SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

NEBILET 5 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Nebilet tablet contains 5 mg of nebivolol (as nebivolol hydrochloride): 2.5 mg of SRRR-nebivolol (or d-nebivolol) and 2.5 mg of RSSS-nebivolol (or l-nebivolol).

Excipient with known effect: each tablet contains 141.75 mg of lactose monohydrate (see section 4.4 and 6.1).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.
White, round, cross-scored tablet.
The tablet can be divided in equal quarters.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Hypertension
Treatment of essential hypertension.

Chronic heart failure (CHF)
Treatment of stable mild and moderate chronic heart failure in addition to standard therapies in elderly patients ≥ 70 years.

4.2. Posology and method of administration

Posology

Hypertension
Adults
The dose is one tablet (5 mg) daily, preferably at the same time of the day.
The blood pressure lowering effect becomes evident after 1-2 weeks of treatment. Occasionally, the optimal effect is reached only after 4 weeks.

Combination with other antihypertensive agents
Beta-blockers can be used alone or concomitantly with other antihypertensive agents. To date, an additional antihypertensive effect has been observed only when Nebilet 5 mg is combined with hydrochlorothiazide 12.5-25 mg.

Patients with renal insufficiency
In patients with renal insufficiency, the recommended starting dose is 2.5 mg daily. If needed, the daily dose may be increased to 5 mg.

Patients with hepatic insufficiency
Data in patients with hepatic insufficiency or impaired liver function are limited. Therefore the use of Nebilet in these patients is contra-indicated.

Older people
In patients over 65 years, the recommended starting dose is 2.5 mg daily. If needed, the daily dose may be increased to 5 mg. However, in view of the limited experience in patients above 75 years, caution must be exercised and these patients monitored closely.

Paediatric population
The efficacy and safety of Nebilet in children and adolescents aged below 18 years has not been established. No data are available. Therefore, use in children and adolescents is not recommended.

Chronic heart failure (CHF)
The treatment of stable chronic heart failure has to be initiated with a gradual uptitration of dosage until the optimal individual maintenance dose is reached.
Patients should have stable chronic heart failure without acute failure during the past six weeks. It is recommended that the treating physician should be experienced in the management of chronic heart failure.
For those patients receiving cardiovascular drug therapy including diuretics and/or digoxin and/or ACE inhibitors and/or angiotensin II antagonists, dosing of these drugs should be stabilised during the past two weeks prior to initiation of Nebilet treatment.

The initial uptitration should be done according to the following steps at 1-2 weekly intervals based on patient tolerability:
1.25 mg nebivolol, to be increased to 2.5 mg nebivolol 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.

Initiation of therapy and every dose increase should be done under the supervision of an experienced physician over a period of at least 2 hours to ensure that the clinical status (especially as regards blood pressure, heart rate, conduction disturbances, signs of worsening of heart failure) remains stable.
Occurrence of adverse events may prevent all patients being treated with the maximum recommended dose. If necessary, the dose reached can also be decreased step by step and reintroduced as appropriate.
During the titration phase, in case of worsening of the heart failure or intolerance, it is recommended first to reduce the dose of nebivolol, or to stop it immediately if necessary (in case of severe hypotension, worsening of heart failure with acute pulmonary oedema, cardiogenic shock, symptomatic bradycardia or AV block).
Treatment of stable chronic heart failure with nebivolol is generally a long-term treatment.
The treatment with nebivolol is not recommended to be stopped abruptly since this might lead to a transitory worsening of heart failure. If discontinuation is necessary, the dose should be gradually decreased divided into halves weekly.

Patients with renal insufficiency
No dose adjustment is required in mild to moderate renal insufficiency since uptitration to the maximum tolerated dose is individually adjusted. There is no experience in patients with severe renal insufficiency (serum creatinine $\geq$ 250μmol/L). Therefore, the use of nebivolol in these patients is not recommended.

Patients with hepatic insufficiency
Data in patients with hepatic insufficiency are limited. Therefore the use of Nebilet in these patients is contra-indicated.

Older people
No dose adjustment is required since uptitration to the maximum tolerated dose is individually adjusted.

Paediatric population
The efficacy and safety of Nebilet in children and adolescents aged below 18 years has not been established. Therefore, use in children and adolescents is not recommended. No data are available.

Method of administration
Oral use.
Tablets may be taken with meals.

4.3. Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Liver insufficiency or liver function impairment.
- Acute heart failure, cardiogenic shock or episodes of heart failure decompensation requiring i.v. inotropic therapy.

In addition, as with other beta-blocking agents, Nebilet is contra-indicated in:

- sick sinus syndrome, including sino-atrial block.
- second and third degree heart block (without a pacemaker).
- history of bronchospasm and bronchial asthma.
- untreated phaeochromocytoma.
- metabolic acidosis.
- bradycardia (heart rate < 60 bpm prior to start therapy).
- hypotension (systolic blood pressure < 90 mmHg).
- severe peripheral circulatory disturbances.

