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Economic Evaluation

Prevention of Heart Failure With Icosapent Ethyl Results in Cost-Savings in the Spanish Population With Established Cardiovascular Disease

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ABSTRACT

Objectives: To estimate the budget impact resulting from reducing heart failure incidence through the introduction of icosapent ethyl to the Spanish healthcare system.

Methods: A cost-offset model was developed to estimate the budget impact resulting from introducing icosapent ethyl in Spanish hospitals in patients at high risk for cardiovascular diseases with established cardiovascular disease. Population and cost inputs were sourced from Spanish databases and clinically validated published literature. Clinical inputs were sourced from clinical trials or clinically validated published literature. The comparator was best supportive care, consisting of background statin with or without ezetimibe therapy, which reflects current treatments used in Spanish centers for the target population.

Results: Over 5 years, icosapent ethyl prevented 383 heart failures, corresponding to 1722 total days spent in hospital. This resulted in cost savings of €2 469 888 (1.8%).

Conclusions: This study demonstrated that the use of icosapent ethyl in patients at high risk for cardiovascular diseases with established cardiovascular disease will result in cost savings in Spanish hospitals, as the benefits of preventing heart failure outweigh the acquisition costs of icosapent ethyl.

Keywords: budget impact, cost offset, heart failure, icosapent ethyl, IPE, major adverse cardiovascular events, secondary prevention, Vazkepa.

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Introduction

Myocardial infarction (MI) remains the most common cause of heart failure (HF) worldwide.[1] Previous MI leads to an increased risk of HF 10 times higher during the first year after the MI, and up to 20 times in the following years (versus no previous MI).[2] HF after MI is the major driver of morbidity and mortality. Therefore, a reduction in MI incidence would result in a reduction in HF incidence, and an improvement in morbidity and mortality.

HF represents a major and growing economic problem. Between 2015 and 2019, total HF-associated costs were €15 373 per person in Spain, with hospitalizations making up 51% of the cost.[3] Similarly, an economic burden study of patients with newly diagnosed HF by Escobar et al (2023) reported that mean HF-related healthcare costs in Spain were €2510 per patient in the first year after diagnosis, decreasing to €1235 in the fourth year.[4] Therefore, a reduction in HF because of fewer cases of MI is expected to result in cost savings to the Spanish healthcare system.

The 2022 American Heart Association/American College of Cardiology/Heart Failure Society of America Guideline for the Management of Heart Failure states that omega-3 polyunsaturated fatty acid supplementation may be reasonable to use as adjunctive therapy to reduce mortality and cardiovascular (CV) hospitalizations in patients with HF class II to IV symptoms.[5]

Icosapent ethyl (IPE) (brand name Vazkepa®) is a highly purified and stable eicosapentaenoic acid (EPA) ethyl ester. The Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial (REDUCE-IT) was a phase IIIb, multicenter, randomized, double-blind, placebo-controlled trial conducted in over 8000 patients, which compared the efficacy and safety of IPE against placebo in preventing CV events.[6] Patients were enrolled if they were 45 years of age or older with established cardiovascular disease (CVD) (secondary prevention subgroup), or 50 years of age or older with diabetes in combination with at least 1 additional risk factor for developing CVD (primary prevention subgroup). The primary efficacy endpoint was a composite 5-point major adverse cardiac event (MACE) endpoint, which included a composite of CV death, nonfatal stroke, nonfatal MI, unstable angina, or coronary revascularization; the secondary endpoint was a 3-point composite MACE endpoint of CV death, nonfatal stroke, or nonfatal MI.

