

Package leaflet: Information for the user

Twilev 2.5 mg/5 mg film-coated tablets

Twilev 5 mg/5 mg film-coated tablets

Twilev 10 mg/5 mg film-coated tablets

ramipril/nebivolol

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- 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 only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Twilev is and what it is used for
2. What you need to know before you take Twilev
3. How to take Twilev
4. Possible side effects
5. How to store Twilev
6. Contents of the pack and other information

1. What Twilev is and what it is used for

Twilev contains two active substances called nebivolol and ramipril. Both of these substances help to control your high blood pressure:

- ramipril belongs to a group of substances called “ACE-inhibitors” (Angiotensin Converting Enzyme Inhibitors). Ramipril decreases your body’s production of substances that could raise your blood pressure. It also makes your blood vessels relax and widen, which contributes to lower blood pressure.
- 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, controls heart pumping strength. It also exerts a dilating action on blood vessels, which contributes to lower blood pressure.

Twilev is used to treat high blood pressure in adult patients who already receive ramipril and nebivolol from separate tablets at the same doses.

2. What you need to know before you take Twilev

Do not take Twilev:

- if you are allergic to nebivolol or any other beta-blocker, to ramipril or any other ACE-inhibitor, or to any of the other ingredients of this medicine (listed in section 6).
- if you have liver problems
- if you have heart failure, which has just occurred or which has recently become worse, or you are receiving treatment by intravenous drip feed for circulatory shock due to acute heart failure to help your heart work
- if you have certain serious heart rhythm problems (e.g. 2nd and 3rd degree atrioventricular block, heart conduction disorders)
- if you have very slow heartbeat (less than 60 beats per minute)
- if you have very low or unstable blood pressure. Your doctor will need to make this

assessment.

- if you have asthma or wheezing (now or in the past)
- if you have serious circulation problems in the arms or legs
- if you have untreated phaeochromocytoma (a tumour located in the adrenal glands, which are located on top of the kidneys)
- if you have a metabolic disorder (metabolic acidosis)
- if you have ever had a serious allergic reaction called “angioedema”. The signs include itching, hives (urticaria), red marks on the hands, feet and throat, swelling of the throat and tongue, swelling around the eyes and lips, difficulty breathing and swallowing
- during the last 6 months of pregnancy (see section below on “Pregnancy and breast-feeding”)
- if you are treated with a blood pressure lowering medicine containing aliskiren and have concomitantly diabetes or impaired kidney function
- if you are having dialysis or blood filtration by any other method. Depending on the machine used, Twilev may not be suitable for you
- if you have kidney problems where the blood supply to your kidney is reduced (renal artery stenosis)
- if you have taken or are currently taking sacubitril/valsartan, a medicine used to treat a type of long-term (chronic) heart failure in adults

Do not take Twilev if any of the above conditions apply or have applied to you. If you are not sure, talk to your doctor before taking Twilev.

Warnings and precautions

Talk to your doctor or pharmacist before taking Twilev

In particular, tell your doctor if you:

- have untreated chronic heart failure, or any other heart conditions, including a type of chest pain due to spontaneously occurring heart cramp which is called “Prinzmetal angina” or have 1st degree heart block (a kind of light heart conduction disorder that affects heart rhythm)
- have abnormally slow heartbeat
- have poor circulation in the arms or legs, e.g. Raynaud’s disease or syndrome, cramp-like pains when walking
- have diabetes: this medicine has no effect on blood sugar, but it could conceal the warning signs of a low sugar level (e.g. palpitations, fast heartbeat) and could increase the risk of severe hypoglycaemia when used with certain type of antidiabetic drugs called sulfonylureas (e.g. gliquidone, gliclazide, glibenclamide, glipizide, glimepiride or tolbutamide)
- have overactive thyroid gland: this medicine may mask the signs of an abnormally fast heart rate due to this condition
- have prolonged breathing problems
- have psoriasis (a skin disease - scaly pink patches) or if you have ever had psoriasis
- have allergy: this medicine may intensify your reaction to pollen or other substances you are allergic to
- are going to receive an anaesthetic. This may be given for an operation or any dental work. Always inform your anaesthetist or ask your doctor for advice as you may need to stop your treatment with Twilev one day beforehand
- have liver or kidney problems
- have lost a lot of body salts or fluids (through being sick (vomiting), having diarrhoea, sweating more than usual, being on a low salt diet, taking diuretics (water tablets) for a long time or having had dialysis)
- are going to have treatment to reduce your allergy to bee or wasp stings (desensitization)
- have high amounts of potassium in your blood (shown in blood test results)
- are taking medicines or have conditions which may decrease sodium levels in your blood. Your doctor may carry out regular blood tests, particularly for checking the levels of sodium in your blood especially if you are elderly
- are taking medicines that may increase the risk of angioedema, a serious allergic reaction, such as mTOR inhibitors (e.g. temsirolimus, everolimus, sirolimus), vildagliptin, neprilysin

