PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986
The medicine is dispensed with a doctor's prescription only

Tritace Comp 2.5 mg / 12.5 mg Tablets
Tritace Comp 5 mg / 25 mg Tablets

SANOFI

Active ingredients:
Each **Tritace Comp 2.5 mg / 12.5 mg** tablet contains:
Ramipril 2.5 mg + Hydrochlorothiazide 12.5 mg
Each **Tritace Comp 5 mg / 25 mg** tablet contains:
Ramipril 5 mg + Hydrochlorothiazide 25 mg

Inactive ingredients: see section 2 ("Important information about some of the ingredients in this medicine") and section 6.

Read this 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 you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

This medicine is used to treat hypertension in patients whose blood pressure cannot be controlled by ramipril alone.
Therapeutic group: Antihypertensive, from the ACE inhibitor group + thiazide diuretic.

2. BEFORE USING THE MEDICINE

Do not use the medicine:
- if you are sensitive to ramipril, or to any other preparation from the ACE inhibitor group, or to hydrochlorothiazide, or to other thiazide diuretics, or to sulfonamides, or to any of the additional ingredients contained in the medicine (see section 6). The signs of an allergic reaction may include: rash, swallowing or breathing difficulties, swelling of the lips, face, throat or tongue.
- if you have suffered in the past from a severe allergic reaction called angioedema. The signs include: itching, hives (urticaria), red blotches on the hands, legs and neck, swelling of the throat and tongue, swelling around the eyes and lips, breathing and swallowing difficulties.
- if you have taken in the past or are taking sacubitril/valsartan, a medicine used to treat a type of chronic heart failure in adults.
- if you are undergoing dialysis or any other type of blood filtration. Depending on the type of machine in use, Tritace Comp may not be suitable for you.
- if you have severe liver problems.
- if you are suffering from abnormal salt levels (calcium, potassium, sodium) in your blood.
- if you are suffering from a kidney problem in which the blood supply to your kidney is reduced (renal artery stenosis).
- during the **last six months of pregnancy** (see "Pregnancy, breastfeeding and fertility" section below).
- if you are breastfeeding (see "Pregnancy, breastfeeding and fertility" section below).
- if you are suffering from diabetes or impaired kidney function and are being treated with a blood pressure lowering medicine containing aliskiren.

Do not take Tritace Comp if any of the aforementioned apply to you. If you are uncertain, consult your doctor before taking Tritace Comp.

Special warnings regarding use of the medicine:

Before treatment with the medicine, tell the doctor if:
- you are suffering from heart, liver or kidney problems.
- you lost a large amount of salts or fluids (as a result of vomiting, diarrhea, increased sweating, low-salt diet, taking diuretics for a prolonged period or if you have undergone dialysis).
- you are about to undergo treatment to reduce allergy to bee or wasp stings (desensitization).
- you are about to receive anesthetics during surgery or dental treatment. You may have to stop treatment with Tritace Comp one day beforehand; consult your doctor.
- your blood potassium level is high (as per blood test results).
- you are taking medicines that may lower your blood sodium level or you suffer from a medical condition that may lower your blood sodium level. Your doctor may refer you for periodic blood tests, particularly to test your blood sodium levels, especially if you are elderly.
- you are taking medicines that may increase the risk of a severe allergic reaction called angioedema, such as mTOR inhibitors (e.g., temsirolimus, everolimus, sirolimus), vildagliptin, neprilysin (NEP) inhibitors (such as racecadotril) or sacubitril/valsartan. For sacubitril/valsartan see also section "Do not use the medicine".
- you are suffering from connective tissue diseases such as scleroderma or systemic lupus erythematosus.
- you must tell your doctor if you think that you are pregnant (or might become pregnant). Tritace Comp is not recommended in the first 3 months of pregnancy and may cause serious harm to your baby after the third month of pregnancy (see "Pregnancy, breastfeeding and fertility" section below).
- you have a decrease in your vision or have eye pain. These could be symptoms of fluid accumulation in the vascular layer of the eye (choroidal effusion) or an increase of pressure in your eye (glaucoma) and can happen within hours to weeks of taking Tritace Comp. This can lead to permanent vision loss, if not treated. If you have had a penicillin or sulfonamide allergy in the past, you may be at higher risk of developing this. You should discontinue Tritace Comp treatment and seek prompt medical attention.
- you are taking any of the following medicines used to treat hypertension:
  - Angiotensin-II receptor blockers (also known as sartans – for example: valsartan, telmisartan, irbesartan) especially if you suffer from diabetes-related kidney problems.
  - Aliskiren.

