SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

CORONIS (CARVEDILOL) 6.25mg Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 6,25 mg carvedilol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Hypertension:

Carvedilol is also indicated for the management of essential hypertension. It can be used alone or in combination with other antihypertensive agents, especially thiazide-type diuretics.

Coronary Heart Failure:

The efficacy of Coronis has been established in coronary heart disease. Its efficacy has been shown in patients with silent myocardial ischemia and instable angina.

Chronic Heart Failure:

Carvedilol is indicated for the treatment of mild to severe heart failure of ischemic or non-ischemic origin. In addition to diuretics, ACE inhibitor, and digitalis, it decreases the mortality and morbidity and delays the progression of the disease in the treatment of chronic heart failure.

Carvedilol may be used in adjunct to the standard treatment. It may be also used in patients that are not administered digitalis, hydrazaline and nitrate.

4.2 Posology and method of administration

Duration of treatment

Coronis therapy is a long term treatment.

Treatment should not be withdrawn abruptly and it should be discontinued gradually in weeks. This is especially important for the patients with coronary artery diseases.

Unless otherwise recommended by the physician

Essential hypertension

For the initial two days of the treatment the recommended dose is 12, 5 mg once daily. Then, 25 mg once daily is used. The daily dose may be increased to maximum 50 mg that is administered once or twice daily if needed. Dosage adjustments should be made with at least two week intervals.

Coronary heart disease

For the initial two days of the treatment the recommended dose is 12, 5 mg twice daily. Then, 25 mg once daily is used. The daily dose may be increased to maximum 100 mg that is administered in divided doses (twice daily) if needed. Dosage adjustments should be made with at least two week intervals.

Symptomatic, stabilized, chronic heart failure:

Dosage must be individualized and monitored during up titration. In patients using digital, diuretic and ACE inhibitors, prior to initiating carvedilol therapy, the doses of these drugs must be stabilized. The recommended starting dose of the therapy is 3,125 mg twice daily for two weeks; if this dose is well tolerated, with at least two week intervals, the dose may be increased to first 6,25 mg twice daily, then to 12,5 mg twice daily and then to 25 mg twice daily. The dose must be increased up to a level where the patient can most tolerate. A maximum dose of 25 mg twice daily is recommended in patients with mild-to-moderate heart failure weighing over 85 kg. Prior to every dose increase, the patient must be observed by a doctor for symptoms of worsening heart failure or vasodilatation. Temporary worsening of heart failure or fluid retention must be cured by increased doses of diuretics; rarely the lowering carvedilol dosage or stopping the carvedilol therapy temporarily might be needed. If the carvedilol therapy has been stopped for over one week period, the therapy should be initiated with lesser doses twice daily and increased as recommended above. If the carvedilol therapy has been stopped for over two weeks, the therapy should be initiated with 3,125 mg twice daily and increased as recommended above.

For treatment of vasodilatation symptoms, initially the dosages of diuretics must be decreased. If the symptoms continue, the dosage of ACE inhibitor (if being used) may be decreased, and carvedilol dosage might be decreased if needed. Under these conditions, the dosage of carvedilol must be increased until the worsening of heart failure or vasodilatation symptoms are stabilized.

Special dosage instructions

Renal Insufficiency

According to the available pharmacokinetic data of patients with different levels of renal function impairment (including renal insufficiency), no change in carvedilol dosage chart is recommended to patients with mild to severe renal insufficiency.

Hepatic Impairment

Carvedilol should not be given to patients with severe hepatic impairment (See Contraindications).

Elderly patients

There is not enough data to support dose adjustment.

Usage Instructions

Tablets must be swallowed with sufficient amount of liquid.

4.3 Contraindications

Coronis is contraindicated in patients with:

- Hypersensitivity to carvedilol or any other components of the product.
- Instable or decompensate cardiac failure.
- Clinically significant hepatic insufficiency.

