SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF HUMAN MEDICINAL PRODUCT
BLOXER 5 mg tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet:
Active substance:
Contains 5.45 mg nebivolol hydrochloride equivalent to 5 mg nebivolol

Excipients:
Lactose monohydrate (produced from cow's milk) 85,96 mg
See section 6.1 for excipients.

3. PHARMACEUTICAL FORM
Tablet.
White, round, biconvex tablets, notched on one side.

4. CLINICAL PARTICULARS
4.1.Therapeutic indications
Hypertension
Treatment of essential hypertension.

Chronic Heart Failure (CHF)
Treatment of stable, mild to moderate chronic heart failure in addition to standard therapies in patients aged 70 years and older.

4.2. Posology and method of administration
Posology
Hypertension
Adults
The dose is one tablet (5 mg) per day. It should preferably always be taken at the same time of day. The blood pressure lowering effect starts to appear after 1-2 weeks of treatment.
Sometimes, the optimal effect is reached only after 4 weeks. In patients requiring further reduction in blood pressure, the dose may be increased up to 40 mg at 2-week intervals.

Combination with other antihypertensive medicines
Beta-blockers can be used alone or in combination with other antihypertensive drugs. To date, an additive antihypertensive effect has only been observed when BLOXER is combined with hydrochlorothiazide 12.5-25 mg.

Chronic heart failure (CHF)
Treatment of stable chronic heart failure should be initiated with a graded titration of the dose and continued until the optimal individual maintenance dose is reached.
Patients must have stable chronic heart failure without acute failure in the last 6 weeks. It is recommended that the treating physician should be experienced in the treatment of chronic heart failure.

In patients receiving cardiovascular drug therapy such as diuretics and/or digoxin and/or Angiotensin Converting Enzyme inhibitors, these drug doses should be stabilized for two weeks before starting treatment with BLOXER.

Initial titration should be done at 1-2 week intervals according to the following steps, depending on patient tolerance:
1.25 mg nebivolol once daily is first increased to 2.5 mg once daily, then to 5 mg once daily and then to 10 mg once daily.

The maximum recommended dose is 10 mg nebivolol once daily.

To ensure that the patient's clinical condition remains stable (especially with regard to blood pressure, heart rate, conduction disturbances and signs of worsening heart failure), initiation of treatment and subsequent dose increases should be made over a period of at least 2 hours under the supervision of an experienced physician.

The occurrence of adverse events may prevent all patients from being treated with the maximum recommended dose. If necessary, the dose reached can also be gradually reduced and re-administered as appropriate.

In case of worsening of heart failure or intolerance during the titration phase, it is recommended to reduce the dose of nebivolol first or, if necessary, to discontinue treatment immediately (severe hypotension, worsening of heart failure with acute pulmonary edema, cardiogenic shock, symptomatic bradycardia or AV block).

Treatment of stable chronic heart failure with nebivolol is usually a long-term therapy.

It is recommended not to stop BLOXER treatment abruptly as this may cause a temporary aggravation of heart failure. If it is necessary to discontinue treatment, the dose should be reduced gradually by halving it weekly.

Frequency and duration of administration:
The duration of treatment should be decided by the physician.

Method of administration:
BLOXER can be taken orally at any time of the day on an empty or full stomach.
The tablets should be swallowed with sufficient amount of liquid without chewing.
The tablets should preferably be taken at the same time every day.

Additional information on special populations:
Renal failure:
The recommended starting dose in hypertensive patients with renal failure is 2.5 mg daily. If necessary, the daily dose can be increased to 5 mg.

In patients with mild to moderate renal impairment with chronic heart failure, no dose adjustment is required when the maximum tolerated dose is adjusted. There is no experience with the use of this drug in patients with severe renal impairment (serum creatinine ≥ 250 micromol/L). Therefore, the use of nebivolol is not recommended in these patients.

BLOXER should be administered with caution in dialysis patients as no studies have been conducted in these patients.

Liver failure:
Data in patients with liver failure or impaired liver function are limited. Therefore, BLOXER is contraindicated in these patients.

Pediatric population:
In children under 18 years of age and adolescents, the safety and efficacy of nebivolol have not been established. There are no available data. Therefore, its use in children and adolescents is not recommended.

