

Package leaflet: Information for the patient

Tolucombi 40 mg/12.5 mg tablets

Tolucombi 80 mg/12.5 mg tablets

Tolucombi 80 mg/25 mg tablets

telmisartan/hydrochlorothiazide

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 Tolucombi is and what it is used for
2. What you need to know before you take Tolucombi
3. How to take Tolucombi
4. Possible side effects
5. How to store Tolucombi
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1. What Tolucombi is and what it is used for

Tolucombi is a combination of two active substances, telmisartan and hydrochlorothiazide in one tablet. Both of these substances help to control high blood pressure.

- Telmisartan belongs to a group of medicines called angiotensin II receptor antagonists. Angiotensin II is a substance produced in your body which causes your blood vessels to narrow thus increasing your blood pressure. Telmisartan blocks the effect of angiotensin II so that the blood vessels relax, and your blood pressure is lowered.
- Hydrochlorothiazide belongs to a group of medicines called thiazide diuretics, which cause your urine output to increase, leading to a lowering of your blood pressure.

High blood pressure, if not treated, can damage blood vessels in several organs, which could lead sometimes to heart attack, heart or kidney failure, stroke, or blindness. There are usually no symptoms of high blood pressure before damage occurs. Thus it is important to regularly measure blood pressure to verify if it is within the normal range.

Tolucombi (40 mg/12.5 mg, 80 mg/12.5 mg) is used to treat high blood pressure (essential hypertension) in adults whose blood pressure is not controlled enough when telmisartan is used alone. **Tolucombi (80 mg/25 mg) is used to** treat high blood pressure (essential hypertension) in adults whose blood pressure is not adequately controlled by Tolucombi 80 mg/12.5 mg or in patients who have been previously stabilised by telmisartan and hydrochlorothiazide given separately.

2. What you need to know before you take Tolucombi

Do not take Tolucombi:

- if you are allergic to telmisartan or any other ingredients of this medicine (listed in section 6).
- if you are allergic to hydrochlorothiazide or to any other sulfonamide-derived medicines.
- if you are more than 3 months pregnant. (It is also better to avoid Tolucombi in early pregnancy-see pregnancy section.)

- if you have severe liver problems such as cholestasis or biliary obstruction (problems with drainage of the bile from liver and the gall bladder) or any other severe liver disease.
- if you have severe kidney disease.
- if your doctor determines that you have low potassium levels or high calcium levels in your blood that do not get better with treatment.
- if you have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren.

If any of the above applies to you, tell your doctor or pharmacist before taking Tolucombi.

Warnings and precautions

Talk to your doctor before taking Tolucombi if you are suffering or have ever suffered from any of the following conditions or illnesses:

- Low blood pressure (hypotension), likely to occur if you are dehydrated (excessive loss of body water) or have salt deficiency due to diuretic therapy (water tablets), low-salt diet, diarrhoea, vomiting, or haemodialysis.
- Kidney disease or kidney transplant.
- Renal artery stenosis (narrowing of the blood vessels to one or both kidneys).
- Liver disease.
- Heart trouble.
- Diabetes.
- Gout.
- Raised aldosterone levels (water and salt retention in the body along with imbalance of various blood minerals).
- Systemic lupus erythematosus (also called “lupus” or “SLE”) a disease where the body’s immune system attacks the body.
- The active substance hydrochlorothiazide can cause an unusual reaction, resulting in a decrease in vision and eye pain. These could be symptoms of an increase of pressure in your eye and can happen within hours to weeks of taking Tolucombi. This can lead to permanent vision impairment, if not treated.
- If you have had skin cancer or if you develop an unexpected skin lesion during the treatment. Treatment with hydrochlorothiazide, particularly long term use with high doses, may increase the risk of some types of skin and lip cancer (non-melanoma skin cancer). Protect your skin from sun exposure and UV rays while taking Tolucombi.

Talk to your doctor before taking Tolucombi, if you are taking:

- digoxin.
- any of the following medicines used to treat high blood pressure:
 - an ACE-inhibitor (for example enalapril, lisinopril, ramipril), in particular if you have diabetes-related kidney problems.
 - aliskiren.

You must tell your doctor if you think you are (or might become) pregnant. Tolucombi is not recommended in early pregnancy, and must not be taken if you are more than 3 months pregnant, as it may cause serious harm to your baby if used at that stage (see pregnancy section).