4.4. Special warnings and precautions for use

See also 4.8 Undesirable effects.

The following warnings and precautions apply to beta-adrenergic antagonists in general.

Anaesthesia
Continuation of beta-blockade reduces the risk of arrhythmias during induction and intubation. If beta-blockade is interrupted in preparation for surgery, the beta-adrenergic antagonist should be discontinued at least 24 hours beforehand.
Caution should be observed with certain anaesthetics that cause myocardial depression. The patient can be protected against vagal reactions by intravenous administration of atropine.

Cardiovascular
In general, beta-adrenergic antagonists should not be used in patients with untreated congestive heart failure (CHF), unless their condition has been stabilised.
In patients with ischaemic heart disease, treatment with a beta-adrenergic antagonist should be discontinued gradually, i.e. over 1-2 weeks. If necessary replacement therapy should be initiated at the same time, to prevent exacerbation of angina pectoris.

Beta-adrenergic antagonists may induce bradycardia: if the pulse rate drops below 50-55 bpm at rest and/or the patient experiences symptoms that are suggestive of bradycardia, the dosage should be reduced.
Beta-adrenergic antagonists should be used with caution:
in patients with peripheral circulatory disorders (Raynaud's disease or syndrome, intermittent claudication), as aggravation of these disorders may occur;
in patients with first degree heart block, because of the negative effect of beta-blockers on conduction time;
in patients with Prinzmetal's angina due to unopposed alphareceptor mediated coronary artery vasoconstriction: beta-adrenergic antagonists may increase the number and duration of anginal attacks.
Combination of nebivolol with calcium channel antagonists of the verapamil and diltiazem type, with Class I antiarrhythmic drugs, and with centrally acting antihypertensive drugs is generally not recommended, for details please refer to section 4.5.

Metabolic/Endocrinological
Nebilet does not affect glucose levels in diabetic patients. Care should be taken in diabetic patients however, as nebivolol may mask certain symptoms of hypoglycaemia (tachycardia, palpitations).
Beta-adrenergic blocking agents may mask tachycardic symptoms in hyperthyroidism. Abrupt withdrawal may intensify symptoms.

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

Other
Patients with a history of psoriasis should take beta-adrenergic antagonists only after careful consideration.
Beta-adrenergic antagonists may increase the sensitivity to allergens and the severity of anaphylactic reactions.

The initiation of Chronic Heart Failure treatment with nebivolol necessitates regular monitoring. For the posology and method of administration please refer to section 4.2. Treatment discontinuation should not be done abruptly unless clearly indicated. For further information please refer to section 4.2.

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

Children and adolescents
No studies have been conducted in children and adolescents. Therefore, use in children and adolescents is not recommended.

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

Pharmacodynamic interactions:

The following interactions apply to beta-adrenergic antagonists in general.

Combinations not recommended:
Class I antiarrhythmics (quinidine, hydroquinidine, cibenzoline, flecainide, disopyramide, lidocaine, mexiletine, propafenone): effect on atrio-ventricular conduction time may be potentiated and negative inotropic effect increased (see section 4.4).

Calcium channel antagonists of verapamil/diltiazem type: negative influence on contractility and atrio-ventricular conduction. Intravenous administration of verapamil in patients with ß- blocker treatment may lead to profound hypotension and atrio-ventricular block (see section 4.4).

Centrally-acting antihypertensives (clonidine, guanfacin, moxonidine, methyldopa, rilmenidine): concomitant use of centrally acting antihypertensive drugs may worsen heart failure by a decrease in the central sympathetic tonus (reduction of heart rate and cardiac output, vasodilatation) (see section 4.4). Abrupt withdrawal, particularly if prior to beta-blocker discontinuation, may increase risk of "rebound hypertension".

Combinations to be used with caution

Class III antiarrhythmic drugs (Amiodarone): effect on atrio-ventricular conduction time may be potentiated.

Anaesthetics - volatile halogenated: concomitant use of beta-adrenergic antagonists and anaesthetics may attenuate reflex tachycardia and increase the risk of hypotension (see section 4.4). As a general rule, avoid sudden withdrawal of beta-blocker treatment. The anaesthesiologist should be informed when the patient is receiving Nebilet.

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

Baclofen (antispastic agent), amifostine (antineoplastic adjuct): concomitant use with antihypertensives is likely to increase the fall in blood pressure, therefore the dosage of the antihypertensive medication should be adjusted accordingly.

Combinations to be considered

Digitalis glycosides: concomitant use may increase atrio-ventricular conduction time. Clinical trials with nebivolol have not shown any clinical evidence of an interaction. Nebivolol does not influence the kinetics of digoxin.

Calcium antagonists of the dihydropyridine type (amlodipine, felodipine, lacidipine, nifedipine, nicardipine, nimodipine, nitrendipine): concomitant use may increase the risk of hypotension, and an increase in the risk of a further deterioration of the ventricular pump function in patients with heart failure cannot be excluded.

Antipsychotics, antidepressants (tricyclics, barbiturates and phenothiazines): concomitant use may enhance the hypothensive effect of the beta-blockers (additive effect).