After a median follow-up of 4.9 years in the REDUCE-IT trial, the primary composite MACE endpoint occurred in 17.2% of patients in the IPE group versus 22.0% of patients in the mineral oil placebo group (hazard ratio [HR] 0.75; $P < .001$), representing a 25% relative risk reduction (RRR) in CV events with IPE in the intention-to-treat (ITT) population. This corresponded to a percentage point reduction of 4.8% in the primary endpoint, and a number needed to treat (NNT) of 21 to prevent 1 CV event. The key secondary composite MACE endpoint occurred in 11.2% of patients receiving IPE versus 14.8% receiving placebo (HR 0.74; $P < .001$) in the ITT population. In the secondary prevention population, the primary composite MACE endpoint occurred in 19.3% of patients in the IPE group versus 25.5% of patients in the mineral oil placebo group (HR 0.73; $P < 0.0001$), representing a 27% RRR in CV events with IPE. This corresponded to a percentage point reduction of 6.2% in the primary endpoint, and an NNT of 16 to prevent 1 CV event. The key secondary composite MACE endpoint occurred in 12.5% of patients receiving IPE versus 16.9% of patients receiving placebo (HR 0.72; $P < 0.0001$) in the secondary prevention population.[6,7]

In the ITT population of the REDUCE-IT trial, 6.1% of patients receiving IPE experienced a fatal or nonfatal MI versus 8.7% receiving placebo (HR 0.69; $P < 0.001$). This corresponded to a percentage point reduction of 2.6% and a RRR of 31%. In the secondary prevention population, 7.2% of patients receiving IPE experienced a fatal or nonfatal MI versus 10.5% receiving placebo (HR 0.67; $P < 0.0001$). This corresponded to a percentage point reduction of 3.3% and an RRR of 33%.[6,7]

The REDUCE-IT trial therefore demonstrated that IPE significantly reduced the risk of CV events, including MI, in adults on a stable dose of statins with established CVD and elevated triglycerides compared to placebo. The REDUCE-IT trial, however, did not include HF as a clinical outcome, and therefore, to date, HF has not been considered in published economic analyses of IPE. By reducing the risk of MI, IPE may also reduce the number of HF cases that occur as a result of MI, and therefore, the costs associated with these HF cases. We developed a cost-offset model to calculate the potential budget impact of introducing IPE on the management and cost of HF in patients with established CVD, in Spanish hospitals over 5 years.

Methods

A cost-offset model was developed to calculate the costs of 2 hypothetical scenarios over 5 years: 1 scenario considering patients receiving current management for reducing the risk of CV events—that is, best supportive care (BSC)—consisting of background statin with or without ezetimibe therapy (market without IPE available for clinical use), and a second scenario considering a proposed management with patients treated with both BSC and IPE (market with IPE available for clinical use). The difference in costs between these 2 scenarios was calculated as the budget impact resulting from the introduction of IPE. Cost categories included in the model included treatment acquisition costs, hospitalization costs, adverse event costs, and the costs of complications related to HF. The model adopts a Spanish health care system perspective. BSC was chosen as the relevant comparator since Spain follows the European Society of Cardiology Guidelines on CVD prevention in clinical practice, adapted locally by the Spanish Society of Cardiology, which recommends a high-intensity statin to reach a low-density lipoprotein cholesterol goal of less than 55 mg/dL (<1.4 mmol/liter).[8,9] BSC also aligns with the comparator arm in the REDUCE-IT trial.[6]

A targeted literature review was conducted to identify the most relevant and appropriate data that best reflected common clinical practice in Spain. Assumptions were made in the absence of data, and an independent Spanish clinical expert validated sources, inputs, assumptions, and calculations, confirming that the structure and sources used were appropriate for modeling the cost-offset of preventing HF in patients with established CVD in Spain.

Model Structure

The model cohort was estimated to use epidemiology parameters to reflect the population eligible to receive IPE. In each year over a 5-year period, an annual population growth rate was applied to include incident patients eligible to receive IPE, and an annual all-cause mortality rate was applied. Market share values for IPE and BSC were applied in each year for the "market without IPE available for clinical use" and the "market with IPE available for clinical use" scenarios to calculate the number of patients receiving each treatment in each year.

In each year of the model, the proportion of patients having an MI was applied based on the proportion of patients experiencing a first or second CV event in each year of the REDUCE-IT trial, combined with the proportion of these CV events being MI. The cumulative annual incidence of HF after a first MI, or a subsequent MI in patients with previous MI history, between years 1 to 5 was then applied to the proportion of patients in the model who had experienced 1 or 2 MIs, respectively, to calculate the proportion patients with HF (either newly diagnosed or diagnosed in a previous year in the model). It was assumed that patients cannot experience a third MI in the model, and once patients have developed HF, it is irreversible. Costs associated with HF were applied in the year the patient first experienced HF and all subsequent years of the model until death.

