

Produktinformationen för Carvsanna filmdragerad tablett 6,25, 12,5, och 25 mg , MTnr 26019, 26020, 26021, gäller vid det tillfälle då läkemedlet godkändes. Informationen kommer inte att uppdateras eftersom läkemedlet inte marknadsförs i Sverige. Av samma anledning finns inte någon svensk produktinformation.

Den engelska produktinformationen kommer dock att uppdateras för de produkter där Sverige är referensland.

Om läkemedelsnamnet i följande produktinformation inte stämmer med namnet på dokumentet, beror det på att läkemedlet i Sverige är godkänt under ett annat namn.

SUMMARY OF THE PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Carvsanna 6.25 mg film-coated tablet

Carvsanna 12.5 mg film-coated tablet

Carvsanna 25 mg film-coated tablet

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains 6.25 mg, 12.5 mg or 25 mg carvedilol.

Excipient: 25mg/50mg/100mg of lactose monohydrate

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet

6.25 mg film-coated tablets: white, oval, scored on both sides and marked "6" on one side.

12.5 mg film-coated tablets: white, oval, scored on both sides and marked "12" on one side.

25 mg film-coated tablets: white, oval, scored on both sides and marked "25" on one side

The tablets can be divided into equal halves.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Essential hypertension.

Chronic stable angina pectoris

Adjunctive treatment in moderate to severe stable heart failure.

4.2 Posology and method of administration

Carvsanna is available in 3 strengths: 6.25 mg, 12.5 mg and 25 mg

Essential hypertension:

Carvedilol may be used for the treatment of hypertension alone or in combination with other antihypertensives, especially thiazide diuretics. Once daily dosing is recommended, however the recommended maximum single dose is 25 mg and the recommended maximum daily dose is 50 mg.

Adults

The recommended initial dose is 12.5 mg once a day for the first two days. Thereafter, the treatment is continued at the dose 25 mg/day. If necessary, the dose may be further increased gradually at intervals of two weeks or more rarely.

Elderly:

The recommended initial dose in hypertension is 12.5 mg once a day, which may also be sufficient for continued treatment. However, if the therapeutic response is inadequate at this

dose, the dose may be further increased gradually at intervals of two weeks or more rarely.

Chronic stable angina pectoris

Adults:

The recommended initial dose is 12.5 mg twice daily for two days. Thereafter, the treatment is continued at the dose 25 mg twice daily. If necessary, the dose may be further increased gradually at intervals of two weeks or more rarely. The recommended maximum daily dose is 100 mg in divided doses (twice daily).

Elderly:

The recommended initial dose is 12.5 mg twice daily for two days. Thereafter, the treatment is continued at the dose 25 mg twice daily, which is the recommended maximum daily dose.

Heart failure

Treatment of moderate to severe heart failure in addition to conventional basic therapy with diuretics, ACE inhibitors, digitalis, and/or vasodilators. The patient should be clinically stable (no change in NYHA-class, no hospitalisation due to heart failure) and the basic therapy must be stabilised for at least 4 weeks prior to treatment. Additionally the patient should have a reduced left ventricular ejection fraction and heart frequency should be > 50 bpm and systolic blood pressure > 85 mm Hg (see section 4.3).

The initial dose is 3.125 mg twice a day for two weeks. If the initial dose is well tolerated, the carvedilol dose can be increased at intervals of two weeks or more rarely, first to 6.25 mg twice daily, then 12.5 mg twice daily followed by 25 mg twice daily. It is recommended that the dose is increased to the highest level tolerated by the patient.

The recommended maximum dose is 25 mg given twice daily in patients weighing less than 85 kg and 50 mg twice daily in patients weighing more than 85 kg, provided that the heart failure is not severe. A dose increase to 50 mg twice daily should be performed carefully under close medical supervision of the patient.