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

Sympathicomimetic agents: concomitant use may counteract the effect of beta-adrenergic antagonists. Beta-adrenergic agents may lead to unopposed alpha-adrenergic activity of sympathicomimetic agents with both alpha- and beta-adrenergic effects (risk of hypertension, severe bradycardia and heart block).

Pharmacokinetic interactions:

As nebivolol metabolism involves the CYP2D6 isoenzyme, co-administration with substances inhibiting this enzyme, especially paroxetine, fluoxetine, thioridazine and quinidine may lead to increased plasma levels of nebivolol associated with an increased risk of excessive bradycardia and adverse events.

Co-administration of cimetidine increased the plasma levels of nebivolol, without changing the clinical effect. Co-administration of ranitidine did not affect the pharmacokinetics of nebivolol. Provided Nebilet is taken with the meal, and an antacid between meals, the two treatments can be co-prescribed.
Combining nebivolol with nicardipine slightly increased the plasma levels of both drugs, without changing the clinical effect. Co-administration of alcohol, furosemide or hydrochlorothiazide did not affect the pharmacokinetics of nebivolol. Nebivolol does not affect the pharmacokinetics and pharmacodynamics of warfarin.

4.6. Fertility, pregnancy and lactation

Pregnancy

Nebivolol has pharmacological effects that may cause harmful effects on pregnancy and/or the foetus/newborn. In general, beta-adrenoceptor blockers reduce placental perfusion, which has been associated with growth retardation, intrauterine death, abortion or early labour. Adverse effects (e.g. hypoglycaemia and bradycardia) may occur in the foetus and newborn infant. If treatment with beta-adrenoceptor blockers is necessary, $beta_1$-selective adrenoceptor blockers are preferable.
Nebivolol should not be used during pregnancy unless clearly necessary. If treatment with nebivolol is considered necessary, the uteroplacental blood flow and the foetal growth should be monitored. In case of harmful effects on pregnancy or the foetus alternative treatment should be considered. The newborn infant must be closely monitored. Symptoms of hypoglycaemia and bradycardia are generally to be expected within the first 3 days.

Breast-feeding

Animal studies have shown that nebivolol is excreted in breast milk. It is not known whether this drug is excreted in human milk. Most beta-blockers, particularly lipophilic compounds like nebivolol and its active metabolites, pass into breast milk although to a variable extent. Therefore, breastfeeding is not recommended during administration of nebivolol.

4.7. Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed . Pharmacodynamic studies have shown that Nebilet 5 mg does not affect psychomotor function. When driving vehicles or operating machines it should be taken into account that dizziness and fatigue may occasionally occur.

4.8. Undesirable effects

Adverse events are listed separately for hypertension and CHF because of differences in the background diseases.

Hypertension

The adverse reactions reported, which are in most of the cases of mild to moderate intensity, are tabulated below, classified by system organ class and ordered by frequency:

SYSTEM ORGAN CLASS	Common (≥1/100 to < 1/10)	Uncommon (≥1/1,000 to ≤1/100)	Very Rare (≤1/10,000)	Not Known
Immune system disorders				angioneurotic oedema, hypersensitivity
Psychiatric disorders		nightmares; depression		

Nervous system disorders	headache, dizziness, paraesthesia		syncope	
Eye disorders		impaired vision		
Cardiac disorders		bradycardia, heart failure, slowed AV conduction/AV-block		
Vascular disorders		hypotension, (increase of) intermittent claudication		
Respiratory, thoracic and mediastinal disorders	dyspnoea	bronchospasm		
Gastrointestinal disorders	constipation, nausea, diarrhoea	dyspepsia, flatulence, vomiting		
Skin and subcutaneous tissue disorders		pruritus, rash erythematous	psoriasis aggravated	urticaria
Reproductive system and breast disorders		impotence		
General disorders and administration site conditions	tiredness, oedema			

The following adverse reactions have also been reported with some beta-adrenergic antagonists: hallucinations, psychoses, confusion, cold/cyanotic extremities, Raynaud phenomenon, dry eyes, and oculo-mucocutaneous toxicity of the practolol-type.

Chronic heart failure

Data on adverse reactions in CHF patients are available from one placebo-controlled clinical trial involving 1067 patients taking nebivolol and 1061 patients taking placebo. In this study, a total of 449 nebivolol patients (42.1%) reported at least possibly causally related adverse reactions compared to 334 placebo patients (31.5%). The most commonly reported adverse reactions in nebivolol patients were bradycardia and dizziness, both occurring in approximately 11% of patients. The corresponding frequencies among placebo patients were approximately 2% and 7%, respectively.

The following incidences were reported for adverse reactions (at least possibly drug-related) which are considered specifically relevant in the treatment of chronic heart failure:

- Aggravation of cardiac failure occurred 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 1.0% of placebo patients.
- Drug intolerance occurred in 1.6% of nebivolol patients compared to 0.8% of placebo patients.
- First degree atrio-ventricular block occurred in 1.4% of nebivolol patients compared to 0.9% of placebo patients.

