Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

CARVIDAY® 10
Carvedilol Phosphate Controlled Release Tablets 10 mg
CARVIDAY® 20
Carvedilol Phosphate Controlled Release Tablets 20 mg
CARVIDAY® 40
Carvedilol Phosphate Controlled Release Tablets 40 mg
CARVIDAY® 80
Carvedilol Phosphate Controlled Release Tablets 80 mg

2. Qualitative and quantitative composition:

Each film coated controlled release tablet contains:
Carvedilol Phosphate Hemihydrate
Eq. to Carvedilol Phosphate 10 mg
Excipient Q.S
(For a full list of excipients, see section 6.1)

Each film coated controlled release tablet contains:
Carvedilol Phosphate Hemihydrate
Eq. to Carvedilol Phosphate 20 mg
Excipient Q.S
(For a full list of excipients, see section 6.1)

Each film coated controlled release tablet contains:
Carvedilol Phosphate Hemihydrate
Eq. to Carvedilol Phosphate 40 mg
Excipient Q.S
(For a full list of excipients, see section 6.1)

Each film coated controlled release tablet contains:
Carvedilol Phosphate Hemihydrate
Eq. to Carvedilol Phosphate 80 mg
Excipient Q.S
(For a full list of excipients, see section 6.1)

3. Pharmaceutical form:

Film coated tablets.
CARVIDAY® 10
A light brown coloured, round shaped biconvex film coated tablet.
CARVIDAY® 20
A yellow coloured, round shaped biconvex film coated tablet.
CARVIDAY® 40
A white coloured, round shaped biconvex film coated tablet.
CARVIDAY® 80

A grey coloured, round shaped biconvex film coated tablet.

4. Clinical particulars

4.1 Therapeutic indications

Carvedilol is used to treat the symptoms of Congestive Heart Failure, Chest Pain (Angina Pectoris), Left Ventricular Dysfunction following Myocardial Infarction and High blood pressure (Hypertension). It may be used alone or with other medications.
Carvedilol belongs to a class of drugs called Beta blockers, Alpha activity.

4.2 Posology and method of administration

Posology:
Carviday® is an extended-release capsule intended for once-daily administration.
Patients controlled with immediate-release carvedilol tablets alone or in combination with other medications may be switched to Carviday® extended-release capsules based on the total daily doses shown in Table below:

Daily Dose of Immediate-Release Carvedilol Tablet	**Daily Dose[a] of Carviday®**
6.25 mg (3.125 mg twice daily)	10 mg once daily
12.5 mg (6.25 mg twice daily)	20 mg once daily
25 mg (12.5 mg twice daily)	40 mg once daily
50 mg (25 mg twice daily)	80 mg once daily
[a] When switching from carvedilol 12.5 mg or 25 mg twice daily, a starting dose of Carviday® 20 mg or 40 mg once daily, respectively, may be warranted for elderly patients or those at increased risk of hypotension, dizziness, or syncope. Subsequent titration to higher doses should, as appropriate, be made after an interval of at least 2 weeks.	

Heart Failure
Prior to initiation of Carviday®, it is recommended that fluid retention be minimized. The recommended starting dose of Carviday® is 10 mg once daily for 2 weeks. Patients who tolerate a dose of 10 mg once daily may have their dose increased to 20, 40, and 80 mg over successive intervals of at least 2 weeks. Patients should be maintained on lower doses if higher doses are not tolerated.

Left Ventricular Dysfunction Following Myocardial Infarction
Treatment with Carviday® may be started as an inpatient or outpatient and should be started after the patient is hemodynamically stable and fluid retention has been minimized. It is recommended that Carviday® be started at 20 mg once daily and increased after 3 to 10 days, based on tolerability, to 40 mg once daily, then again to the target dose of 80 mg once daily. A lower starting dose may be used (10 mg once daily) and/or the rate of up-titration

may be slowed if clinically indicated (e.g., due to low blood pressure or heart rate, or fluid retention). Patients should be maintained on lower doses if higher doses are not tolerated.

