Package leaflet: Information for the user

Trinomia 100 mg/40 mg/10 mg hard capsules
Trinomia 100 mg/40 mg/5 mg hard capsules
Trinomia 100 mg/40 mg/2.5 mg hard capsules
Acetylsalicylic acid/atorvastatin /ramipril

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 Trinomia is and what it is used for

Trinomia capsules contain three substances called Acetylsalicylic acid, atorvastatin and ramipril.

- Acetylsalicylic acid belongs to a group of substances called antiplatelet agents that help prevent your blood cells sticking together and forming a blood clot.
- Atorvastatin belongs to a group of substances called statins, which are lipid (fat) regulating medicines that are used to lower lipids known as cholesterol and triglycerides in the blood when a low fat diet and life style changes on their own have failed. If you are at an increased risk of heart disease, atorvastatin can also be used to reduce such risk even if your cholesterol levels are normal. You should maintain a standard cholesterol lowering diet during treatment.
- Ramipril belongs to a group of substances called ACE inhibitors (Angiotensin Converting Enzyme Inhibitors) that works by decreasing your body's production of substances that could raise your blood pressure; making your blood vessels relax and widen and making it easier for your heart to pump blood around your body.

Trinomia is used as substitution therapy in adult patients adequately controlled with the three substances (acetylsalicylic acid, atorvastatin and ramipril) taken at the same time at equivalent doses, to minimise the risk of having a cardiovascular accident, in patients who have already suffered a previous cardiovascular event.

2. What you need to know before you take Trinomia

Do not take Trinomia:

- if you are allergic to acetylsalicylic acid , to other salicylates or to tartrazine (colouring agent). Signs of an allergic reaction may include a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue.
- if you are allergic to ramipril or to any other ACE inhibitor medicine
- if you are allergic to atorvastatin , to any similar medicines used to lower blood lipids or to any of the other ingredients of the medicine (listed in section 6).
- if you are allergic to to soya or peanut.
- if you have had asthma attacks or other hypersensitive reactions to certain medicines for pain, fever or inflammation (salicylates or other non-steroid anti-inflammatory drugs) in the past.
- if you have active, or history of recurrent peptic ulcer and/or gastric/intestinal haemorrhage, or other kinds of bleeding such as cerebrovascular haemorrhages if you have a high risk of bleeding (haemophilia).
- if you have heart disease that is not sufficiently controlled (severe heart failure).
- if you take 15 mg or more of methotrexate per week.
- if you have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren.
- if you have nasal polyps (inflamed swellings inside the nose) associated with asthma.
- if you have severe liver or kidney disease.
- if you have had any unexplained abnormal blood tests for liver function.
- if you are a woman able to have children and not using reliable contraception.
- if you are pregnant or trying to become pregnant.
- if you are breast-feeding.
- if you are taking:
    - HIV protease inhibitors such as tipranavir or ritonavir (medicines used in the treatment of HIV).
    - ciclosporin (a medicine often used in organ transplant patients).
- 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.
- if you are having dialysis or any other type of blood filtration. Depending on the machine that is used, Trinomia may not be suitable for you.
- if you have kidney problems where the blood supply to your kidney is reduced (renal artery stenosis).
- if your blood pressure is abnormally low or unstable. Your doctor will need to make this assessment.
- if you are under 18 years of age. In case of children under 16 years with fever, flu or chicken pox exist risk of Reye syndrome.
- if you use the combination of glecaprevir/pibrentasvir in the treatment of hepatitis C.
- 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, as the risk of angioedema (rapid swelling under the skin in an area such as the throat) is increased.
- If you are taking any of the following medicines, the risk of angioedema may be increased:
    - Racecadotril, a medicine used to treat diarrhoea;
    - Medicines used to prevent organ transplant rejection and for cancer (e.g., temsirolimus, sirolimus, everolimus).
    - Vildagliptin, a medicine used to treat diabetes.

In particular, talk to your doctor or pharmacist if you are taking, have recently taken or might take any of the following medicines:

Potassium supplements (including salt substitutes), potassium-sparing diuretics and other medicines that can increase the amount of potassium in your blood (e.g. trimethoprim and co-trimoxazole for infections caused by bacteria; ciclosporin, an immunosuppressant medicine used to prevent organ transplant rejection; and heparin, a medicine used to thin blood to prevent clots).