In each year of the model, a proportion of the patients with HF experienced complications associated with HF (arrhythmia, stroke, and thromboembolism, or CV death). For the proportion of patients experiencing a complication event in each year of the model, the annual cost of the complication was applied. Patients experiencing CV death were removed from the model cohort in the subsequent year after dying.

Target Population

The population included in the cost-offset model was aligned with the inclusion and exclusion criteria of the REDUCE-IT trial secondary prevention population, as this was the population in which the protective effects of IPE against MI and other CV events were observed. Patients in this population were 45 years of age and older, receiving statin treatment with elevated fasting triglycerides (≥ 150 mg/dL [≥ 1.7 mmol/liter]), established CVD, and controlled low-density lipoprotein cholesterol (> 40mg/dL [> 1.04 mmol/liter] and ≤ 100 mg/dL [≤ 2.60 mmol/liter]). Established CVD was defined as a history of any of the following:[7] (1) acute coronary syndrome (such as MI or unstable angina requiring hospitalization); (2) coronary or other arterial revascularization procedures; (3) coronary heart disease; (4) ischemic stroke; and (5) peripheral arterial disease.

Default population inputs were sourced from clinically validated published literature to align the population of the model with that of the REDUCE-IT trial. The total population of Spain 48 196 693 was sourced from the Instituto Nacional de Estadística (INE), and the population growth rate of Spain, 0.40%, was sourced from the World Bank.[10,11] The proportion of the population aged 45 to 79 years was sourced from the INE as 42.65% and the percentage of the Spanish population with established CVD of 9.80% was sourced from the Ministerio de Sanidad.[12,13] The proportion of these patients with atherosclerotic established CVD was sourced from Wilkins et al[14] as 71.00% and the

percentage of these patients treated with statins of 94.60% was sourced from Pérez de Isla et al.[15] The percentage of these patients with elevated triglycerides (≥ 150 mg/dL [≥ 1.7 mmol/liter]), 21.89%, and annual mortality of 4% were sourced from De Backer et al.[16] Finally, the general population mortality was sourced from INE as 0.25%.[12]

Hypothetical market share estimate data showing the proportions of patients on each treatment were provided by Amarin. Market share estimates for the current scenario (without IPE) were assumed to be 100% for BSC, since no other treatments are available in this indication. Market share estimates for the proposed scenario were based on Amarin's internal market share projections for years 1 to 3 and were assumed to continue the same trend for years 4 and 5 (Table 1). It should be noted that these hypothetical market share estimates were based on specific market conditions in Spain and are not applicable to other markets where reimbursement conditions may differ.

Clinical Inputs

Clinical inputs were applied in the model to calculate the number of patients who experience MI, HF, and HF complications with and without IPE treatment (Fig. 1).

The proportion of patients experiencing a first or second CV event in each year (Table 2) and the proportion of these CV events that were MIs (IPE: 28.69%; BSC: 27.77%) were sourced from the REDUCE-IT trial.[6] To account for uncertainty regarding the observed treatment effect of IPE in the REDUCE-IT trial (discussed further in the Limitations section), a 1.5% reduction in the treatment effect was applied by negatively adjusting the proportion of patients experiencing an event at each time point in the BSC arm.

The proportion of patients with a previous MI who experienced HF in each year was then sourced from Faridi et al[17] in the base case (Table 3), with an alternative scenario using data from Butler[18] for year 1 (31.30%). Finally, the proportions of patients with HF who experienced stroke/thromboembolism, arrhythmia, or CV death as a complication of HF were sourced from Watson et al[19] (2% of patients with HF experienced stroke/thromboembolism, 33.33% of patients with HF experienced arrhythmia, and 25% of patients with HF experienced CV death annually as a complication of HF).