(NEP) inhibitors (such as racecadotril) or sacubitril/valsartan. For sacubitril/valsartan, see section 2 'Do not take Twilev'

- have collagen vascular disease such as scleroderma or systemic lupus erythematosus
- think that you are (or might become) pregnant. Twilev is not recommended in the first 3 months of pregnancy and may cause serious harm to your baby after 3 months of pregnancy (see section below on "Pregnancy and breast-feeding")
- are of Black ethnicity, as there is a higher risk of angioedema, and the medication may be less effective in lowering blood pressure than in patients of other ethnicities
- are taking any of the following medicines used to treat high blood pressure:
 - an angiotensin II receptor blocker (ARBs) (also known as sartans-for example valsartan, telmisartan, irbesartan), in particular if you have diabetes-related kidney problems.
 - aliskiren

Your doctor may check your kidney function, blood pressure, and the amount of electrolytes (e.g. potassium) in your blood at regular intervals.

See also information under the heading 'Do not take Twilev'

Children and adolescents

Because of the lack of data on the use of the product in children and adolescents under the age of 18, **Twilev** is not recommended for use in them.

Other medicines and Twilev

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is because Twilev can affect the way some other medicines work. Also, some medicines can affect the way Twilev works. This interaction may make one or both medicines less effective, or it may increase the risk or severity of side effects.

In particular, tell your doctor if you are taking any of the following medicines:

- **Medicines for controlling blood pressure or heart conditions** (such as amiodarone, cibenzoline, clonidine, digoxin, diltiazem, disopyramide, felodipine, flecainide, guanfacin, hydroquinidine, lacidipine, lidocaine, methyldopa, mexiletine, moxonidine, nicardipine, nifedipine, nimodipine, nitrendipine, procainamide, propafenone, quinidine, rilmenidine, verapamil).
- **Other medicines for high blood pressure** including an angiotensin II receptor blocker (ARB) or aliskiren (see also information under the headings "Do not take Twilev" and "Warnings and precautions"), or diuretics (water tablets) such as furosemide.
- **Medicines which can increase the amount of potassium** in your blood, such as spironolactone, triamterene, amiloride, potassium salts, trimethoprim alone or in combination with sulfamethoxazole (for infections) and heparin (for thinning blood).
- Medicines such as **ephedrine**, **noradrenaline** or **adrenaline**, used for the treatment of low blood pressure, shock, cardiac failure, asthma or allergies. Your doctor will need to check your blood pressure.
- **Medicines used to treat diarrhea** (such as racecadotril).
- **Medicines containing sacubitril and valsartan** – used for treating a type of long term (chronic) heart failure in adults (see also information under the headings "Do not take Twilev" and "Warning and Precautions").
- **Lithium**, a medicine used to treat mental health problems.
- **Certain medicines for depression** such as amitriptyline, paroxetine, fluoxetine.
- **Barbiturates**, a group of medicine used as sedative and therapy for psychosis, but also for epilepsy, anxiety, insomnia and seizure disorders.
- **Phenothiazine**, a group of medicine used as sedative and therapy for psychosis, but also for vomiting and nausea.
- **Thioridazine**, a group of medicine used as sedative and therapy for psychosis.
- **Anesthetics** used in surgical procedures.
- **Immunosuppressant medicines** (medicines that reduces the body's immune response), such as ciclosporin, everolimus, sirolimus and tacrolimus, used to stop the rejection of organs after

a transplant.

- **Medicines for cancer**, including certain medicines used in chemotherapy such as temsirolimus and amifostine (a protective medicine used during chemotherapy).
- **Allopurinol**, used to lower the uric acid in your blood.
- **Medicines for asthma, blocked nose or certain eye disorders** such as glaucoma (increased pressure in the eye) or dilation (widening) of the pupil.
- **Baclofen**, used to treat muscle stiffness in diseases like multiple sclerosis.
- **Medicines for treating excessive stomach acid or ulcers** (antacid drug): you should take this Twilev during a meal and the antacid drug between meals.
- **Steroid medicines for inflammation** such as prednisolone.
- **Medicines for diabetes** such as insulin and oral antidiabetic medicines: Twilev may lower your blood sugar amounts, especially if taken with a group of antidiabetic drugs called sulfonylureas (see also information under the heading “Warning and Precautions”), and it could conceal the warning signs of a low sugar level (e.g. palpitations, fast heartbeat). Check your blood sugar amounts closely while taking this medicine.
- **Medicines used to relieve pain and inflammation** (e.g. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) such as ibuprofen or indomethacin and aspirin).