Treatment with hydrochlorothiazide may cause electrolyte imbalance in your body. Typical symptoms of fluid or electrolyte imbalance include dry mouth, weakness, lethargy, drowsiness, restlessness, muscle pain or cramps, nausea (feeling sick), vomiting, tired muscles, and an abnormally fast heart rate (faster than 100 beats per minute). If you experience any of these you should tell your doctor.

You should also tell your doctor, if you experience an increased sensitivity of the skin to the sun with symptoms of sunburn (such as redness, itching, swelling, blistering) occurring more quickly than normal.

In case of surgery or anaesthetics, you should tell your doctor that you are taking Tolucombi.

Tolucombi may be less effective in lowering the blood pressure in black patients.

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 Tolucombi”.

Children and adolescents

The use of Tolucombi in children and adolescents up to the age of 18 years is not recommended.

Other medicines and Tolucombi

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Your doctor may need to change the dose of these other medications or take other precautions. In some cases you may have to stop taking one of the medicines. This applies especially to the medicines listed below taken at the same time with Tolucombi:

- Lithium containing medicines to treat some types of depression.
- Medicines associated with low blood potassium (hypokalaemia) such as other diuretics, ('water tablets'), laxatives (e.g. castor oil), corticosteroids (e.g. prednisone), ACTH (a hormone), amphotericin (an antifungal medicine), carbenoxolone (used to treat mouth ulcers), penicillin G sodium (an antibiotic), and salicylic acid and derivatives.
- Medicines that may increase blood potassium levels such as potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium, ACE inhibitors, cyclosporin (an immunosuppressant drug) and other medicinal products such as heparin sodium (an anticoagulant).
- Medicines that are affected by changes of the blood potassium level such as heart medicines (e.g. digoxin) or medicines to control the rhythm of your heart (e.g. quinidine, disopyramide, amiodarone, sotalol), medicines used for mental disorders (e.g. thioridazine, chlorpromazine, levomepromazine) and other medicines such as certain antibiotics (e.g. sparfloxacin, pentamidine) or certain medicines to treat allergic reactions (e.g. terfenadine).
- Medicines for the treatment of diabetes (insulins or oral agents such as metformin).
- Cholestyramine and colestipol, medicines for lowering blood fat levels.
- Medicines to increase blood pressure, such as noradrenaline.
- Muscle relaxing medicines, such as tubocurarine.
- Calcium supplements and/or vitamin D supplements.
- Anti-cholinergic medicines (medicines used to treat a variety of disorders such as gastrointestinal cramps, urinary bladder spasm, asthma, motion sickness, muscular spasms, Parkinson's disease and as an aid to anaesthesia) such as atropine and biperiden.
- Amantadine (medicine used to treat Parkinson's disease and also used to treat or prevent certain illnesses caused by viruses).
- Other medicines used to treat high blood pressure, corticosteroids, painkillers (such as non-steroidal anti-inflammatory drugs [NSAIDs]), medicines to treat cancer, gout, or arthritis.
- If you are taking an ACE-inhibitor or aliskiren (see also information under the headings “Do not take Tolucombi” and “Warnings and precautions”).
- Digoxin.

Tolucombi may increase the blood pressure lowering effect of other medicines used to treat high blood pressure or of medicines with blood pressure lowering potential (e.g. baclofen, amifostine). Furthermore, low blood pressure may be aggravated by alcohol, barbiturates, narcotics or antidepressants. You may notice this as dizziness when standing up. You should consult with your doctor if you need to adjust the dose of your other medicine while taking Tolucombi.

The effect of Tolucombi may be reduced when you take NSAIDs (non steroidal anti-inflammatory medicines, e.g. acetylsalicylic acid or ibuprofen).

Tolucombi with food and alcohol

You can take Tolucombi with or without food.

Avoid taking alcohol until you have talked to your doctor. Alcohol may make your blood pressure fall more and/or increase the risk of you becoming dizzy or feeling faint.

Pregnancy and breast-feeding

Pregnancy

You must tell your doctor if you think you are (or might become) pregnant. Your doctor will normally advise you to stop taking Tolucombi before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of Tolucombi. Tolucombi is not recommended during pregnancy, and must not be taken when more than 3 months pregnant, as it may cause serious harm to your baby if used after the third month of pregnancy.

Breast-feeding

Tell your doctor if you are breast-feeding or about to start breast-feeding. Tolucombi 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

Some people feel dizzy or tired when taking Tolucombi. If you feel dizzy or tired, do not drive or operate machinery.