- Oedema of the lower limb were reported by 1.0% of nebivolol patients compared to 0.2% of placebo patients.

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 the national reporting system.

4.9. Overdose

No data are available on overdosage with Nebilet.

Symptoms
Symptoms of overdosage with beta-blockers are: bradycardia, hypotension, bronchospasm and acute cardiac insufficiency.

Treatment
In case of overdosage or hypersensitivity, the patient should be kept under close supervision and be treated in an intensive care ward. Blood glucose levels should be checked. Absorption of any drug residues still present in the gastro-intestinal tract can be prevented by gastric lavage and the administration of activated charcoal and a laxative. Artificial respiration may be required. Bradycardia or extensive vagal reactions should be treated by administering atropine or methylatropine. Hypotension and shock should be treated with plasma/plasma substitutes and, if necessary, catecholamines. The beta-blocking effect can be counteracted by slow intravenous administration of isoprenaline hydrochloride, starting with a dose of approximately 5 μg/minute, or dobutamine, starting with a dose of 2.5 μg/minute, until the required effect has been obtained. In refractory cases isoprenaline can be combined with dopamine. If this does not produce the desired effect either, intravenous administration of glucagon 50-100 μg/kg i.v. may be considered. If required, the injection should be repeated within one hour, to be followed -if required- by an i.v. infusion of glucagon 70 μg/kg/h. In extreme cases of treatment-resistant bradycardia, a pacemaker may be inserted.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Beta-blocking agent, selective.
ATC code: C07AB12
Nebivolol is a racemate of two enantiomers, SRRR-nebivolol (or d-nebivolol) and RSSS-nebivolol (or l-nebivolol). It combines two pharmacological activities:

- It is a competitive and selective beta-receptor antagonist: this effect is attributed to the SRRR-enatiomer (d-enantiomer).
- It has mild vasodilating properties due to an interaction with the L-arginine/nitric oxide pathway.

Single and repeated doses of nebivolol reduce heart rate and blood pressure at rest and during exercise, both in normotensive subjects and in hypertensive patients. The antihypertensive effect is maintained during chronic treatment.
At therapeutic doses, nebivolol is devoid of alpha-adrenergic antagonism.
During acute and chronic treatment with nebivolol in hypertensive patients systemic vascular resistance is decreased. Despite heart rate reduction, reduction in cardiac output during rest and exercise may be limited due to an increase in stroke volume. The clinical

relevance of these haemodynamic differences as compared to other beta1 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.

In a mortality–morbidity, placebo-controlled trial performed in 2128 patients ≥ 70 years (median age 75.2 years) with stable chronic heart failure with or without impaired left ventricular ejection fraction (mean LVEF: 36 ± 12.3%, with the following distribution: LVEF less than 35% in 56% of patients, LVEF between 35% and 45% in 25% of patients and LVEF greater than 45% in 19% of patients) followed for a mean time of 20 months, nebivolol, on top of standard therapy, significantly prolonged the time to occurrence of deaths or hospitalisations for cardiovascular reasons (primary end-point for efficacy) with a relative risk reduction of 14% (absolute reduction: 4.2%). This risk reduction developed after 6 months of treatment and was maintained for all treatment duration (median duration: 18 months). The effect of nebivolol was independent from age, gender, or left ventricular ejection fraction of the population on study. The benefit on all cause mortality did not reach statistical significance in comparison to placebo (absolute reduction: 2.3%).
A decrease in sudden death was observed in nebivolol treated patients (4.1% vs 6.6%, relative reduction of 38%).

In vitro and in vivo experiments in animals showed that Nebivolol has no intrinsic sympathicomimetic activity.
In vitro and in vivo experiments in animals showed that at pharmacological doses nebivolol has no membrane stabilising action.
In healthy volunteers, nebivolol has no significant effect on maximal exercise capacity or endurance.
Available preclinical and clinical evidence in hypertensive patients has not shown that nebivolol has a detrimental effect on erectile function.