If any of the above apply to you (or you are not sure), talk to your doctor before taking Twilev.

Twilev with food and drink and alcohol

Twilev can be taken with food or on an empty stomach.

Take care when drinking alcohol while you are taking Twilev, as you may feel faint or dizzy. If this happens to you, do not drink any alcohol, including wine, beer or alcopop (beverage containing fruit juices or other flavours and with a low alcohol content).

Pregnancy and breast-feeding

Pregnancy

Inform your doctor if you are pregnant, if you think you may be pregnant or are planning to have a baby. Your doctor will normally advise you to stop taking Twilev before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of this medicine. You should not take Twilev in the first 12 weeks of pregnancy and you must not take them at all from the 13th week as their use during pregnancy may possibly be harmful to the baby. In case of use during the first 12 weeks of pregnancy, careful monitoring of the condition of the fetus and the newborn may be necessary.

Breast-feeding

If you are breast-feeding or about to start breast-feeding ask your doctor for advice before taking this medicine. Twilev is not recommended for mothers who are breast-feeding, and your doctor may choose another treatment for you if you wish to breast-feed.

Driving and using machines

Twilev may affect your ability to drive or use machines. If the medicine makes you feel sick, dizzy or tired, or gives you a headache, do not drive or use machines and contact your doctor immediately.

This medicine contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially ‘**sodium-free**’.

3. How to take Twilev

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is one tablet daily, preferably at the same time each day.

Twilev may be taken before, during or after the meal, but, alternatively, you can take it independently of meals. The tablet is best taken with some water, without being chewed.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

If you take more Twilev 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 low blood pressure with fainting (hypotension) with possible increased heart rate (reflex tachycardia), very slow heart beat (bradycardia), changes in blood chemical (electrolytes), kidney disfunction, breathlessness such as in asthma (bronchospasm), and acute heart failure.

If you forget to take Twilev

If you forget a dose of Twilev, 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 to make up for a forgotten tablet. Repeated skipping, however, should be avoided.

If you stop taking Twilev

Always consult your doctor before stopping Twilev treatment.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Stop taking Twilev and see a doctor straight away, if you notice any of the following serious side effects - you may need urgent medical treatment:

- Swelling of the face, lips or throat which make it difficult to swallow or breathe, as well as itching and rashes. This could be a sign of a severe allergic reaction to Twilev
- Severe skin reactions including rash, ulcers in your mouth, worsening of a pre-existing skin disease, reddening, blistering or detachment of skin (such as Stevens-Johnson syndrome, toxic epidermal necrolysis or erythema multiforme).

Tell your doctor immediately if you experience:

- Faster heart rate, uneven or forceful heartbeat (palpitations), chest pain, tightness in your chest or more serious problems including heart attack and stroke
- Shortness of breath or a cough. These could be signs of lung problems
- Bruising more easily, bleeding for longer than normal, any sign of bleeding (e.g. bleeding from the gums), purple spots blotching on the skin or getting infections more easily than usual, sore throat and fever, feeling tired, faint, dizzy or having pale skin.
These can be signs of blood or bone marrow problems.
- Severe stomach pain which may reach through to your back. This could be a sign of pancreatitis (inflammation of the pancreas)
- Fever, chills, tiredness, loss of appetite, stomach pain, feeling sick, yellowing of your skin or eyes (jaundice).
These can be signs of liver problems such as hepatitis (inflammation of the liver) or liver damage.

The following other side effects have been reported. If any of these cause you problems, you should contact your doctor.

Other possible side effects with Twilev:

Common side effects (may affect up to 1 in 10 people):

- fatigue
- hypotension (abnormally low blood pressure), especially when you stand or sit up quickly
- inflammation of your sinuses (sinusitis) or bronchitis
- stomach, gut or abdominal pain
- indigestion
- nausea
- vomiting
- altered bowel habits (including diarrhoea and constipation)
- headache
- burning, crawling, itching, numbness, prickling, "pins and needles", or tingling feelings
- cramps or pain in muscles
- swollen hands or feet (oedema)
- blood tests showing more potassium than usual in your blood.

