

**ARB[®]**

Candesartan

Angiotensin Receptor Blocker**COMPOSITION**

ARB[®] 8 Tablet : Each tablet contains Candesartan cilexetil 8 mg INN.

ARB[®] 16 Tablet : Each tablet contains Candesartan cilexetil 16 mg INN.

PHARMACOLOGY

General : Candesartan cilexetil is rapidly and completely bioactivated by ester hydrolysis during absorption from the gastrointestinal tract to candesartan, a selective AT1 subtype angiotensin II receptor antagonist. Candesartan is mainly excreted unchanged in urine and feces (via bile). It undergoes minor hepatic metabolism by O-deethylation to an inactive metabolite. The elimination half-life of candesartan is approximately 9 hours. After single and repeated administration, the pharmacokinetics of candesartan are linear for oral doses up to 32 mg of candesartan cilexetil. Candesartan and its inactive metabolite do not accumulate in serum upon repeated once-daily dosing.

Following administration of candesartan cilexetil, the absolute bioavailability of candesartan was estimated to be 15%. After tablet ingestion, the peak serum concentration (C_{max}) is reached after 3 to 4 hours. Food with a high fat content does not affect the bioavailability of candesartan after candesartan cilexetil administration.

Metabolism and Excretion : Total plasma clearance of candesartan is 0.37 mL/min/kg with a renal clearance of 0.19 mL/min/kg. When candesartan is administered orally, about 26% of the dose is excreted unchanged in urine. Following an oral dose of ¹⁴C-labeled candesartan cilexetil, approximately 33% of radioactivity is recovered in urine and approximately 67% in feces. Following an intravenous dose of ¹⁴C-labeled candesartan approximately 59% of radioactivity is recovered in urine and approximately 36% in feces. Biliary excretion contributes to the elimination of candesartan.

Distribution : The volume of distribution of candesartan is 0.13 L/kg. Candesartan is highly bound to plasma proteins (>99%) and does not penetrate red blood cells. The protein binding is constant at candesartan plasma concentrations well above the range achieved with recommended doses.

INDICATIONS AND USES

It is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents.

DOSAGE AND ADMINISTRATION

Dosage must be individualized. Blood pressure response is dose related over the range of 2 mg to 32 mg. The usual recommended starting dose of candesartan is 16 mg once daily when it is used as monotherapy in patients who are not volume depleted. Candesartan can be administered once or twice daily with total daily doses ranging from 8 mg to 32 mg. Larger doses do not appear to have a greater effect, and there is relatively little experience with such doses. Most of the antihypertensive effect is present within 2 weeks, and maximal blood pressure reduction is generally obtained within 4 to 6 weeks of treatment with candesartan.

No initial dosage adjustment is necessary for elderly patients, for patients with mildly impaired renal function, or for patients with mildly impaired hepatic function. For patients with possible depletion of intravascular volume (eg. patients treated with diuretics, particularly those with impaired renal function), candesartan should be initiated under close medical supervision and consideration should be given to administration of a lower dose.

Candesartan may be administered with or without food.

If blood pressure is not controlled by candesartan alone, a diuretic may be added. Candesartan may be administered with other antihypertensive agents.

CONTRAINDICATION

Candesartan is contraindicated in patients who are hypersensitive to any component of this product.

SIDE EFFECT

Body as a Whole : Asthenia, fever.

Central and Peripheral Nervous System : Paresthesia, vertigo.

Gastrointestinal System Disorder : Dyspepsia, gastroenteritis.

Heart Rate and Rhythm Disorders : Tachycardia, palpitation.

Metabolic and Nutritional Disorders : Creatine phosphokinase increased, hyperglycaemia, hypertriglyceridemia, hyperuricemia.

Musculoskeletal System Disorders : Myalgia.

Platelet/ Bleeding-Clotting Disorders : Epistaxis.

Psychiatric Disorders : Anxiety, depression, somnolence.

Skin and appendages Disorders : Rash, sweating increased.

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Urinary system Disorders : Hematuria.

WARNING

Drugs that act directly on the renin-angiotensin system can cause fetal and neonatal morbidity and death when administered to pregnant women. Several dozen cases have been reported in the world literature in patients who were taking angiotensin-converting enzyme inhibitors. When pregnancy is detected, candesartan 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, aptient ductus arteriosus have also been reported, although it is not clear whether these occurrences were due to exposure to the drug.

These adverse effects do not appear to have resulted from intrauterine drug exposure that has been limited to the first trimester. Mothers whose embryos and fetuses are exposed to an angiotensin II receptor antagonist only during the first trimester should be informed. Nonetheless, when patients become pregnant, physicians should have the patient discontinue the use of candesartan as soon as possible.

DRUG INTERACTION

No significant drug interactions have been reported in studies of candesartan cilexetil given with other drugs such as glyburide, nifedipine, digoxin, warfarin, hydrochlorothiazide and oral contraceptives in healthy volunteers. Because candesartan is not significantly metabolized by the cytochrome P450 system and at therapeutic concentrations has no effects of P450 enzymes, interactions with drugs that inhibit or are metabolized by these enzymes would not be expected.

USE IN PREGNANCY AND LACTATION

Use in pregnancy : Not indicated. When pregnancy is detected candesartan should be discontinued as soon as possible.

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Use in nursing mother : It is not known whether candesartan is excreted in human milk, but candesartan has been shown to be present in rat milk. Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

USE IN PEDIATRIC PATIENT

Safety and effectiveness in pediatric patients have not been established.

STORAGE CONDITION

Store in a cool & dry place. Protect from light and moisture.

HOW SUPPLIED

ARB® 8 Tablet : Each box contains 3x10 tablets in blister pack.

ARB® 16 Tablet : Each box contains 3x10 tablets in blister pack.



CARDIOVASCULAR PREPARATIONS

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