Transient worsening of symptoms of heart failure may occur at the beginning of treatment, or due to a dose increase, especially in patients with severe heart failure and/or under high dose diuretic treatment. This does usually not call for discontinuation of treatment, but the dose should not be increased. The patient should be monitored by a physician/cardiologist after starting carvedilol treatment or increasing the dose. Before each dose increase, an examination should be performed for potential symptoms of worsening heart failure or for symptoms of excessive vasodilatation (e.g. renal function, body weight, blood pressure, heart rate and heart rhythm). Worsening of heart failure or fluid retention is treated by increasing the dose of diuretic, and the dose of carvedilol should not be increased until the patient is stabilised. If bradycardia appears or in case of lengthening of AV conduction time, the level of digoxin should first be monitored. Occasionally it may be necessary to reduce the carvedilol dose or temporarily discontinue treatment altogether. Even in these cases, carvedilol dose titration can often be successfully continued.

If carvedilol therapy is discontinued for more than two weeks, it should be reinitiated at 3.125 mg twice daily and increased gradually in accordance with the above recommendation.

Renal insufficiency.

Dosage must be determined for each patient individually, but according to pharmacokinetic parameters there is no evidence that dose adjustment of carvedilol in patients with renal failure is necessary.

Moderate hepatic dysfunction.

Dose adjustment may be required.

Children and adolescents.

There is no experience in children and adolescents.

Elderly.

Elderly patients may be more susceptible to the effects of carvedilol and should be monitored more carefully.

As with other beta-blockers and especially in coronary patients, the withdrawal of carvedilol should be done gradually (*see section 4.4*).

Method of administration.

The tablets do not need to be taken with a meal. However, 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.

4.3 Contraindications

- Hypersensitivity to carvedilol or to any of the excipients.
- Unstable/decompensated heart failure.
- Clinically manifest liver dysfunction.
- Metabolic acidosis.
- 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 special precautions for use

Chronic Congestive Heart Failure

In congestive heart failure patients, worsening cardiac 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 may be necessary to lower the carvedilol dose or, in rare cases, temporarily discontinue it. Such episodes do not preclude subsequent successful titration of carvedilol. Carvedilol should be used with caution in combination with digitalis glycosides, as both drugs slow AV conduction.

Renal function in Congestive Heart Failure

Reversible deterioration of renal function has been observed with carvedilol therapy in chronic heart failure patients with low blood pressure (systolic < 100 mm Hg), ischaemic heart disease and diffuse vascular disease, and/or underlying renal insufficiency.

Left ventricular dysfunction following acute myocardial infarction

Before treatment with carvedilol is initiated the patient must be clinically stable and should have received an ACE inhibitor for at least the preceding 48 hours, and the dose of the ACE inhibitor should have been stable for at least the preceding 24 hours.

Labile or secondary hypertension

Since there is limited clinical experience, carvedilol should not be administered in patients with labile or secondary hypertension

First degree heart block

Because of its negative dromotropic action, carvedilol should be administered with caution to patients with first degree heart block.

Chronic obstructive pulmonary disease

Carvedilol should be used with caution, in patients with chronic obstructive pulmonary disease (COPD) with a bronchospastic component who are not receiving oral or inhaled medication, and only if the potential benefit outweighs the potential risk.

In patients with a tendency to bronchospasm, respiratory distress can occur as a result of a possible increase in airway resistance. Patients should be closely monitored during initiation and up-titration of carvedilol and the dose of carvedilol should be reduced if any evidence of bronchospasm is observed during treatment.

Diabetes

Care should be taken in the administration of carvedilol to patients with diabetes mellitus, as the early signs and symptoms of acute hypoglycaemia may be masked or attenuated. In chronic heart failure patients with diabetes, the use of carvedilol may be associated with worsening control of blood glucose.

Peripheral vascular disease

Carvedilol should be used with caution in patients with peripheral vascular disease as β -blockers can precipitate or aggravate symptoms of arterial insufficiency.

Raynaud's phenomenon

Carvedilol should be used with caution in patients suffering from peripheral circulatory disorders (eg Raynaud's phenomenon) as there may be exacerbation of symptoms.

Thyreotoxicosis

Carvedilol may obscure the symptoms of thyrotoxicosis.

Anesthesia and major surgery

Caution should be exercised in patients undergoing general surgery, because of the synergistic negative inotropic effects of carvedilol and anaesthetic drugs.

