Pharmacotherapeutic report on colesevelam (Cholestagel®) in combination with ezetimibe, with or without a statin, in adult patients with primary hypercholesterolemia, including patients with familial hypercholesterolemia

Medicine. Colesevelam (as hydrochloride). Tablet, 625 mg, film-coated.

Summary of the therapeutic value

Intended effects. Patients with primary hypercholesterolemia who received colesevelam and ezetimibe had an additional mean 0.5 mmol/l (11%) reduction in low-density lipoprotein cholesterol (LDL-C) levels compared with patients receiving ezetimibe monotherapy. The total 32% reduction in LDL-C with combination therapy is comparable with the reduction that can be expected with statin monotherapy. Combination treatment with colesevelam and ezetimibe is intended for patients who are not adequately controlled with ezetimibe monotherapy and who do not tolerate statins or for whom statins are contraindicated. The effect of combination therapy has not been evaluated among the intended target population.

Patients with familial hypercholesterolemia and an LDL-C >2.5 mmol/l who received colesevelam as an add-on therapy, alongside a maximally-tolerated and stable regimen of a statin and ezetimibe, had an additional mean 0.6 mmol/l (12%) reduction in LDL-C levels compared with patients receiving combination therapy with a statin and ezetimibe. In total, 79% of the patients received the maximal dose of a statin.

No data are available on combination therapy with cholestyramine (another bile-acid sequestrant). It was therefore impossible to compare the effects of the combination therapy with colesevelam with those of combination therapy with cholestyramine.

Unintended effects. The incidence of gastrointestinal adverse events was higher with combination therapy. No unexpected adverse events occurred. In general, the adverse events were considered mild to moderate in intensity. Due to the small number of patients included in the studies, no conclusions can be drawn regarding rare but serious side-effects as a result of combination therapy with colesevelam.

Experience. Sufficient experience has been gained with colesevelam and considerable experience with cholestyramine. However, the number of patients being prescribed colesevelam (or cholestyramine) who are also using ezetimibe (with or without a statin) is unknown.

Applicability. In general, the contraindications and drug interactions recorded in the SPCs of colesevelam and cholestyramine are similar. However, colesevelam may possibly have fewer clinically important drug-drug interactions than cholestyramine, which could result in a broader applicability for colesevelam. However, evidence for this broader applicability is limited. As a result, no definitive conclusions can be drawn.

Ease of use. In contrast with cholestyramine, colesevelam can be used concomitantly with ezetimibe (with or without a statin). However, its use is restricted by the large number of tablets that need to be taken each day.

Final conclusion. The combination of colesevelam and ezetimibe has a lower therapeutic value than ezetimibe, because no data are available on the efficacy of the combination therapy among

patients who are not adequately controlled with ezetimibe monotherapy and who do not tolerate statins or for whom statins are contra-indicated.
The triple combination (colesevelam, ezetimibe and a statin) has an added therapeutic value in comparison with a combination treatment with a statin and ezetimibe. The triple combination should only be used for patients with familial hypercholesterolemia who do not achieve an LDL-C ≤ 2.5 mmol/l with the maximally-tolerated dose of a statin and ezetimibe.
Other important information. In 2007, colesevelam was evaluated for the (main) indication: co-administered with a HMG-CoA reductase inhibitor (statin) is indicated as adjunctive therapy to diet to provide an additive reduction in LDL-C levels in adult patients with primary hypercholesterolemia who are not adequately controlled with a statin alone (CFH report 07/25).