

**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE
PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986**

The medicine is dispensed with a doctor's prescription only

Duplex 5/80

Coated Tablets

Composition:

Each tablet contains:
Amlodipine (as
besilate) 5 mg
Valsartan 80 mg

Duplex 5/160

Coated Tablets

Composition:

Each tablet contains:
Amlodipine (as
besilate) 5 mg
Valsartan 160 mg

Duplex 10/160

Coated Tablets

Composition:

Each tablet contains:
Amlodipine (as
besilate) 10 mg
Valsartan 160 mg

Inactive ingredients: See section 6 "Further information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

For treatment of essential hypertension.

Duplex is indicated for patients whose blood pressure is not adequately controlled on monotherapy.

Therapeutic group:

Amlodipine – calcium channel blocker.

Valsartan – angiotensin II receptor antagonist.

Duplex tablets contain two substances called amlodipine and valsartan. These two substances are intended for the treatment of hypertension in adults, when treatment with each ingredient separately does not provide satisfactory results.

- Amlodipine belongs to a group of substances called "calcium channel blockers". Amlodipine stops calcium from penetrating into the walls of the blood vessels, which prevents blood vessels from tightening.
- Valsartan belongs to a group of substances called "angiotensin II receptor antagonists". Angiotensin II is a substance produced by the body and causes the blood vessels to tighten, thus increasing the blood pressure. Valsartan works by blocking the effect of angiotensin II.

Both substances help prevent the blood vessels from tightening. As a result, the blood vessels relax and blood pressure is lowered.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to amlodipine or to any one of the other calcium channel blockers. This may manifest in itching, redness of the skin or breathing difficulties.

- You are sensitive (allergic) to valsartan or to any one of the additional ingredients contained in the medicine (detailed in section 6 “Further information”). If you think you may be allergic, refer to the doctor before taking **Duplex**.
- You have severe liver problems, or bile problems such as biliary cirrhosis or obstruction of biliary flow in the liver.
- You are more than three months pregnant (it is also advisable to avoid **Duplex** in early pregnancy, see the “Pregnancy, breastfeeding and fertility” section).
- You have severe low blood pressure (hypotension).
- You have narrowing of the aortic valve (aortic stenosis) or cardiogenic shock (a condition where your heart is unable to supply enough blood to the body).
- You suffer from heart failure after a heart attack.
- You have diabetes or impaired kidney function and you are being treated with an antihypertensive medicine containing aliskiren.

If any of these sections apply to you, tell your doctor before taking Duplex.

Special warnings regarding use of the medicine

Before treatment with Duplex, tell the doctor if:

- You are sick (vomiting or diarrhea).
- You have liver or kidney problems.
- You underwent a kidney transplant or have been diagnosed as suffering from narrowing of the renal arteries.
- You have a problem affecting adrenal gland function, called primary hyperaldosteronism.
- You have heart failure or have previously had a heart attack. Carefully follow the doctor’s instructions regarding the starting dosage. The doctor may also check your kidney function.
- A doctor has diagnosed that you are suffering from a narrowing of valves in the heart (aortic or mitral stenosis), or abnormal thickening of the heart muscle (obstructive hypertrophic cardiomyopathy).
- You have ever had swelling, mainly of the face and throat, while taking other medicines (including ACE inhibitors). If these symptoms apply to you, **stop taking Duplex and refer to your doctor immediately. In this case, never take Duplex again.**
- You experience abdominal pain, nausea, vomiting or diarrhea after taking **Duplex**. Your doctor will decide whether to continue the treatment. Do not stop taking **Duplex** by your own decision.
- You are taking any of the following medicines used to treat high blood pressure:
 - ACE inhibitors (for example: enalapril, lisinopril, ramipril), in particular if you have diabetes-related kidney problems.
 - Aliskiren.

Children and adolescents

Duplex is not recommended for children and adolescents under 18 years of age.

Tests and follow-up

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

See additional information in this section “Do not use the medicine if”.

If any of these sections apply to you, inform the doctor before taking Duplex.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, inform the doctor or pharmacist.

Your doctor may need to change the dosage or take other precautions; in some cases, you may have to stop taking one of the medicines.

Especially, inform the doctor or pharmacist if you are taking medicines from the following groups:

- ACE inhibitors or aliskiren (see information in section 2 “Do not use the medicine if” and “Special warnings regarding use of the medicine”).
- Diuretics (a type of medicine that increases urine output).
- Lithium, a medicine used to treat certain types of depression.
- Potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium, or other substances that may increase potassium levels.
- Certain types of pain killers called non-steroidal anti-inflammatory drugs (NSAIDs) or selective cyclooxygenase 2 inhibitors (Cox-2 inhibitors). The doctor may also check your kidney function.
- Anticonvulsants (such as carbamazepine, phenobarbital, phenytoin, fosphenytoin, primidone preparations).
- A herbal extract for sedation – Hypericum perforatum (St. John’s wort).
- Nitroglycerin and other nitrates, or other medicines that belong to the vasodilator group.
- Medicines used to treat HIV/AIDS (such as ritonavir, indinavir, nelfinavir).
- Medicines used to treat fungal infections (such as ketoconazole, itraconazole).
- Medicines used to treat bacterial infections (such as rifampicin, erythromycin, clarithromycin, telithromycin).
- Verapamil, diltiazem (heart medicines).
- Simvastatin (a medicine used to lower cholesterol levels).
- Dantrolene (infusion for body temperature abnormalities).
- Tacrolimus (used to prevent transplant rejection by your body’s immune system).
- Medicines used to protect against transplant rejection (ciclosporin).