Hypertension
The recommended starting dose of Carviday® is 20 mg once daily. If this dose is tolerated, using standing systolic pressure measured about one hour after dosing as a guide, the dose should be maintained for 7 to 14 days, and then increased to 40 mg once daily if needed, based on trough blood pressure, again using standing systolic pressure one hour after dosing as a guide for tolerance. This dose should also be maintained for 7 to 14 days and can then be adjusted upward to 80 mg once daily if tolerated and needed. Although not specifically studied, it is anticipated the full antihypertensive effect of Carviday® would be seen within 7 to 14 days as had been demonstrated with immediate-release carvedilol. Total daily dose should not exceed 80 mg.

Geriatric use
When switching elderly patients (65 years of age or older) who are taking the higher doses of immediate-release carvedilol tablets (25 mg twice daily) to Carviday®, a lower starting dose (40 mg) of Carviday® should be considered to minimize the potential for dizziness, syncope, or hypotension. Patients who have switched and who tolerate Carviday® should, as appropriate, have their dose increased after an interval of at least 2 weeks.

Method of administration: Oral
Carviday® should be taken once daily in the morning with food. Carviday® tablets should be swallowed as a whole. Carviday® and/or its contents should not be crushed, chewed or taken in divided doses.

4.3 Contraindications
- Hypersensitivity to the carvedilol or to any of the excipients listed in section 6.1.
- Bronchial asthma or related bronchospastic conditions
- Second- or third-degree AV block
- Sick sinus syndrome
- Severe bradycardia (unless a permanent pacemaker is in place)
- Patients with cardiogenic shock or who have decompensated heart failure requiring the use of intravenous inotropic therapy
- Patients with severe hepatic impairment

4.4 Special warnings and precautions for use

Glycaemic control in Type 2 Diabetes: Carvedilol may mask symptoms and signs of acute hypoglycaemia. Impaired glucose control may occasionally occur in patients with diabetes mellitus and heart failure in connection with the use of carvedilol.

Thyrotoxicosis: Carvedilol may mask features (symptoms and signs) of thyrotoxicosis

Bradycardia: Carvedilol may cause bradycardia, if there is a decrease in pulse rate to less than 55 beats per minute, and symptoms associated with bradycardia occur, the carvedilol dose should be reduced.

Bronchospasm: Patients with Chronic Obstructive Pulmonary Disease with a tendency towards bronchospasm who are not treated with oral or inhalation medicine should only be given carvedilol if the expected improvement outweighs the possible risk.

Cessation of therapy: Patients with coronary artery disease, who are being treated with Carviday®, should be advised against abrupt discontinuation of therapy. Severe exacerbation of angina and the occurrence of myocardial infarction and ventricular arrhythmias have been reported in angina patients following the abrupt discontinuation of therapy with B-blockers.

Peripheral Vascular Disease: B-blockers can precipitate or aggravate symptoms of arterial insufficiency in patients with peripheral vascular disease. Caution should be exercised in such individuals.

4.5 Interaction with other medicinal products and other forms of interaction

Hypotensive Agents
Patients taking both agents with B-blocking properties and a drug that can deplete catecholamines (e.g., reserpine and monoamine oxidase inhibitors) should be observed closely for signs of hypotension and/or severe bradycardia.

Cyclosporine
Modest increases in mean trough cyclosporine concentrations were observed following initiation of carvedilol treatment in 21 renal transplant patients suffering from chronic vascular rejection. Due to wide interindividual variability in the dose adjustment required, it is recommended that cyclosporine concentrations be monitored closely after initiation of carvedilol therapy and that the dose of cyclosporine be adjusted as appropriate.

Digitalis Glycosides
Both digitalis glycosides and □-blockers slow atrioventricular conduction and decrease heart rate. Concomitant use can increase the risk of bradycardia. Digoxin concentrations are increased by about 15% when digoxin and carvedilol are administered concomitantly.

Inducers/Inhibitors of Hepatic Metabolism
Rifampin reduced plasma concentrations of carvedilol by about 70%.

