Package leaflet: Information for the patient

Lipocomb 40 mg/10 mg hard capsules

rosuvastatin and ezetimibe

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

1. What Lipocomb is and what it is used for

Lipocomb contains two different active substances in one capsule. One of the active substances is rosuvastatin, belonging to the group of so-called statins, the other active substance is ezetimibe.

Lipocomb is a medicine used to lower levels of total cholesterol, "bad" cholesterol (LDL cholesterol) and fatty substances called triglycerides in your blood. In addition, it also raises levels of "good" cholesterol (HDL cholesterol). This medicine works to reduce your cholesterol in two ways: it reduces the cholesterol absorbed in your digestive tract, as well as the cholesterol your body makes by itself.

For most people, high cholesterol does not affect the way they feel because it does not produce any symptoms. However, if it is left untreated, fatty deposits can build up in the walls of your blood vessels causing them to narrow.
Sometimes, these narrowed blood vessels can get blocked which can cut off the blood supply to the heart or brain leading to a heart attack or a stroke. By lowering your cholesterol levels, you can reduce your risk of having a heart attack, a stroke or related health problems.

Lipocomb is used in patients whose cholesterol levels cannot be controlled by a cholesterol lowering diet alone. You should stay on your cholesterol lowering diet while taking this medicine.
Your doctor may prescribe Lipocomb if you are already taking both rosuvastatin and ezetimibe at the same dose level.

Lipocomb is used in patients with heart disease. Lipocomb reduces the risk of heart attack, stroke, surgery to increase heart blood flow, or hospitalisation for chest pain.

Lipocomb does not help you lose weight.

2. What you need to know before you take Lipocomb

Do not take Lipocomb if you:

- are allergic to rosuvastatin, ezetimibe or any of the other ingredients of this medicine (listed in section 6).
- have liver disease.
- have moderate or severe kidney impairment.
- have repeated, unexplained muscle aches or pains (myopathy).
- take a combination of sofosbuvir/velpatasvir/voxilaprevir (medicines used for viral infection of the liver called hepatitis C).
- have had any repeated or unexplained muscle pain, a personal or family history of muscle problems, or a previous history of muscle problems when taking other cholesterol-lowering medicines.
- take a medicine called ciclosporin (used for example, after organ transplants).
- are pregnant or breast-feeding. If you become pregnant while taking Lipocomb stop taking it immediately and tell your doctor. Women should avoid becoming pregnant while taking Lipocomb by using suitable contraceptive measures.
- have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking Lipocomb or other rosuvastatin-containing medicine.
- have thyroid gland that is not working properly (hypothyroidism).
- regularly drink large amounts of alcohol.
- are of Asian origin (Japanese, Chinese, Filipino, Vietnamese, Korean and Indian).
- take other medicines called fibrates to lower your cholesterol (see section "Other medicines and Lipocomb".

If any of the above applies to you (or you are in doubt), contact your doctor.

Warnings and precautions

Talk to your doctor or pharmacist before taking Lipocomb if you:

- have problems with your kidneys.
- have problems with your liver.
- have had repeated or unexplained muscle aches or pains, a personal or family history of muscle problems, or a previous history of muscle problems when taking other cholesterol-lowering medicines. Tell your doctor immediately if you have unexplained muscle aches or pains especially if you feel unwell or have a fever. Also tell your doctor or pharmacist if you have a muscle weakness that is constant.
- 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).
- have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking Lipocomb or other rosuvastatin-containing medicine.
- are of Asian origin (Japanase, Chinese, Filipino, Vietnamese, Korean and Indian). Your doctor needs to choose the right dose of Lipocomb to suit you.
- take medicines used to fight infections, including HIV or hepatitis C infection e.g. lopinavir/ritonavir and/or atazanavir see "Other medicines and Lipocomb".
- have severe respiratory failure.
- take other medicines called fibrates to lower your cholesterol. See "Other medicines and Lipocomb".
- regularly drink large amounts of alcohol.
- have thyroid gland that is not working properly (hypothyroidism).

- are more than 70 years old (as your doctor needs to choose the right dose of Lipocomb to suit 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 Lipocomb can lead to serious muscle problems (rhabdomyolysis).

If any of the above applies to you (or if you are not sure):
Do not take Lipocomb 40 mg/10 mg hard capsules (the highest dose) and check with your doctor or pharmacist before you actually start taking any dose of Lipocomb.

Serious skin reactions including Stevens-Johnson syndrome and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in association with rosuvastatin treatment. **Stop using Lipocomb and seek medical attention immediately** if you notice any of the symptoms described in section 4.

In a small number of people, statins can affect the liver. This is identified by a simple test which looks for increased levels of liver enzymes in the blood. For this reason, your doctor will regularly out this blood test (liver function test) during treatment with Lipocomb. It is important to go to the doctor for the prescribed laboratory checks.

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.

Children and adolescents
The use of Lipocomb is not recommended in children and adolescents under the age of 18 years.