Geriatric population:
For hypertensive patients over 65 years of age, the recommended starting dose is 2.5 mg daily. If necessary, the daily dose can be increased to 5 mg. However, since there is limited data on patients over 75 years of age, it should be used with caution in these patients and patients should be closely monitored.
In patients with chronic heart failure, no dose adjustment is required after adjustment for the maximum tolerated dose.

4.3. Contraindications
BLOXER is contraindicated;
- In patients with hypersensitivity to its active substance or any of its excipients
- In liver failure or impaired liver function.

- In acute heart failure, cardiogenic shock or decompensated heart failure requiring IV inotropic therapy.

In addition, as with other beta blockers, BLOXER is contraindicated in the following conditions:
- Sick sinus syndrome, including sino-atrial block
- Second and third degree heart block (without pacemaker)
- Those with a history of bronchospasm and bronchial asthma
- Untreated pheochromocytoma
- Metabolic acidosis
- Bradycardia (heart rate < 60 beats/minute before starting treatment).
- Hypotension (systolic blood pressure < 90 mmHg)
- Severe peripheral circulatory disorders.

4.4. Special warnings and precautions for use

See also section 4.8.
The following warnings and precautions apply generally to beta-adrenergic antagonists.

Anesthesia
Maintenance of beta blockade reduces the risk of arrhythmias during induction and intubation. If beta blockade is to be interrupted during preparation for surgery, beta-adrenergic antagonists should be discontinued at least 24 hours before surgery.

Caution should be exercised when using certain anesthetics that cause myocardial depression. The patient should be protected against vagal reactions due to intravenous atropine administration.

Cardiovascular
In general, beta-adrenergic antagonists should not be used in patients with untreated congestive heart failure (CHF) until their condition has stabilized.

In patients with ischemic heart disease, beta-adrenergic antagonist treatment should be discontinued slowly (e.g. over 1-2 weeks). If necessary, other treatment should be started concurrently to prevent exacerbations of angina pectoris.

Beta-adrenergic antagonists may cause bradycardia: Dosage should be reduced if the pulse rate falls below 50-55 beats/minute at rest and/or if the patient experiences symptoms suggestive of bradycardia.

Beta-antagonists should be used with caution in the following conditions:

- Patients with peripheral circulatory disorders (Raynaud's disease or syndrome, intermittent claudication) as they may exacerbate these disorders;
- In patients with first-degree heart block, because of the negative effect of beta-blockers on conduction time;
- In patients with Prinzmetal angina due to unopposed alpha receptor-mediated coronary artery vasoconstriction: Beta-adrenergic antagonists may increase the number and prolong the duration of angina attacks.

Nebivolol is generally not recommended in combination with calcium channel antagonists such as verapamil and diltiazem, class I anti-arrhythmic drugs and centrally acting antihypertensive drugs; please see section 4.5 for details.

Metabolic/Endocrinologic
BLOXER does not affect glucose levels in diabetic patients. However, caution should be exercised in diabetic patients as nebivolol may mask some symptoms of hypoglycemia (tachycardia, palpitation).

Beta-adrenergic blockers may mask tachycardic symptoms in hyperthyroidism. Sudden discontinuation of the drug may exacerbate symptoms.

Respiratory
In patients with chronic obstructive pulmonary disease, beta-adrenergic antagonists should be used with caution as airway constriction may be exacerbated.

Other
In patients with a history of psoriasis, beta-adrenergic antagonists should be used after careful evaluation of the patient's condition.

Beta-adrenergic antagonists may increase sensitization to allergens and the severity of anaphylactic reactions.

Initiation of treatment of chronic heart failure with nebivolol requires regular observation of patients. Please see section 4.2 for posology and method of administration. Treatment should not be abruptly discontinued unless explicitly indicated. See section 4.2 for additional information.

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

4.5. Interactions with other medicinal products and other forms of interaction

Pharmacodynamic interactions:

The following interactions are commonly observed with beta-adrenergic antagonists:

Combinations not recommended for use together:

Class l anti-arrhythmics (quinidine, hydroquinidine, sibenzoline, flecainide, disopyramide, lidocaine, mexiletine, propafenone): The effect on atrioventricular conduction time may be exacerbated and the negative inotropic effect may be increased (see section 4.4).

