CELCARV 3.125/6.25
Carvedilol Tablets USP 3.125mg/6.25mg

CELCARV 3.125
COMPOSITION
Each Film Coated Tablet Contains:
Carvedilol USP 3.125mg
Excipients q.s.
Colour: Sunset Yellow

CELCARV 6.25
COMPOSITION
Each Film Coated Tablets Contains:
Carvedilol USP 6.25mg
Excipients q.s.
Colour: Titanium Dioxide BP

DESCRIPTION
CELCARV 3.125/6.25 contains carvedilol is used to treat high blood pressure and heart failure

PHARMACODYNAMICS
Pharmacotherapeutic group: Alpha and beta blocking agents.
ATC code: C07AG02
Carvedilol is a vasodilatory non-selective beta-blocker, which reduces the peripheral vascular resistance by selective alpha 1- receptor blockade and suppresses the renin-angiotensin system through non-selective beta-blockade. Plasma renin activity is reduced and fluid retention is rare.
Carvedilol has no intrinsic sympathomimetic activity (ISA). Like propranolol, it has membrane stabilising properties.
Carvedilol is a racemate of two stereoisomers. Both enantiomers were found to have alpha-adrenergic blocking activity in animal models. Non-selective beta - and beta - adrenoceptor blockade is attributed mainly to the S (-) enantiomer.

PHARMACOKINETIC
Absorption
Carvedilol is rapidly absorbed after oral administration. In healthy subjects, maximum serum concentration is achieved approximately 1 hour after administration. The absolute bioavailability of carvedilol in humans is approximately 25%.
Distribution
Carvedilol is highly lipophilic. The plasma protein binding is about 98 to 99%. The volume of distribution is approximately 2 l / kg and increases in patients with liver cirrhosis.
Biotransformation
In humans and in animal species studied, carvedilol is extensively metabolized to several metabolites which are excreted primarily in bile. The first pass effect after oral administration is about 60-75%. Carvedilol is extensively metabolized in the liver, glucuronidation being one of the main reactions.
Elimination
The average half-life of elimination of carvedilol is approximately 6 hours. The plasma clearance is approximately 500-700 ml / min. Elimination is mainly via the bile, and excretion mainly via the faeces. A minor part is eliminated renally in the form of various metabolites

THERAPEUTIC INDICATIONS:
Essential hypertension
Chronic stable angina pectoris
Adjunctive treatment of moderate to severe stable chronic heart failure

POSOLOGY AND METHOD OF ADMINISTRATION:
Essential Hypertension
In patients with high blood pressure, the recommended maximum single dose is 25 mg and the recommended maximum daily dose is 50 mg.
Adults:
The usual starting dose is 12.5 mg once a day for the first two days, increasing to 25 mg once a day. If necessary, your doctor may gradually increase the dose further at intervals of two weeks or more.
Elderly:
Your doctor will usually start you on 12.5 mg a day and continue with this dose for the length of your treatment. However, if necessary, your doctor may gradually increase your dose at intervals of two weeks or more.

Angina:
Adults
The usual starting dose is 12.5 mg twice a day for two days.
After two days the dose is usually 25 mg, twice a day.
If your angina is not under control, your doctor may increase your dose slowly, over several weeks up to 50 mg twice a day.
Elderly
Your doctor will decide both your starting dose and the best dose for you to take in the longer term.
The usual maximum dose is 50 mg each day, taken in smaller amounts (divided doses)

Congestive heart failure:
Adults and elderly
While taking carvedilol, make sure that you continue with your other treatments for heart failure as advised by your doctor.
In heart failure patients, treatment with carvedilol is recommended to be started and supervised by a hospital specialist.
The tablets should be taken twice a day – in the morning and in the evening.
The usual starting dose is one 3.125 mg tablet twice a day for two weeks.
Your doctor will then increase the dose slowly, over several weeks, up to 25 mg twice a day.
For patients with a body weight of less than 85 kg, the recommended maximum single dose is 25 mg and the recommended maximum daily dose is 50 mg.
For patients with a body weight above 85 kg, the recommended maximum single dose is 50 mg and the recommended maximum daily dose is 100 mg.
Patients with kidney problems
Dose adjustment may be required, depending on your blood pressure. Your doctor will decide which dose is best suited for you.
Patients with liver disease
carvedilol should not be taken by patients with liver problems.
Patients undergoing surgery
Tell your hospital doctor you are taking carvedilol if you need to have an anaesthetic for surgery. This is because some anaesthetics can lower your blood pressure and it may become too low.
Use in children and adolescents
Carvedilol tablets are not recommended for use in children under 18 years of age.