Cost and Resource Use Data

The costs of HF in the scenarios with and without IPE were calculated based on the following cost categories: treatment acquisition costs, adverse event costs, the direct cost of HF hospitalization, unit costs of HF (primary care visits, laboratory tests, radiology, and other tests, specialized visits, emergency room visits, hospitalizations, and HF medication), and the cost of HF complications (arrhythmia, stroke/thromboembolism, or CV death). All costs were inflated to a cost year of 2024 using the Spanish Consumer Price Index for Health.[20] The costs of HF complications were applied to the proportion of the model cohort who experienced these complications after HF. A cost of €152.00 per pack of 120 capsules of IPE was used in the model, corresponding to an annual cost of €1850.60, assuming that patients receiving IPE were administered 4 capsules per day with no wastage.[21] The annual cost of background therapy (statins ± ezetimibe) was applied to patients who received IPE or BSC in the model, and the average annual cost of background therapy was sourced from a previously published cost-effectiveness study of evolocumab versus statins and ezetimibe for hypercholesterolemia in Spain.[22] The annual cost of statins with or without ezetimibe applied in the model was €422.88. Resource use units per year and costs per event for HF-associated healthcare resources were sourced from a published study of HF-associated costs and resource use in Spain.[3] The cost and resource use inputs used in the model and their sources are presented below in Table 4.[3,21-24]

Table 1. Current market share and hypothetical market uptake used in the model.

Year	IPE	BSC
Current scenario (without IPE)		
Years 1-5	0%	100%
Hypothetical future scenario (with IPE)		
Year 1	1%	99%
Year 2	5%	95%
Year 3	9%	91%
Year 4	15%	85%
Year 5	20%	80%

BSC indicates best supportive care; IPE, icosapent ethyl.

Results

The total number of patients in the Spanish population eligible to receive IPE was 296 148 in year 1 of the model, increasing to 304 888 in year 5. Of these patients, 3266 received IPE in year 1 of the proposed scenario, increasing to 60 978 in Year 5.

The introduction of IPE into the market resulted in 383 cases of HF avoided over the 5 years captured in the model. This resulted in the NNT of 130 patients in the established CVD population to prevent one case of HF, corresponding to a reduction of the risk of HF by 0.77%. Additionally, 128 subsequent cases of arrhythmia, 8 cases of stroke or thromboembolism, and 96 CV deaths were prevented over the 5 years captured in the model. This corresponded to the prevention of 1722 total days spent in the hospital and 191 emergency room visits.

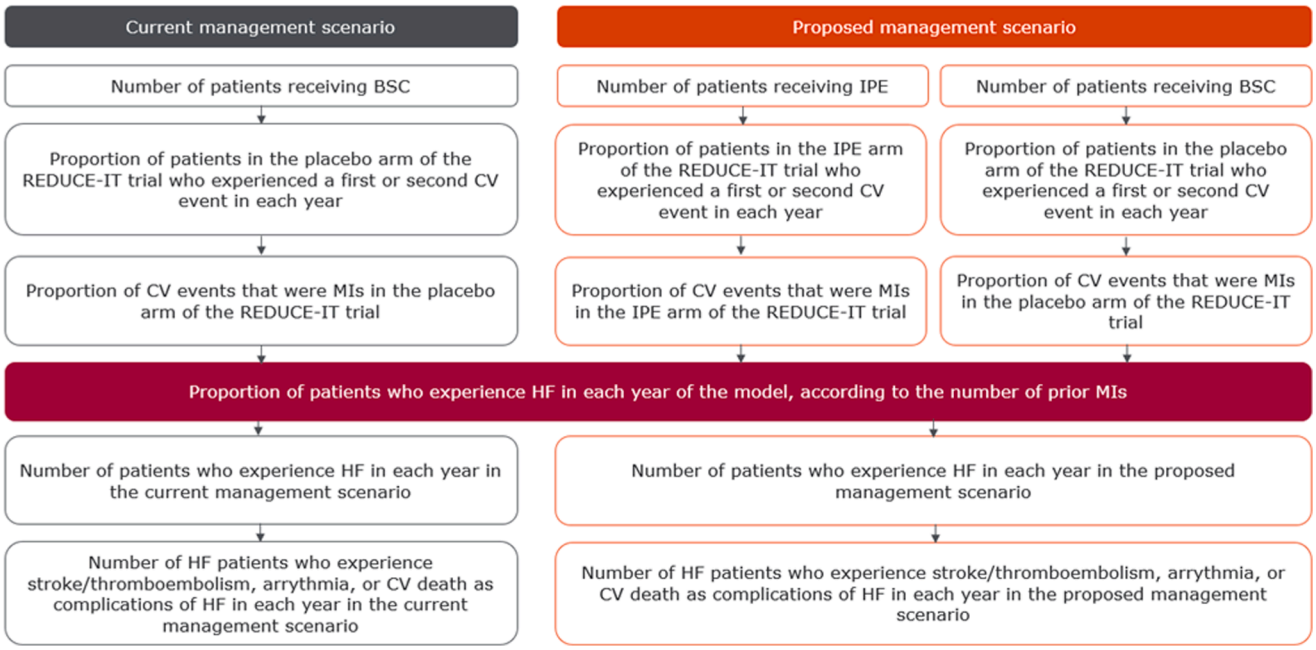
Total costs associated with HF in the base case were determined to be €135 725 520 in the "market without IPE available for clinical use" (€448.53 per patient). This decreased to €133 255 633 in the "market with IPE available for clinical use" (€440.39 per patient), resulting in an overall net saving of €2 469 888 (1.8%) over the 5 years captured in the model (€8.14 per patient). The budget impact per year ranged from cost-savings of €8257 in year 1 (€0.03 per patient) to cost-savings of €1 279 430 in year 5 (€4.20 per patient). The largest drivers of cost-savings over the 5 years captured in the model were direct hospital costs of HF (savings of €3 271 443 [€10.77 per patient]), followed by costs of HF complications (savings of €2 310 941 [€7.61 per patient]) and costs and resource use of HF (savings of €2 142 208 [€7.05 per patient]), whereas treatment acquisition costs increased by €3 508 580 (€11.55 per patient) and adverse event costs increased by €4806 (€0.02 per patient) with the introduction of IPE. Base case results are presented in Figure 2.

