

Ezetimibe

Indications

Ezetimibe is only licensed for use in heterozygous-familial and non-familial hypercholesterolaemia i.e. patients with high cholesterol concentrations not due to an underlying cause (NICE states serum cholesterol >7.5 mmol/l¹).

What NICE says¹

Ezetimibe monotherapy is recommended as an option for the treatment of adults with primary (heterozygous-familial or non-familial) hypercholesterolaemia who would otherwise be initiated on statin therapy but who are unable to do so because of contraindications to initial statin therapy or intolerance to statin therapy.

Ezetimibe, co-administered with initial statin therapy, is recommended as an option for the treatment of adults with primary (heterozygous-familial or non-familial) hypercholesterolaemia who have been initiated on statin therapy when: serum total or low-density lipoprotein (LDL) cholesterol concentration is not appropriately controlled either after appropriate dose titration of initial statin therapy or because dose titration is limited by intolerance to the initial statin therapy and consideration is being given to changing from initial statin therapy to an alternative statin.

Does it work?

Although ezetimibe lowers LDL-cholesterol levels, until recently there have been no published data to say whether or not ezetimibe alone or added to a statin reduces the chance of having a cardiovascular event. The ENHANCE study, in people with familial hypercholesterolaemia, found no beneficial effects of ezetimibe plus simvastatin 80mg versus simvastatin 80mg plus placebo on carotid intima-media thickness.²

The SEAS trial in people with asymptomatic aortic stenosis found no benefit from simvastatin 40mg plus ezetimibe 10mg versus placebo on the risk of major CV events over 1 year.³

Is it safe?

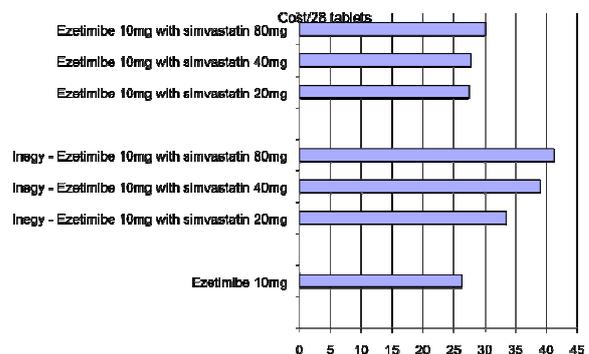
Raised liver enzymes and myalgia are described in the SPC as common (1/100 to $<1/10$) when co-prescribed with a statin but are uncommon as monotherapy.⁴

The SEAS unexpectedly raised concerns about the safety of ezetimibe, because it found a 55% relative increase in the risk of new cancers in the active treatment group. However an analysis of interim data from two much larger ongoing studies of simvastatin plus ezetimibe did not find an increased risk of cancer.⁵

Recommendation

Statins remain the treatment of choice in most patients. Ezetimibe only has a role, as supported by NICE guidance, for those with primary hypercholesterolaemia (ie have had a serum cholesterol >7.5 mmol/l) who are truly intolerant of statin treatment or where statins are contraindicated; or for those whose cholesterol levels are still high despite being prescribed an appropriate dose of a statin.⁶

A statin plus ezetimibe prescribed separately is less expensive than the combination product.



References

1. Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia. NICE technology appraisal guidance 132. November 2007.
2. Kastelein J, Akdim F, Stroes E, et al. Simvastatin with or without ezetimibe in familial hypercholesterolemia. *New Engl J Med* 2008;358:1431-43 (the ENHANCE study)
3. Rossebø A, Pedersen T, Boman K, et al for the SEAS Investigators. Intensive lipid lowering with simvastatin and ezetimibe in aortic stenosis. *N Engl J Med* 2008;359:1343-56
4. Ezitrol data sheet. <http://www.medicines.org.uk/EMC/medicine/12091/SPC/Ezetrol+10mg+Tablets/>
5. Peto R, Emberson J, Landray M, et al. Analyses of cancer data from three ezetimibe trials. *N Engl J Med* 2008;359:1357-1366
6. Ezetimibe in hypercholesterolaemia: NICE guidance. *MeReC Extra* No 32. March 2008.

