Package leaflet: Information for the user

ATOZET 10 mg/10 mg film-coated tablets
ATOZET 10 mg/20 mg film-coated tablets
ATOZET 10 mg/40 mg film-coated tablets
ATOZET 10 mg/80 mg film-coated tablets

ezetimibe and atorvastatin

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

1. What ATOZET is and what it is used for

ATOZET is a medicine to lower increased levels of cholesterol. ATOZET contains ezetimibe and atorvastatin.

ATOZET is used in adults to lower levels of total cholesterol, “bad” cholesterol (LDL cholesterol), and fatty substances called triglycerides in the blood. In addition, ATOZET raises levels of “good” cholesterol (HDL cholesterol).

ATOZET 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.

Cholesterol is one of several fatty substances found in the bloodstream. Your total cholesterol is made up mainly of LDL and HDL cholesterol.

LDL cholesterol is often called “bad” cholesterol because it can build up in the walls of your arteries forming plaque. Eventually this plaque build-up can lead to a narrowing of the arteries. This narrowing can slow or block blood flow to vital organs such as the heart and brain. This blocking of blood flow can result in a heart attack or stroke.

HDL cholesterol is often called “good” cholesterol because it helps keep the bad cholesterol from building up in the arteries and protects against heart disease.

Triglycerides are another form of fat in your blood that may increase your risk for heart disease.

ATOZET is used for patients who cannot control their cholesterol levels by diet alone. You should stay on a cholesterol-lowering diet while taking this medicine.

ATOZET is used in addition to your cholesterol-lowering diet if you have:

- a raised cholesterol level in your blood (primary hypercholesterolaemia [heterozygous familial and non-familial]) or elevated fat levels in your blood (mixed hyperlipidaemia)
  - that is not well controlled with a statin alone;
  - for which you have used a statin and ezetimibe as separate tablets.

- a hereditary illness (homozygous familial hypercholesterolaemia) that increases the cholesterol level in your blood. You may also receive other treatments.

- heart disease. ATOZET reduces the risk of heart attack, stroke, surgery to increase heart blood flow, or hospitalisation for chest pain.

ATOZET does not help you lose weight.

2. What you need to know before you take ATOZET

Do not take ATOZET if
- you are allergic to ezetimibe, atorvastatin or any of the other ingredients of this medicine (listed in section 6),
- you have or have ever had a disease that affects the liver,
- you have had any unexplained abnormal blood tests for liver function,
- you are a woman able to have children and are not using reliable contraception,
- you are pregnant, trying to become pregnant or are breast-feeding,
- you use the combination of glecaprevir/pibrentasvir in the treatment of hepatitis C.

Warnings and precautions
Talk to your doctor or pharmacist before taking ATOZET if
- you have had a previous stroke with bleeding into the brain, or have small pockets of fluid in the brain from previous strokes,
- you have kidney problems,
- you have an under-active thyroid gland (hypothyroidism),
- you have had repeated or unexplained muscle aches or pains, a personal history or family history of muscle problems,
- you have had previous muscular problems during treatment with other lipid-lowering medicines (e.g. other “statin” or “fibrate” medicines),
- you regularly drink a large amount of alcohol,
- you have a history of liver disease,
- you are older than 70 years,
- you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this product,
- 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 ATOZET can lead to serious muscle problems (rhabdomyolysis).
- 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 promptly if you experience unexplained muscle pain, tenderness, or weakness while taking ATOZET. This is because on rare occasions, muscle problems can be serious, including muscle breakdown resulting in kidney damage. Atorvastatin is known to cause muscle problems, and cases of muscle problems have also been reported with ezetimibe.

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.

Check with your doctor or pharmacist before taking ATOZET:
- if you have severe respiratory failure.

If any of these apply to you (or you are not sure), talk to your doctor or pharmacist before taking ATOZET because your doctor will need to carry out a blood test before and possibly during your ATOZET 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 ATOZET").

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.

Tell your doctor about all your medical conditions including allergies.

The combined use of ATOZET and fibrates (medicines for lowering cholesterol) should be avoided since the combined use of ATOZET and fibrates has not been studied.

Children
ATOZET is not recommended for children and adolescents.

Other medicines and ATOZET
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines, including those obtained without prescription.