Warnings and precautions

Talk to your doctor or pharmacist before taking Trinomia:

- if you are allergic to other pain medicines or anti-inflammatory drugs, other medicines for fever, rheumatism other than acetylsalicylic acid or to other substances that cause allergies.
- if you have other allergies (for example skin reactions, itching, hives).
- if you have bronchial asthma, hay fever, swelling of the nasal mucous membranes or chronic lung diseases.
- before operations or small interventions such as tooth extraction, because there may be a greater tendency for bleeding. You may need to stop taking Trinomia for a short time.
- if you have had stomach or intestinal ulcers or bleeding in the past.
- if you are taking simultaneous treatment with medicines to prevent blood clotting, medicines for pain, fever or inflammation (non-steroid anti-inflammatory drugs e.g. ibuprofen), corticosteroids (used to treat allergy or inflammation), antidepressants e.g. Selective Serotonin Re-uptake Inhibitors (SSRIs).
- if you are taking or have taken in the last 7 days a medicine called fusidic acid, (a medicine for bacterial infection) orally or by injection. The combination of fusidic acid and Trinomia can lead to serious muscle problems (rhabdomyolysis).
- if you 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 Trinomia”.
- if you have or have ever had heart, liver or kidney problems. Trinomia may not be right for you.
- if you have a lack of glucose 6-phosphate dehydrogenase.
- if you are at risk for gout, because acetylsalicylic acid may reduce the excretion of uric acid. Under certain circumstances, this may cause an attack of gout.
- your doctor should do a blood test before you start taking Trinomia and regularly during the treatment. This is to check how well your liver is working.
- if you drink large amounts of alcohol.
- if you have severe respiratory failure.
- if you 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 for a long time or having had dialysis).
- if you are going to have treatment to reduce your allergy to bee or wasp stings (desensitization).
- if you have high amounts of potassium in your blood (shown in blood test results).
- if you have collagen vascular disease such as scleroderma or systemic lupus erythematosus.
- If you have or have had myasthenia (a disease with general muscle weakness including in some cases muscles used when breathing), or ocular myasthenia (a disease causing eye

muscle weakness) as statins may sometimes aggravate the condition or lead to the occurrence of myasthenia (see section 4).

Contact your doctor immediately if you experience unexplained muscle pain, tenderness or weakness. This is because on rare occasions, muscle problems can be serious, including muscle breakdown resulting in kidney damage; and very rare deaths have occurred.

Also tell your doctor or pharmacist if you have a muscle weakness that is constant. Additional tests and medicines may be needed to diagnose and treat this.

The risk of muscle breakdown is greater in certain patients. Tell your doctor if any of the following applies to you:

- o if you have had a previous stroke with bleeding into the brain, or have small pockets of fluid in the brain from previous strokes
- o you have kidney problems.
- o you have thyroid problems.
- o you have ever had muscle problems during treatment with other lipid-lowering medicines (e.g. other '-statin' or '-fibrate' medicines).
- o you or close family members have a hereditary muscle disorder.
- o you regularly consume large amounts of alcohol.
- o you are more than 70 years old.

If any of these apply to you, your doctor will need to carry out a blood test before and possibly during your treatment to predict your risk of muscle related side effects. The risk of muscle related side effects e.g rhabdomyolysis is known to increase when certain medicines are taken at the same time (see Section 2 "Other medicines and Trinomia").

While you are on this medicine your doctor will monitor you closely if you have diabetes or are at risk of developing diabetes. You are likely to be at risk of developing diabetes if you have high levels of sugars and fats in your blood, are overweight and have high blood pressure.

Generally, it is recommended to correct dehydration, hypovolaemia or salt depletion before initiating treatment (in patients with heart failure, however, such corrective action must be carefully weighed out against the risk of volume overload).

Other medicines and Trinomia

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is because Trinomia can affect the way some other medicines work. Also some medicines can affect the way Trinomia works.

Trinomia contains acetylsalicylic acid and this substance can affect the way some other medicines work. Also some medicines can affect the way acetylsalicylic acid works. Please tell your doctor if you are taking any of the following medicines that may increase the chance of getting side effects:

- Anticoagulation medicines (for example coumarin and heparin) and medicines that dissolve blood clots may increase the risk of bleeding. Pay careful attention to signs of inner and outer bleeding (for example bruises) before treatment with these medicines.
- Other inhibitors of platelet aggregation (medicines that inhibit the cohesion or sticking of blood platelets) like ticlopidin and clopidogrel may increase the risk of bleeding.
- Medicines that contain cortisone or substances equivalent to cortisone such as prednisolone (with the exception of products that are applied on the skin or in cortisone therapy for Addison's disease) increase the risk of undesirable effects in the gastrointestinal tract.

- Other medicines for pain or inflammation (non-steroid analgesics such as ibuprofen or indometacin) and other rheumatism medicines in general increase the risk of bleeding and gastrointestinal ulcers.
- Medicines to reduce the blood glucose level (antidiabetic drugs) may cause low blood glucose levels.
- Digoxin (medicine to strengthen the heart).
- Methotrexate (treatment of cancer and certain rheumatic diseases).
- Valproic acid for treatment of convulsions attacks (epilepsy).
- Selective serotonin reuptake inhibitors (for treatment of depressions) may increase the risk of bleeding in the gastrointestinal tract.
- Ciclosporin (a medicine often used in organ transplant patients).
- Vancomycin (a type of antibiotic) can cause hearing problems.