Bradycardia

Carvedilol may induce bradycardia. If the patient's pulse rate decreases to less than 55 beats per minute, the carvedilol dose should be reduced.

Hypersensitivity

Care should be taken in administering carvedilol to patients with a history of serious hypersensitivity reactions, and in those undergoing desensitisation therapy, as beta-blockers may increase both the sensitivity towards allergens and the seriousness of anaphylactic reactions.

Psoriasis

Patients with a history of psoriasis associated with beta-blocker therapy should take carvedilol only after consideration of the risk-benefit ratio.

Concomitant use of calcium channel blockers

Careful monitoring of ECG and blood pressure is necessary in patients receiving concomitant therapy with calcium channel blockers of the verapamil or diltiazem type or other antiarrhythmic drugs (specifically amiodarone).

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 pharmacological activities, there is no experience with its use in this condition. Caution should therefore 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 is no clinical experience with carvedilol in these patients although the alpha-blocking activity of carvedilol may prevent such symptoms. Caution should, however, be taken in the administration of carvedilol to patients suspected of having Prinzmetal's variant angina.

Contact lenses

Wearers of contact lenses should bear in mind the possibility of reduced lacrimation.

Debrisoquine metabolism

Patients who are known as poor metabolisers of debrisoquine, should be closely monitored during initiation of therapy (see section 5.2).

Withdrawal syndrome

Carvedilol treatment should not be discontinued abruptly, particularly in patients suffering from ischaemic heart disease. The withdrawal of carvedilol should be gradual (over a period of two weeks).

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction*Antiarrhythmics*

Isolated cases of conduction disturbance, rarely with haemodynamic disruption, have been observed in patients taking carvedilol and (oral) diltiazem, verapamil and/or amiodarone. As with other beta-blockers, careful monitoring of the ECG and blood pressure should be undertaken when co-administering calcium channel-blockers of the verapamil and diltiazem type as the risk of AV conduction disorders or risk of cardiac failure are increased (synergistic effect). Close monitoring should be done when co-administering carvedilol, and either a class I antiarrhythmics or amiodarone (oral). Bradycardia, cardiac arrest, and ventricular fibrillation have been reported shortly after initiation of beta-blocker treatment in patients receiving amiodarone. There is a risk of cardiac failure in case of class Ia or Ic antiarrhythmics concomitant intravenous therapy.

Concomitant treatment with reserpine, guanethidine, methyldopa, guanfacine and monoamine-oxidase inhibitors (exception MAO-B-inhibitors) can lead to additional decrease in heart rate. Monitoring of vital signs is recommended.

Dihydropyridines

The administration of dihydropyridines and carvedilol should be done under close supervision as heart failure and severe hypotension have been reported.

Nitrates

Increased hypotensive effects.

Cardiac glycosides

An increase of steady state digoxin levels by approximately 16% and of digitoxin by approximately 13% has been seen in hypertensive patients in connection with the concomitant use of carvedilol and digoxin. Monitoring of plasma digoxin concentrations is recommended when initiating, discontinuing or adjusting treatment with carvedilol.

Other antihypertensive drugs

Carvedilol may potentiate the effects of other concomitantly administered antihypertensives (e.g. α_1 -receptor antagonists) and drugs with antihypertensive side effects such as barbiturates, phenothiazines, tricyclic antidepressants, vasodilating agents and alcohol.

Ciclosporin

The plasma level of ciclosporin is increased when carvedilol is co-administered. It is recommended that ciclosporin concentrations are carefully monitored.

Antidiabetics including insulin

The blood sugar lowering effect of insulin and oral diabetic drugs may be intensified. Symptoms of hypoglycaemia may be masked. In diabetic patients regular monitoring of blood glucose levels is necessary.

Clonidine

When combination treatment with carvedilol and clonidine is discontinued, carvedilol should be withdrawn several days before gradually decreasing the dose of clonidine.

Inhalational anaesthetics

Attention should be paid to the potential negative inotropic and hypotensive interactions of carvedilol and anaesthetics in association with anaesthesia.

NSAIDs, oestrogens and corticosteroids

The antihypertensive effect of carvedilol is decreased due to water and sodium retention.