In the scenario analysis using an alternative proportion of patients with previous MI who experience HF in year 1, total costs associated with HF were determined to be €148 364 797 in the "market without IPE available for clinical use" and €145 880 060 in the "market with IPE available for clinical use," resulting in an overall net saving of €2 484 737 (1.7%) over the 5 years captured in the model.

Discussion

This model demonstrates that introducing IPE in Spain to reduce the risk of CV events in adult statin-treated patients at high CV risk with elevated triglycerides and established CVD is

Figure 1. Application of clinical inputs in the model.



BSC indicates best supportive care; CV, cardiovascular; HF, heart failure; IPE, icosapent ethyl; MI, myocardial infarction.

likely to also lead to a reduction in the incidence of HF, resulting in cost savings and a reduction in hospital stays.

IPE is a novel treatment indicated to reduce the risk of CV events in adult statin-treated patients. The results of this study demonstrate that IPE would be cost-saving through its potential effects on the risk of HF as a result of preventing CV events such as MIs. The cost-savings are derived through the direct costs of preventing HF occurrence, and the savings associated with the prevention of subsequent complications related to HF, outweighing the treatment acquisition costs associated with the introduction of IPE in Spanish clinical practice.

HF subsequent to MI also represents a significant regional issue in the broader European population. In the Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies (SWEDEHEART) registry, 28% of incident hospital admissions for MI in Sweden in 2008 were complicated by HF.[25,26] Similarly, in Norway between 2001 and 2009, 18.7% of patients with a first MI presented with HF or developed HF during hospitalization.[27] In addition, in the ESC Heart Failure Long-Term Registry, which included 211 cardiology centers from 21 European and Mediterranean countries, 53.6% of patients with HF had a previous MI.[28] This suggests that preventing MI would likely reduce the incidence of subsequent HF in European populations beyond Spain. Therefore, although this cost-offset model focuses on the Spanish healthcare system perspective, it is likely that cost-savings as a result of preventing subsequent HF would also be found in other European countries through the introduction of IPE for the prevention of CV events in adult statin-treated patients.