Please tell your doctor if you are taking any of the following medicines that can make acetylsalicylic acid work less well:
- Particular medicines that result in an increased excretion of urine (diuretics, aldosterone antagonists like spironolactone and canrenoate, loop diuretics like furosemide).
- Medicines which promote the excretion of uric acid (for example probenecid and benzbromarone).
- Ibuprofen: the antiplatelet effect of acetylsalicylic acid can be attenuated.
- Metamizole: Metamizole (substance to decrease pain and fever) may reduce the effect of acetylsalicylic acid on platelet aggregation (blood cells sticking together and forming a blood clot), when taken concomitantly. Therefore, this combination should be used with caution in patients taking low dose aspirin for cardioprotection.

Please tell your doctor if you are taking any of the following medicines. They may be affected by acetylsalicylic acid:
- Interferon α: acetylsalicylic acid reduce the activity of interferon α.
- Medicines to treat manic-depressive illness (lithium).
- Antiacids (used to treat indigestion).
- Barbiturates (used in the treatment of seizure disorders).
- Zidovudine (used in the treatment of HIV).
- Phenytoin (a medicine used to treat epilepsy).
- Acetylsalicylic acid may alter blood and urine tests.

Trinomia contains atorvastatin and this substance can also affect the way some other medicines work. Also some medicines can affect the way atorvastatin works. Alternatively it could increase the risk or severity of side-effects, including the important muscle wasting condition described in the above section “Warning and precautions”). Please tell your doctor if you are taking any of the following medicines:
- Ciclosporin (a medicine often used in organ transplant patients).
- Certain antibiotics or antifungal medicines, e.g. erythromycin, clarithromycin, telithromycin, ketoconazole, itraconazole, voriconazole, fluconazole, posaconazole, rifampin.
- If you need to take oral fusidic acid to treat a bacterial infection you will need to temporarily stop using this medicine. Your doctor will tell you when it is safe to restart Trinomia. Taking Trinomia with fusidic acid may rarely lead to muscle weakness, tenderness or pain (rhabdomyolysis). See more information regarding rhabdomyolysis in section 4.
- Medicines used in the treatment of HIV e.g. ritonavir, lopinavir, atazanavir, indinavir, darunavir, saquinavir, efavirenz, the combination of tipranavir/ritonavir etc.
- Other medicines to regulate lipid levels, e.g. gemfibrozil, other fibrates, colestipol

- Some medicines used in the treatment of hepatitis C e.g. telaprevir, boceprevir and the combination of elbasvir/grazoprevir.
- Some calcium channel blockers used for angina or high blood pressure, e.g. amlodipine, diltiazem; medicines to regulate your heart rhythm e.g. digoxin, verapamil, amiodarone.
- Other medicines known to interact with atorvastatin include ezetimibe (which lowers cholesterol), warfarin (which reduces blood clotting), oral contraceptives, stiripentol (an anti-convulsant for epilepsy), phenazone (a painkiller), cimetidine (an H_2-receptor antagonists), colchicine (used to treat gout) and antacids (indigestion products containing aluminium or magnesium).
- Medicines obtained without a prescription: St John's Wort

Trinomia contains ramipril and this substance can also affect the way some other medicines work. Also some medicines can affect the way ramipril works. Please tell your doctor if you are taking any of the following medicines that may increase the chance of getting side effects:
- Medicines for cancer (chemotherapy).
- Medicines to stop the rejection of organs after a transplant such as ciclosporin.
- Diuretics such as furosemide.
- Medicines which can increase the amount of potassium in your blood such as spironolactone, triamterene, amiloride, potassium salts and heparin (for thinning blood).
- Steroid medicines for inflammation such as Prednisolone.
- Allopurinol (used to lower the uric acid in your blood).
- Procainamide (for heart rhythm problems).

Please tell your doctor if you are taking any of the following medicines that can make ramipril work less well:
- Medicines used for the treatment of low blood pressure, shock, cardiac failure, asthma or allergies such as ephedrine, noradrenaline or adrenaline. Your doctor will need to check your blood pressure.

Please tell your doctor if you are taking any of the following medicines. They may be affected by ramipril:
- Medicines for diabetes such as oral glucose lowering medicines and insulin. Ramipril may lower your blood sugar amounts. Check your blood sugar amounts closely while taking Trinomia.
- Lithium (for mental health problems). Ramipril may increase the amount of lithium in your blood. Your lithium amount will need to be closely checked by your doctor.

Your doctor may need to change your dose and/or to take other precautions:
If you are taking an angiotensin II receptor blocker (ARB) or aliskiren (see also information under the headings "Do not take Trinomia" and "Warnings and precautions".

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

Trinomia with food, drink and alcohol
Alcohol increases the risk of stomach and intestinal ulcers and bleeding. Additionally alcohol can have additive effects with medicines used to reduce blood pressure. Therefore it is not recommended to drink alcohol while taking Trinomia.
Grapefruit juice contains one or more components that alter how the body uses some medicinal products, including Trinomia. Consuming grapefruit juice should be avoided.
Trinomia should be taken preferably after a meal (see section 3).