Verapamil and diltiazem-type calcium channel antagonists: Adverse effect on contractility and atrioventricular conduction. Intravenous administration of verapamil to patients receiving beta-blocker therapy may cause severe hypotension and atrioventricular block (see section 4.4). Caution should be exercised in patients receiving verapamil and diltiazem-type calcium channel blockers concomitantly with beta-blockers; ECG and blood pressure monitoring should be performed.

Centrally acting antihypertensives (clonidine, guanfacine, moxonidine, methyldopa, rilmenidine): Concomitant use of centrally acting antihypertensive drugs may exacerbate heart failure through a decrease in central sympathetic tone, such as decreased heart rate and cardiac output, vasodilation (see section 4.4). Abrupt discontinuation of the drug may increase the risk of "rebound hypertension", especially if this occurs before discontinuation of beta-blocker therapy.

Combinations that require caution when administered together:

Class III anti-arrhythmic drugs (Amiodarone): The effect on atrioventricular conduction time may be exacerbated.

Anesthetics - volatile halogens: Concomitant use of beta-adrenergic antagonists with anesthetics may reduce reflex tachycardia and increase the risk of hypotension (see section 4.4). As a general rule, abrupt discontinuation of beta-blocker therapy should be avoided. The anesthesiologist should be informed if the patient is on BLOXER.

Insulin and oral antidiabetic drugs: Although nebivolol does not affect glucose levels, concomitant use may mask certain symptoms of hypoglycemia (palpitations, tachycardia).

Baclofen (antispastic agent), amifostine (antineoplastic adjuvant medicine): Concomitant use with antihypertensives may increase the fall in blood pressure, so the dose of antihypertensive medication should be adjusted accordingly.

Combinations that can be used together:
Digitalis glycosides: Concomitant use may increase atrioventricular conduction time. Clinical studies with nebivolol have not revealed any clinical evidence of interaction. Nebivolol does not affect the kinetics of digoxin.

Dihydropyridine-type calcium antagonists (amlodipine, felodipine, lasidipine, nifedipine, nicardipine, nimodipine, nitrendipine): Concomitant use may increase the risk of hypotension and should be considered in patients with heart failure as it may increase the risk of further deterioration of ventricular pump function.

Antipsychotics, antidepressants (tricyclics, barbiturates and phenothiazines): Concomitant use may increase the hypotensive effect of beta-blockers (additive effect).

Non-steroidal anti-inflammatory drugs (NSAIDs): It has no effect on the blood pressure-lowering effect of nebivolol.

Sympathomimetic agents: Concomitant use may abolish the effect of beta-adrenergic antagonists. Beta-adrenergic agents may lead to unopposed alpha-adrenergic activity of sympathomimetic agents with both alpha- and beta-adrenergic effects (risk of hypertension, severe bradycardia and heart block).

Pharmacokinetic interactions:
Since the CYP2D6 isoenzyme is involved in the metabolism of nebivolol, concomitant use with substances that inhibit this enzyme, in particular paroxetine, fluoxetine, thioridazine and quinidine, may lead to elevated plasma levels of nebivolol accompanied by excessive bradycardia and increased risk of adverse events.

Co-administration of nebivolol with cimetidine increased blood levels without altering the clinical effects of nebivolol. Co-administration with ranitidine did not affect nebivolol pharmacokinetics. BLOXER may be co-prescribed provided that BLOXER is taken with meals and antacids are taken between meals.

The combination of nebivolol with nicardipine slightly increased plasma levels of both drugs without altering their clinical effects. Co-administration of alcohol, furosemide or hydrochlorothiazide did not affect the pharmacokinetics of nebivolol. Nebivolol does not affect the pharmacokinetics and pharmacodynamics of warfarin.

Additional information on special populations
There are no interaction studies for special populations.

Pediatric population:

There are no interaction studies in the pediatric population.

4.6. Pregnancy and Lactation
General recommendation:
Pregnancy category: C

Women of childbearing potential/Birth control
It is not recommended for use in women planning to become pregnant. If pregnancy occurs during treatment, BLOXER should be discontinued.

Pregnancy
There are insufficient data on the use of BLOXER in pregnant women. Animal studies have shown reproductive toxicity (see section 5.3). The potential risk to humans is unknown.

BLOXER has harmful pharmacological effects on pregnancy and/or fetus/newborn.

In general, beta-adrenoreceptor blockers reduce placental perfusion, which is associated with growth retardation, intrauterine death, miscarriage or preterm delivery.