  Your doctor may perform periodic tests of kidney function, blood pressure and the amount of electrolytes (e.g., potassium) in your blood.
  See also information under "Do not use the medicine" section.
- you have had skin cancer in the past or if you develop an unexpected skin lesion while using the medicine.
  Use of hydrochlorothiazide, particularly long-term use with high doses, may increase the risk of developing skin and lip cancer (non-melanoma-type skin cancer).
  Protect your skin from exposure to the sun and UV radiation while using Tritace Comp.

Children and adolescents
Tritace Comp is not recommended for use in children and adolescents below 18 years of age, since the efficacy and safety of Tritace Comp in these age groups have not yet been established.

If any of the aforementioned apply to you (or if you are uncertain), consult your doctor before taking Tritace Comp.

Tests and follow-up
Check with your doctor or pharmacist before using the medicine if:
- you are due to undergo a parathyroid function test. Tritace Comp might affect the results of the test.
- you are a sports person due to undergo an anti-doping test. Tritace Comp may result in a positive test result.

Drug interactions:
If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.
This is because Tritace Comp may affect the activity of other medicines and other medicines may affect the activity of Tritace Comp.

Tell your doctor if you are taking any of the following medicines. They can reduce the effectiveness of Tritace Comp:
- Medicines used to relieve pain and inflammation (e.g., NSAIDs such as ibuprofen or indomethacin and aspirin)
- Medicines for the treatment of low blood pressure, shock, heart failure, asthma or allergies such as ephedrine, noradrenaline or adrenaline. The doctor will need to monitor your blood pressure.

Tell your doctor if you are taking any of the following medicines. Combination with the following medicines may increase the chance of side effects:
- Sacubitril/valsartan – used for treating a type of chronic heart failure in adults (see also information in the "Do not use the medicine" section)
- Medicines used to relieve pain and inflammation (e.g., NSAIDs such as ibuprofen or indomethacin and aspirin)
- Medicines which may lower the amount of potassium in your blood, such as medicines for constipation, diuretics, amphotericin B (used for fungal infections) and ACTH (used to test adrenal glands functioning)
- Medicines to treat cancer (chemotherapy)
- Medicines for heart problems, including problems with your heart rate
- Medicines to prevent rejection of a transplant, such as cyclosporine
- Diuretics, such as furosemide
- Medicines which may 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)
- Steroids to treat inflammation, such as prednisolone
- Calcium supplements
- Allopurinol (used to lower the uric acid level in your blood)
- Procainamide (to treat heart rhythm problems)
- Cholestyramine (to lower the amount of fats in your blood)
- Carbamazepine (for epilepsy)
- Heparin (for thinning the blood)
- Temsirolimus (for cancer)
- Sirolimus, everolimus (for prevention of graft rejection)
- Vildagliptin (used for treating type 2 diabetes)
- Racecadotril (used against diarrhea)
- Your doctor may need to change the dosage and/or to take other precautions: If you are taking an angiotensin II receptor blocker (ARB) or aliskiren (see also information in sections "Do not take the medicine" and "Special warnings regarding use of the medicine")

Tell your doctor if you are taking any of the following medicines. Tritace Comp may affect their activity:
- Medicines for diabetes such as oral glucose-lowering medicines and insulin. Tritace Comp may lower your blood sugar level. Carefully monitor your blood sugar levels while taking Tritace Comp
- Lithium (for mental problems). Tritace Comp may increase the level of lithium in your blood. Your doctor must closely monitor your lithium level
- Muscle relaxants
- Quinine (for malaria)
- Medicines that contain iodine, these may be used in a hospital during a scan or X-ray
- Penicillin (for infections)
- Medicines to thin the blood that are administered orally, such as warfarin

If any of the above apply to you (or if you are uncertain), consult your doctor before taking Tritace Comp.

Use of the medicine and food
The medicine can be taken with or without food.

Use of the medicine and alcohol consumption
Drinking alcohol during the course of treatment with Tritace Comp may cause dizziness. Consult your doctor regarding the possibility of drinking alcohol during the course of treatment with Tritace Comp, since alcohol can have an additional effect on lowering blood pressure.