Amiodarone

Amiodarone, and its metabolite desethyl amiodarone, inhibitors of CYP2C9 and P-glycoprotein, increased concentrations of the S (-) enantiomer of carvedilol by at least 2-fold. The concomitant administration of amiodarone or other CYP2C9 inhibitors such as fluconazole with Carviday® may enhance the B-blocking properties of carvedilol resulting in further slowing of the heart rate or cardiac conduction. Patients should be observed for signs of bradycardia or heart block, particularly when one agent is added to pre-existing treatment with the other.

Calcium Channel Blockers
Conduction disturbance (rarely with hemodynamic compromise) has been observed when carvedilol is co-administered with diltiazem. As with other agents with B-blocking properties, if Carviday® is to be administered orally with calcium channel blockers of the verapamil or diltiazem type, it is recommended that ECG and blood pressure be monitored.

Insulin or Oral Hypoglycemics
Agents with B-blocking properties may enhance the blood-sugar-reducing effect of insulin and oral hypoglycemics. Therefore, in patients taking insulin or oral hypoglycemics, regular monitoring of blood glucose is recommended.

4.6 Pregnancy and lactation
Pregnancy: There are no adequate data from the use of carvedilol in pregnant women.

Lactation: Carvedilol is lipophilic and according to results from the lactating animals, carvedilol and its metabolites are excreted in the breast milk and therefore, mothers receiving carvedilol should not breast feed.

4.7 Effects on ability to drive and use machines.
This drug can cause dizziness, drowsiness, and fatigue. During initiation of therapy, the patient should be cautioned to avoid situations such as driving or hazardous tasks, where injury could result should the symptoms occur.

4.8 Undesirable effects
The risk of most adverse reactions associated with carvedilol is similar across all indications.
Frequency categories are as follows:
Very common ≥ 1/10
Common ≥ 1/100 and < 1/10
Uncommon ≥ 1/1,000 and < 1/100
Rare ≥ 1/10,000 and < 1/1,000
Very rare < 1/10,000

Infections and infestations
Common: Bronchitis, pneumonia, upper respiratory tract infection, urinary tract infection

Blood and lymphatic system disorders

Common: Anaemia
Rare: Thrombocytopaenia
Very rare: Leukopenia

Immune system disorders
Very rare: Hypersensitivity (allergic reaction)

Metabolism and nutrition disorders
Common: Weight increase, hypercholesterolaemia, impaired blood glucose control (hyperglycaemia, hypoglycaemia) in patients with pre-existing diabetes

Psychiatric disorders
Common: Depression, depressed mood
Uncommon: Sleep disorders, confusion

Nervous system disorders
Very common: Dizziness, headache
Uncommon: Presyncope, syncope, paraesthesia

Eye disorders
Common: Visual impairment, lacrimation decreased (dry eye), eye irritation

Cardiac disorders
Very common: Cardiac failure
Common: Bradycardia, oedema, hypervolaemia, fluid overload
Uncommon: Atrioventricular block, angina pectoris

Vascular disorders
Very common: Hypotension
Common: Orthostatic hypotension, disturbances of peripheral circulation (cold extremities, peripheral vascular disease, exacerbation of intermittent claudication and Reynaud's phenomenon), Hypertension

Respiratory, thoracic and mediastinal disorders
Common: Dyspnoea, pulmonary oedema, asthma in predisposed patients
Rare: Nasal congestion

Gastrointestinal disorders
Common: Nausea, diarrhoea, vomiting, dyspepsia, abdominal pain
Uncommon: Constipation
Rare: dry mouth

Hepatobiliary disorders
Very rare: Alanine aminotransferase (ALT), aspartate aminotransferase (AST) and gammaglutamyltransferase (GGT) increased

Skin and subcutaneous tissue disorders

Uncommon: Skin reactions (e.g. allergic exanthema, dermatitis, urticaria, pruritus, psoriatic and lichen planus like skin lesions and increased sweating), alopecia
Very rare: Severe cutaneous adverse reactions (e.g. Erythema multiforme, Stevens-Johnson syndrome, Toxic epidermal necrolysis)

Musculoskeletal and connective tissue disorders
Common: Pain in extremities

Renal and urinary disorders
Common: Renal failure and renal function abnormalities in patients with diffuse vascular disease and/or underlying renal insufficiency, micturition disorders
Very rare: Urinary incontinence in women

Reproductive system and breast disorders
Uncommon: Erectile dysfunction

General disorders and administration site conditions
Very common: Asthenia (fatigue)
Common: Pain, Oedema

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org.