As with the other β-blockers, carvedilol should not be used in patients with:

- Second- or third-degree AV block (unless a permanent pacemaker is in place)
- Severe bradycardia (<50 bpm)
- Sick sinus syndrome (including sino-atrial block)
- Severe hypotension (systolic blood pressure <85 mmHg)
- Cardiogenic shock
- History of bronchospasm or asthma

4.4 Special warnings and precautions for use

Chronic congestive heart failure: In patients with congestive heart failure, worsening heart failure or fluid retention may occur during up-titration of carvedilol. If such symptoms occur,

diuretics should be increased and the carvedilol dose should not be advanced until clinical stability resumes. Occasionally it is necessary to lower the carvedilol dose or temporarily discontinue it. Such episodes do not preclude subsequent successful titration of, or a favorable response to, carvedilol. Since both drugs reduce the AV conduction, carvedilol should not be used in combination with digitalis glycosides.

Renal function in congestive heart failure: Rarely, use of carvedilol in patients with congestive heart failure has resulted in reversible deterioration of renal function. Patients at risk appear to be those with low blood pressure (systolic blood pressure <100 mm Hg), ischemic heart disease and diffuse vascular disease, and/or underlying renal insufficiency.

Chronic obstructive lung failure: In the patients with chronic obstructive pulmonary disease (COPD) who has attacks of bronchospasm and who do not use oral or inhaled medications for this disease, carvedilol should be used only if the potential benefits are greater than the potential risks. In patents with tendency to bronchospasm, respiratory distress may occur due to the possible increased in the airway resistance. Patients should be closely monitored during the initiation of the treatment and the titration of the dose of the carvedilol and the dose should be decreased if bronchospasm occurs during treatment.

Diabetes: Since it may mask the early symptoms and signs of the acute hypoglycemia, carvedilol should be used with caution in patients with diabetes mellitus. Carvedilol may affect the control of blood glucose levels in diabetic patients with chronic heart failure. Because of the β-blocker properties of the drug, latent diabetes mellitus may become significant, present diabetes may be aggravated and blood glucose regulation may be inhibited.

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

Reynaud phenomenon: Since carvedilol may cause the aggravation of the symptoms in patients with peripheral vascular disease, it should be used with caution.

Thyrotoxicosis: As with all β-blockers, carvedilol also may mask clinical signs of thyrotoxicosis.

Anesthesia and Major Surgery: Caution should be exercised in patients who undergone an operation due to the synergic negative inotropic affect of anesthetics and carvedilol.

Bradycardia: Carvedilol may cause bradycardia. In case heartbeat per minute less than 55, Carvedilol dosage should be decreased.

Hypersensitivity: Since the β-blockers may increase the sensitivity to allergens and the degree of anaphylactoid reactions, carvedilol should be used with caution in patients with history of hypersensitivity and in patients who undergo desensitization treatment.

Psoriasis: In patients with history of psoriasis caused by β-blockers, carvedilol should be only used if benefit overweighs the risks to the patient.

Co-administration with calcium channel blockers: In patients in whom carvedilol is concomitantly administered with calcium channel blockers such as verapamil and diltiazem and other antiarrythmic agents, ECG and blood pressure should be closely monitored.

Pheochromocytoma: In patients with pheochromocytoma, an (alpha)-blocking agent should be initiated prior to the use of any (beta)-blocking agent. Although carvedilol has both (alpha)- and (beta)-blocking pharmacologic activities, there has been no experience with its use in this condition. Therefore, caution should be taken in the administration of carvedilol to patients suspected of having pheochromocytoma.

Prinzmetal's variant angina: Agents with non-selective (beta)-blocking activity may provoke chest pain in patients with Prinzmetal's variant angina. There has been no clinical experience with carvedilol in these patients although the (alpha)-blocking activity may prevent such symptoms. However, caution should be taken in the administration of carvedilol to patients suspected of having Prinzmetal's variant angina.

Contact lenses: Contact lens wearers may experience decrease in the lacrimation.

Withdrawal syndrome: Especially in patients with ischemic heart disease, carvedilol treatment should not be withdrawn abruptly. Carvedilol treatment should be ceased gradually. (Within 2 weeks).

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacokinetic Drug-Drug Interactions

Digoxin: Following concomitant administration of carvedilol and digoxin, digoxin concentrations increase by 15%. Both carvediol and heart glycosides slow down the transmittance of AV. When initiating the carvedilol therapy, adjusting the dose or when stopping the therapy, careful monitoring of digoxin levels is recommended.

