pkg.Dev**			
ART WORK SIZE :	S/S		Reviewed By	**Pkg.Dev**			
DATE :	22-07-2016	Black	Approved By	**Quality**			