Methods of administration
The tablets should be taken with the adequate supply of fluid. It is recommended that heart failure patients take their carvedilol medication with food to allow the absorption to be slower and the risk of orthostatic hypotension to be reduced.

CONTRAINDICATION:
- Hypersensitivity to the carvedilol or to any of the excipients
- Heart failure belonging to NYHA Class IV of the heart failure classification with marked fluid retention or overload requiring intravenous inotropic treatment.
- Chronic obstructive pulmonary disease with bronchial obstruction.
- Clinically significant hepatic dysfunction.
- Bronchial asthma.
- AV block, degree II or III (unless a permanent pacemaker is in place).
- Severe bradycardia (<50 bpm).
- Sick sinus syndrome (incl. sino-atrial block).
- Cardiogenic shock.
- Severe hypotension (systolic blood pressure below 85 mmHg).
- Prinzmetal angina.
- Untreated pheochromocytoma.
- Metabolic acidosis.
- Severe peripheral arterial circulatory disturbances.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE:
Check with your doctor or pharmacist before taking Carvedilol if:
- you have a condition called Prinzmetal's angina (cardiac chest pain that occurs at rest)
- you suffer from any other heart problems.
- you have lung disease (this includes asthma and chronic obstructive pulmonary disease). This medicine may cause wheezing or spasm in the lung.
- you have had any problems with your liver, kidneys or thyroid.
- you have diabetes (high blood sugar). Symptoms of low blood sugar may be masked if you are taking carvedilol.
- you have a skin condition known as psoriasis, after taking beta-blocker medicines.
- you have a circulation disorder (usually affecting the fingers) called Raynaud's phenomenon.
- you have an allergy and are having treatment to desensitize you.
- you have ever had a serious allergic reaction (for example, sudden swelling causing difficulty breathing or swallowing, swelling of the hands, feet or ankles, or a severe rash).
- you wear contact lenses (you may notice that your eyes become drier than usual).
- you have problems with your blood vessels (peripheral vascular disease).
- you have phaeochromocytoma (a tumour of the adrenal gland causing high blood pressure). An initial treatment with appropriate medicines (alpha-blockers) should be started before using any beta-blocker.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION:
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
Be sure to advise if you are taking any of the following medicines:
- calcium channel blockers e.g. verapamil or diltiazem (for irregular heartbeat)
- antiarrhythmics, e.g. amiodarone (for irregular heartbeat)
- any other medicine that may additionally decrease the heart rate, e.g. reserpine
- medicines known as monoamine oxidase inhibitors e.g. isocarboxide and phenelzine (for depression)
- fluoxetine and paroxetine (used to treat depression)
- digoxin (for heart failure)
- medicines for your blood pressure, including diuretics (water tablets) (Carvedilol may intensify the effect of these medicines)
- antidiabetic medicines (metformin) or insulin (Carvedilol may intensify the effects of these medicines)
- clonidine (for migraine, menopausal flushing, high blood pressure or Tourette's syndrome)
- ciclosporin (for preventing rejection of a transplanted organ)
- rifampicin (used to treat bacterial infections, including tuberculosis)
- non-steroidal anti-inflammatory drugs (NSAIDs)
- beta-agonist bronchodilators (used to treat chest tightness and wheezing due to asthma or other chest conditions).

PREGNANCY AND LACTATION
Pregnancy
There are no adequate data from the use of carvedilol in pregnant women. Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown.
Beta-blockers reduce placental perfusion which may result in intrauterine fetal death and immature and premature deliveries. In addition, adverse reactions (especially hypoglycaemia, hypotension, bradycardia, respiratory depression and hypothermia) may occur in the fetus and neonate. There is an increased risk of cardiac and pulmonary complications in the neonate in the postnatal period. Carvedilol should not be used during pregnancy unless clearly necessary (that is if the potential benefit for the mother outweighs the potential risk for the fetus/neonate). The treatment should be stopped 2-3 days before expected birth. If this is not possible the new-born has to be monitored for the first 2-3 days of life.
Breastfeeding
Carvedilol is lipophilic and according to results from studies with lactating animals, carvedilol and its metabolites are excreted in breast milk and, therefore, mothers receiving carvedilol should not breast-feed.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
This medicinal product has minor influence on the ability to drive and use machines. Some individuals may have reduced alertness especially on initiation and adjustment of medication.

ADVERSE REACTION:
Like all medicines, this medicine can cause side effects, although not everybody gets them. The possible side effects and how likely you are to get them will depend on the reason you are being treated with Carvedilol.
Very common (affect more than 1 in 10 people):
- Feeling dizzy.
- Headache.
- Feeling weak and tired.
- Problems with your heart. The signs include chest pains, tiredness, shortness of breath and swelling of your arms and legs.
- Low blood pressure. The signs include feeling dizzy or lightheaded.