Pregnancy, breast-feeding and fertility

Do not take Trinomia if you are pregnant, think you may be pregnant or are planning to have a baby. If you get pregnant while taking Trinomia, stop taking it immediately and contact your doctor. A switch to a suitable alternative treatment should be carried out in advance of a planned pregnancy.
Do not take Trinomia if you are breast-feeding.
Women of child-bearing potential should use effective contraception during treatment.
Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
You may feel dizzy, while taking Trinomia. This is more likely to happen when you change from other medicines to Trinomia or when taking a higher dose. If this happens, do not drive or use any tools or machines.

Trinomia contains lactose, sodium and soya lecithin
Trinomia contains a sugar called lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

This medicine contains less than 1 mmol sodium (23 mg) per hard capsule, that is to say essentially 'sodium-free'.

Trinomia contains soya oil. If you are allergic to peanut or soya, do not use this medicinal product.

3. How to take Trinomia

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

Taking this medicine
- Take this medicine by mouth preferably after a meal.
- Swallow the capsules whole with liquid.
- Do not open, crush or chew the capsules.

How much to take
The usual dose is one capsule once daily.
Your doctor will determine the appropriate strength for you, depending on your condition, your current treatment and your personal risk status.

If you take more Trinomia than you should
Dizziness and buzzing in the ears, especially in older patients, may be symptoms of a serious intoxication.
Tell a doctor or go to the nearest hospital casualty department straight away. Do not drive to the hospital, get somebody else to take you or call for an ambulance. Take the medicine pack with you. This is so the doctor knows what you have taken.

If you forget to take Trinomia
- If you miss a dose, take your normal dose when it is next due.
- Do not take a double dose to make up for a forgotten capsule.

If you stop taking Trinomia
Please do not interrupt or stop the treatment with Trinomia until you have spoken with your doctor.

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.

The evaluation of side effects is based on the following frequencies:

Very common	affects more than 1 in 10 people
Common	affects less than 1 in 10 people
Uncommon	affects less than 1 in 100 people
Rare	affects less than 1 in1,000 people
Very rare	affects less than 1 in 10,000 people
Not known	frequency cannot be estimated from the available data

Stop taking Trinomia and see a doctor straight away, if you notice any of the following serious side effects or symptoms - you may need urgent medical treatment, tell to your doctor immediately or go to the nearest hospital accident and emergency deparment:

- In very rare occasions tarry stools or vomiting of blood (signs of severe bleeding in the stomach) have been reported.
- In rare occasions hypersensitive reactions of the skin, the respiratory tract, the gastrointestinal tract and the cardiovascular system, especially in case of asthma patients have been reported. The following disease symptoms may occur: low blood pressure, attacks of respiratory distress, rhinitis, nasal congestion, allergic shock, swelling of the face, tongue and larynx (Quincke's oedema).
- Severe bleeding, such as cerebral bleeding, is rarely or very rarely reported and especially in patients who have uncontrolled high blood pressure and/or simultaneous treatment with anticoagulants (medicines that inhibit the clotting of blood) it can be life-threatening.
- Muscle pain, tenderness, weakness, rupture, cramps or red-brown discolouration of urine. If you experience muscle weakness, tenderness, pain or red-brown discolouration of urine and at the same time, you feel unwell or have a high temperature it may be caused by an abnormal muscle breakdown which can be life-threatening and lead to kidney problems. Very rare deaths have occurred.
- In rare occasions hypersensitivity (allergic) reactions have been reported including: Swelling of the face, tongue and throat which make it difficult to swallow or breathe, as well as itching and rashes.
- Serious illness with severe peeling and swelling of the skin, blistering of the skin, mouth, eyes, genitals and fever. Skin rash with pink-red blotches especially on palms of hands or soles of feet which may blister.
- Rarely, inflammation of the liver with yellowing of the skin and eyes, itching, dark-coloured urine or pale-coloured stool, liver failure (very rare).
- Rarely, inflammation of the pancreas often with severe abdominal pain.
- Lupus-like disease syndrome (including rash, joint disorders and effects on blood cells)

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.

Side effects with acetylsalicylic acid, atorvastatin or ramipril alone:
Please tell your doctor if any of the following gets serious or lasts longer than a few days.

Acetylsalicylic acid

Very common (may affect more than 1 in 10 people):
- Gastrointestinal complaints such as heartburn, nausea, vomiting, stomach ache and diarrhoea.
- Insignificant blood loss from the gastrointestinal tract (micro-bleeding).

Uncommon (may affect up to 1 in 100 people):
- Gastrointestinal bleeding and ulcers.
- After long-term administration of Trinomia iron deficiency anaemia may occur due to hidden blood losses from the gastrointestinal tract.
- Gastrointestinal ulcers may occur, but they very rarely perforate the lining.
- Gastrointestinal inflammation.
- Skin reactions.

Rare to very rare (may affect up to 1 in 1,000 people):
- Bleeding such as nosebleed, bleeding of the gums, bleeding skin or bleeding in the urinary tract and reproductive organs may also come with a prolonged bleeding time. This effect can continue over 4 up to 8 days after the treatment.

