

**The Cost Effectiveness of Omacor® post-myocardial
infarction in the Irish Healthcare Setting**



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1. Omacor® is a concentrated preparation of omega-3-acid ethyl esters that contains 46% eicosapentaenoic acid (EPA) ethyl ester and 38% docosahexaenoic acid (DHA) ethyl ester. Omacor® is indicated as an adjuvant treatment in secondary prevention after myocardial infarction in addition to other standard therapy. It is also indicated for the treatment of endogenous hypertriglyceridaemia as a supplement to diet when dietary measures alone are insufficient to produce an adequate response. In February 2013 Abbott Laboratories submitted an economic dossier to the National Centre for Pharmacoeconomics, outlining the cost-effectiveness of Omacor® post-myocardial infarction in the Irish Healthcare Setting.
2. The economic evaluation assessed the cost-effectiveness of adding Omacor® treatment to current secondary prevention therapy after acute myocardial infarction in Ireland. It also aimed to estimate the budget impact of adding Omacor® to current secondary prevention therapy following acute myocardial infarction. Evidence on the cost-effectiveness in hypertriglyceridaemia was not presented. The perspective of the analysis was that of the Health Service Executive (HSE).
3. The main source of efficacy data incorporated into the economic evaluation was the GISSI-Prevenzione (GISSI-P) trial. This trial investigated the effect of dietary supplementation with n-3 poly unsaturated fatty acids and vitamin E after myocardial-infarction. The primary combined efficacy endpoint was death, non-fatal myocardial-infarction and stroke. Treatment with n-3 PUFA, but not vitamin E, significantly lowered the risk of the primary endpoint (relative risk decrease 10% by 2 way analysis, 15% by 4 way analysis).
4. The NCPE review group considered the main limitation, for the purpose of this evaluation, was that the approach to secondary prevention therapy was significantly different in the GISSI-P study to what would be considered the standard of care today. In the GISSI-P trial only 5%

of patients had coronary revascularization at baseline. Only 4.7% of patients were on cholesterol lowering drugs following discharge from hospital and although statin usage increased to approximately 45% at the end of the study, it was still remarkably low and well below what would be expected today. Similarly in other therapeutic areas ACE inhibitors and beta-blockers were used in less than 50% of patients in the GISSI-P study the majority of patients' post-myocardial infarction today would be expected to be on these agents. Therefore, the main criticism of the evidence used to populate the economic model, was that it is derived from a study where secondary prevention measures could not be considered compatible with the current standard of care.

5. The evaluation also considered the OMEGA study which was a randomised, placebo-controlled trial to test the effect of highly purified omega-3 fatty acids on top of modern guideline adjusted therapy after myocardial infarction. The authors concluded that the application of omega-3 fatty acids in addition to guideline adjusted therapy did not further lower the rate of sudden cardiac death and other clinical events. One of the limitations of the OMEGA trial was that the study had low power to detect a difference given the small event rate which may raise a question as to the efficacy of Omega-3 fatty acids in this setting. The ORIGIN trial also concluded that omega-3 fatty acid supplementation, did not reduce the rate of cardiovascular events in high risk patients. The results of a recent meta-analysis concluded that omega-3 PUFA supplementation was not associated with a lower risk of all cause mortality, cardiac death, sudden death, myocardial infarction or stroke based on relative and absolute measures of association. Having considered the evidence, the NCPE review group, had concerns in relation to the efficacy of Omacor® post-myocardial infarction in patients already receiving the standard of care.
6. In the economic evaluation a peer reviewed Markov cohort model was developed using Excel software using data from the GISSI-P trial concerning average age, drug usage and efficacy for the trial duration.

Post trial data was obtained from the literature. The model was run with a cohort of 1,000 patients and consisted of 9 different health states to reflect the outcomes used in the GISSI-P trial. Patients could transit within the health states during the 41 yearly cycles over which the model was run i.e. until patients had reached the age of 100 years. The survival curves at 4 years were derived from the GISSI-P trial and for survival data beyond the 42-month duration of the trial the GISSI-P survival curves were fitted with survival curves from a Canadian study involving a similar population of patients. The perspective was that of the HSE and discounting at 4% was applied to health effects and costs. Primary outcome of the analysis was cost per QALY with a secondary outcome of cost per life year gained.

7. The base case cost-effectiveness analysis indicated that treatment with Omacor® leads to 0.261 life years gained and 0.198 quality adjusted life years with additional costs of €1,627 which resulted in a cost-effectiveness ratio of €6,233/LYG. The cost per QALY gained when using Omacor® was estimated at €8,223/QALY.

8. A one way sensitivity analysis was conducted on a number of the parameters. The base case ICER was €8,223/QALY. When the discount rate was changed with costs and effects discounted at 0%, the ICER was €7,324/QALY and when the discount rate was increased to 6% for both costs and effects the ICER increased to €8,754/QALY. The costing of myocardial infarction or acute stroke did not impact significantly on the ICER. Follow up costs of stroke increased the ICER to €10,185/QALY when post stroke costs were doubled. The efficacy of Omacor® and the risk of death was a significant driver in the model and when the efficacy of Omacor® was reduced to a relative risk of 0.95, the ICERs increased significantly to €22,214/QALY. The probabilistic sensitivity analysis indicated that the probability of Omacor® being cost-effective was 98% when considering a threshold of €45,000/QALY.

9. The submission included a budget impact analysis where the cost of Omacor® was estimated at €0.72 per day for the 1gm dose resulting in an annual cost of €263. The budget impact was structured on the assumption that the market share for Omacor® would increase from 25% in year 1 to 80% in year 5. The estimated incremental cost increased from €275,873 per annum in year 1 to €2,910,025 per annum in year 5 resulting in a cumulative budget impact of €7.79million over the 5 year period.

10. The NCPE review group had concerns in relation to the clinical data used to populate this economic model. Recent publications question whether Omacor® has any additional effect over and above the standard of care for secondary prevention of coronary heart disease. Consequently the reliability of the ICER values presented in this submission is uncertain. Furthermore, GMS database analysis indicates that approximately 39% of Omacor® is used for the post myocardial infarction indication and 61% of Omacor® use is for the treatment of hypertriglyceridaemia. This submission does not include any evidence that Omacor® is cost effective for the treatment of hypertriglyceridaemia.

11. In view of the concerns relating to the efficacy of Omacor in the post myocardial infarction setting and the absence of any evidence to support the cost-effectiveness of Omacor® for the treatment of hypertriglyceridaemia we cannot recommend the reimbursement of this product at this point in time.