CANDESARTAN

GIRAN-8
8 mg Tablet

GIRAN-16
16 mg Tablet

Angiotensin-2-Receptor Blockers

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FORMULATION:

Giran-8
Each tablet contains:
Candesartan (as Cilexetil) ..... 8 mg.

Giran-16
Each tablet contains:
Candesartan (as Cilexetil) ..... 16 mg.

PRODUCT DESCRIPTION:

Giran-8:
A light blue colored, square and biconvex tablet, having cross breakline on both sides.

Giran-16:
A light pink colored, square and biconvex tablet, having cross breakline on both sides.

PHARMACOLOGY:
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. Candesartan blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT_1 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 AT_2 receptor found in many tissues, but AT_2 is not known to be associated with cardiovascular homeostasis. Candesartan has much greater affinity (>10,000-fold) for the AT_1 receptor than for the AT_2 receptor. 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 candesartan does not inhibit ACE (kininase II), it does not affect the response to bradykinin. Whether this difference has clinical relevance is not yet known. Candesartan 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 candesartan on blood pressure.

PHARMACOKINETICS:
Candesartan cilexetil is an ester prodrug that is hydrolysed during absorption from the gastrointestinal tract to the active form candesartan. The absolute bioavailability for candesartan is about 40% when candesartan cilexetil is given as a solution and about 14% when given as tablets. Peak plasma concentrations of candesartan occur about 3 to 4 hours after oral doses as tablets. Candesartan is more than 99% bound to plasma proteins. It is excreted in urine and bile mainly as unchanged drug and a small amount of inactive metabolites. The terminal elimination half-life is about 9 hours. Candesartan is not removed by haemodialysis.

INDICATIONS:
It is used in the management of hypertension and may also be used in heart failure in patients with impaired left ventricular systolic function, either when ACE inhibitors are not tolerated, or in addition to ACE inhibitors.

DRUG INTERACTIONS:
The anti-hypertensive effects of Candesartan may be potentiated by drugs or other agents that lower blood pressure. An additive hyperkalaemic effect is possible with potassium supplements, potassium-sparing diuretics, or other drugs that can cause hyperkalaemia; losartan and potassium-sparing diuretics should not generally be given together. NSAIDs should be used with caution in patients taking Candesartan as the risk of renal impairment may be increase, particularly in those who are inadequately hydrated; use of NSAIDs may also attenuate the hypotensive effect of Candesartan. Candesartan and some other angiotensin II receptor antagonists are metabolized by cytochrome P450 isoenzymes and interactions may occur with drugs that affect these enzymes.

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

REPORTING OF SUSPECTED ADVERSE REACTIONS:
To allow continued monitoring of the benefit/risk balance of the medicinal product, reporting of suspected adverse reaction is necessary. Healthcare professionals are encouraged to report any suspected adverse reactions, directly to the importer/distributor and/or to FDA: www.fda.gov.ph.
Patients are advised to seek immediate medical attention at the first sing/s of adverse reactions.

ADVERSE EFFECTS:
Adverse effects of Candesartan have been reported to be usually mild and transient, and include dizziness, headache, and dose-related orthostatic hypotension. Hypotension may occur particularly in patients with volume depletion (for example those who have received high-dose diuretics).

Impaired renal function and, rarely, rash, urticaria, pruritis, angioedema, and raised liver enzyme values may occur. Hyperkalaemia, myalgia, and arthralgia have been reported. Candesartan appears less likely than ACE inhibitors to cause cough. Other adverse effects that have been reported with angiotensin II receptor antagonists include respiratory-tract disorders, back pain, gastrointestinal disturbances, fatigue, and neutropenia. Rhabdomyolysis has been reported rarely.

SPECIAL PRECAUTIONS:

Fetal Toxicity: Candesartan can cause fetal harm when administered to a pregnant woman. Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. Resulting oligohydramnios can be associated with fetal lung hypoplasia and skeletal deformations. Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure and death. When pregnancy is detected, discontinue Candesartan as soon as possible.

Morbidity in Infants: Children < 1 year of age must not receive Candesartan for hypertension. Drugs that act directly on the renin-angiotensin system (RAS) can have effects on the development of immature kidneys.

Hypotension: Candesartan can cause symptomatic hypotension. Symptomatic hypotension is most likely to occur in patients who have been volume and/or salt depleted as a result of prolonged diuretic therapy, dietary salt restriction, dialysis, diarrhea, or vomiting. Patients with symptomatic hypotension may require temporarily reducing the dose of Candesartan, diuretic or both, and volume repletion. Volume and/or salt depletion should be corrected before initiating therapy with Candesartan.

Impaired Renal Function: Monitor renal function periodically in patients treated with Candesartan. Changes in renal function including acute renal failure can be caused by drugs that inhibit the renin-angiotensin system. Patients whose renal function may depend, in part, on the activity of the renin-angiotensin system (e.g., patient with renal artery stenosis, chronic kidney disease, severe heart failure, or volume depletion) may be at particular risk of developing oliguria, progressive azotemia or acute renal failure when treated with Candesartan. Consider withholding or discontinuing therapy in patients who develop a clinically significant decrease in renal function on Candesartan.

Hyperkalemia: Drugs that inhibit the renin-angiotensin system can cause hyperkalemia. Concomitant use of Candesartan with drugs that increase potassium levels may increase the risk of hyperkalemia.

DOSAGE AND ADMINISTRATION:

Candesartan is given orally as the ester prodrug candesartan cilexetil. Onset of antihypertensive action occurs about 2 hours after a dose and a maximum effect is achieved within about 4 weeks of starting therapy.

In the management of hypertension the usual initial dose of candesartan cilexetil is 8 mg once daily in the UK, or 16 mg once daily in the USA. The dose should be adjusted according to response; the usual maintenance dose is 8 mg once daily, but doses up to 32 mg daily, as a single dose or in 2 divided doses, may be used. Lower initial doses should be considered in patients with intravascular volume depletion; in the UK an initial dose of 4 mg once daily is suggested. Patients with renal or hepatic impairment may also require lower initial doses. In heart failure, candesartan cilexetil is given in an initial dose of 4 mg once daily; the dose should be doubled at intervals of not less than two weeks up to 32 mg once daily if tolerated.

Or as prescribed by the physician.

PREGNANCY AND LACTATION:

Pregnancy: Candesartan can cause fetal harm when administered to a pregnant woman. Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. Most epidemiologic studies examining fetal abnormalities after exposure to antihypertensive use in the first trimester have not distinguished drugs affecting the renin-angiotensin system from other antihypertensive agents. When pregnancy is detected, discontinue Candesartan as soon as possible.

Lactation: 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 serious adverse reactions in breastfed infants, advise a nursing woman that breastfeeding is not recommended during treatment with Candesartan.

OVERDOSAGE & TREATMENT:

The most likely manifestation of overdosage with Candesartan would be hypotension, dizziness, and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted. Candesartan cannot be removed by hemodialysis.

In managing overdose, the possibilities of multiple-drug overdoses, drug-drug interactions, and altered pharmacokinetics in the patient needs to be considered.

CAUTION:

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

STORAGE CONDITION:

Store at temperatures not exceeding 30°C.

AVAILABILITY:

GIRAN-8: Alu/Clear PVC Blister Pack x 10's (Box of 30's)

FDA Registration Number	: DRP-6257
Date of Renewal of Authorization	: 17 June 2019

GIRAN-16: Alu/Clear PVC Blister Pack x 10's (Box of 30's)

FDA Registration Number	: DRP-6036
Date of Renewal of Authorization	: 08 January 2018
Date of Revision of package Insert	: 25 April 2022

Manufactured by:
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