

PACKAGE LEAFLET

NEBILET PLUS 5 mg / 12.5 mg film-coated tablets

Nebivolol / Hydrochlorothiazide

Read all this leaflet carefully before you start using this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

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1. What Nebilet Plus is and what it is used for
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1. WHAT NEBILET PLUS IS AND WHAT IT IS USED FOR

Nebilet Plus contains nebivolol and hydrochlorothiazide as the active ingredients.

- Nebivolol is a cardiovascular drug belonging to the group of selective beta-blocking agents (i.e. with a selective action on the cardiovascular system). It prevents increased heart rate and controls heart pumping strength. It also widens blood vessels, which helps to lower your blood pressure.
- Hydrochlorothiazide is a diuretic, that acts by increasing the amount of urine you produce.

Nebilet Plus is a one-tablet combination of nebivolol and hydrochlorothiazide and is used for the treatment of raised blood pressure (hypertension). It is used instead of the two separate products for those patients who are already taking them together.

2. BEFORE YOU TAKE NEBILET PLUS

Do not take Nebilet Plus

- if you are allergic (hypersensitive) to nebivolol or to hydrochlorothiazide or to any of the other ingredients of Nebilet Plus (see end of Section 2, and Section 6).
- if you are allergic (hypersensitive) to other sulphonamide-derived substances (like hydrochlorothiazide, which is a sulphonamide-derived drug)
- if you have one or more of the following disorders:
 - very slow heartbeat (less than 60 beats per minute)
 - certain other serious heart rhythm problems (e.g. sick sinus syndrome, sino-atrial block, 2nd and 3rd degree atrioventricular block).
 - heart failure, which has just occurred or which has recently become worse, or you are receiving treatment for circulatory shock due to acute heart failure by intravenous drip feed to help your heart work
 - low blood pressure
 - serious circulation problems in the arms or legs
 - untreated phaeochromocytoma, a tumour located on top of the kidneys (in the adrenal glands)
 - severe kidney problems, complete absence of urine (anuria)
 - a metabolic disorder (metabolic acidosis), e.g., diabetic ketoacidosis.
 - asthma or wheezing (now or in the past)
 - liver function disorder
 - high blood calcium, low blood potassium, low blood sodium levels that are persistent and resistant to treatment
 - high uric acid levels with gout symptoms

Take special care with Nebilet Plus

- Inform your doctor if you have or develop one of the following problems:
 - a type of chest pain due to spontaneously occurring heart cramp, called Prinzmetal angina
 - 1st degree heart block (a kind of mild heart conduction impairment that affects heart rhythm)
 - abnormally slow heartbeat
 - untreated chronic heart failure
 - lupus erythematosus (a disorder of the immune system, i.e. your body's defence system)
 - psoriasis (a skin disease characterised by scaly pink patches) or if you have ever had psoriasis
 - overactive thyroid gland: this medicine may mask the signs of an abnormally fast heart rate due to this condition
 - poor circulation in the arms or legs, e.g. Raynaud's disease or syndrome, cramp-like pains when walking
 - allergy: this medicine may intensify your reaction to pollen or other substances you are allergic to
 - prolonged breathing problems
 - diabetes: this medicine could conceal the warning signs of a low sugar level (e.g. palpitations, fast heartbeat); your doctor will also tell you to check your blood sugar more often while taking Nebilet Plus, as the dose of your antidiabetic drugs may need to be adjusted
 - kidney problems: your doctor will check your kidney function to make sure it does not get worse. If you have serious kidney problems do not take Nebilet Plus (see section 'Do not take Nebilet Plus')
 - if you tend to have low blood potassium, and especially if you suffer from prolonged QT syndrome (a kind of ECG abnormality) or you are taking digitalis (to help your heart pump); you are more likely to have low blood potassium if you suffer from liver cirrhosis, or have had too rapid a loss of water due to a strong diuretic treatment, or if your intake of potassium with food and drinks is inadequate
 - if you have to have surgery, always inform your anaesthetist that you are on Nebilet Plus before being anaesthetised.