Very rare (may affect up to 1 in 10,000 people):
- Increased values in liver function tests.
- Kidney function disorders.
- Reduction of blood glucose (hypoglycaemia).
- The acetylsalicylic acid in small dosage reduces the excretion of uric acid. For patients at risk, this can cause an attack of gout in certain circumstances.
- Skin rashes with fever and participation of the mucosa (Erythema multiforme)

Not known (frequency cannot be estimated from the available data):
Headache, dizziness, mental confusion, hearing disorders or buzzing in the ears (tinnitus), especially in case of older patients, may be symptoms of an overdose (see section “If you take more than you should”).

Atorvastatin

The following adverse events have been reported with some statins (medicines of the same type):
- Sexual difficulties.
- Depression.
- Breathing problems including persistent cough and or shortness of breath or fever.
- Diabetes. This is more likely if you have high levels of sugars and fats in your blood, are overweight and have high blood pressure. Your doctor will monitor you while you are taking this medicine.

Common (may affect up to 1 in 10 people):
- Inflammation of the nasal passages, pain in the throat, nose bleed.
- Allergic reactions.

- Increases in blood sugar levels (if you have diabetes continue careful monitoring of your blood sugar levels), increase in blood creatine kinase.
- Headache.
- Nausea, constipation, wind, indigestion, diarrhoea.
- Joint pain, muscle pain and back pain.
- Blood test results that show your liver function can become abnormal.

Uncommon (may affect up to 1 in 100 people):
- Anorexia (loss of appetite), weight gain, decreases in blood sugar levels (if you have diabetes you should continue careful monitoring of your blood sugar levels).
- Having nightmares, insomnia.
- Dizziness, numbness or tingling in the fingers and toes, reductions of sensation to pain or touch, change in sense of taste, loss of memory.
- Blurred vision.
- Ringing in the ears and/or head.
- Vomiting, belching, abdominal pain upper and lower, pancreatitis (inflammation of the pancreas leading to stomach pain).
- Hepatitis (liver inflammation).
- Rash, skin rash and itching, hives, hair loss.
- Neck pain, muscle fatigue.
- Fatigue, feeling unwell, weakness, chest pain, swelling especially in the ankles (oedema), raised temperature.
- Urine tests that are positive for white blood cells.

Rare (may affect up to 1 in 1,000 people):
- Visual disturbance.
- Numbness or tingling in fingers and toes.
- Unexpected bleeding or bruising.
- Cholestasis (yellowing of the skin and whites of the eyes).
- Tendon injury.

Very rare (may affect up to 1 in 10,000 people):
- An allergic reaction - symptoms may include sudden wheezing and chest pain or tightness, swelling of the eyelids, face, lips, mouth, tongue or throat, difficulty breathing, collapse.
- Hearing loss.
- Gynecomastia (breast enlargement in men and women).
- Severe liver problems.

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

- Muscle weakness that is constant.
- Myasthenia gravis (a disease causing general muscle weakness including in some cases muscles used when breathing).
- Ocular myasthenia (a disease causing eye muscle weakness).

Talk to your doctor if you experience weakness in your arms or legs that worsens after periods of activity, double vision or drooping of your eyelids, difficulty swallowing, or shortness of breath.

<u>Ramipril</u>

Common (may affect up to 1 in 10 people):
- Headache or feeling tired.

- Feeling dizzy. This is more likely to happen when you start taking Trinomia or start taking a higher dose.
- Fainting, hypotension (abnormally low blood pressure), especially when you stand or sit up quickly.
- Dry tickly cough, inflammation of your sinuses (sinusitis) or bronchitis, shortness of breath.
- Stomach or gut pain, diarrhoea, indigestion, feeling or being sick.
- Skin rash with or without raised area.
- Chest pain.
- Cramps or pain in your muscles.
- Blood tests showing more potassium than usual in your blood.

Uncommon (may affect up to 1 in 100 people):
- Balance problems (vertigo).
- Itching and unusual skin sensations such as numbness, tingling, pricking, burning or creeping on your skin (paraesthesia).
- Loss or change in the way things taste.
- Sleep problems.
- Feeling depressed, anxious, more nervous than usual or restless.
- Blocked nose, difficulty breathing or worsening of asthma.
- A swelling in your gut called “intestinal angioedema” presenting with symptoms like abdominal pain, vomiting and diarrhoea.
- Heartburn, constipation or dry mouth.
- Passing more water (urine) than usual over the day.
- Sweating more than usual.
- Loss or decrease of appetite (anorexia).
- Increased or irregular heartbeats.
- Swollen arms and legs. This may be a sign of your body holding onto more water than usual.
- Flushing.
- Blurred vision.
- Pain in your joints.
- Fever.
- Sexual inability in men, reduced sexual desire in men or women.
- An increased number of certain white blood cells (eosinophilia) found during a blood test.
- Blood tests showing changes in the way your liver, pancreas or kidneys are working.