Adverse effects (such as hypoglycemia and bradycardia) may occur in the fetus and newborn. If treatment with beta-adrenoreceptor blockers is necessary, $beta_1$-selective adrenoreceptor blockers should be preferred.

BLOXER should not be used during pregnancy unless necessary. If it is considered necessary, uteroplacental blood flow and fetal growth should be monitored. In case of harmful effects on pregnancy or fetus, alternative treatment should be considered.
Newborns should be closely monitored. Symptoms of hypoglycemia and bradycardia are usually expected within the first 3 days.

Lactation
Animal studies have shown that nebivolol passes into breast milk. It is not known whether this medicine is excreted in human milk. Most beta-blockers, especially lipophilic compounds such as nebivolol and its active metabolites, pass into breast milk at varying rates. This risk for newborns/babies cannot be excluded. Therefore, mothers taking nebivolol should not breastfeed.

Reproductive ability/ Fertility
No effect of nebivolol on mouse fertility has been observed in rats and mice, except at doses several times higher than the maximum recommended dose for humans, at which adverse effects on male and female reproductive organs were observed. However, the effect of nebivolol on human fertility is unknown.

A randomized, double-blind, placebo and active-controlled, parallel group study in healthy male volunteers was conducted to determine the effect of nebivolol on adrenal function, luteinizing hormone and testosterone levels. This study showed that a daily dose of 10 mg nebivolol for 6 weeks had no significant effect on ACTH stimulated male serum cortisol AUX 0-120 minutes, serum LH or serum total testosterone.

Spermatogenesis effects were observed in male rats and mice at dosages of 10 and 5 times the MRHD, respectively. In rats, spermatogenesis effects were not reversible and worsened during the four-week recovery period. However, the effects of nebivolol on sperm in mice are partially reversible.

4.7. Effects on ability to drive and use machines

There are no studies on the effects of nebivolol on the ability to drive and use machines. Pharmacodynamic studies have shown that Nebivolol does not affect psychomotor function. However, it should be noted that dizziness and fatigue may sometimes occur when driving or operating machinery.

4.8. Undesirable effects

Undesirable effects are listed by System Organ Class and grouped under headings using the following frequency definitions: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); unknown (cannot be estimated based on available data).

Side effects for hypertension and chronic heart failure are listed separately due to the differences in the diseases.

Hypertension

Reported side effects, most of which were mild or moderate in severity, are given below by organ system class and frequency.

Diseases of the immune system:
Unknown: Angioneurotic edema, hypersensitivity

Psychiatric disorders:
Uncommon: Nightmares, depression

Diseases of the nervous system:
Common: Headache, dizziness, paresthesia
Very rare: Syncope

Eye diseases:
Uncommon: Visual disturbances

Cardiac diseases:
Uncommon: Bradycardia, heart failure, slowing of AV conduction/AV block

Vascular diseases:
Uncommon: Hypotension, intermittent claudication (increased)

Respiratory, chest and mediastinal disorders:
Common: Dyspnea
Uncommon: Bronchospasm

Gastrointestinal diseases:
Common: Constipation, nausea, diarrhea
Uncommon: Dyspepsia, flatulence, vomiting

Skin and subcutaneous tissue diseases:
Uncommon: Itching, erythematous rash
Very rare: Psoriasis flare-up
Unknown: Urticaria

Reproductive and breast diseases:
Uncommon: Erectile dysfunction

General disorders and diseases related to the administration site:
Common: Fatigue, edema

The following undesirable effects have also been reported for some beta-adrenergic antagonists: Hallucinations, psychoses, confusion, cold/cyanotic extremities, Raynaud's phenomenon, dry eye and practolol-type oculo-mucocutaneous toxicity.

Chronic heart failure
Data on side effects in patients with chronic heart failure were obtained from a placebo-controlled clinical trial involving 1067 patients taking nebivolol and 1061 patients taking placebo. In this study, at least possible causally related side effects were reported in 449 patients on nebivolol (42.1%) compared with 334 patients on placebo (31.5%). The most commonly reported side effects in patients receiving nebivolol were bradycardia and dizziness, which occurred in approximately 11% of patients. The incidence of these side effects in patients on placebo was 2% and 7%, respectively.