Insulin and orally administered hypoglysemics: Agents with (beta)-blocking properties may increase the serum glucose–lowering effects of insulin and orally administered hypoglysemics. Hypoglycemia symptoms might be masked or lowered (especially tachycardia). Therefore regular monitoring of blood glucose is recommended in patients using insulin or orally administered hypoglysemics.

Inducers and inhibitors of liver metabolism: Rifampisin reduces plazma concentrations of carvedilol by about 70%. Cimetidine increases the AUC of carvedilol by about 30% but does not affect Cmax (maximum concentration). Since Carvedilol plasma levels may decrease and Cimetidine plasma levels may increase in patients administering mixed functioned oxidase inducers such as rifampicin, these patients must be closely monitored. Since Cimetidine has low effect on Carvedilol levels, any possibility of clinical interaction is at minimum level.

Catecholamine-depleting agents: Patients who are using agents with (beta)-blocking properties concomitantly with a catecholamine-depleting agent (such as Reserpine and/or monoamine oxidase inhibitors) must be closely observed in terms of hypotension and/or severe bradycardia.

Cyclosporin: Modest increases in mean trough cyclosporine concentrations were observed following initiation of carvedilol treatment in 21 renal transplant patients suffering from chronic vascular rejection. In about 30% of patients, the dose of cyclosporine had to be reduced in order to maintain cyclosporine concentrations within the therapeutic range, while in the remainder no adjustment was needed. On the average for the group, the dose of cyclosporine was reduced about 20% in these patients. Due to wide inter-individual 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.

Verapamil, diltiazem and other antiarythmics: Concurrent use with Carvedilol may increase the risk of AV transmittance disorders (See Warnings/Precautions).

Pharmacokinetic Drug-Drug Interactions

Clonidine: Concomitant administration of clonidine with agents with β-blocking properties may potentiate blood-pressure- and heart-rate-lowering effects. When concomitant treatment with agents with β-blocking properties and clonidine is to be terminated, the (beta)-blocking

agent should be discontinued first. Clonidine therapy can then be discontinued several days later by gradually decreasing the dosage.

Calcium channel blockers: (See Warnings/Precautions) Isolated cases of conduction disturbance (rarely with hemodynamic ompromise) have been observed when carvedilol is co-administered with diltiazem. As with other agents with β-blocking properties, if carvedilol 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. As with other agents that have beta-blocking activity, carvedilol may increase the efficacy of anti-hypertensive drugs (Such as $Alpha_1$ receptor antagonists) or other drugs that have hypotension as a part of their adverse effect profile. The synergistic negative inotropic and hypotensive effects of carvedilol and other anesthetic agents should be considered during anesthesia.

4.6 Fertility, pregnancy and lactation

Use in Pregnancy and Lactation:

Pregnancy: Pregnancy category is C in 1^{st} trimester and D in 2^{nd} and 3^{rd} trimester.

β-blockers may cause intrauterine fetal death or immature / premature births due to the inhibition of the placental perfusion. Additionally, adverse effects may occur in fetus or newborn (especially hypoglycemia and bradycardia). If the risk of cardiac or pulmonary complication is high in newborns during the postnatal period, caredilol should not e used.

Lactation: It is not known whether carvedilol is excreted to maternal milk or not. Therefore, carvedilol is not recommended for the use during lactation.

4.7 Effects on ability to drive and use machines

No studies have been conducted on the effect of carvedilol on patients' ability to drive or use machines. The ability to drive, use machines, or work without support may be impaired due to individually variable reactions (dizziness, fatigue). This applies particularly at the start of treatment, after dose increase, when changing medication, and when used with alcohol.

4.8 Undesirable effects

*I*ncidence is described as follows:

≥ 10 %: very frequent,

≥ 1% - <10%: frequent,

≥ 0,1% - <1%,: occasional,

≥ 0,01% - <0,1%: rare,

<0,01%: very rare that includes isolated cases.

The incidence of adverse effects is not dose dependent except vertigo.