Rare (may affect up to 1 in 1,000 people):
- Feeling shaky or confused.
- Red and swollen tongue.
- Severe flaking or peeling of the skin, itchy, lumpy rash.
- Nail problem (e.g. loosening or separation of a nail from its bed).
- Skin rash or bruising.
- Blotches on your skin and cold extremities.
- Red, itchy, swollen or watery eyes.
- Disturbed hearing and ringing in your ears.
- Feeling weak.
- Blood tests showing a decrease in the number of red blood cells, white blood cells or platelets or in the amount of haemoglobin.

Very rare (may affect up to 1 in 10,000 people):
- Being more sensitive to the sun than usual.

Not known (frequency cannot be estimated from the available data):
- Disturbance in attention
- Swollen mouth.

- Blood tests showing too few blood cells in your blood.
- Blood tests showing less sodium than usual in your blood.
- Fingers and toes changing colour when you are cold and then tingling or feeling painful when you warm up (Raynaud's phenomenon).
- Breast enlargement in men.
- Slowed or impaired reactions.
- Burning sensation.
- Change in the way things smell.
- Hair loss.

Side effects of Trinomia (acetylsalicylic acid, atorvastatin or Ramipril)

Very common (may affect more than 1 in 10 people):
- Gastrointestinal complaints such as heartburn, nausea, vomiting, stomach ache and diarrhoea.
- Insignificant blood loss from the gastrointestinal tract (micro-bleeding).

Common (may affect up to 1 in 10 people):
- Inflammation of the nasal passages, pain in the throat, nose bleed.
- Dry tickly cough, inflammation of your sinuses (sinusitis) or bronchitis, shortness of breath.
- Chest pain.
- Constipation, wind, indigestion.
- Stomach or gut pain, being sick.
- Headache or feeling tired.
- Feeling dizzy. This is more likely to happen when you start taking Trinomia or start taking a higher dose.
- Fainting, hypotension (abnormally low blood pressure), especially when you stand or sit up quickly.
- Allergic reactions.
- Skin rash with or without raised area.
- Cramps or pain in your muscles.
- Joint pain and back pain.
- Blood test results that show your liver function can become abnormal.
- Increases in blood sugar levels (if you have diabetes continue careful monitoring of your blood sugar levels), increase in blood creatine kinase.
- Blood tests showing more potassium than usual in your blood.

Uncommon (may affect up to 1 in 100 people):
- Gastrointestinal bleeding and ulcers but they very rarely perforate the lining.
- Gastrointestinal inflammation.
- Anorexia (loss of appetite), decrease of appetite, weight gain, decreases in blood sugar levels (if you have diabetes you should continue careful monitoring of your blood sugar levels).
- Belching, abdominal pain upper and lower, pancreatitis (inflammation of the pancreas leading to stomach pain).
- A swelling in your gut called “intestinal angioedema” presenting with symptoms like abdominal pain, vomiting and diarrhoea.
- After long-term administration of Trinomia iron deficiency anaemia may occur due to hidden blood losses from the gastrointestinal tract.
- Skin reactions.
- Rash, itching, hives, hair loss.
- Having nightmares, insomnia.
- Sleep problems.
- Dizziness, numbness or tingling in the fingers and toes, reductions of sensation to pain or touch, change in sense of taste, loss of memory.
- Balance problems (vertigo).
- Blurred vision.

- Ringing in the ears and/or head.
- Loss or change in the way things taste.
- Itching and unusual skin sensations such as numbness, tingling, pricking, burning or creeping on your skin (paraesthesia).
- Feeling depressed, anxious, more nervous than usual or restless.
- Hepatitis (liver inflammation).
- Neck pain, muscle fatigue.
- Fatigue, feeling unwell, weakness, swelling especially in the ankles (oedema), raised temperature.
- Blocked nose, difficulty breathing or worsening of asthma.
- Dry mouth.
- Sweating more than usual.
- Passing more water (urine) than usual over the day.
- Swollen arms and legs. This may be a sign of your body holding onto more water than usual.
- Flushing.
- Fever.
- Increased or irregular heartbeats.
- Sexual inability in men, reduced sexual desire in men or women.
- Urine tests that are positive for white blood cells.
- An increased number of certain white blood cells (eosinophilia) found during a blood test.
- Blood tests showing changes in the way your liver, pancreas or kidneys are working.

Rare to very rare (may affect up to 1 in 1,000 people):
- Bleeding such as nosebleed, bleeding of the gums, bleeding skin or bleeding in the urinary tract and reproductive organs may also come with a prolonged bleeding time. This effect can continue over 4 up to 8 days after the treatment.

Rare (may affect up to 1 in 1,000 people):
- Numbness or tingling in fingers and toes.
- Unexpected bleeding or bruising.
- Cholestasis (yellowing of the skin and whites of the eyes).
- Tendon injury.
- Feeling shaky or confused.
- Red and swollen tongue.
- Severe flaking or peeling of the skin, itchy, lumpy rash.
- Nail problem (e.g. loosening or separation of a nail from its bed).
- Blotches on your skin and cold extremities.
- Red, itchy, swollen or watery eyes.
- Disturbed hearing.