- Nibilet Plus may increase blood fat levels and uric acid. It may affect the levels of certain chemicals in your blood, called electrolytes: your doctor will check them from time to time via a blood test.
- The hydrochlorothiazide in Nibilet Plus may cause your skin to be oversensitive to sunlight or artificial UV light. Stop taking Nibilet Plus and tell your doctor if you get a rash, itchy spots or sensitive skin during treatment (see also Section 4).
- Anti-dope test: Nibilet Plus could cause a positive anti-dope test.

Children and adolescents

Because of the lack of data on the use of the product in children and adolescents, Nibilet Plus is **not** recommended for use in them.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, **including** medicines obtained without a prescription. Certain medicines cannot be used at the same time, while other drugs require specific changes (in the dose, for example).

Always tell your doctor if you are using or receiving any of the following medicines in addition to Nibilet Plus:

- Medicines that, as well as Nibilet Plus, may influence the blood pressure and/or heart function:

- Medicines for controlling blood pressure or medicines for heart problems (such as amiodarone, amlodipine, cibenzoline, clonidine, digoxin, diltiazem, disopyramide, dofetilide, felodipine, flecainide, guanfacine, hydroquinidine, ibutilide, lacidipine, lidocaine, mexiletine, methyldopa, moxonidine, nicardipine, nifedipine, nimodipine, nitrendipine, propafenone, quinidine, rilmenidine, sotalol, verapamil)
- Sedatives and therapies for psychosis (a mental illness) e.g. amisulpiride, barbiturates (also used for epilepsy), chlorpromazine, cyamemazine, droperidol, haloperidol, levomepromazine, narcotic drugs, phenothiazine (also used for vomiting and nausea), pimozide, sulpiride, sultopride, thioridazine, tiapride trifluoperazine
- Medicines for depression e.g. amitriptyline, fluoxetine, paroxetine
- Medicines used for anaesthesia during an operation
- Medicines for asthma, blocked nose or certain eye disorders such as glaucoma (increased pressure in the eye) or dilation (widening) of the pupil

- Medicines whose effect or toxicity may be increased by Nibilet Plus:

- Lithium, used as a mood stabilizer
- Cisapride (used for digestive problems)
- Bepridil (used for angina)
- Diphepanil (used for excessive sweating)
- Medicines used for infections: erythromycin given by infusion or injection, pentamidine and sparflaxacin, amphotericin and penicillin G sodium, halofantrine (used for malaria)
- Vincamine (used for brain circulation problems)
- Mizolastine and terfenadine (used for allergy)
- Diuretics and laxatives
- Medicines used to treat acute inflammation: steroids (e.g. cortisone and prednisone), ACTH (adrenocorticotrophic hormone) and medicines derived from salicylic acid (e.g. acetylsalicylic acid/ aspirin and other salicylates)
- Carbenoxolone (used for heartburn and stomach ulcer)
- Calcium salts, used as supplements for bone health
- Medicines used to relax muscles (e.g. tubocurarine)
- Diaxozide, used to treat low blood sugar and high blood pressure
- Amantadine, an antiviral medicine
- Cyclosporine, used to suppress the body's immune response
- Iodinated contrast media, used for contrast in X-ray scans
- Anti-cancer medicines (e.g. cyclophosphamide, fluorouracil, methotrexate)

- Medicines whose effect may be decreased by Nibilet Plus:

- Blood sugar-lowering medicines (insulin and oral antidiabetic drugs, metformin)
- Medicines for gout (e.g. allopurinol, probenecid and sulfapyrazone)
- Medicines like noradrenalin, used to treat low blood pressure or slow heart rate

- Medicines for pain and inflammation (non-steroidal anti-inflammatory drugs), as they may reduce the blood pressure lowering effect of Nibilet Plus

- Medicines for treating excessive stomach acid or ulcers (antacid), e.g. cimetidine: you should take Nibilet Plus during a meal and the antacid between meals.