Congestive Heart Failure:

In clinical studies conducted with patients with congestive heart failure, the adverse events occurring most frequently with carvediol than with placebo are listed below:

-Central nervous system: Very frequent: Especially during the initiation of the treatment, mild vertigo, headache and fatigue occur. Asthenia (including fatigue) is also frequently seen.

-Cardiovascular system

Frequent: Bradycardia, hypotension, edema (general, peripheral and genital edema, leg edema, hypovolemia and increase in the fluid overload).

Occasional: Syncope (including presyncope), AV-block and heart failure during dosa adjustments.

-Gastrointestinal system

Frequently nausea, diarrhea and vomiting.

-Haematology

Rarely thrombocytopenia and leucopenia in isolated cases.

-Metabolism

Frequently increase in the body weight and hypercholesterolemia. Hypoglycemia and worsening of the blood glucose control are frequently seen in diabetic patients.

-Others

Frequently vision disturbances and rarely distributed vascular disease and / or renal failure in patients with renal function abnormalities (See Warnings / Precautions).

Adverse effects in the hypertension treatment and long-term treatment of coronary heart disease

The adverse reaction profile related with the intake of carvedilol in hypertension and angina pectoris is in harmony with the profile observed in congestive heart failure; however the incidence of adverse events is much lower in the previous group.

The side effects reported in clinical studies conducted with patients with hypertension and coronary heart disease:

-Central nervous system

Especially in the beginning of the therapy, mild dizziness, headache and fatigue, may be seen frequently. Occasionally, depression, sleep disorders and paresthesia may be seen.

-Cardiovascular system

Especially in the beginning of the therapy, frequently bradycardia, postural hypotension, rarely syncope; occasionally, peripheral circulation disorders (in limbs, peripheral vascular disease, frequently cladication, aggravation of symptoms in Raynaud's phenomenon), AV blockage, angina pectoris, heart failure, peripheral edema symptoms.

-Respiratory system

In predisposed patients, frequently asthma and dyspnea, rarely nasal congestion.

-Gastrointestinal track

Nausea, abdominal pain, diarrhea, occasionally constipation and vomiting.

-Skin

Occasionally skin rash (for example rarely allergic exanthema, dermatitis, urticaria, itching.

-Blood chemistry and hematology

In isolated cases, elevations in ALT, AST and gamma-GT and thrombocytopenia and leucopenia are observed.

-Other

Frequently, pain in extremities, decrease in tears and eye irritation, occasionally sexual impotence and visual disorders, rarely dryness in mouth and urination disorder, allergic reactions in isolated instances.

IN CASE OF AN UNEXPECTED SIDE EFFECT, CONSULT YOUR PHYSICIAN.

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 EFDA yellow Card Scheme, online at https://primaryreporting.who-umc.org/ET or toll free call 8482 to Ethiopian food and drug authority (EFDA).

4.9 Overdose

Intoxication symptoms:

Over dosage 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.

Intoxication therapy:

Along with general procedures, the patient should be kept under observation and treated under intensive-care conditions. The supporting therapy may be administered:

The patient should be placed in a supine position.

Atropine: 0, 5-2 mg IV (for excessive bradycardia)

Glucagon: In the beginning of the therapy, 1 to 10 mg IV, then a continuous infusion of 2- 5 mg/hour (to support cardiovascular function). Sympathomimetics which may be used according to body weight and effect are: Dobutamine, isoprenaline, orsiprenaline and adrenaline). If positive inothropic effect is needed, use of phosfosiesterase inhibitors such as milrinon must be considered. If peripheral vasodilatation dominates in the event of intoxication, it may be necessary to administer adrenaline or noradrenaline with continuous monitoring of circulatory conditions. . For therapy-resistant bradycardia, pacemaker therapy should be performed.

Bronchospasm Therapy: For bronchospasm, (beta)-sympathomimetics (as aerosol or IV) or aminophylline IV should be given.

Seizure Therapy: In the event of seizures, slow IV injection of diazepam or clonazepam is recommended.