  Blood tests showing a decrease in the number of red blood cells, white blood cells or platelets or in the amount of haemoglobin.

Very rare (may affect up to 1 in 10,000 people):
- Increased values in liver function tests.
- Severe liver problems.
- The acetylsalicylic acid in small dosage reduces the excretion of uric acid. For patients at risk, this can cause an attack of gout in certain circumstances.
- An allergic reaction - symptoms may include sudden wheezing and chest pain or tightness, swelling of the eyelids, face, lips, mouth, tongue or throat, difficulty breathing, collapse.
- Being more sensitive to the sun than usual.
- Hearing loss.
- Gynecomastia (breast enlargement in men and women).

Not known (frequency cannot be estimated from the available data):
- Disturbance in attention

- Swollen mouth.
- Fingers and toes changing colour when you are cold and then tingling or feeling painful when you warm up (Raynaud's phenomenon).
- Slowed or impaired reactions.
- Burning sensation.
- Change in the way things smell.
- Blood tests showing too few blood cells in your blood.
- Blood tests showing less sodium than usual in your blood.

The following adverse events could also been reported with some statins:
- Sexual difficulties.
- Depression.
- Breathing problems including persistent cough and or shortness of breath or fever.

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 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 Trinomia

Keep this medicine out of the sight and reach of children.
Store below 25°C.
Do not use Trinomia after the expiry date which is stated on the carton and blister. The expiry date refers to the last day of that month.
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 Trinomia contains

- *Trinomia 100 mg/40 mg/ 10 mg hard capsules*: The active substances are acetylsalicylic acid, atorvastatin and ramipril. Each capsule contains 100 mg acetylsalicylic acid, 40 mg atorvastatin (as atorvastatin calcium trihydrate) and 10 mg ramipril.
- *Trinomia 100 mg/40 mg/ 5 mg hard capsules*: The active substances are acetylsalicylic acid, atorvastatin and ramipril. Each capsule contains 100 mg acetylsalicylic acid, 40 mg atorvastatin (as atorvastatin calcium trihydrate) and 5 mg ramipril.
- *Trinomia 100 mg/40 mg/ 2,5 mg hard capsules:* The active substances are acetylsalicylic acid, atorvastatin and ramipril. Each capsule contains 100 mg acetylsalicylic acid, 40 mg atorvastatin (as atorvastatin calcium trihydrate) and 2.5 mg ramipril.

- The other ingredients (excipients, for all the strength) are:
  Core: microcrystalline cellulose (E460); talc (E553); sodium starch glycolate (type A); lactose monohydrate; pregelatinised starch (maize); calcium carbonate (E170); Hydroxypropylcellulose (E463); Polysorbate 80 (E433); crospovidone (type A); silica colloidal anhydrous; magnesium stearate; hypromellose (E464); sodium stearyl fumarate.

  Trinomia 100 mg/40 mg/ 10 mg hard capsules:
  Film-coating: polyvinyl alcohol; titanium dioxide (E171); talc (E553); soya lecithin (E322); xanthan gum (E415); ; hypromellose (E464);); triethyl citrate (E1505); povidone; yellow iron oxide (E172); red iron oxide (E172).

Capsule shell: gelatin (E441); titanium dioxide (E171); yellow iron oxide (E172); red iron oxide (E172), shellac, black iron oxide (E172).

Trinomia 100 mg/40 mg/ 5 mg hard capsules:
Film-coating: polyvinyl alcohol; titanium dioxide (E171); talc (E553); soya lecithin (E322); xanthan gum (E415); hypromellose (E464); triethyl citrate (E1505); povidone; yellow iron oxide (E172); red iron oxide (E172).
Capsule shell: gelatin (E441); titanium dioxide (E171); yellow iron oxide (E172); red iron oxide (E172), shellac, black iron oxide (E172).

Trinomia 100 mg/40 mg/ 2,5 mg hard capsules:
Film-coating: polyvinyl alcohol; titanium dioxide (E171); talc (E553); soya lecithin (E322); xanthan gum (E415); hypromellose (E464); triethyl citrate (E1505); povidone; yellow iron oxide (E172); red iron oxide (E172).
Capsule shell: gelatin (E441); titanium dioxide (E171); shellac, black iron oxide (E172).

What Trinomia looks like and contents of the pack

Trinomia 100 mg/40 mg/10 mg hard capsules are size 0 hard shell gelatin capsules (approx. length: 21.7 mm) with opaque orange-coloured cap and body, imprinted with "AAR 100/40/10", containing two 50 mg acetylsalicylic white or nearly white film-coated tablets engraved "AS", two 20 mg atorvastatin pink film-coated tablets engraved "AT" and one 10 mg ramipril pale yellow film-coated tablet engraved "R1".