5.2. Pharmacokinetic properties

Both nebivolol enantiomers are rapidly absorbed after oral administration. The absorption of nebivolol is not affected by food; nebivolol can be given with or without meals.
Nebivolol is extensively metabolised, partly to active hydroxy-metabolites. Nebivol is metabolised via alicyclic and aromatic hydroxylation, N-dealkylation and glucuronidation; in addition, glucuronides of the hydroxy-metabolites are formed. The metabolism of nebivolol by aromatic hydroxylation is subject to the CYP2D6 dependent genetic oxidative polymorphism. The oral bioavailability of nebivolol averages 12% in fast metabolisers and is virtually complete in slow metabolisers. At steady state and at the same dose level, the peak plasma concentration of unchanged nebivolol is about 23 times higher in poor metabolisers than in extensive metabolisers. When unchanged drug plus active metabolites are considered, the difference in peak plasma concentrations is 1.3 to 1.4 fold. Because of the variation in rates of metabolism, the dose of Nebilet should always be adjusted to the individual requirements of the patient: poor metabolisers therefore may require lower doses.
In fast metabolisers, elimination half-lives of the nebivolol enantiomers average 10 hours. In slow metabolisers, they are 3-5 times longer. In fast metabolisers, plasma levels of the RSSS-enantiomer are slightly higher than for the SRRR-enantiomer. In slow metabolisers, this difference is larger. In fast metabolisers, elimination half-lives of the hydroxymetabolites of both enantiomers average 24 hours, and are about twice as long in slow metabolisers.
Steady-state plasma levels in most subjects (fast metabolisers) are reached within 24 hours for nebivolol and within a few days for the hydroxy-metabolites.
Plasma concentrations are dose-proportional between 1 and 30 mg. The pharmacokinetics of nebivolol are not affected by age.
In plasma, both nebivolol enantiomers are predominantly bound to albumin.
Plasma protein binding is 98.1% for SRRR-nebivolol and 97.9% for RSSS-nebivolol.
One week after administration, 38% of the dose is excreted in the urine and 48% in the

faeces. Urinary excretion of unchanged nebivolol is less than 0.5% of the dose.

5.3. Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of genotoxicity and carcinogenic potential.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Polysorbate 80 (E433)
Hypromellose (E464)
Lactose monohydrate
Maize starch
Croscarmellose sodium (E468)
Microcrystalline cellulose (E460)
Silica, colloidal anhydrous (E551)
Magnesium stearate (E572)

6.2. Incompatibilities

Not applicable

PACKAGING AND REGISTRATION NUMBER
Box, 2 Blister of 14 tablets, Reg. No. DKI1529800210A1

HARUS DENGAN RESEP DOKTER

Imported by
PT. Menarini Indria Laboratories
Bekasi – Indonesia

Licensed by:
A. Menarini Asia-Pacific Holdings Pte. Ltd., Singapore

Manufacturer
Berlin-Chemie AG
Glienicker Weg 125, 12489 Berlin, Germany

Storage at temperature store below 30°C
Protect from light

MENARINI

148 mm

630 mm

NEBILET 5 mg tablets

Nebivolol

Baca leaflet ini sebelum Anda menggunakan obat ini karena berisi informasi penting bagi Anda.
- Simpan leaflet ini. Anda bisa membacanya lagi.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter atau apoteker.
- Obat ini diresepkan hanya untuk Anda. Jangan berikan obat ini kepada orang lain. Obat ini bisa membahayakan mereka, meskipun gejala penyakitnya sama seperti Anda.
- Jika Anda mengalami efek samping, bicarakan dengan dokter atau apoteker atau perawat. Termasuk kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Lihat bagian 4.

Isi leaflet ini:

1. Nebilet dan kegunaannya

Nebilet mengandung nebivolol, obat kardiovaskular yang termasuk golongan obat penghambat beta selektif (misalnya dengan tindakan selektif pada sistem kardiovaskular). Obat ini mencegah peningkatan denyut jantung, mengendalikan kekuatan memompa jantung. Obat ini juga memberikan tindakan dilatasi pada pembuluh darah, yang bisa menurunkan tekanan darah.

Obat ini digunakan untuk mengobati tekanan darah tinggi (hipertensi).

Nebilet juga digunakan untuk mengobati gagal jantung kronis ringan dan sedang pada pasien berusia 70 atau lebih, di samping terapi lain.

2. Yang perlu Anda ketahui sebelum mengonsumsi Nebilet

Jangan mengonsumsi Nebilet
- jika Anda alergi terhadap nebivolol atau bahan lain obat ini (tercantum dalam bagian 6).
- jika Anda mengalami satu atau lebih gangguan berikut:
  - tekanan darah rendah
  - masalah sirkulasi serius di lengan atau kaki
  - detak jantung sangat lambat (kurang dari 60 kali per menit)
  - masalah irama jantung serius lainnya (misalnya gangguan blok atrioventrikular tingkat 2 dan 3, konduksi jantung).
  - gagal jantung, yang baru terjadi atau yang akhir-akhir ini menjadi lebih parah, atau Anda sedang menjalani pengobatan syok sirkulasi karena gagal jantung akut dengan pemberian infus intravena untuk membantu kerja jantung Anda.
  - asma atau mengi (sekarang atau di masa lalu).
  - pheochromocytoma yang tidak diobati, tumor yang terletak di atas ginjal (di kelenjar adrenal).
  - gangguan fungsi hati.
  - gangguan metabolisme (asidosis metabolik), misalnya, ketoasidosis diabetik.

Peringatan dan pencegahan
Bicarakan dengan dokter atau apoteker sebelum mengonsumsi Nebilet.

