ARBITEN

Valsartan

Valsartan, Angiotensin II Antagnoists.

Composition:

Arbiten 80: each film-coated tablet contains 80 mg valsartan.

Arbiten 160: each film-coated tablet contains 160 mg valsartan.

Action:

As a prodrug, valsartan produces direct antagonism of the angiotensin II (AT2) receptors, unlike the ACE inhibitors. It displaces angiotensin II from the AT1 receptor and produces its blood pressure lowering effects by antagonizing AT-1 induced vasoconstriction, aldosterone release, catecholamine release, arginine vasopressin release, water intake and hypertrophic responses. This action results in more efficient blockade of the cardiovascular effects of angiotensin II and fewer side effects than the ACE inhibitors (Angiotensin II antagonists are unlikely to be associated with cough).

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.

Valsartan abrupt withdrawal has not been associated with rebound hypertension or other adverse clinical events.

Valsartan had no notable effects on total cholesterol, fasting triglycerides, fasting serum glucose, or uric acid.

Indications:

- treatment of hypertension.
- treatment of heart failure (NYHA class II-IV)

Valsartan significantly reduces hospitalizations for heart failure consequently improves morbidity.

Also slows the progression of heart failure, improves NYHA functional class, ejection fraction and signs and symptoms of heart failure and improves quality of life versus placebo.

Contraindications:

Hypersensitivity to valsartan. Pregnancy (see "pregnany and lactation").

Warnings and precautions:

Sodium -and /or volume - depleted patients

Symptomatic hypotension may occur in rare cases after initiation of therapy with valsartan in severely sodium-depleted and/ or volume--depleted patients, such as those receiving high doses of diuretics.

This condition should be corrected prior to administration of valsartan.

If 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.

Renal artery stenosis

It was reported that short-term administration of valsartan in patients with renovascular hypertension secondary to unilateral renal artery stenosis did not induce any significant changes in renal haemodynamics, serum creatinine, or blood urea nitrogen (BUN). Monitoring is recommended as a safety measure because other drugs that affect the rennin-angiotensin-aldosterone system may increase blood urea and serum creatinine in patients with bilateral or unilateral renal artery stenosis.

Impaired renal function

No dosage adjustment for valsartan is required in patients with renal impairment because valsartan renal clearance is only 30% to total plasma clearance, no correlation was seen between renal function and systemic exposure to valsartan. Caution is advised in severe cases (creatinine clearance <10ml/min) no data are available.

No information is available in patients undergoing dialysis. Though, valsartan is highly bound to plasma protein and is unlikely to be removed by dialysis.

Hepatic impairment

No dose adjustment for valsartan is necessary in patients with hepatic insufficiency of non-biliary origin and without cholestasis because 70% of the absorbed dose is excreted in the bile mainly as unchanged and patients with biliary obstructive disorders showed lower valsartan clearance. Particular caution should be exercised when administering valsartan to theses patients.

Heart failure

Caution should be observed when initiating therapy in patients with heart failure because when given these patients valsartan commonly have some reduction in blood pressure. Discontinuation of therapy because of continuing symptomatic hypotension usually is not necessary when dosing instructions are followed.

Evaluation of patients with heart failure should always include assessment of renal function because renal function may be anticipated in susceptible individuals as a consequence of inhibiting the rennin-angiotensin-aldosterone system changes in patients with severe heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with angiotensin-converting enzyme inhibitors and angiotensin receptor antagonists has been associated with oliguria and/ or progressive azotemia and (rarely) with acute renal failure and/ or death.

In patients with heart failure, valsartan is not recommended in the triple combination of an ACE inhibitor, a beta-blocker and an ARB (Angiotensin II receptor blocker).

Elderly

A somewhat higher systemic exposure to valsartan was observed in some elderly subjects than in young subjects, however, this has not been shown to have any clinical significance.

Interactions:

It was reported that no drug interactions of clinical significance have been found.