Trinomia 100 mg/40 mg/10 mg hard capsules are available in blister packs of 7, 14, 28, 56, 84 or 98 capsules.

Trinomia 100 mg/40 mg/5 mg hard capsules are size 0 hard shell gelatine capsules (approx. length: 21.7 mm) with opaque orange -coloured cap and opaque white-coloured body, imprinted with "AAR 100/40/5" containing two 50 mg acetylsalicylic white or nearly white film-coated tablet engraved "AS", two 20 mg atorvastatin pink film-coated tablets engraved "AT" and one 5 mg ramipril pale yellow film-coated tablet engraved "R5".

Trinomia 100 mg/40 mg/5 mg hard capsules are available in blister packs of 7, 14, 28, 56, 84 or 98 capsules.

Trinomia 100 mg/40 mg/2.5 mg hard capsules are size 0 hard shell gelatine capsules (approx. length: 21.7 mm) with opaque white -coloured body and cap, imprinted with "AAR 100/40/2.5" containing two 50 mg acetylsalicylic white or nearly white film-coated tablet engraved "AS", two 20 mg atorvastatin pink film-coated tablets engraved "AT and one 2.5 mg ramipril pale yellow film-coated tablet engraved "R2".

Trinomia 100 mg/40 mg/2.5 mg hard capsules are available in blister packs of 7, 14, 28, 56, 84 or 98 capsules.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:	*Manufacturer:*
Ferrer Internacional, S.A. Gran Vía Carlos III, 94	Ferrer Internacional S.A. Joan Buscallà, 1-9

08028 Barcelona (Spain) 08173 Sant Cugat del Vallès (Barcelona, Spain)

For any information about this medicine, please contact the Marketing Authorisation Holder.

This medicinal product is authorised in the Member States of the EEA under the following names:

Belgium:	Trinomia 100 mg/40 mg/10 mg gélule
Bulgaria:	Trinomia 100 mg/40 mg/10 mg твърди капсули
Germany:	Iltria 100 mg/40 mg/10 mg hartkapseln
Finland:	Trinomia 100 mg/40 mg/10 mg kapseli, kova
France:	Iltria 100 mg/40 mg/10 mg gélules
Greece:	Trinomia 100 mg/40 mg/10 mg καψάκια σκληρά
Ireland:	Trinomia 100 mg/40 mg/10 mg hard capsules
Italy:	Trinomia 100 mg/40 mg/10 mg capsule rigide
Austria:	Trinomia 100 mg/40 mg/10 mg hartkapseln
Portugal:	Trinomia 100 mg/40 mg/10 mg cápsulas
Romania:	Trinomia 100 mg/40 mg/10 mg capsule
Spain:	Trinomia 100 mg/40 mg/10 mg cápsulas duras
Sweden:	Trinomia 100 mg/40 mg/10 mg kapslar, hårda

Belgium:	Trinomia 100 mg/40 mg/5 mg gélule
Bulgaria:	Trinomia 100 mg/40 mg/5 mg твърди капсули
Germany:	Iltria 100 mg/40 mg/5 mg hartkapseln
Finland:	Trinomia 100 mg/40 mg/5 mg kapseli, kova
France:	Iltria 100 mg/40 mg/5 mg gélules
Greece:	Trinomia 100 mg/40 mg/5 mg καψάκια σκληρά
Ireland:	Trinomia 100 mg/40 mg/5 mg hard capsules
Italy:	Trinomia 100 mg/40 mg/5 mg capsule rigide
Austria:	Trinomia 100 mg/40 mg/5 mg hartkapseln
Portugal:	Trinomia 100 mg/40 mg/5 mg cápsulas
Romania:	Trinomia 100 mg/40 mg/5 mg capsule
Spain:	Trinomia 100 mg/40 mg/5 mg cápsulas duras
Sweden:	Trinomia 100 mg/40 mg/5 mg kapslar, hårda
Belgium:	Trinomia 100 mg/40 mg/2.5 mg gélule
Bulgaria:	Trinomia 100 mg/40 mg/2.5 mg твърди капсули
Germany:	Iltria 100 mg/40 mg/2.5 mg hartkapseln
Finland:	Trinomia 100 mg/40 mg/2.5 mg kapseli, kova
France:	Iltria 100 mg/40 mg/2.5 mg gélules
Greece:	Trinomia 100 mg/40 mg/2.5 mg καψάκια σκληρά
Ireland:	Trinomia 100 mg/40 mg/2.5 mg hard capsules
Italy:	Trinomia 100 mg/40 mg/2.5 mg capsule rigide
Austria:	Trinomia 100 mg/40 mg/2.5 mg hartkapseln
Portugal:	Trinomia 100 mg/40 mg/2.5 mg cápsulas
Romania:	Trinomia 100 mg/40 mg/2.5 mg capsule
Spain:	Trinomia 100 mg/40 mg/2.5 mg cápsulas duras
Sweden:	Trinomia 100 mg/40 mg/2.5 mg kapslar, hårda

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