Pregnancy, breastfeeding and fertility
Pregnancy
You must tell your doctor if you think you are pregnant or might become pregnant.
Tritace Comp is not recommended in the first 12 weeks of pregnancy and must not be used at all from week 13, since it can cause harm to the baby.
If you become pregnant while on Tritace Comp, tell your doctor immediately. Switch to an alternative suitable treatment before a planned pregnancy.
Breastfeeding
Do not use Tritace Comp during breastfeeding.
Consult your doctor or the pharmacist before taking any medicine.

Driving and operating machinery
You may feel dizzy while taking Tritace Comp; this is more likely to occur at the beginning of treatment or when increasing the dosage. If this happens, do not drive or use any tools or machines.

Important information about some of the ingredients in this medicine

Tritace Comp contains sodium. This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say it is essentially "sodium-free".

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.
The dosage and treatment regimen will be determined by the doctor only.

Treatment of hypertension

Your doctor will adjust the dosage until control of your blood pressure is attained.

Elderly patients

Your doctor may lower the starting dosage and increase it slowly during the treatment.

Do not exceed the recommended dose.

Method of administration

- Take the tablet orally, at the same time every day, usually in the morning.
- Swallow the medicine with a liquid.
- Do not chew or crush the tablets.
- The Tritace Comp 2.5 mg / 12.5 mg and Tritace Comp 5 mg / 25 mg tablet can be halved on the score line to equal halves, and the half dose taken when needed.

If you accidentally took a higher dosage or if a child 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 so that the doctor will know what you took.
Do not drive by yourself; ask someone else to drive you or call for an ambulance.

If you forgot to take the medicine:

- If you forgot to take this medicine at the designated time, take the next dose at the regular time and consult a doctor.
- Do not take a double dose to make up for the forgotten dose!

Adhere to the treatment regimen as recommended by the doctor.
Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.
If you have further questions regarding use of the medicine, consult a doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Tritace Comp may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Discontinue treatment with Tritace Comp and refer to a doctor immediately if you experience any of the following serious side effects – you may need urgent medical treatment:

- Swelling of the face, lips or throat causing swallowing or breathing difficulties, as well as itching and rash. These can be signs of a severe allergic reaction to Tritace Comp
- A severe skin reaction including rash, mouth ulcers, worsening of a pre-existing skin disease, redness, blistering or detachment of the skin (such as Stevens-Johnson syndrome, toxic epidermal necrolysis or erythema multiforme).

Report to the doctor immediately if you experience any of the following side effects:

- Increased heart rate, forceful or uneven heartbeat (palpitations), chest pain, tightness in the chest or more serious problems such as heart attack or stroke
- Shortness of breath, coughing or fever lasting 2-3 days and reduced appetite; these could be signs of a lung problem, including inflammation of the lungs
- Bruising more easily, bleeding for longer than normal, any sign of bleeding (e.g., bleeding from the gums), purple spots, blotches on the skin or getting infections more easily than usual, sore throat and fever, feeling tired, fainting, dizziness or pallor. These can be signs of blood or bone marrow problems
- Severe abdominal pain which can radiate to the back. This could be a sign of pancreatitis
- Fever, chills, tiredness, loss of appetite, abdominal pain, nausea, yellowing of the skin or eyes (jaundice). These can be signs of liver problems such as hepatitis (inflammation of the liver) or liver damage
- Decrease in vision or pain in your eyes due to high pressure (possible signs of fluid accumulation in the vascular layer of the eye (choroidal effusion) or acute angle-closure glaucoma).

Additional side effects include:

Tell your doctor if any of the following effects worsen or last longer than a few days.

Common effects (occurring in up to 1 user in 10)

- Headache, feeling weak or tired
- Feeling dizzy – likely to happen at the beginning of Tritace Comp treatment or when the dosage of Tritace Comp is increased
- Dry tickly cough or bronchitis
- Blood tests showing higher blood sugar levels than usual. If you have diabetes, this may exacerbate your disease
- Blood tests showing higher uric acid or fat levels than usual in your blood
- Pain, redness and swelling of the joints.