Medicines inducing or inhibiting cytochrome P450 enzymes

Patients receiving medicines that induce (e.g. rifampicin and barbiturates) or inhibit (e.g. cimetidine, ketoconazole, fluoxetine, haloperidol, verapamil, erythromycin) cytochrome P450 enzymes have to be monitored closely during concomitant treatment with carvedilol as serum carvedilol concentrations may be reduced by enzyme inducers and increased by the enzyme inhibitors.

Sympathomimetics with alpha-mimetic and beta-mimetic effects

Risk of hypertension and excessive bradycardia.

Ergotamine

Vasoconstriction increased.

Neuromuscular blocking agents

Increased neuromuscular block.

4.6 Pregnancy and lactation

There is no adequate clinical experience with carvedilol in pregnant women.

Animal studies are insufficient with respect to effects on pregnancy, embryonal/foetal development, parturition and postnatal development (see section 5.3). The potential risk for humans is unknown.

Carvedilol should not be used during pregnancy unless the potential benefit outweighs the potential risk.

Beta-blockers reduce placental perfusion which may result in intrauterine foetal death and immature and premature deliveries. In addition, adverse reactions (especially hypoglycaemia, bradycardia) may occur in the foetus and neonate). There may be an increased risk of cardiac and pulmonary complications in the neonate in the postnatal period. Animal studies have not shown substantive evidence of teratogenicity with carvedilol (see also section 5.3).

Animal studies demonstrated that carvedilol or its metabolites are excreted in breast milk. It is not known whether carvedilol is excreted in human milk. Breast feeding is therefore not recommended during administration of carvedilol.

4.7 Effects on ability to drive and use machines

No studies have been performed on the effects of carvedilol on patients' fitness to drive or to operate machinery.

Because of individually variable reactions (e.g. dizziness, tiredness), the ability to drive, operate machinery, or work without firm support may be impaired. This applies particularly at the start of treatment, after dose increases, on changing products, and in combination with alcohol.

4.8 Undesirable effects

(a) Summary of the safety profile

The frequency of adverse reactions is not dose-dependent, with the exception of dizziness, abnormal vision and bradycardia.

(b) Tabulated list of adverse reactions

The risk of most adverse reactions associated with carvedilol is similar across all indications. Exceptions are described in subsection (c).

Frequency categories are as follows:

Very common $\geq 1/10$

Common $\geq 1/100$ and $< 1/10$

Uncommon $\geq 1/1,000$ and $< 1/100$

Rare $\geq 1/10,000$ 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)

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

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

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

(c) Description of selected adverse reactions

Dizziness, syncope, headache and asthenia are usually mild and are more likely to occur at the beginning of treatment.

In patients with congestive heart failure, worsening cardiac failure and fluid retention may occur during up-titration of carvedilol dose (see section 4.4).

Cardiac failure is a commonly reported adverse event in both placebo and carvedilol-treated patients (14.5% and 15.4% respectively, in patients with left ventricular dysfunction following acute myocardial infarction).

Reversible deterioration of renal function has been observed with carvedilol therapy in chronic heart failure patients with low blood pressure, ischaemic heart disease and diffuse vascular disease and/or underlying renal insufficiency (see section 4.4).

As a class, beta-adrenergic receptor blockers may cause latent diabetes to become manifest, manifest diabetes to be aggravated, and blood glucose counter-regulation to be inhibited.

Carvedilol may cause urinary incontinence in women which resolves upon discontinuation of the medication.

4.9 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 generalised 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 norfenefrine 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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 α_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 α -adrenergic blocking activity in animal models. Non-selective β_1 - and β_2 -adrenoceptor blockade is attributed mainly to the S(-) enantiomer.

The antioxidant properties of carvedilol and its metabolites have been demonstrated in *in vitro* and *in vivo* animal studies and *in vitro* in a number of human cell types.

In hypertensive patients, a reduction in blood pressure is not associated with a concomitant increase in peripheral resistance, as observed with pure beta-blocking agents. Heart rate is slightly decreased. Stroke volume remains unchanged. Renal blood flow and renal function remain normal, as does peripheral blood flow, therefore, cold extremities, often observed with beta-blockers, are rarely seen. In hypertensive patients carvedilol increases the plasma norepinephrine concentration.