4.9 Overdose.
Overdosage may cause severe hypotension, bradycardia, cardiac insufficiency, cardiogenic shock, and cardiac arrest. Respiratory problems, bronchospasms, vomiting, lapses of consciousness, and generalized seizures may also occur. The patient should be placed in a supine position and, where necessary, kept under observation and treated under intensive-care conditions.

5. Pharmacological properties
5.1 Pharmacodynamic properties
Mechanism of Action:
Carvedilol is a racemic mixture in which nonselective β- adrenoreceptor blocking activity is present in the S (-) enantiomer and α1-adrenergic blocking activity is present in both R (+) and S (-) enantiomers at equal potency. Carvedilol has no intrinsic sympathomimetic activity. Like propranolol, it has membrane stabilising properties. 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.

5.2 Pharmacokinetic properties

Absorption:

Carvedilol is rapidly and extensively absorbed following oral administration of immediate release carvedilol tablets, with an absolute bioavailability of approximately 25% to 35% due to a significant degree of first-pass metabolism. Carviday® controlled release tablets have approximately 85% of the bioavailability of immediate-release carvedilol tablets. The exposure (AUC, Cmax, trough concentration) of carvedilol as Carviday® controlled release tablets is equivalent to those of immediate-release carvedilol tablets when both are administered with food. The absorption of carvedilol from Carviday® is slower and more prolonged compared with the immediate release carvedilol tablet with peak concentrations achieved approximately 5 hours after administration. Plasma concentrations of carvedilol increase in a dose-proportional manner over the dosage range of Carviday® 10 to 80 mg. Within-subject and between-subject variability for AUC and Cmax is similar for Carviday® and immediate-release carvedilol.

Distribution:

Carvedilol is more than 98% bound to plasma proteins, primarily with albumin. The plasma protein binding is independent of concentration over the therapeutic range. Carvedilol is a basic, lipophilic compound with a steady-state volume of distribution of approximately 115 L, indicating substantial distribution into extravascular tissues.

Metabolism and Excretion:

Carvedilol is extensively metabolized. Following oral administration of radiolabelled carvedilol to healthy volunteers, carvedilol accounted for only about 7% of the total radioactivity in plasma as measured by AUC. Less than 2% of the dose was excreted unchanged in the urine. Carvedilol is metabolized primarily by aromatic ring oxidation and glucuronidation. The oxidative metabolites are further metabolized by conjugation via glucuronidation and sulfation. The metabolites of carvedilol are excreted primarily via the bile into the feces. Demethylation and hydroxylation at the phenol ring produce 3 active metabolites with β-receptor blocking activity. Based on preclinical studies, the 4'- hydroxyphenyl metabolite is approximately 13 times more potent than carvedilol for β-blockade. Compared with carvedilol, the 3 active metabolites exhibit weak vasodilating activity. Plasma concentrations of the active metabolites are about one-tenth of those observed for carvedilol and have pharmacokinetics similar to the parent. Carvedilol undergoes stereoselective first-pass metabolism with plasma levels of R(+)-carvedilol approximately 2 to 3 times higher than S(-)-carvedilol following oral administration of Carviday® in healthy subjects. Apparent clearance is 90 L per h and 213 L per h for R(+)- and S(-)-carvedilol, respectively. The primary P450 enzymes responsible for the metabolism of both R(+) and S(-)-carvedilol in human liver microsomes were CYP2D6 and CYP2C9 and to a lesser extent CYP3A4, 2C19, 1A2, and 2E1. CYP2D6 is