Important Note:

In the event of severe intoxication where there are symptoms of shock, supporting treatment must be continued for a sufficiently long period of time because half-life of carvedilol may be elongated or it may re-distributed from deeper compartments. The period of supporting/antidote therapy depends on the severity of the overdose. Adjuvant therapy must be continued until the patient’s condition is stabilized.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Carvedilol is an adrenergic receptor blocker with α_1, β_1 and β_2 adrenergic receptor blocking properties. Carvedilol has been shown to have organ protecting affects. Carvedilol is a potent antioxidant, a scavenger of reactive oxygen radicals. Carvedilol is rasemic and both of its R (+) and S (-) isomers exhibit α_1 adrenergic receptor blockage and antioxidant properties. Carvedilol has antiproliferative affect on the human vascular smooth muscle cells. In clinical trials, chronic carvedilol treatment has been shown to decrease in oxidative stress measured by variable parameters. β-adrenergic receptor blockage property that is associated with S (-) enantiomer is not selective for β_1 and β_2 adrenergic receptors. Carvedilol has no intrinsic sympathomimetic activity and like propranolol, it has membrane stabilizing properties. Carvedilol reduces the peripheral vascular resistance through vasodilatation and suppresses the renin-angiotensin-aldosterone system through beta-blockade. The activity of plasma renin is reduced and fluid retention is rare. Carvedilol decreases the peripheral vascular resistance with its selective α_1 blockage affect. Carvedilol decreases the increase in the blood pressure caused by phenylephrine which is a α_1 receptor antagonist but not the increase caused by angiotensin II. Carvedilol does not have a negative affect on lipid profile. It preserves the ratio between high density lipoproteins and low density lipoproteins (HDL/LDL)

Efficacy:

According to the results of the clinical trials:

Hypertension:

Carvedilol decreases the blood pressure in hypertensive patients with its β - blocker affect and vasodilatation affect which is mediated by α_1. The reduction in blood pressure is not associated with a concomitant increase in total peripheral resistance, as observed with pure beta-blocking agents. Heart rate is slightly decreased. Renal blood flow and renal function are maintained. Carvedilol has been shown to preserve cardiac output and decrease the total peripheral resistance. The amount of blood in the particular organ and vascular beds is not affected by carvedilol such as kidney, skeletal muscle, forearm, leg, skin, brain or carotid artery. Cold extremities and early tiredness during physical activity are rarely seen. Long-term effects of carvedilol on hypertension have been shown by double-blind controlled clinical trials.

Coronary Heart Disease:

In coronary heart disease patients, carvedilol has been shown to have a stable anti- ischemic (improvements in total exercise time, time to ST segment depression of 1 mm and time to angina) and anti-anginal affects. Acute hemodynamic studies demonstrated that carvedilol

reduces myocardial oxygen consumption and sympathetic over activity significantly. Additionally carvedilol reduces ventricular pre-load (pulmonary arterial pressure and pulmonary capillary wedge pressure) and after-load (total peripheral resistance).

Chronic Heart Failure:

Carvedilol significantly reduces all-cause mortality and cardiovascular hospitalization. It also increases the ejection fraction. Carvedilol improves the symptoms of ischemic and non-ischemic chronic heart failure. This effect of carvedilol is dose dependent.

5.2 Pharmacokinetic properties

Absorption

Carvedilol is rapidly absorbed following the oral administration. Serum levels peak at approximately 1 hour after an oral dose. Its effect begins in 1-2 hours. Maximum antihypertensive effect is achieved within 1-2 hours. Absolute bioavailability of carvedilol in humans is approximately 25-35 %.

Distribution

Carvedilol is highly lipophilic; approximately 98% to 99% is bound to plasma proteins. The distribution volume is approximately 2 L/kg.

Metabolism

Most of the administered carvedilol is metabolized to various metabolites that are primarily excreted via the bile. Following the oral administration, first-pass effect is accounted for approximately 60-75 %. Carvedilol is metabolized primarily in the liver and glucuronidation is one of the essential reactions. Demethylation and hydroxylation at the phenol ring produce three active metabolites with (beta)-receptor blocking activity. Based on preclinical studies, the 4'-hydroxyphenyl metabolite is approximately 13 times more potent than carvedilol for (beta)-blockade. Compared to carvedilol, the three 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. Two of the hydroxy-carbazole metabolites of carvedilol are 30-80 times more potent antioxidants than the parent compound.