In prolonged treatment of patients with angina, carvedilol has been seen to have an anti-ischaemic effect and to alleviate pain. Haemodynamic studies demonstrated that carvedilol reduces ventricular pre- and after-load. In patients with left ventricular dysfunction or congestive heart failure, carvedilol has a favourable effect on haemodynamics and left ventricular ejection fraction and dimensions.

Carvedilol has no negative effect on the serum lipid profile or electrolytes. The ratio of HDL (high-density lipoproteins) and LDL (low-density lipoproteins) remains normal.

5.2 Pharmacokinetic properties

General description. The absolute bioavailability of orally administered carvedilol is approximately 25 %. Plasma levels peak at approximately 1 hour after dosing. There is linear correlation between the dose and plasma concentrations. In patients with slow hydroxylation of debrisoquine, plasma carvedilol concentrations increased up to 2 – 3 -fold compared to rapid debrisoquine metabolisers. Food does not affect bioavailability although the time to reach maximum plasma concentration is delayed. Carvedilol is a highly lipophilic compound. Approximately 98 % to 99 % of carvedilol is bound to plasma proteins. Its volume of distribution is approximately 2 l/kg. The first pass effect after oral administration is approximately 60 – 75 %.

The average elimination half-life of carvedilol ranges from 6 to 10 hours. Plasma clearance is approximately 590 ml/min. Elimination is mainly biliary. The primary route of excretion of carvedilol is via the faeces. A minor portion is eliminated via the kidneys as metabolites.

Carvedilol is found to be extensively metabolised into various metabolites, which are mainly eliminated in bile. Carvedilol is metabolised in the liver mainly through aromatic ring oxidation and glucuronidation. Demethylation and hydroxylation at the phenol ring yield three active metabolites with beta-blocking activity. Compared to carvedilol, these three active metabolites have a weak vasodilatory effect. On the basis of preclinical studies, the 4'-hydroxyphenolmetabolite has a beta-blocking activity 13 times more potent than that of carvedilol. However, the metabolite concentrations in humans are approximately 10 times lower than those of carvedilol. Two of the hydroxycarbazole metabolites of carvedilol are highly potent antioxidants, with a 30 - 80-fold potency compared to carvedilol.

Properties in the patient. The pharmacokinetics of carvedilol are affected by age; plasma levels of carvedilol are approximately 50 % higher in the elderly compared to young subjects. In a study in patients with liver cirrhosis, the bioavailability of carvedilol was four times greater and the peak plasma level five times higher and the volume of distribution three times higher than in healthy subjects. In some of the hypertensive patients with moderate (creatinine clearance 20 - 30 ml/min) or severe (creatinine clearance < 20 ml/min) renal insufficiency, an

increase in plasma carvedilol concentrations of approximately 40 – 55 % was seen compared to patients with normal renal function. However, there was a large variation in the results.

5.3 Preclinical safety data

Carvedilol was not teratogenic in rats and rabbits. Embryo/fetotoxic effects occurred in rabbits at dose levels not toxic to the does.

Standard in vitro and in vivo tests did not show any relevant mutagenic or carcinogenic potential of carvedilol.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Cellulose microcrystalline

Lactose monohydrate

Crospovidone CL

Povidone K30

Silica, colloidal anhydrous

Magnesium stearate

Tablet coat:

Hypromellose

Titanium dioxide (E 171)

Triethyl citrate

Macrogol 8000

Polydextrose

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

HDPE bottles: 2 years.

Blisters: 3 years

6.4 Special precautions for storage

Store in the original package, in order to protect from light.

Blisters: Do not store above 30°C.

HDPE-bottles: Do not store above 25°C.

6.5 Nature and content of container

Plastic bottle (HDPE) with polypropylene closure material or blister (PVC/Aluminium)

Pack sizes: 10, 14, 28, 30, 50, 56, 60, 98 and 100 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

To be completed nationally

8 MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

2007-06-04

10 DATE OF REVISION OF THE TEXT

2011-05-04