For adverse reactions considered to be of particular significance in the treatment of chronic heart failure (at least possibly related to the drug), the following incidences were reported:

- Heart failure worsened in 5.8% of nebivolol patients compared to 5.2% of placebo patients.
- Postural hypotension was reported in 2.1% of nebivolol patients compared to 1% of placebo patients.
- Intolerance to the drug developed in 1.6% of nebivolol patients compared to 0.8% of placebo patients.
- First-degree atrioventricular block developed in 1.4% of nebivolol patients compared to 0.9% of placebo patients.
- Lower limb edema was reported in 1% of nebivolol patients compared to 0.2% of placebo patients.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization 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 the national reporting system.

4.9. Overdose and treatment

There are no data on overdose of BLOXER.

Symptoms

Symptoms of overdose with beta-blockers include: Bradycardia, hypotension, bronchospasm and acute heart failure

Treatment

In case of overdose or hypersensitivity, the patient should be closely monitored and treated in the intensive care unit. Blood glucose levels should be checked. Absorption of any drug residue that may still be present in the gastrointestinal tract should be prevented by gastric lavage, activated charcoal and a laxative should be administered. Artificial respiration may be necessary. Bradycardia or excessive vagal reactions should be treated with atropine or methyltropine. Hypotension and shock should be treated with plasma/plasma substitutes and, if necessary, catecholamines. The beta-blocking effect can be overcome by starting with isoprenaline hydrochloride at a dose of approximately 5 micrograms/minute or dobutamine at 2.5 micrograms/minute until the desired effect is achieved by slow intravenous administration. In refractory cases, isoprenaline can be combined with dopamine. If this fails to produce the desired effect, intravenous administration of 50-100 micrograms/kg glucagon may be considered. If necessary, the injection should be repeated within one hour and followed by i.v. glucagon infusion at a dose of 70 micrograms/kg/hour if necessary. In extreme cases of treatment-resistant bradycardia, a pacemaker may be implanted.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Antihypertensives, Selective beta-blockers
ATC code: C07AB12

Nebivolol is a selective beta-blocker.

Nebivolol is a racemate of two enantiomers, SRRR-nebivolol (or *d*-nebivolol) and RSSS-nebivolol (or /*l*-nebivolol). Nebivolol combines two pharmacological activities:

- It is a competitive and selective beta-receptor antagonist: This effect is due to the SRRR-enantiomer (*d*-enantiomer).
- It has a mild vasodilator effect due to interaction with the L-arginine/nitric oxide pathway.

Single and repeated doses of nebivolol lower heart rate and blood pressure at rest and during exercise, both in normotensive and hypertensive patients. The antihypertensive effect is maintained during chronic treatment.

At therapeutic doses, nebivolol has no alpha-adrenergic antagonistic effect.

During acute and chronic treatment of hypertensive patients with nebivolol, systemic vascular resistance is reduced. Despite the reduction in heart rate, the decrease in cardiac output at rest and during exercise may be limited due to the increase in stroke volume. The clinical relevance of these hemodynamic differences compared with other $beta_1$ receptor antagonists has not been fully established.

In hypertensive patients, nebivolol increases the NO-mediated vascular response to Acetylcholine (ACh), which is reduced in patients with endothelial dysfunction.

With or without impaired left ventricular ejection fraction (mean LVEF: 36 ± 12.3% Distribution was as follows: 56% of patients with LVEF below 35%, 25% of patients with LVEF between 35% and 45%, and 19% of patients with LVEF above 45%), in a placebo-controlled mortality-morbidity study in 2128 stable chronic heart failure patients aged ≥70 years (mean age 75.2 years), after a median observation period of 20 months, nebivolol given at the start of standard therapy was associated with a relative risk reduction of 14% (absolute reduction: 4.2%), with a relative risk reduction of 14% (absolute reduction: 4.2%), significantly prolonged the time to death or hospitalizations due to cardiovascular causes (the primary endpoint for efficacy). This reduction in risk occurred after the 6th month of treatment and was sustained for the entire duration of treatment (median duration: 18 months). The effect of nebivolol was independent of the age, sex or left ventricular ejection fraction of the study population. The benefit of nebivolol on all-cause mortality did not reach statistical significance compared to placebo (absolute reduction: 2.3%). In patients treated with

nebivolol, a reduction in sudden death was observed (4.1% and 6.6%, relative reduction of 38%).