Elimination

Elimination half-life of carvedilol is approximately 6 hours. Plasma clearance ranges from 500 to 700 mL/min. Its main elimination route is feces. It is excreted mainly via the bile. A small amount of administered carvedilol is excreted via the kidneys as various metabolites.

Pharmacokinetics in Special Populations:

Renal Insufficiency: During the chronic treatment with carvedilol, autoregulatuar blood flow is preserved and glomerular filtration is not effected. In patients with hypertension and renal failure, the area under the curve (AUC), elimination half-life and maximum plasma concentration are not significantly changed. The renal elimination of unchanged drug is decreased in patients with renal failure; however, pharmacokinetic parameters are not altered significantly. Clinical trials have been demonstrated that carvedilol is an effective agent in the treatment of hypertension caused by renal disorders. This is also valid for the patients with chronic renal insufficiency, hemodialysis or renal transplantation. Carvedilol reduces the blood pressure both in the days of hemodialysis and also in the days that the hemodialysis is not performed and this effect is comparable with the blood pressure lowering effect in patients with normal renal function. Consistent with its high degree of plasma protein-binding, carvedilol does not appear to be cleared significantly by hemodialysis. Based on the result of the clinical trials in patients with hemodialysis, it is concluded that carvedilol is more effective and better tolerated than calcium channel blockers.

Hepatic impairment: In patients with cirrhotic liver disease, systemic bioavailability of the drug is increased to 80% because of the lacking first-pass effect. Therefore, carvedilol is contraindicated in patients with significant hepatic failure (See. Contraindications).

Elderly: Pharmacokinetics of carvedilol in hypertensive patients is not altered by the age of the patient. A clinical study conducted with older hypertensive patients demonstrated that adverse effects profile was similar compared to younger patients. In another clinical study conducted in elder coronary heart disease patients, it is reported that the adverse events were similar compared to younger patients.

Children: Limited data is available about the pharmacokinetics of carvedilol under the age of 18.

Diabetic patients: Carvedilol has no effect on fasting and post-prandial blood glucose concentration, glycosilated hemoglobulin A_1 or dose adjustment needs fort the anti-diabetic agents in hypertensive patients with non-insulin dependent diabetes.

Carvediol is shown to have no statistically significant effect on glucose tolerance test. Carvedilol improved the insulin sensitivity in non-diabetic hypertensive patients with decreased insulin sensitivity (Syndrome X). The same results have been achieved in hypertensive non-insulin dependent diabetes patients.

5.3 Preclinical safety data

In carcinogenicity studies conducted in rats and mice at doses up to 75 mg/kg/day and 200 mg/kg/day, respectively (38 to 100 times the maximum recommended human dose [MRHD]), carvedilol had no carcinogenic effects.

Carvedilol was not mutagenic in in vivo and in vitro tests in mammals and non-mammals.

Administration of carvedilol at maternally toxic doses (≥200 mg/kg, ≥100 times the MHRD) resulted in fertility disorders (poor mating, decreased corpora lutea, implantation and embryonic response). Doses >60 mg/kg (>30 times the MHRD) caused delays in the physical growth/development of offspring. Embryotoxicity (increased post-implantation deaths) was observed, but no malformations were seen in rats and rabbits that received the drug at doses of 200 mg/kg and 75 mg/kg, respectively (38 to 100 times the maximum recommended human dose [MHRD]). A summary of all preclinical safety information can be found in expert reports from October 1999 to March 2000.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate (from cow's milk)
Sucrose
Povidone K25
Crospovidone
Colloidal anhydrous silica
Magnesium stearate
Yellow iron oxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 MONTHS

6.4 Special precautions for storage

-Store in a dry place below 30°C.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

It is packed in Al/PVC/PVDC folio blisters of 28 tablets in a cardboard box with a patient information leaflet.

6.6 Special precautions for disposal <and other handling>

Any unused medicinal product or waste material should be disposed of in accordance with "Regulation on Control of Medical Waste" and "Regulation on Control of Packaging and Packaging Wastes".

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

Certificate No: 05038/07209/REN/2020

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Mar 4, 2020

10. DATE OF REVISION OF THE TEXT

September 2023