Beritahu dokter jika Anda mengalami atau merasakan masalah berikut:
- kelainan detak jantung yang melambat
- nyeri dada yang disebabkan kram jantung spontan disebut Prinzmetal angina
- gagal jantung kronis yang tidak diobati
- blok jantung tingkat 1 (gangguan konduksi jantung ringan yang mempengaruhi irama jantung)
- sirkulasi yang buruk di lengan atau kaki, misalnya penyakit atau sindrom Raynaud, nyeri seperti kram ketika berjalan
- masalah pernapasan berkepanjangan
- diabetes: Obat ini tidak berpengaruh terhadap gula darah, tetapi bisa menghilangkan tanda-tanda peringatan kadar gula rendah (misalnya jantung berdebar, detak jantung cepat).
- kelenjar tiroid yang terlalu aktif: Obat ini bisa menghilangkan tanda-tanda kelainan detak jantung cepat yang disebabkan kondisi ini
- Alergi: Obat ini bisa meningkatkan reaksi Anda terhadap serbuk sari atau zat lain yang membuat Anda alergi.
- psoriasis (penyakit kulit - bercak merah muda bersisik) atau jika Anda pernah mengalami psoriasis
- jika Anda harus menjalani operasi, beri tahu ahli anestesi bahwa Anda sedang mengonsumsi Nebilet sebelum dibius.

Jika Anda mengalami masalah ginjal yang serius jangan konsumsi Nebilet untuk gagal jantung dan beritahu dokter.
Anda akan dipantau secara teratur pada awal pengobatan gagal jantung kronis oleh dokter yang berpengalaman (lihat bagian 3).
Pengobatan ini tidak boleh dihentikan secara tiba-tiba kecuali dengan jelas dinyatakan dan dievaluasi oleh dokter (lihat bagian 3).

Anak-anak dan remaja
Karena kurangnya data tentang penggunaan produk pada anak-anak dan remaja, Nebilet **tidak** dianjurkan untuk dikonsumsi oleh anak-anak dan remaja.

Obat lain dan Nebilet
Beritahu dokter atau apoteker jika Anda sudah mengonsumsi, baru saja mengonsumsi atau akan mengonsumsi obat lain.
Selalu beritahu dokter jika Anda mengonsumsi obat berikut selain Nebilet:
- Obat untuk mengendalikan tekanan darah atau obat untuk masalah jantung (seperti *amiodarone, amlodipin, cibenzoline, klonidin, digoksin, diltiazem, disopiramid, felodipin, flecainide, guanfacin, hidrokuinidin, lacidipine, lidokain, metildopa, mexiletine, moxonidine, nicardipine, nifedipin, nimodipine, nitrendipine, propafenone, kuinidin, rilmenidine,* verapamil).
- Obat penenang dan terapi untuk psikosis (penyakit kejiwaan) misalnya barbiturat (juga digunakan untuk epilepsi), fenotiazin (juga digunakan untuk muntah dan mual) dan tioridazin.
- Obat untuk depresi misalnya amitriptyline, paroxetine, fluoxetine.
- Obat yang digunakan untuk anestesi selama operasi.
- Obat untuk asma, hidung tersumbat atau gangguan mata seperti glaukoma (peningkatan tekanan pada mata) atau pelebaran pupil.
- Baclofen (obat antispasmodik); Amifostine (obat pelindung yang digunakan selama pengobatan kanker)
- Seluruh obat ini dan nebivolol bisa mempengaruhi tekanan darah dan/atau fungsi jantung.
- Obat untuk asam lambung yang berlebihan atau maag (obat antasida), Anda harus mengonsumsi Nebilet saat makan dan obat antasida di antara waktu makan.

Nebilet dengan makanan dan minuman
Silakan lihat bagian 3.

Hamil dan menyusui
Nebilet tidak boleh dikonsumsi selama kehamilan, kecuali jika sangat diperlukan.
Tidak dianjurkan untuk dikonsumsi saat menyusui.
Jika Anda sedang hamil atau menyusui, kemungkinan akan hamil atau berencana untuk memiliki bayi, tanyakan kepada dokter atau apoteker untuk meminta nasihat sebelum mengonsumsi obat ini.

Mengemudi dan menggunakan mesin
Obat ini bisa menyebabkan pusing atau kelelahan. Jika terpengaruh, **jangan** mengemudi atau mengoperasikan mesin.

Nebilet mengandung laktosa
Produk ini mengandung **laktosa** . Jika Anda telah diberitahu oleh dokter bahwa Anda memiliki intoleransi terhadap beberapa gula, **hubungi dokter sebelum** mengonsumsi obat ini.

3. Cara mengonsumsi Nebilet

Selalu konsumsi obat ini seperti yang dikatakan dokter Anda. Tanyakan pada dokter atau apoteker jika Anda tidak yakin.
Nebilet dapat diminum sebelum, selama atau setelah makan, tetapi, sebagai alternatif, Anda bisa meminumnya tanpa disertai makanan.
Tablet ini sebaiknya diminum dengan air.

Pengobatan tekanan darah tinggi (hipertensi)
- Dosis yang biasa digunakan adalah 1 tablet per hari. Sebaiknya dosis dikonsumsi pada waktu yang sama setiap hari.
- Pasien lansia dan pasien dengan gangguan ginjal biasanya akan mulai dengan ½ (setengah) tablet setiap hari.
- Efek terapeutik pada tekanan darah menjadi jelas setelah 1-2 minggu pengobatan. Terkadang, hasil yang optimal tercapai setelah 4 minggu.