Other medicines and Lipocomb
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Tell your doctor if you are taking any of the following:
- Ciclosporin (used for example, after organ transplants to prevent rejection of the transplanted organ. The effect of rosuvastatin is increased with concomitant use). **Do not take Lipocomb while taking ciclosporin.**
- Blood thinners e.g. warfarin, acenocoumarol or fluindione (their blood thinning effect and the risk of bleeding may be increased while taken concomitantly with Lipocomb), ticagrelor or clopidogrel.
- Other medicines to lower your cholesterol called fibrates, which correct also blood triglyceride levels (e.g. gemfibrozil and other fibrates). During concomitant use, the effect of rosuvastatin is increased. **Do not take the Lipocomb 40 mg/10 mg hard capsules with concomitant use of a fibrate.**
- Colestyramine (a medicine also used to lower cholesterol), because it affects the way ezetimibe works.
- Regorafenib (used to treat cancer).
- Darolutamide (used to treat cancer).
- Any of the following medicines used to treat viral infections, including HIV or hepatitis C infection, alone or in combination (see Warnings and precautions): ritonavir, lopinavir, atazanavir, sofosbuvir, voxilaprevir, ombitasvir, paritaprevir, dasabuvir, velpatasvir, grazoprevir, elbasvir, glecaprevir, pibrentasvir.
- Indigestion remedies containing aluminium and magnesium (used to neutralise acid in your stomach; they decrease the plasma level of rosuvastatin.) This effect may be mitigated with taking this type of medicine 2 hours after rosuvastatin.

- Erythromycin (an antibiotic). The effect of rosuvastatin is decreased with their concomitant use.
- Fusidic acid. 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 Lipocomb. Taking Lipocomb with fusidic acid may rarely lead to muscle weakness, tenderness or pain (rhabdomyolysis). See more information regarding rhabdomyolysis in section 4.
- An oral contraceptive (the pill). The levels of sexual hormones absorbed from the pill are increased.
- Capmatinib (used to treat cancer).
- Hormone replacement therapy (increased hormone levels in the blood).
- Fostamatinib (used to treat low platelet counts).
- Febuxostat (used to treat and prevent high blood levels of uric acid).
- Teriflunomide (used to treat multiple sclerosis).
- Leflunomide (used to treat rheumathoid arthritis).
- Roxadustat (used to treat anaemia in patients with chronic kidney disease).
- Tafamidis (used to treat a disease called transthyretin amyloidosis).
- Momelotinib (used to treat myelofibrosis in adults with anemia).

The effects of these medicines could be changed by Lipocomb or they could change the effect of Lipocomb.

If you go into hospital or receive treatment for another condition, tell the medical staff that you are taking Lipocomb.

Lipocomb with alcohol
Do not take Lipocomb 40 mg/10 mg hard capsules (the highest dose), if you regularly drink large amounts of alcohol.

Pregnancy and breast-feeding
Do not take Lipocomb if you are pregnant, are trying to get pregnant or think you may be pregnant. If you get pregnant while taking Lipocomb, stop taking it immediately and tell your doctor. Women should use contraceptive measures during the treatment with Lipocomb.
Do not take Lipocomb, if you are breast-feeding, because it is not known if the medicine is passed into breast milk.

Driving and using machines
Lipocomb are not expected to interfere with your ability to drive or to use machinery. However, it should be taken into account that some people get dizzy after taking Lipocomb. If you get dizzy, talk to your doctor before driving or using machines.

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

3. How to take Lipocomb

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

<u>You should keep on being on low-cholesterol diet and doing exercises while taking Lipocomb.</u>

The recommended daily dose for adults is one capsule of the given strength.

Take Lipocomb once daily.
You can take it at any time of the day, with or without food. Swallow each capsule whole with a drink of water.
Take your medicine at the same time every day.

Lipocomb is not suitable to start a treatment. Treatment initiation or dose adjustment, if necessary, should only be done by giving the active substances separately and after setting the appropriate doses the switch to Lipocomb of the appropriate strength is possible.
The maximum daily dose of rosuvastatin is 40 mg. It is only for patients with high cholesterol levels and a high risk of heart attacks or stroke whose cholesterol levels are not lowered enough with 20 mg.

Regular cholesterol checks
It is important to go back to your doctor for regular cholesterol checks to make sure your cholesterol has reached and is staying at the correct level.

If you take more Lipocomb than you should
Contact your doctor or the emergency department of the nearest hospital because you might need medical help.

If you forget to take Lipocomb
Don't worry, skip the missed dose and take your next scheduled dose at the correct time. Do not take a double dose to make up for a forgotten dose.

If you stop taking Lipocomb
Talk to your doctor if you want to stop taking Lipocomb. Your cholesterol levels might increase again if you stop taking Lipocomb.

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.

It is important that you are aware of what these side effects may be.