Clinically relevant drug-drug interactions in the form of metabolic induction or inhibition of the cytochrome p450 system are not expected with valsartan because valsartan is not metabolized to a significant extent.

Although valsartan is highly bound to plasma proteins, invitro 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.

As with other drugs that block angiotensin II or its effects, concomitant use of potassium-sparing diuretics (e.g. Spironolactone, triametrene, 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.

Caution is advised when comedication is considered necessary.

Pregnancy and lactation:

Pregnancy risk factor: C (first trimester) and D (second and third trimesters).

Medications which act on the renin-angiotensin system are reported to have the following with fetal and neonatal effects, including hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death. Oligohydramnios is also reported. These effects are reported to occur with exposure during the second and third trimesters of pregnancy. Valsartan should be discontinued as soon as possible after pregnancy is detected.

Excretion in breast milk is unknown. Valsartan was excreted in the milk of lactating rats. Therefore, it is not advisable to use valsartan in lactating mothers.

Effects on ability to drive and use machines:

Caution is advised when driving or operating machinery as with other antihypertensive agents.

Adverse reactions:

The incidence of adverse reactions showed no association of race, age and gender.

It was reported that none of the adverse reactions did their incidence appear to be related to dose or duration of treatment; therefore, adverse reactions occurring on all doses of valsartan were pooled.

The following adverse reactions are reported with valsartan with an incidence of 1% or more: headache, dizziness, viral infection, upper respiratory tract infection, coughing, diarrhea, fatigue, rhinitis, sinusitis, back pain, abdominal pain, nausea, pharyngitis and arthralgia.

Other reported adverse reactions with a frequency below 1% included: oedema; asthenia; insomnia; rash; decreased libido, vertigo. It is unknown whether these effects were casually related to valsartan therapy.

The following post-marketing data was reported with valsartan in very rare cases of angioedema, rash, pruritis, and other hypersensitivity allergic reactions including serum sickness, and vasculitis. Very rare cases of impaired renal function have also been reported.

Laboratory findings:

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

In rare cases, valsartan may be associated with decreases in haemoglobin and haematocrit.

Neutropenia was observed in 1.9% of patients treated with valsartan versus 1.6% of patients treated with an ACE inhibitor.

It was observed significant increases in serum creatinine, potassium and total bilirubin.

Also it was reported in patients treated with valsartan occasional elevations of liver function values.

In heart failure patients, it was observed greater than 50% increases in serum creatinine and greater than 20% increases in serum potassium. Also in heart failure trials, greater than 50% increases in blood urea nitrogen (BUN) were observed.

Overdose:

Although there is no experience of overdosage 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.

Dosage and administration:

Adults: Oral

Hypertension

The recommended dose of Arbiten is 80 mg once daily, irrespective of race, age, or gender; majority of effect within 2 weeks and maximal are seen after 4 weeks. In patients whose blood pressure is not adequately controlled, the daily dose may be increased to 160 mg or a diuretic may be added.

Heart failure

The recommended starting dose of valsartan is 40 mg twice daily; titrate dose to 80 mg -160 mg twice daily, as tolerated; maximum daily dose is 320 mg in divided doses. Consideration should be given to reducing the dose of concomitant diuretics.

Evaluation of patients with heart failure should always include assessment of renal function. The safety and efficacy of valsartan have not been established in children.

No dosage adjustment is required for patients with renal impairment or for patients with hepatic insufficiency of non-biliary origin and without cholestasis. Valsartan may also be administered with other anti--hypertensive agents.

Patient information:

Do not stop taking this medication unless instructed by a physician, do not take this medication during pregnancy or lactation; take a missed dose as soon as possible unless it is almost time for your next dose; call your doctor immediately if you have symptoms of allergy or develop side effects including headache and dizziness.

Pack size:

Arbiten 80: 30 film coated tablets.

Arbiten 160: 30 film coated tablets.

- A medicament is a product that 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 dispensed the medicament.
- The doctor and the pharmacist are experts in medicine.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep medicaments out of the reach of children.

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