Feeling dizzy, having a headache and feeling weak and tired are usually mild and more likely to happen at the beginning of your treatment.
Common (affect less than 1 in 10 people):
- Infections of the airway (bronchitis), lung (pneumonia), nose and throat (upper respiratory tract). The signs include wheezing, shortness of breath, chest tightness and sore throat.
- Infections of the urinary tract which can cause problems in passing water.
- Low numbers of red blood cells (anaemia). The signs include feeling tired, pale skin, a fluttering sensation in your heart (palpitations) and being short of breath.
- Increase in weight.
- Increase in cholesterol levels (shown by a blood test).
- Loss of control of blood sugar in people with diabetes.
- Feeling depressed.
- Problems with your sight, sore or dry eyes due to fewer tears being made.
- A slow heart beat.
- Feeling dizzy or light-headed after standing up.
- Fainting.
- Fluid retention. The signs include: overall swelling of your body, swelling of parts of your body, for example your hands, feet, ankles and legs, and an increase in how much blood you have in your body.
- Problems with blood circulation in your arms and legs. The signs include cold hands and feet, whiteness, tingling and pain in your fingers and a pain in your leg which gets worse when you walk.
- Breathing problems or asthma.
- Fluid build-up in the lungs (pulmonary oedema).
- Feeling sick or being sick.
- Diarrhoea.
- Stomach pain/indigestion.
- Pain, possibly in your hands and feet.
- Problems with your kidneys, including changes to how often you pass urine.

Uncommon (affect less than 1 in 100 people):
- Disturbed sleep.
- Tingling or numbness of your hands or feet.
- Chest pain (angina pectoris).
- Heart failure.
- Problems with your skin, including skin rashes which may cover a lot of your body, a lumpy rash (hives), feeling itchy and dry skin patches.
- Hair loss.
- Being unable to get an erection (erectile dysfunction).
- Constipation.

Rare (affect less than 1 in 1,000 people):
- Low number of platelets in your blood. The signs include bruising easily and nose bleeds.
- A stuffy nose, wheezing and flu-like symptoms.
- A dry mouth.

Very rare (affect less than 1 in 10,000 people):
- Low numbers of all types of white blood cells. The signs include infections of the mouth, gums, throat and lungs.
- Allergic (hypersensitivity) reactions. The signs may include difficulty breathing or swallowing caused by sudden swelling of the throat, or face or swelling of your hands, feet and ankles or severe skin reactions.
- Changes in liver function which show up in a blood test.
- Some women may have difficulty with bladder conotrol when they pass water (urinary incontinence). This normally will get better when treatment is stopped.

Carvedilol can also cause development of the signs of diabetes in people who have a very mild form of diabetes called 'latent diabetes'.

OVERDOSE
Symptoms and signs
In the event of overdose, there may be severe hypotension, bradycardia, heart failure, cardiogenic shock and cardiac arrest. There may also be respiratory problems, bronchospasm, vomiting, disturbed consciousness and generalized seizures.
Treatment
In addition to general supportive treatment, the vital parameters must be monitored and corrected, if necessary, under intensive care conditions.
Atropine can be used for excessive bradycardia, while to support ventricular function intravenous glucagon, or sympathomimetics (dobutamine, isoprenaline) are recommended. If positive inotropic effect is required, phosphodiesterase inhibitors (PDE) should be considered. If peripheral vasodilation dominates the intoxication profile then norfenephrine or noradrenaline should be administered with continuous monitoring of the circulation. In the case of drug-resistant bradycardia, pacemaker therapy should be initiated.
For bronchospasm, β-sympathomimetics (as aerosol or intravenous) should be given, or aminophylline may be administered intravenously by slow injection or infusion. In the event of seizures, slow intravenous injection of diazepam or clonazepam is recommended.
Carvedilol is highly protein-bound. Therefore, it cannot be eliminated by dialysis.
In cases of severe overdose with symptoms of shock, supportive treatment must be continued for a sufficiently long period, i.e. until the patient's condition has stabilised, as a prolongation of elimination half-life and redistribution of carvedilol from deeper compartments are to be expected.

INCOMPATIBILITY:
Not applicable.

SHELF LIFE:
36 Months

PACKAGING:
10 tablets are packed in Alu-Alu blister; such 3 blisters are packed in printed carton along with pack insert.

STORAGE CONDITION:
Stored at a temperature not exceeding 30°C. Protect from light and moisture.
Keep the medicine out of reach of children.

Imported by:

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MANUFACTURED BY:
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