Use of the medicine and food

Do not consume grapefruits and grapefruit juice when taking **Duplex**. This is because grapefruits and grapefruit juice may increase the levels of the active ingredient amlodipine in the blood, which can cause an unexpected increase in the blood pressure-lowering effect. **Duplex** may be taken with or without food.

Pregnancy, breastfeeding and fertility

Pregnancy

You must inform your doctor if you think that you may be pregnant or if you may become pregnant. Your doctor will generally recommend that you stop taking **Duplex** before you become pregnant or as soon as you find out that you are pregnant and will recommend that you take another medicine instead of **Duplex**. **Duplex** is not recommended in early pregnancy (in the first three months of pregnancy), and **must not** be taken if you are more than three months pregnant, as it may cause serious harm to the unborn baby if used after the third month of pregnancy.

Breastfeeding

Tell your doctor if you are breastfeeding or are planning to start breastfeeding. **Small amounts of amlodipine pass into breast milk.** It is not recommended to take **Duplex** when breastfeeding, and your doctor may recommend another treatment for you if you wish to breastfeed, especially if the baby was just born or born prematurely.

Consult the doctor or pharmacist before using any medicine.

Driving and operating machinery

This medicine may cause dizziness and affect your ability to concentrate. Therefore, if you do not know how this medicine will affect you, do not drive, do not operate machinery and do not perform other activities that require concentration.

3. HOW SHOULD YOU USE THE MEDICINE?

Always take the preparation according to the doctor's instructions.

Check with the doctor or pharmacist if you are not sure about the dosage and treatment regimen of the preparation.

This will help to achieve the best results and reduce the risk of side effects.

The dosage and treatment regimen will be determined by the doctor only.

The usual dosage is generally one coated tablet per day:

- It is preferable to take the medicine at the same time each day.
- **Duplex** is intended for oral administration only.
- Swallow the tablets with a glass of water.
- **Duplex** can be taken with or without food. Do not take **Duplex** with grapefruit or with grapefruit juice.
- If necessary, the tablet can be halved for immediate use. There is no information regarding crushing or chewing the tablet.

Depending on your response to the treatment, the doctor may suggest a higher or lower dosage.

Do not exceed the recommended dose.

Duplex in the elderly (aged 65 and above)

Your doctor will exercise caution when increasing the dosage. If you have further questions regarding use of the medicine, ask your doctor or pharmacist.

If you accidentally take a higher dosage

If you took an overdose or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

Excess fluid may accumulate in your lungs (pulmonary edema) causing shortness of breath which may develop up to 24-48 hours after taking.

If you forget to take the medicine

If you forgot to take the medicine at the designated time, take a dose as soon as you remember. Then, take the next dose at the regular time. However, if it is almost time to take the next dose, do not take the forgotten dose. Do not take a double dose to make up for the forgotten dose. Take the next dose at the regular time and consult the doctor.

Adhere to the treatment regimen as recommended by the doctor.

Even if there is an improvement in your health, do not discontinue treatment with the medicine without consulting the doctor.

If you stop taking the medicine

Stopping **Duplex** treatment may cause worsening of your illness. Do not stop taking the medicine unless the doctor has instructed you to do so.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, the use of **Duplex** may cause side effects in some of the users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

There are serious side effects that require immediate medical treatment:

Few patients have experienced these serious side effects.

If any of the following side effects occurs refer to the doctor immediately:

Rare side effects – effects that occur in 1-10 users in 10,000:

An allergic reaction with symptoms such as rash, itching, swelling of the face or lips or tongue, breathing difficulties, low blood pressure (feeling faint, feeling dizzy).

Very rare side effects – effects that occur in less than one user in 10,000:

Intestinal angioedema: swelling in the intestine that occurs with symptoms such as abdominal pain, nausea, vomiting and diarrhea.

Additional side effects that may occur with Duplex:

Common side effects – effects that occur in 1-10 users in 100:

Flu; nasal congestion, sore throat and discomfort when swallowing; headache; swelling of the arms, palms of the hands, legs, ankles or soles of the feet; tiredness; weakness; redness and warm feeling of the face and/or the neck.

Uncommon side effects – effects that occur in 1-10 users in 1,000:

Dizziness; nausea and abdominal pain; dry mouth; drowsiness; tingling or numbness of the palms of the hands or soles of the feet; vertigo; fast heartbeat including palpitations; dizziness upon standing up; cough; diarrhea; constipation; skin rash; redness of the skin; joint swelling, back pain; pain in joints.