There are some medicines that may change the effect of ATOZET or their effect may be changed by ATOZET (see section 3). This type of interaction could make one or both of the medicines less effective. Alternatively it could increase the risk or severity of side effects, including the important muscle wasting condition known as "rhabdomyolysis" described in section 4:
- ciclosporin (a medicine often used in organ transplant patients),
- erythromycin, clarithromycin, telithromycin, fusidic acid**, rifampicin (medicines for bacterial infections),
- ketoconazole, itraconazole, voriconazole, fluconazole, posaconazole (medicines for fungal infections),
- gemfibrozil, other fibrates, nicotinic acid, derivatives, colestipol, cholestyramine (medicines for regulating lipid levels),
- some calcium channel blockers used for angina or high blood pressure, e.g. amlodipine, diltiazem,
- digoxin, verapamil, amiodarone (medicines to regulate your heart rhythm),
- medicines used in the treatment of HIV, e.g. ritonavir, lopinavir, atazanavir, indinavir, darunavir, the combination of tipranavir/ritonavir, etc. (medicines for AIDS),
- some medicines used in the treatment of hepatitis C, e.g. telaprevir, boceprevir and the combination of elbasvir/grazoprevir,
- daptomycin (a medicine used to treat complicated skin and skin structure infections and bacteraemia).

****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 ATOZET. Taking ATOZET with fusidic acid may rarely lead to muscle weakness, tenderness or pain (rhabdomyolysis). See more information regarding rhabdomyolysis in section 4.**

- Other medicines known to interact with ATOZET
  - oral contraceptives (medicines for preventing pregnancy),
  - stiripentol (an anticonvulsant medicine for epilepsy),
  - cimetidine (a medicine used for heartburn and peptic ulcers),
  - phenazone (a painkiller),
  - antacids (indigestion products containing aluminium or magnesium),
  - warfarin, phenprocoumon, acenocoumarol or fluindione (medicines to prevent blood clots),
  - colchicine (used to treat gout),
  - St John's wort (a medicine to treat depression).

ATOZET with food and alcohol
See section 3 for instructions on how to take ATOZET. Please note the following:

Grapefruit juice
Do not take more than one or two small glasses of grapefruit juice per day because large quantities of grapefruit juice can change the effects of ATOZET.

Alcohol
Avoid drinking too much alcohol while taking this medicine. See section 2 "Warnings and precautions" for details.

Pregnancy and breast-feeding
Do not take ATOZET if you are pregnant, are trying to get pregnant or think you may be pregnant. Do not take ATOZET if you are able to become pregnant unless you use reliable contraceptive measures. If you get pregnant while taking ATOZET, stop taking it immediately and tell your doctor.

Do not take ATOZET if you are breast-feeding.

The safety of ATOZET during pregnancy and breast-feeding has not yet been proven.

Ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines
ATOZET is not expected to interfere with your ability to drive or to use machinery. However, it should be taken into account that some people may get dizzy after taking ATOZET.

ATOZET contains lactose
ATOZET tablets contain 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.

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

3. How to take ATOZET

Always take this medicine exactly as your doctor has told you. Your doctor will determine the appropriate tablet strength for you, depending on your current treatment and your personal risk status. Check with your doctor or pharmacist if you are not sure.
- Before starting ATOZET, you should be on a diet to lower your cholesterol.
- You should keep on this cholesterol-lowering diet while taking ATOZET.

<u>How much to take</u>
The recommended dose is one ATOZET tablet by mouth once a day.

When to take
Take ATOZET at any time of the day. You can take it with or without food.

If your doctor has prescribed ATOZET along with cholestyramine or any other bile acid sequestrant (medicines for lowering cholesterol), you should take ATOZET at least 2 hours before or 4 hours after taking the bile acid sequestrant.

If you take more ATOZET than you should
Please contact your doctor or pharmacist.

If you forget to take ATOZET
Do not take an extra dose; just take your normal amount of ATOZET at the usual time the next day.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, ATOZET can cause side effects, although not everybody gets them.

If you experience any of the following serious side effects or symptoms, stop taking your tablets and tell your doctor immediately or go to the nearest hospital accident and emergency department.
- serious allergic reaction which causes swelling of the face, tongue and throat that can cause great difficulty in breathing

- 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

- muscle weakness, tenderness, pain or rupture or red-brown discolouration of urine and particularly, if 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

- lupus-like disease syndrome (including rash, joint disorders and effects on blood cells)

You should consult your doctor as soon as possible if you experience problems with unexpected or unusual bleeding or bruising, because this may be suggestive of a liver complaint.

The following common side effects were reported (may affect up to 1 in 10 people):
- diarrhoea,
- muscle aches.

The following uncommon side effects were reported (may affect up to 1 in 100 people):
- the flu,
- depression; trouble sleeping; sleep disorder,
- dizziness; headache; tingling sensation,
- slow heartbeat,
- hot flush,
- shortness of breath,
- abdominal pain; abdominal bloating; constipation; indigestion; flatulence; frequent bowel movements; inflammation of the stomach; nausea; stomach discomfort; upset stomach,
- acne; hives,
- joint pain; back pain; leg cramps; muscle fatigue, spasms, or weakness; pain in arms and legs,
- unusual weakness; feeling tired or unwell; swelling, especially in the ankles (oedema),

- elevations in some laboratory blood tests of liver or muscle (CK) function,
- weight gain.