Tolucombi contains lactose, sorbitol and sodium

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

Tolucombi 40 mg/12.5 mg contains 147.04 mg sorbitol in each tablet, which is equivalent to 5 mg/kg/day, if the body weight is 29.8 kg.

Tolucombi 80 mg/12.5 mg and Tolucombi 80 mg/25 mg contain 294.08 mg sorbitol in each tablet, which is equivalent to 5 mg/kg/day, if the body weight is 58.8 kg.

Patients weighing 58.8 kg or less must take into consideration that sorbitol is a source of fructose and if your doctor has told you that you (or your child) have an intolerance to some sugars or if you have been diagnosed with hereditary fructose intolerance (HFI), a rare genetic disorder in which a person cannot break down fructose, talk to your doctor before you (or your child) take or receive this medicine.

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

3. How to take Tolucombi

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 of Tolucombi is one tablet a day. Try to take a tablet at the same time each day. You can take Tolucombi with or without food. The tablets should be swallowed with some water or other non-alcoholic drink. It is important that you take Tolucombi every day until your doctor tells you otherwise.

If your liver is not working properly, the usual dose should not exceed 40 mg/12.5 mg once a day.

If you take more Tolucombi than you should

If you accidentally take too many tablets you may experience symptoms such as low blood pressure and rapid heartbeat. Slow heartbeat, dizziness, vomiting, reduced kidney function including kidney failure, have also been reported. Due to the hydrochlorothiazide component, markedly low blood pressure and low blood levels of potassium can also happen, which may result in nausea, sleepiness

and muscle cramps and/or irregular heartbeat associated with the concomitant use of drugs such as digitalis or certain anti-arrhythmic treatments. Contact your doctor, pharmacist, or your nearest hospital emergency department immediately.

If you forget to take Tolucombi

If you forget to take a dose, do not worry. Take it as soon as you remember then carry on as before. If you do not take your tablet on one day, take your normal dose on the next day. **Do not** take a double dose to make up for forgotten individual doses.

If you have 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.

Some side effects can be serious and need immediate medical attention:

You should see your doctor immediately if you experience any of the following symptoms:

Sepsis* (often called "blood poisoning"), is a severe infection with whole-body inflammatory response, rapid swelling of the skin and mucosa (angioedema); blistering and peeling of the top layer of skin (toxic epidermal necrolysis); these side effects are rare (may affect up to 1 in 1,000 people) or of unknown frequency (toxic epidermal necrolysis) but are extremely serious and patients should stop taking the medicine and see their doctor immediately.

If these effects are not treated they could be fatal. Increased incidence of sepsis has been observed with telmisartan only, however can not be ruled out for Tolucombi.

Possible side effects of Tolucombi:

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

Dizziness.

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

Decreased blood potassium levels, anxiety, fainting (syncope), sensation of tingling, pins and needles (paraesthesia), feeling of spinning (vertigo), fast heart beat (tachycardia), heart rhythm disorders, low blood pressure, a sudden fall in blood pressure when you stand up, shortness of breath (dyspnoea), diarrhoea, dry mouth, flatulence, back pain, muscle spasm, muscle pain, erectile dysfunction (inability to get or keep an erection), chest pain, increased blood uric acid levels.

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

Inflammation of the lung (bronchitis), activation or worsening of systemic lupus erythematosus (a disease where the body's immune system attacks the body, which causes joint pain, skin rashes and fever); sore throat, inflamed sinuses; feeling sad (depression), difficulty falling asleep (insomnia), impaired vision, difficulty breathing, abdominal pain, constipation, bloating (dyspepsia), feeling sick (vomiting), inflammation of the stomach (gastritis), abnormal liver function (Japanese patients are more likely to experience this side effect), redness of the skin (erythema), allergic reactions such as itching or rash, increased sweating, hives (urticaria), joint pain (arthralgia) and pain in extremities, muscle cramps, flu-like-illness, pain, low levels of sodium, increased levels of creatinine, hepatic enzymes or creatine phosphokinase in the blood.

Adverse reactions reported with one of the individual components may be potential adverse reactions with Tolucombi, even if not observed in clinical trials with this product.

Telmisartan

In patients taking telmisartan alone the following additional side effects have been reported:

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

Upper respiratory tract infection (e.g. sore throat, inflamed sinuses, common cold), urinary tract infections, deficiency in red blood cells (anaemia), high potassium levels, slow heart rate (bradycardia), kidney impairment including acute kidney failure, weakness, cough.