Rare side effects – effects that occur in 1-10 users in 10,000:

Anxiety; tinnitus; fainting; passing more urine than usual or feeling an increased urge to pass urine; inability to achieve or maintain an erection; sensation of

heaviness; low blood pressure with symptoms such as dizziness, light-headedness; excessive sweating; skin rash all over the body; itching; muscle spasms.

If any of the effects listed above affect you severely, refer to your doctor.

Additional side effects that have been reported upon use of amlodipine or valsartan when taken alone, that do not occur when using Duplex, or occur more frequently than when using Duplex:

Amlodipine

Refer to the doctor immediately if you experience any of these very rare and severe side effects after taking the medicine:

- Sudden wheezing, chest pain, shortness of breath or breathing difficulties.
- Swelling of the eyelids, face or lips.
- Swelling of the tongue and throat causing severe breathing difficulty.
- Severe skin reactions including severe skin rash, hives, generalized skin reddening, intense itching, blistering, skin peeling and swelling, inflammation of the mucosal tissue (Stevens-johnson syndrome, toxic epidermal necrolysis), or other allergic reactions.
- Myocardial infarction, irregular heart rate.
- Inflammation of the pancreas which may cause severe abdominal and back pain accompanied by a general unwell feeling.

The following side effects have been reported. If the following effects cause you problems or if they last for more than one week, refer to your doctor:

Common side effects – effects that occur in 1-10 users in 100: Dizziness, sleepiness, palpitations (awareness of heart beat), flushing, swelling of the ankles (edema), abdominal pain, nausea.

Uncommon side effects – effects that occur in 1-10 users in 1,000: Mood swings, anxiety, depression, insomnia, tremor, changes in sense of taste, fainting, loss of pain sensation, visual disturbances, visual impairment, ringing in the ears, low blood pressure, sneezing/runny nose caused by inflammation of the nasal tissue (rhinitis), indigestion, vomiting, hair loss, excessive sweating, itchy skin, skin discoloration, urination disorder, increased need to urinate at night, more frequent urination, inability to achieve an erection, discomfort or enlargement of the breasts in men, pain, malaise, muscle pain, muscle cramps, weight gain or loss.

Rare side effects – effects that occur in 1-10 users in 10,000: Confusion.

Very rare side effects – effects that occur in less than one user in 10,000: Decreased number of white blood cells, decreased number of blood platelets which may result in easily bruising or bleeding (red blood cell damage), excess blood sugar (hyperglycemia), swelling of the gums, abdominal bloating (gastritis), abnormal liver function, inflammation of the liver (hepatitis), yellowing of the skin (jaundice), increase in liver enzymes which may have an effect on certain medical tests, increased muscle tension (tone), inflammation of blood vessels occasionally accompanied by skin rash, sensitivity to light, disorders that combine stiffness, tremor and/or movement difficulties.

Valsartan

Side effects of unknown frequency (effects whose frequency has not yet been determined): Decrease in red blood cells, fever, sore throat or mouth

sores due to infections; spontaneous bleeding or bruising; high levels of potassium in the blood; abnormal liver test results; decreased renal function or a severe decrease in renal function; swelling mainly of the face and the throat; muscle pain; rash, purplish-red spots, fever; itching; allergic reactions; skin blisters (symptoms of a condition called dermatitis bullous).

If you experience these effects, refer to your doctor immediately!

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:

<http://sideeffects.health.gov.il/>

Additionally, you can report to "Unipharm Ltd.".

5. HOW TO STORE THE MEDICINE?

- Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- Store below 25°C and in a place protected from light.

6. FURTHER INFORMATION

In addition to the active ingredients, the medicine also contains:

Silicified microcrystalline cellulose, Crospovidone, Magnesium stearate, Colloidal silicon dioxide, White coating blend (HPMC 2910/hypromellose, Titanium dioxide, Macrogol/PEG), Brown coating blend (Hypromellose, Talc, Macrogel/PEG, Iron oxide yellow, Titanium dioxide, Iron oxide red, Iron oxide black).

There are packages containing 5, 10, 14, 15, 20, 28, 30 or 56 tablets. Not all package sizes may be marketed.

What the medicine looks like and the contents of the package:

Duplex 5/80 are round, film coated, biconvex pink-brown tablets, with a score line on one side.

Duplex 5/160 are round, film coated, biconvex light pink tablets, with a score line on one side.

Duplex 10/160 are round, film coated, biconvex, pink-brown tablets, with a score line on one side.

Registration holder and address: Unipharm Ltd., P.O. Box 16545, Tel Aviv, 6116401.

Manufacturer and address: Unipharm Ltd., "Mevo Carmel" Industrial Park.

Revised in March 2025.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

Duplex 5/80: 153 59 34303 01

Duplex 5/160: 152 73 34093 01

Duplex 10/160: 153 26 34298 01



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