thought to be the major enzyme in the 4'- and 5'-hydroxylation of carvedilol, with a potential contribution from 3A4. CYP2C9 is thought to be of primary importance in the O-methylation pathway of S(-)-carvedilol. Carvedilol is subject to the effects of genetic polymorphism with poor metabolizers of debrisoquin (a marker for cytochrome P450 2D6) exhibiting 2- to 3-fold higher plasma concentrations of R(+)-carvedilol compared with extensive metabolizers. In contrast, plasma levels of S(-)-carvedilol are increased only about 20% to 25% in poor metabolizers, indicating this enantiomer is metabolized to a lesser extent by cytochrome P450 2D6 than R(+)-carvedilol. The pharmacokinetics of carvedilol do not appear to be different in poor metabolizers of S-mephenytoin (patients deficient in cytochrome P450 2C19).

6. Pharmaceutical particulars

6.1 List of Excipients:

Carviday® 10

- Lactose
- Ethylcellulose
- Hydroxy propyl methyl cellulose K-100M
- Microcrystalline cellulose
- Povidone K-30 %
- Isopropyl alcohol
- Microcrystalline cellulose PH 102
- Magnesium stearate
- Purified talc
- Colloidal Silicon Dioxide
- Methylene Dichloride

Carviday® 20

- Lactose
- Ethylcellulose
- Hydroxy propyl methyl cellulose K-100M
- Microcrystalline cellulose
- Povidone K-30 %
- Isopropyl alcohol
- Microcrystalline cellulose PH 102
- Magnesium stearate
- Purified talc
- Colloidal Silicon Dioxide
- Yellow Ferric oxide of iron ready mix coat
- Methylene Dichloride

Carviday® 40

- Lactose
- Ethylcellulose
- Hydroxy propyl methyl cellulose K-100M
- Microcrystalline cellulose
- Povidone K-30 %
- Isopropyl alcohol
- Microcrystalline cellulose PH 102
- Magnesium stearate
- Purified talc
- Colloidal Silicon Dioxide
- Precoat Titanium Dioxide Ready mix Non-Aqueous
- Methylene Dichloride

Carviday® 80

- Lactose
- Ethylcellulose
- Hydroxy propyl methyl cellulose K-100M
- Microcrystalline cellulose
- Povidone K-30 %
- Isopropyl alcohol
- Microcrystalline cellulose PH 102
- Magnesium stearate
- Purified talc
- Colloidal Silicon Dioxide
- Methylene Dichloride

6.2 Incompatibilities

Not applicable.

6.3 Shelf life
Carviday® 10, Carviday® 20, Carviday® 40 and **Carviday® 80**
36 months

6.4 Special precautions for storage
Store below 30°C. Protect from direct sunlight, heat & moisture.

6.5 Nature and contents of container
Carviday® 10, Carviday® 20, Carviday® 40 and Carviday® 80 are each available in a pack of 3 x 10 tablets in Alu-Alu Blister pack.

6.6 Special precautions for disposal and other
Any unused medicine product or waste material should be disposed of in accordance with the local requirements.

7. Marketing authorization holder and manufacturing site addresses
Carviday® 10 / 20 / 40 / 80

Manufactured in India by:
HBC HEALTH CARE PVT. LTD.
Block/ Survey No.: 609 Paiki 002, Ambasan
(Amipura), Near Shanku Water Park,
Ahmedabad-Mehsana Highway, Dist-Mehsana

Manufactured For & Marketed by:
KRISHNA CHEMISTS LTD.
P.O. BOX 3328-00506
NAIROBI, KENYA.

8. Marketing Authorization Number
Carviday® 10
H2021/CTD6066/2046ER
Carviday® 20
H2021/CTD6068/2047ER
Carviday® 40
H2021/CTD6072/2048ER
Carviday® 80
H2021/CTD6074/2049ER

9. Date of first authorization/renewal of the authorization
Carviday® 10, Carviday® 20, Carviday® 40 and **Carviday® 80**
Date of first authorization – 16/09/2021

10. Date of revision of the text
11/12/2025