Elevated cholesterol levels: Benefit of ezetimibe is not proven

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Elevated blood cholesterol levels are regarded as a risk factor for heart attacks and other cardiovascular diseases. However, this does not necessarily mean that every cholesterol-lowering drug can also prevent heart attacks. For example, the benefit of the cholesterol-lowering drug ezetimibe is unclear. In particular, proof is lacking that patients have a greater benefit if they take ezetimibe in addition to statins for the prevention of heart attacks. This is the result of the final report published by the German Institute for Quality and Efficiency in Health Care (IQWiG) on 12 September 2011.

Prescribed largely in combination with statins

Ezetimibe is a cholesterol-absorption inhibitor. If taken orally, it acts in the small intestine by inhibiting the absorption of cholesterol into the body from ingested food, which leads to a reduction in blood cholesterol levels. It is hoped that this also reduces the risk of heart disease. Ezetimibe is currently prescribed mainly in combination with a statin, which is also used for the prevention of heart attacks in certain patients. For specific statins, various studies have demonstrated that in such patients they not only lower cholesterol levels but may also prevent heart attacks and other cardiovascular complications. Patients with elevated cholesterol levels who do not tolerate these drugs can also take ezetimibe without a statin.

IQWiG has now investigated whether ezetimibe - particularly in

combination with statins - also lowers the risk of the complications mentioned.

Benefit of combination therapy not proven

A total of 2 studies were identified for the benefit assessment. In both studies, all patients received a statin as basic therapy. In the 24-month ENHANCE study, one half of the study participants additionally received ezetimibe, the others placebo. In the 14-month ARBITER-6-HALTS study, ezetimibe was compared with niacin (nicotinic acid). Relevant studies investigating ezetimibe as monotherapy were not available.

IQWiG analysed the results of the ENHANCE and ARBITER-6-HALTS studies particularly with regard to deaths, cardiovascular complications, health-related quality of life, and adverse effects. With regard to patient-relevant outcomes, neither of the 2 studies showed robust differences between the group of patients receiving ezetimibe plus a statin and the control group. In summary, the data provide no indication that ezetimibe shows more benefit or harm than niacin or placebo. However, the studies available so far are too small and too short to conclusively clarify the benefit and harm of this drug.

The attention of health care professionals is currently focused on an ongoing study (IMPROVE-IT). It is the first study with the primary aim of comparing the effect of simvastatin plus ezetimibe versus simvastatin plus placebo on cardiovascular outcomes. The study includes high-risk patients with acute coronary syndrome whose condition has already been stabilized. The results are expected in 2013.

Procedure of report production

IQWiG published the preliminary results in the form of the preliminary

report at the beginning of May 2011 and interested parties were invited to submit comments. When the comments stage ended, the preliminary report was revised and sent as a final report to the contracting agency, the Federal Joint Committee, in July 2011. Only one written comment was received, which was published in a separate document at the same time as the final report. The report was produced in collaboration with external experts.

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