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

Low platelet count (thrombocytopenia), increase in certain white blood cells (eosinophilia), serious allergic reaction (e.g. hypersensitivity, anaphylactic reaction, drug rash), low blood sugar levels (in diabetic patients), upset stomach, eczema (a skin disorder), arthrosis, inflammation of the tendons, decreased haemoglobin (a blood protein), somnolence.

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

Progressive scarring of lung tissue (interstitial lung disease)**

* The event may have happened by chance or could be related to a mechanism currently not known.

** Cases of progressive scarring of lung tissue have been reported during intake of telmisartan. However, it is not known whether telmisartan was the cause.

Hydrochlorothiazide

In patients taking hydrochlorothiazide alone the following additional side effects have been reported:

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

Feeling sick (nausea), low blood magnesium level.

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

Reduction in blood platelets, which increases risk of bleeding or bruising (small purple-red marks in skin or other tissue caused by bleeding), high blood calcium level, headache.

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

Increased pH (disturbed acid-base balance) due to low blood chloride level.

Side effects of unknown frequency (frequency cannot be estimated from the available data):

Inflammation of the salivary gland, skin and lip cancer (Non-melanoma skin cancer), decreases in the number (or even lack) of cells in the blood, including low red and white blood cell count, serious allergic reactions (e.g. hypersensitivity, anaphylactic reaction), decreased or loss of appetite, restlessness, light-headedness, blurred or yellowing of vision, decrease in vision and eye pain (possible signs of acute myopia or acute-angle closure glaucoma), inflammation of blood vessels (vasculitis necrotising), inflamed pancreas, upset stomach, yellowing of the skin or eyes (jaundice), lupus-like syndrome (a condition mimicking a disease called systemic lupus erythematosus where the body's immune system attacks the body); skin disorders such as inflamed blood vessels in the skin, increased sensitivity to sunlight, rash, redness of the skin, blistering of the lips, eyes or mouth, skin peeling, fever (possible signs of erythema multiforme), weakness, kidney inflammation or impaired kidney function, glucose in the urine (glycosuria), fever, impaired electrolyte balance, high blood cholesterol levels, decreased blood volume, increased levels of glucose, difficulties in controlling blood/ urine levels of glucose in patients with a diagnosis of diabetes mellitus, or fat in the blood.

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 the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Tolucombi

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.

This medicinal product does not require any special temperature storage conditions. 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 Tolucombi contains

- The active substances are telmisartan and hydrochlorothiazide.
Each tablet contains 40 mg telmisartan and 12.5 mg hydrochlorothiazide.
Each tablet contains 80 mg telmisartan and 12.5 mg hydrochlorothiazide.
Each tablet contains 80 mg telmisartan and 25 mg hydrochlorothiazide.
- The other ingredients are: hydroxypropylcellulose, lactose monohydrate, magnesium stearate, mannitol, meglumine, povidone (K30), red ferric oxide (E172) – only in 40 mg/12.5 mg and 80 mg/12.5 mg tablets, silica colloidal anhydrous, sodium hydroxide (E524), sodium stearyl fumarate, sorbitol (E420) and yellow ferric oxide (E172) – only in 80 mg/25 mg tablets. See section 2 "Tolucombi contains lactose, sorbitol and sodium".

What Tolucombi looks like and contents of the pack

40 mg/12.5 mg tablets: White to almost white or pinkish white on one side and pink marbled on the opposite side of two-layer biconvex oval tablet, tablet dimensions 15 mm x 7 mm.

80 mg/12.5 mg tablets: White to almost white or pinkish white on one side and pink marbled on the opposite side of two-layer biconvex oval tablet, tablet dimensions 18 mm x 9 mm.

80 mg/25 mg tablets: White to yellowish white on one side and yellow marbled on the opposite side of two-layer biconvex oval tablet, tablet dimensions 18 mm x 9 mm.

Blisters (OPA/Al/PVC foil//Al foil): 14 x 1, 28 x 1, 30 x 1, 56 x 1, 60 x 1, 84 x 1, 90 x 1, 98 x 1 and 100 x 1 tablet in a box.

Blisters (OPA/Al/PE foil with desiccant//Al foil): 14 x 1 and 98 x 1 tablet in a box.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

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Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>