Taking Nibilet Plus with food and drink

Nibilet Plus can be taken with food or on an empty stomach, but the tablet is best taken with some water. Take care when drinking alcohol while you are taking Nibilet Plus, as you may feel faint or dizzy. If this happens to you, do not drink any alcohol, including wine, beer or alcopops.

Pregnancy and breast-feeding

You must tell your doctor if you are pregnant or if you think that you are. Usually, your doctor will advise you to take another medicine instead of Nibilet Plus, as Nibilet Plus is not recommended during pregnancy. This is because the active ingredient hydrochlorothiazide crosses the placenta. The use of Nibilet Plus during pregnancy may cause potentially harmful foetal and neonatal effects. Tell your doctor if you are breast-feeding or about to start breast-feeding. Nibilet Plus is not recommended for mothers who are breast-feeding.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving or operating machines

This medicine may cause dizziness or fatigue. If affected, **do not** drive or operate machinery.

Important information about some of the ingredients of Nibilet Plus

This product contains **lactose**. If you have been told by your doctor that you have an intolerance to some sugars, **contact your doctor before** taking this medicine.

3. HOW TO TAKE NEBILET PLUS

Always take Nebilet Plus exactly as your doctor has told you. You should check with your doctor if you are not sure.

Take 1 tablet a day with some water, preferably at the same time of day.
Nebilet Plus may be taken before, during or after a meal, but you can take it independently of meals.

Do not give Nebilet Plus to children or adolescents.

If you take more Nebilet Plus than you should

If you accidentally take an overdose of this medicine, tell your doctor or pharmacist **immediately**. The most frequent symptoms and signs of overdose are very slow heart beat (bradycardia), low blood pressure with possible fainting, breathlessness such as in asthma, acute heart failure, excessive urination with consequent dehydration, nausea and somnolence, muscle spasms, heart rhythm disturbances (especially if you are also taking digitalis or medicines for heart rhythm problems).

If you forget to take Nebilet Plus

If you forget a dose of Nebilet Plus, but remember a little later on that you should have taken it, take that day's dose as usual. However, if a long delay has occurred (e.g. several hours), so that the next due dose is near, skip the forgotten dose and take the next, scheduled, normal dose at the usual time. Do not take a double dose. Repeated skipping, however, should be avoided.

If you stop taking Nebilet Plus

Always consult your doctor before stopping Nebilet Plus treatment.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Nebilet Plus can cause side effects, although not everybody gets them.

The following side effects have been reported with nebivolol:

Common side effects (affecting more than 1 person in every 100 treated but fewer than 1 person in every 10 treated):

- headache
- dizziness
- tiredness
- an unusual burning, pricking, tickling, or tingling sensation
- diarrhoea
- constipation
- nausea
- shortness of breath
- swollen hands or feet.

Uncommon side effects (affecting more than 1 person in every 1,000 treated, but fewer than 1 person in every 100 treated):

- slow heartbeat or other heart complaints
- low blood pressure
- cramp-like leg pains on walking
- abnormal vision
- impotence
- feelings of depression
- digestive difficulties, gas in stomach or bowel, vomiting
- skin rash, itchiness
- breathlessness such as in asthma, due to sudden cramps in the muscles around the airways (bronchospasm)
- nightmares.

Very rare side effects (affecting fewer than 1 person in every 10,000 treated):

- fainting
- worsening of psoriasis (a skin disease characterised by scaly pink patches).

The following side effects have been reported only in some isolated cases:

- whole-body allergic reactions, with generalised skin eruption (hypersensitivity reactions); rapid-onset swelling, especially around the lips, eyes, or of the tongue with possible sudden difficulty breathing (angioedema).