Uncommon effects (occurring in up to 1 user in 100)

- Skin rash, with or without raised areas
- Flushing, fainting, lower blood pressure than usual, particularly when standing up or sitting up quickly
- Balance problems (vertigo)
- Itching and unusual skin sensation such as numbness, tingling, pricking, burning or paresthesia
- Loss of or change in the sense of taste
- Sleep problems
- Feeling depressed, anxious, more nervous or shaky than usual
- Blocked nose, inflammation of your sinuses (sinusitis), shortness of breath
- Inflammation of the gums, swollen mouth
- In the eyes – redness, itching, swelling or tearing
- Ringing in the ears
- Blurred vision
- Hair loss
- Chest pain
- Muscle pain
- Constipation, abdominal pain
- Indigestion or nausea
- Urinating more than usual over the day
- Sweating more than usual or feeling thirsty
- Decreased or loss of appetite
- Increased or irregular heartbeat
- Swelling of the arms and legs – can be a sign of the body retaining more fluids than usual
- Fever
- Impotence in men
- Blood test results showing a reduction in the number of red blood cells, white blood cells or platelets or in the amount of hemoglobin
- Blood test results indicating changes in function of the liver, pancreas or kidneys
- Blood test results showing a lower blood potassium level than usual.

Very rare effects (occurring in up to 1 user in 10,000)

- Vomiting, diarrhea or heartburn
- Red and swollen tongue or dry mouth
- Blood test results showing a higher than usual potassium level in your blood.

Other reported side effects:

Inform your doctor if any of the effects described below worsen or last longer than a few days.

- Concentration difficulties, feeling restless or confused
- Color change of the fingers and toes when you feel cold and then tingling or painful when you warm up. This may be a phenomenon called Raynaud's phenomenon
- Breast enlargement in men
- Blood clots
- Hearing disturbances
- Less secretion than usual of tears from the eyes
- Objects appearing yellow
- Dehydration
- Swelling, pain and redness of the cheeks (inflammation of the salivary glands)
- Swelling in the gut (intestinal angioedema), manifested by symptoms such as abdominal pain, vomiting or diarrhea
- Higher than normal sensitivity to sunlight
- Severe peeling of the skin, itchy, lumpy rash or other skin reactions such as reddish rash of the face or forehead
- Skin rash or bruises
- Blotches on the skin and sensation of cold in the extremities
- Nail problems (for instance, loosening or detachment of the nail from its bed)
- Musculoskeletal rigidity or inability to move your jaw
- Muscle weakness or cramps
- Reduced sexual desire in men or women
- Appearance of blood in the urine – this may be a sign of a kidney problem
- Higher than usual level of sugar in the urine
- Increase in certain white blood cells (eosinophilia), observed in blood tests
- Blood test results showing a deficiency of blood cells in your blood (pancytopenia)
- Blood test results showing a change in the level of salts, e.g., sodium, calcium, magnesium and chloride in your blood
- Concentrated urine (dark in color), nausea or vomiting, muscle cramps, confusion and fits, which can be the result of a disturbance in the secretion of the hormone that controls the excretion of urine (ADH). If you have these symptoms, refer to the doctor as soon as possible
- Slowed or impaired reactions
- Change in the way things smell
- Breathing difficulties or worsening of asthma
- Skin and lip cancer (Non-melanoma skin cancer).

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in this 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: https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants in order 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/tray (blister).
The expiry date refers to the last day of that month.

Storage conditions:

Storage at a temperature below 25°C.
Do not discard medicines in the sewage system or the household waste bin. Ask your pharmacist how to dispose of medicines that you no longer use. These measures will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredients, Tritace Comp 2.5 mg / 12.5 mg and Tritace Comp 5 mg / 25 mg also contain:
Pregelatinized starch, Microcrystalline cellulose, Hydroxypropylmethylcellulose, Sodium stearyl fumarate.
What the medicine looks like and the contents of the package:
The tablets are packed in a tray package (blister).
The **Tritace Comp 2.5 mg / 12.5 mg** tablets are oblong, white or almost white with a score line. **HNV** and the logo are debossed on each side.
The **Tritace Comp 5 mg / 25 mg** tablets are oblong, white or almost white with a score line. **HNW** and the logo are debossed on each side.
All the strengths are packaged in PVC/Aluminum trays (blisters) of 14 or 28 tablets.
Not all the package sizes may be marketed.
This leaflet does not contain all the information about the preparations. If you have any question or are not sure about something, please refer to your doctor.
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