Uncommon side effects (may affect up to 1 in 100 people):

- slow heartbeat or other heart complaints
- cramp-like leg pains on walking
- feelings of depression, anxious, more nervous than usual or restless
- breathlessness such as in asthma, due to sudden cramps in the muscles around the airways (bronchospasm) or worsening of asthma
- blocked nose
- nightmares
- sleep problems
- increased or irregular heartbeats
- heart failure
- dry mouth
- heartburn
- flatulence
- an increased number of certain white blood cells (eosinophilia) found during a blood test
- loss or decrease of appetite (anorexia)
- balance problems (vertigo)
- loss or change in the way things taste
- blurred vision
- flushing
- blood tests showing changes in the way your liver, pancreas or kidneys are working
- a swelling in your gut called "intestinal angioedema" presenting with symptoms like abdominal pain, vomiting and diarrhea
- sweating more than usual
- pain in your joints
- passing more water (urine) than usual over the day
- sexual inability in men, reduced sexual desire in men or women

Rare side effects (may affect up to 1 in 1,000 people):

- feeling shaky or confused
- blood tests showing a decrease in the number of red blood cells, white blood cells or platelets or in the amount of haemoglobin
- disturbed hearing and ringing in your ears
- red, itchy, swollen or watery eyes
- red and swollen tongue
- nail problem (e.g. loosening or separation of a nail from its bed)
- weakness

Very rare side effects (may affect up to 1 in 10,000 people):

- worsening of psoriasis (a skin disease - scaly pink patches)
- being more sensitive to the sun than usual

Not known (frequency cannot be estimated from the available data):

- blood tests showing too few blood cells in your blood
- blood tests showing less sodium than usual in your blood
- concentrated urine (dark in colour), feel or are sick, have muscle cramps, confusion and fits which may be due to inappropriate ADH (anti-diuretic hormone) secretion. If you have these symptoms contact your doctor as soon as possible
- difficulty concentrating
- slowed or impaired reactions
- burning sensation
- change in the way things smell
- fingers and toes changing colour when you are cold and then tingling or feeling painful when you warm up (Raynaud's phenomenon)
- hair loss
- breast enlargement in men

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Twilev

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and blister after EXP. The expiry date refers to the last day of that month.

Do not store above 30°C.

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

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Twilev contains

- The active substances are ramipril and nebivolol (as nebivolol hydrochloride).
Twilev 2.5 mg/5 mg: each film-coated tablet contains 2.5 mg of ramipril and 5 mg of nebivolol (as nebivolol hydrochloride).
Twilev 5 mg/5 mg: each film-coated tablet contains 5 mg of ramipril and 5 mg of nebivolol (as nebivolol hydrochloride).
Twilev 10 mg/5 mg: each film-coated tablet contains 10 mg of ramipril and 5 mg nebivolol (as nebivolol hydrochloride).
- The other ingredients are:
Tablet core: Cellulose microcrystalline, croscarmellose sodium, maize starch, hypromellose, polysorbate 80, sodium stearyl fumarate.
Film-coating:
Twilev 2.5 mg/5 mg: OPADRY pink (composed of: Hypromellose, Titanium dioxide (E171), Macrogol, Red iron oxide (E172), Carmine (E120);
Twilev 5 mg/5 mg: OPADRY yellow (composed of: Hypromellose, Titanium dioxide (E171),

Macrogol, Yellow iron oxide (E172));
Twilev 10 mg/5 mg: OPADRY white (composed of: Hypromellose, Titanium dioxide (E171), Macrogol).

What Twilev looks like and contents of the pack

Twilev 2.5 mg/5 mg film-coated tablets are pink, oval, film-coated plain on both sides.

Twilev 5 mg/5 mg film-coated tablets are yellow, oval, film-coated tablet with score line on one side and plain on the other.

Twilev 10 mg/5 mg film-coated tablets are white, oval, film-coated tablet with score lines on both sides.

Twilev is available in oPA/Alu/PVC//Alu blisters.

Pack sizes of 14, 28, 30, 56, 60, 84, 90 film-coated tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

MENARINI INTERNATIONAL O.L.S.A..

1, Avenue de la Gare, L-1611

Luxembourg.

Manufacturer

Menarini Manufacturing Logistic and Services Srl

Via Sette Santi, 3 50131

Firenze

Italy

Or

Saneca Pharmaceuticals, a.s.

Nitrianska 100, 920 27

Hlohovec,

Slovak Republic

This medicine is authorised in the Member States of the European Economic Area under the following names:

Estonia, Austria, Belgium, Bulgaria, Croatia, France, Greece, Hungary, Ireland, Latvia, Lithuania, Luxembourg, Poland, Romania, Slovak Republic, Spain: Twilev

Czech Republic: Nebotruv

Italy, Slovenia: Ezerdence

Portugal: Nebopek

This leaflet was last revised in 02/2026