The following side effects have been reported with hydrochlorothiazide:

Allergic reactions

- whole-body allergic reaction (anaphylactic reaction)

Heart and circulation

- heart rhythm disturbances, palpitations
- changes in the electrocardiogram
- sudden fainting when standing upright, formation of blood clots in veins (thrombosis) and embolism, circulatory collapse (shock)

Blood

- changes in the number of blood cells, such as: decreased white blood cells, decreased blood platelets, decreased red blood cells; impaired production of new blood cells by the bone marrow
- altered levels of body fluids (dehydration) and blood chemicals, in particular decreased potassium, decreased sodium, decreased magnesium, decreased chlorine and increased calcium
- increased uric acid levels, gout, increased blood glucose, diabetes, metabolic alkalosis (a disorder of metabolism), increased blood cholesterol and/or triglycerides

Stomach and gut

- lack of appetite, dry mouth, nausea, vomiting, stomach discomfort, abdominal pain, diarrhoea, fewer bowel movements (constipation), absence of bowel movements (ileus paralytic), flatulence
- inflammation of the glands that produce saliva, inflammation of the pancreas, increased blood amylase level (a pancreatic enzyme)
- yellowing of the skin (jaundice), inflammation of the gall bladder

Chest

- respiratory distress, lung inflammation (pneumonitis), formation of fibrous tissue in the lungs (interstitial lung disease), fluid accumulation in the lung (pulmonary oedema)

Nervous system

- vertigo (spinning sensation)
- convulsions, depressed level of consciousness, coma, headache, dizziness
- apathy, confusional state, depression, nervousness, restlessness, sleep disturbances
- unusual burning, pricking, tickling, or tingling skin sensations
- muscle weakness (paresis)

Skin and hair

- itchiness, purple spots/blotches on the skin (purpura), hives (urticaria), increased sensitivity of your skin to sunlight, rash, facial rash and/or patchy redness that can cause scarring (cutaneous lupus erythematosus), inflammation of blood vessels with consequent death of tissue (vasculitis necrotising), peeling, redness, loosening, and blistering of the skin (toxic epidermal necrolysis)

Eyes and ears

- yellow vision, blurred vision, worsening of myopia, decreased tear production

Joint and muscles

- muscle spasm, muscle pain

Urinary

- kidney dysfunction, acute kidney failure (reduced urine production and build-up of fluid and wastes in your body), inflammation of the connective tissue within the kidneys (interstitial nephritis), sugar in the urine.

Sexual

- Erection disturbances

General/Other

- General weakness, tiredness, fever, thirst

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE NEBILET PLUS

Keep out of the reach and sight of children.

This medicinal product does not require any special storage condition.

Do not take Nebilet Plus after the expiry date ('EXP') which is stated on the box and on the blister pack.

The expiry date refers to the last day of that month.

Nebilet Plus should not be disposed of via wastewater or household waste.

Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Nebilet Plus contains

- The active substance is nebivolol 5 mg (as nebivolol hydrochloride: 2.5 mg of d-nebivolol and 2.5 mg of l-nebivolol) and 12.5 mg of hydrochlorothiazide
- The other ingredients are:
 - tablet core: lactose monohydrate, polysorbate 80 (E433), hypromellose (E464), maize starch, croscarmellose sodium (E468), cellulose microcrystalline (E460), silica colloidal anhydrous (E551), magnesium stearate (E572)
 - coating: macrogol 40 stearate Type I, titanium dioxide (E171), carmines (carminic acid aluminium lake, E120), hypromellose (E464), cellulose microcrystalline (E460).

What Nebilet Plus looks like and contents of the pack

Nebilet Plus is available as almost pink, round, slightly biconvex film-coated tablets with "5/12.5" embossed on one side and a score line on the other side in packs of 7, 14, 28, 30, 56, 90 film-coated tablets.

The break-mark is only to facilitate breaking for ease of swallowing and not to divide the tablets into equal doses.

Tablets are provided in blisters (PP/COC/PP/Aluminium blister).

(Not all pack sizes may be marketed)

Marketing Authorisation Holder

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