

Ezetimibe

What is Ezetimibe?

Ezetimibe (E-zet-im-ibe) is the name of a medicine that lowers cholesterol, it is often referred to as Ezetrol which is the brand name for the drug. It works in a different way to a statin and so is often prescribed alongside a statin because of the added cholesterol lowering it offers. Ezetimibe also comes as a combination medicine with simvastatin under the brand name Inegy

Ezetimibe is a "cholesterol absorption inhibitor" which means it works by partially blocking the reabsorption of cholesterol (from the diet and from bile) in the small intestine. As a result less cholesterol is taken to the liver for re-cycling. This means that the liver has to increase its efforts to take more cholesterol out of the blood. It does this by increasing the number of LDL receptors on the surface of liver cells. These LDL receptors literally catch LDL cholesterol particles and remove them from the blood.

Research studies for Ezetimibe

The SHARP study (Study of Heart and Renal Protection 2011) showed that the combination of ezetimibe 10mg and simvastatin 20mg reduced the incidence of major cardiovascular events, such as heart attacks and strokes in people with chronic kidney disease. This was also seen in the earlier SEAS study (2008) using the same combination in individuals with aortic stenosis, showing a reduction in CV events in the simvastatin–ezetimibe arm versus a dummy (placebo) drug.

In 2015, the IMPROVE IT study looked at very high risk patients with known acute coronary syndrome who were treated with either simvastatin alone or in combination with ezetimibe. This study found that over the research period those treated with ezetimibe had fewer cardiovascular events, including ischaemic stroke. Although the absolute benefit from adding ezetimibe was small it was significant and supported the belief that LDL cholesterol lowering using medication other than statins was beneficial (and without adverse effect). Therefore ezetimibe was recommended as a second line therapy to help achieve therapeutic goals in people who were already on maximum tolerated statin therapy.

How does Ezetimibe stop cholesterol absorption?

Although the exact mechanism is not known, ezetimibe is thought to interact with the Niemann-Pick C1-Like1 (NPC1L1) protein which is located at the surface of the intestine (on the gastrointestinal tract epithelial cells or brush border). Ezetimibe can reduce LDL cholesterol levels by 15-22%, but has little effect on other lipoproteins. If ezetimibe is used in combination with a statin it can provide an additional LDL cholesterol reduction of 15-20%.

Dose and combination

Ezetimibe is taken orally at a dose of 10 mg once daily. Ezetimibe can be combined with a statin to provide a complementary mode of cholesterol reduction. It is not normally a substitute for a statin. This is because, for most people, statins are more effective at lowering cholesterol.

A technology appraisal (NICE TA 385) licenced ezetimibe to be used as a monotherapy (single therapy) for treating those with primary hypercholesterolaemia (heterozygous FH or non-familial) who cannot take statins or for whom statins are ineffective. It also allowed for use in combination with a statin when target LDL cholesterol levels are not being reached. This also includes its use in rare conditions such as homozygous FH and sitosterolaemia.

Similar to other medications, ezetimibe is not recommended in pregnancy and should also be avoided in women who are breastfeeding.

Side effects

When used as a monotherapy any side effects that are experienced are usually mild and temporary. These can include gastrointestinal disturbance, abdominal pain, diarrhoea, flatulence and fatigue. When taken with a statin, the most common side effects include moderate elevations of liver enzymes, muscle pain and headaches. A full list of reported side effects (common, uncommon and rare) are included in the patient information leaflet which is included with the medication.

Can I use plant sterol or stanol fortified foods alongside ezetimibe?

Ezetimibe and cholesterol-lowering foods that have been fortified with plant sterols or stanols are known to lower cholesterol in similar ways.

Whilst there may be subtle differences between their exact mechanisms of action, it is impossible to say with any certainty that plant sterol/stanol fortified foods give any additional cholesterol lowering benefit for people taking ezetimibe.

Typically plant sterol and stanol foods can lower cholesterol by up to 12.5% when taken at optimum doses. See our factsheet [Plant Sterols and Stanols](#) for further information.

References

NICE Technology Appraisal (TA385) – **Ezetimibe for treating primary heterozygous-familial and non-familial hypercholesterolaemia**. 2016

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