The following side effects were reported with frequency not known (frequency cannot be estimated from the available data):
- 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 eyelids, difficulty swallowing, or shortness of breath.

Additionally, the following side effects have been reported in people taking ATOZET, or ezetimibe or atorvastatin tablets:
- allergic reactions including swelling of the face, lips, tongue, and/or throat that may cause difficulty in breathing or swallowing (which requires treatment immediately),
- raised red rash, sometimes with target-shaped lesions,
- liver problems,
- cough,
- heartburn,
- decreased appetite; loss of appetite,
- high blood pressure,
- skin rash and itching; allergic reactions including rash and hives,
- tendon injury,
- gallstones or inflammation of the gallbladder (which may cause abdominal pain, nausea, vomiting),
- inflammation of the pancreas often with severe abdominal pain,
- reduction in blood cell counts, which may cause bruising/bleeding (thrombocytopenia),
- inflammation of the nasal passages; nose bleed,
- neck pain; pain; chest pain; pain in the throat,
- increases and decreases in blood sugar levels (if you have diabetes you should continue careful monitoring of your blood sugar levels),
- having nightmares,
- numbness or tingling in the fingers and toes,
- reduction of sensation to pain or touch,
- change in sense of taste; dry mouth,
- loss of memory,
- ringing in the ears and/or head; hearing loss,
- vomiting,
- belching,
- hair loss,
- raised temperature,
- urine tests that are positive for white blood cells,
- blurred vision; visual disturbances,
- gynaecomastia (breast enlargement in men).

Possible side effects reported with some statins
- 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,

- muscle pain, tenderness, or weakness that is constant and particularly if, at the same time, you feel unwell or have a high temperature that may not go away after stopping ATOZET (frequency not known).

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 (see details below). By reporting side effects you can help provide more information on the safety of this medicine.
Ireland: HPRA Pharmacovigilance Website: www.hpra.ie.
Malta: ADR Reporting at: www.medicinesauthority.gov.mt/adrportal

5. How to store ATOZET

- Keep this medicine out of the sight and reach of children.
- Do not take ATOZET after the expiry date stated on the carton or container after "EXP." The expiry date refers to the last day of that month.
- Store in the original package in order to protect from oxygen.

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 to protect the environment.

6. Contents of the pack and other information

What ATOZET contains
The active substances are ezetimibe and atorvastatin. Each film-coated tablet contains 10 mg ezetimibe and 10 mg, 20 mg, 40 mg, or 80 mg atorvastatin (as atorvastatin calcium trihydrate).

The other ingredients are: calcium carbonate; silica, colloidal anhydrous; croscarmellose sodium; hydroxypropylcellulose; lactose monohydrate; magnesium stearate; cellulose, microcrystalline; polysorbate 80; povidone; sodium laurilsulphate.

The film coating contains: hypromellose, macrogol 8000, titanium dioxide (E171), talc.

What ATOZET looks like and contents of the pack
Capsule-shaped, biconvex, film-coated tablets, white to off white.

ATOZET 10 mg/10 mg tablets: "257" debossed on one side
ATOZET 10 mg/20 mg tablets: "333" debossed on one side
ATOZET 10 mg/40 mg tablets: "337" debossed on one side
ATOZET 10 mg/80 mg tablets: "357" debossed on one side

Pack sizes:
Packs of 10, 30, 90, and 100 film-coated tablets in nitrogen-purged aluminium/aluminium (oPA-Al-PVC cavity with Al lidding) blisters.

Packs of 30 x 1 and 45 x 1 film-coated tablets in unit dose, nitrogen-purged aluminium/aluminium (oPA-Al-PVC cavity with Al lidding) blisters.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
N.V. Organon
Kloosterstraat 6

NL-5349 AB Oss
The Netherlands

Manufacturer
Merck Sharp & Dohme B.V.
Waarderweg 39,
2031 BN Haarlem,
The Netherlands

Organon Heist bv
Industriepark 30
2220 Heist-op-den-Berg
Belgium

Organon N.V.
Kloosterstraat 6, 5349 AB,
Oss, Netherlands.

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

DE/H/3895/001-004/DC
ATOZET: Austria, Belgium, Bulgaria, Croatia, Denmark, Germany, Iceland, Ireland, Italy, Luxembourg, Malta, The Netherlands, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Sweden, United Kingdom
LIPTRUZET: Cyprus, France, Greece, Hungary
ZOLETORV: Czech Republic

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