Pengobatan gagal jantung kronis
- Pengobatan Anda akan dimulai dan diawasi secara ketat oleh dokter yang berpengalaman.
- Dokter akan memulai pengobatan Anda dengan ¼ (seperempat) tablet per hari. Obat bisa ditambah setelah 1-2 minggu menjadi ½ (setengah) tablet per hari, kemudian menjadi 1 tablet per hari dan kemudian menjadi 2 tablet per hari sampai dosis yang tepat untuk Anda. Dokter akan meresepkan dosis yang tepat untuk Anda di setiap tahapan dan Anda harus mengikuti petunjuknya.
- Dosis maksimum yang disarankan adalah 2 tablet (10mg) sehari.
- Anda seharusnya diawasi dengan ketat selama 2 jam oleh dokter yang berpengalaman ketika Anda memulai pengobatan dan setiap peningkatan dosis.
- Dokter akan mengurangi dosis Anda bila perlu.
- Anda **tidak boleh menghentikan pengobatan ini secara tiba-tiba** karena akan memperburuk gagal jantung Anda.
- Penderita dengan masalah ginjal yang serius tidak boleh mengonsumsi obat ini.
- Minum obat Anda sekali sehari, sebaiknya pada waktu yang sama setiap hari.

Jika Anda telah diberitahu dokter untuk mengonsumsi ¼ (seperempat) atau ½ (setengah) tablet setiap hari, lihat petunjuk di bawah ini tentang cara mematahkan Tablet Nebilet 5 mg yang bertanda silang.
- Letakkan tablet ke permukaan yang datar dan keras (misalnya meja atau meja dapur), dengan tanda silang menghadap ke atas.
- Pecahkan tablet dengan menekannya menggunakan dua jari telunjuk yang diletakkan di sepanjang satu patahan (Diagram 1 dan 2).
- Untuk dosis seperempat tablet, tablet setengah dipatahkan dengan cara yang sama (Diagram 3 dan 4).

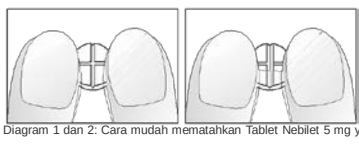

Diagram 1 dan 2: Cara mudah mematahkan Tablet Nebilet 5 mg yang bertanda silang menjadi setengah.

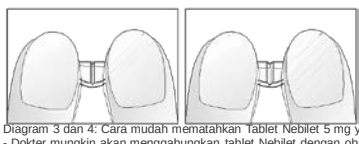

Diagram 3 dan 4: Cara mudah mematahkan Tablet Nebilet 5 mg yang bertanda silang menjadi seperempat.
- Dokter mungkin akan menggabungkan tablet Nebilet dengan obat lain untuk mengobati kondisi Anda.
- Tidak boleh dikonsumsi anak-anak atau remaja.

Jika Anda mengonsumsi lebih banyak Nebilet dari yang seharusnya
Jika Anda tidak sengaja mengonsumsi dosis obat ini secara berlebihan, **segera** beri tahu dokter atau apoteker. Gejala dan tanda overdosis Nebilet yang paling sering adalah detak jantung yang sangat lambat (bradikardi), tekanan darah rendah dengan kemungkinan pingsan (hipotensi), sesak napas seperti pada asma (bronkospasme), dan gagal jantung akut.

Anda bisa mengonsumsi arang aktif (yang tersedia di apotek) sambil menunggu dokter datang.

Jika Anda lupa mengonsumsi Nebilet
Jika Anda lupa mengonsumsi satu dosis Nebilet, kemudian mengetahuinya belum lama setelah waktu seharusnya Anda meminumnya, minum dosis hari tersebut seperti biasa. Namun, jika Anda lupa mengonsumsi pada waktu yang lama (misalnya beberapa jam), sehingga waktu untuk mengonsumsi dosis berikutnya sudah dekat, lewati dosis yang terlupakan dan konsumsi **dosis normal** berikutnya, sesuai jadwal, pada waktu biasanya. Jangan konsumsi dua dosis pada waktu yang sama. Jangan melewatkan dosis berulang kali.

Jika Anda berhenti mengonsumsi Nebilet
Anda harus selalu berkonsultasi dengan dokter sebelum menghentikan pengobatan Nebilet untuk tekanan darah tinggi atau gagal jantung kronis.

Anda tidak boleh menghentikan pengobatan Nebilet secara tiba-tiba karena bisa membuat gagal jantung Anda menjadi lebih buruk. Jika Anda harus menghentikan pengobatan Nebilet untuk gagal jantung kronis, dosis harian harus dikurangi secara bertahap, dengan mengurangi separuh dosis, pada interval mingguan.

Jika Anda memiliki pertanyaan lebih lanjut tentang pemakaian produk ini, tanyakan kepada dokter atau apoteker.