Stop taking Lipocomb and seek medical help immediately if you experience any of the following:
Rare (may affect up to 1 in 1 000 people)
- Allergic reactions such as swelling of the face, lips, tongue and/or throat, which may cause difficulty in breathing and swallowing.
- Unusual muscle aches or pains which go on for longer than you might expect. Rarely this can develop into potentially life threatening muscle damage known as rhabdomyolysis, which leads to malaise, fever and kidney impairment.
- Lupus-like disease syndrome (including rash, joint disorders and effects on blood cells).
- Muscle rupture.

Not known (frequency cannot be estimated from the available data)
- Reddish non-elevated, target-like or circular patches on the trunk, often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes. These serious skin rashes can be preceded by fever and flu-like symptoms (Stevens-Johnson syndrome).
- Widespread rash, high body temperature and enlarged lymph nodes (DRESS syndrome or drug hypersensitivity syndrome).

- Erythema multiforme (life-threatening allergic reactions affecting the skin and mucous membranes).

Other possible side effects

Common (may affect up to 1 in 10 people)
- Headache
- Constipation
- Feeling sick
- Muscle pain
- Feeling weak
- Dizziness
- An increase in the amount of protein in the urine – this usually returns to normal on its own without having to stop taking this medicine.
- 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.
- Abdominal pain (stomach-ache)
- Diarrhoea
- Flatulence (excess gas in the intestinal tract)
- Feeling tired
- Elevations in some laboratory blood tests of liver function (transaminases)

Uncommon (may affect up to 1 in 100 people)
- Rash, itching, hives
- Elevations in some laboratory blood tests of muscle (CK) function
- Cough
- Indigestion
- Heartburn
- Joint pain
- Muscle spasms
- Neck pain
- Decreased appetite
- Pain
- Chest pain
- Hot flush
- High blood pressure
- Tingling sensation
- Dry mouth
- Inflammation of the stomach
- Back pain
- Muscle weakness
- Pain in arms and legs
- Swelling, especially in the hands and feet

Rare (may affect up to 1 in 1 000 people)
- Inflammation of the pancreas, which causes a severe stomach pain which can extend to the back.
- Reduction in blood platelets

Very rare (may affect up to 1 in 10 000 people)
- Jaundice (yellowing of the skin and eyes)

- Inflammation of the liver (hepatitis)
- Traces of blood in your urine
- Damage to the nerves of your legs and arms (such as numbness)
- Memory loss
- Breast enlargement in men (gynecomastia)

Not known (frequency cannot be estimated from the available data)
- Shortness of breath
- Oedema (swelling)
- Sleep disturbances, including insomnia and nightmares
- Sexual difficulties
- Depression
- Breathing problems including persistent cough and/or shortness of breath or fever
- Tendon injury
- Muscle weakness that is constant
- Gallstones or inflammation of the gallbladder (which may cause abdominal pain, nausea, vomiting)
- 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.

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

5. How to store Lipocomb

Store below 30°C.
Store in the original package in order to protect from light and moisture.

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

Do not use this medicine after the expiry date (EXP) which is stated on the carton box and the 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 Lipocomb contains

The active substances are rosuvastatin (as rosuvastatin zinc tetrahydrate) and ezetimibe. The capsules contain rosuvastatin zinc tetrahydrate equivalent to 40 mg rosuvastatin. Each capsule contains 10 mg of ezetimibe.

The other ingredients are:
Core
Silicified Microcrystalline Cellulose (Microcrystalline Cellulose (E460) and Colloidal Anhydrous Silica (E551)), Colloidal Anhydrous Silica (E551), Magnesium stearate (E572), Povidone (E1201), Croscarmellose Sodium (E468), Microcrystalline Cellulose (E460), Mannitol (E421), Sodium laurilsulfate (E514), Low-substituted hydroxypropyl cellulose (E463)
Capsule shell
Cap: Red iron oxide (E172), Titanium dioxide (E171), Yellow iron oxide (E172), Gelatine
Body: Gelatine, Yellow iron oxide (E172), Titanium dioxide (E171)

What Lipocomb looks like and contents of the pack
Unmarked self-closing Coni Snap type, hard gelatine capsule with red coloured cap and yellow coloured body filled with three tablets: one piece of white or almost white round, flat and bevel-edged *Ezetimibe 10 mg tablet* with a stylized E sign on one side of the tablet and 612 code on the other side; two pieces of white or almost white round *Rosuvastatin 20 mg* tablet with  mark on one side of the tablet and no mark on the other side. The length of the capsule is about 21.7 mm (± 0.5 mm).

Packs of 7, 10, 28, 30, 56, 60, 84, 90 hard capsules in cold blister (OPA/Al/PVC//Al) put into folded cardboard box and Patient information leaflet.
Not all pack sizes may be marketed.

Marketing Authorisation Holder

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

The Netherlands	Cholecomb 40 mg/10 mg capsule, hard
Austria	Lipocomb 40 mg/10 mg hartkapseln
Czech Republic	Delipid Plus 40/10 mg
Ireland	Lipocomb 40 mg/10 mg hard capsules
Romania	Lipocomb 40 mg/10 mg capsule
Slovakia	Lipocomb 40 mg/10 mg tvrdé kapsuly

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