In vitro and *in vivo* studies in animals have shown that nebivolol has no intrinsic sympathomimetic activity.
In vitro and *in vivo* studies in animals have shown that nebivolol at pharmacological doses has no membrane stabilizing effect.

Studies in healthy volunteers have shown that nebivolol has no significant effect on reducing maximum exercise capacity or on endurance.

Available preclinical and clinical evidence in hypertensive patients has shown that nebivolol does not have a detrimental effect on erectile function.

5.2. Pharmacokinetic properties
General characteristics:
Absorption:
Both enantiomers of nebivolol are rapidly absorbed after oral administration. Absorption of nebivolol is not affected by food; nebivolol can be taken with meals or on an empty stomach.

The oral bioavailability of nebivolol is approximately 12% in subjects with fast metabolism and almost complete in those with slow metabolism. At steady-state and at the same dose level, the peak plasma concentration of unchanged nebivolol is approximately 23 times higher in subjects with slow metabolism than in subjects with fast metabolism. When unchanged drug and active metabolites are taken into account, the difference in peak plasma concentrations is 1.3 to 1.4-fold. Due to the variation in metabolic rates, the dose of BLOXER should always be adjusted to the individual patient's needs, so those with slow metabolism may require lower doses.

Plasma concentrations are dose-dependent between 1-30 mg. The pharmacokinetics of nebivolol are not affected by age.

Distribution:
In plasma, both nebivolol enanatiomers are mainly bound to albumin. Binding to plasma proteins is 98.1% for SRRR-nebivolol and 97.9% for RSSS-nebivolol.

Biotransformation:
Nebivolol is extensively metabolized, partly to active hydroxy-metabolites. Nebivolol is metabolized by alicyclic and aromatic hydroxylation, N-dealkylation and glucuronidation. It is converted to hydroxy metabolites formed by N-dealkylation and glucuronides by

glucoronidation. The metabolism of nebivolol by aromatic hydroxylation shows CYP2D6-dependent genetic oxidative polymorphism.

Elimination:
In subjects with rapid metabolism, the elimination half-life of nebivolol enantiomers is approximately 10 hours. In subjects with slow metabolism, their half-lives are 3-5 times longer. In subjects with fast metabolism, plasma levels of RSSS-enantiomers are slightly higher than SRRR-enantiomers. This difference is larger in subjects with slow metabolism. The elimination half-life of the hydroxymetabolites of both enantiomers averages 24 hours in subjects with fast metabolism and is twice as long in subjects with slow metabolism.

In most individuals (fast metabolizers) steady-state plasma levels are reached within 24 hours with nebivolol and within a few days with its hydroxymetabolites.

One week after administration, 38% of the dose is excreted in the urine and 48% in the feces. Excretion of unchanged nebivolol in urine is less than 0.5% of the dose.

Linearity/non-linearity:
Nebivolol shows linear pharmacokinetics.

5.3. Preclinical safety data
Preclinical data do not reveal a specific hazard to humans based on conventional studies of genotoxicity, reproductive and developmental toxicity and carcinogenic potential.

Adverse effects on reproductive function have only been recorded at high doses several times the maximum recommended human dose (see section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Lactose Monohydrate (produced from cow's milk)
Crospovidone Type A
Poloxamer 188
Povidone K 30
Microcrystalline Cellulose
Magnesium Stearate

6.2 Incompatibilities
Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage
Store at room temperature below 25ºC.

6.5 Nature and contents of packaging
Blisters with transparent PVC/PE/PVDC on one side and printed aluminum foil on the other side.
Each carton box contains 28 and 84 tablets.

6.6- Special precautions for disposal and other handling
Any unused material should be disposed according to local disposal regulations.

7. MARKETING AUTHORIZATION HOLDER
DEVA HOLDİNG A.Ş.
Halkalı Merkez Mah.Basın Ekspres Cad.
No: 1 34303
Küçükçekmece / İSTANBUL/TÜRKİYE
Phone: +90 212 692 92 92
Fax: +90 212 697 00 24
E-mail: deva@devaholding.com.tr

8. MARKETING AUTHORIZATION NUMBER(S)
235 / 16

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION
Date of first authorization: 27.09.2011
Date of last renewal:

10. DATE OF REVISION OF THE TEXT