4. Kemungkinan efek samping

Seperti semua obat lain, obat ini bisa menyebabkan efek samping, meskipun tidak semua orang mengalaminya.
Jika Nebilet **digunakan untuk pengobatan peningkatan tekanan darah**, kemungkinan efek sampingnya adalah:
Efek samping umum (dialami oleh hingga 1 dari 10 orang):
- sakit kepala
- pusing
- kelelahan
- rasa gatal atau kesemutan yang tidak biasa
- diare
- sembelit
- mual
- sesak napas
- tangan atau kaki bengkak

Efek samping tidak umum (dialami oleh hingga 1 dari 100 orang):
- detak jantung lambat atau keluhan jantung lainnya
- tekanan darah rendah
- nyeri kaki seperti kram saat berjalan
- kelainan penglihatan
- impotensi
- merasa depresi
- nyeri pencernaan (dispepsia), gas di perut atau usus, muntah
- ruam kulit, gatal
- sesak napas seperti pada asma, yang disebabkan oleh kram mendadak pada otot di sekitar saluran napas (bronkospasme)
- mimpi buruk

Efek samping yang sangat jarang (dialami oleh hingga 1 dari 10.000 orang):
- Pingsan
- memburuknya psoriasis (penyakit kulit - bercak merah muda bersisik)

Efek samping berikut telah dilaporkan hanya dalam beberapa kasus selama pengobatan Nebilet:
- reaksi alergi seluruh tubuh, dengan erupsi kulit umum (reaksi hipersensitivitas);
- pembengkakan onset cepat, terutama di sekitar bibir, mata, atau lidah dengan kemungkinan kesulitan bernapas secara mendadak (angioedema);
- jenis ruam kulit seperti benjolan merah pucat, timbul, gatal dari penyebab alergi atau non alergi (urtikaria).

Dalam sebuah studi klinis untuk **gagal jantung kronis**, efek samping berikut pernah dialami:
Efek samping sangat umum (dialami oleh lebih dari 1 dari 10 orang):
- detak jantung lambat
- pusing

Efek samping umum (bisa dialami oleh hingga 1 dari 10 orang):
- gagal jantung memburuk
- tekanan darah rendah (seperti merasa lemas ketika bangun dengan cepat)
- ketidakmampuan untuk mentoleransi obat ini
- jenis gangguan konduksi jantung ringan yang mempengaruhi irama jantung (blok atrioventrikular tingkat 1)
- pembengkakan anggota tubuh bagian bawah (seperti pergelangan kaki bengkak).

Pelaporan efek samping
Jika Anda mengalami efek samping, bicaralah dengan dokter atau apoteker atau perawat. Termasuk kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Anda juga bisa melaporkan efek samping langsung melalui sistem pelaporan nasional. Dengan melaporkan efek samping, Anda bisa membantu memberikan informasi lebih lanjut tentang keamanan obat ini.

5. Cara menyimpan Nebilet

Jauhkan obat ini dari penglihatan dan jangkauan anak-anak.
Produk obat ini tidak memerlukan kondisi penyimpanan khusus. Jangan konsumsi obat ini setelah tanggal kedaluwarsa yang tercantum pada label karton dan blister foil setelah EXP. Tanggal kedaluwarsa merupakan hari terakhir bulan tersebut.

Jangan membuang obat pada air limbah atau limbah rumah tangga.
Tanyakan pada apoteker cara membuang obat yang tidak lagi digunakan. Langkah-langkah ini akan membantu melindungi lingkungan.

6. Isi kemasan dan informasi lain

Kandungan Nebilet
- Zat aktif nebivolol. Setiap tablet mengandung 5 mg nebivolol (sebagai nebivolol hidroklorida): 2,5 mg d-nebivolol dan 2,5 mg l-nebivolol.
- Bahan lain: laktosa monohidrat, polisorbat 80 (E433), hypromellose (E464), pati jagung, natrium kroskarmelosa (E468), selulosa mikrokristalin (E460), silika koloidal anhidrat (E551), magnesium stearat (E572).

Bentuk Nebilet dan isi kemasan
Nebilet merupakan tablet bertanda silang berwarna putih dan berbentuk bulat dalam kemasan tablet 28 (Dus, 2 blister @ 14 tablet). Tablet disediakan dalam kemasan blister (PVC/aluminium blister).
No. Reg. DKI1529800210A1.

HARUS DENGAN RESEP DOKTER.
Simpan pada temperature di bawah 30°C . Lindungi dari sinar matahari langsung.

Diimpor oleh:
PT. Menarini Indria Laboratories
Bekasi - Indonesia

Diproduksi oleh:
Berlin-Chemie AG
Glienicker Weg 125, 12489 Berlin, Jerman
atas lisensi dari A. Menarini Asia-Pacific Holdings Pte. Ltd., Singapura.

MENARINI
SOLUTIONS 2021

DISETUJUI OLEH BPOM : 11/01/2022
EREG10043712100125