The clinical efficacy of IPE in preventing MACE outcomes has previously been demonstrated in the REDUCE-IT trial, which showed a clinically significant ($P < 0.001$) reduction in its 5-point MACE composite endpoint as patients in the IPE arm of the trial demonstrated a reduction in CV events experienced compared to the placebo arm. This prevention of CV events is the rationale for modeling the impact of IPE on the occurrence of subsequent HF events, and demonstrates that IPE would be expected to prevent other CV events in addition to nonfatal MIs.

Table 2. Proportion of patients who experienced a first or second CV event (with 1.5% treatment effect reduction applied).

Year	IPE		BSC	
	First CV event	Second CV event	First CV event	Second CV event
Year 1	4.90%	1.25%	6.58%	2.22%
Year 2	9.56%	2.83%	12.73%	4.95%
Year 3	13.99%	4.52%	18.47%	7.80%
Year 4	18.21%	6.27%	23.83%	10.67%
Year 5	22.21%	8.04%	28.84%	13.50%

BSC indicates best supportive care; CV, cardiovascular; IPE, icosapent ethyl.

Table 3. Proportion of patients with previous MI experiencing HF.

Year	Proportion of patients with 1 previous MI experiencing HF	Proportion of patients with 2 previous MIs experiencing HF
Year 1	7.26%	9.73%
Year 2	10.27%	14.25%
Year 3	12.74%	17.95%
Year 4	14.79%	21.37%
Year 5	16.85%	24.11%

HF indicates heart failure; MI, myocardial infarction.

Table 4. Cost and resource use data used in the model.

Parameter	Cost	Source
Average annual cost of statins ± ezetimibe	€422.88	Olry de Labry Lima et al.[22]
Average annual cost of IPE	€1850.60	Ministerio de Sanidad[21]
Annual adverse event costs (BSC)	€132.58	Consulta Interactiva del SNS[23]
Annual adverse event costs (IPE)	€176.78	
Annual direct hospital cost of HF per patient	€5073.06	Jodar et al.[24]
CV death cost (one-off cost)	€9151.06	
Annual nonfatal stroke cost	€6312.39	
Annual cost of arrythmia	€3,508,77	
Cost per primary care visit	€25.70	Escobar et al.[3]
Primary care visit resource use per patient per year	7.7	
Annual cost of primary care visits	€197.89	
Annual cost of laboratory tests	€34.30	
Annual cost of radiology and other tests	€359.59	
Cost per specialized visit	€100.36	
Specialized visit resource use per patient per year	1.1	
Annual cost of specialized visits	€110.39	
Cost per emergency room visit	€125.84	
Emergency room visit resource use per patient per year	0.5	
Annual cost of emergency room visits	€62.92	
Cost per hospitalization	€510.70	
Hospitalization resource use per patient per year	4.5	
Annual cost of hospitalizations per year	€2,298.17	
Annual cost of HF medication	€258.68	

BSC indicates best supportive care; CV, cardiovascular; HF, heart failure; IPE, icosapent ethyl.

Several previous economic analyses have been conducted using the clinical outcomes of the REDUCE-IT trial to inform the clinical effectiveness of IPE and have shown that the improved clinical outcomes versus BSC result in IPE being a cost-effective treatment in several countries.[29,30] Of particular relevance to this study, cost-effectiveness and budget impact analyses of IPE in patients with recent acute coronary syndrome in Catalonia have shown that IPE is cost-effective at a willingness-to-pay threshold of €30 000,[31] and would have an average annual budget impact of less than €1 million over 5 years.[32] However, these studies only consider the clinical outcomes included in the 5-point composite MACE endpoint of the REDUCE-IT trial (nonfatal stroke, nonfatal MI, unstable angina, coronary revascularization, and CV death) and, therefore, do not represent the full value of IPE as a treatment for preventing CV events. By considering the budget impact on HF, downstream of MI, we build on this previous body of research by demonstrating the additional cost-savings that IPE would have on the Spanish healthcare system through preventing HF after MI.

In future research, it may be relevant to incorporate HF outcomes into cost-effectiveness analyses to investigate the cost-effectiveness of IPE in preventing HF as a subsequent event to MI.

Limitations

First, the association between nonfatal MI risk and HF risk in the model is informed by data sourced from the published literature and not from a prospective study in patients with HF or at high risk for HF or pre-HF with a primary endpoint of new/worsening HF cases or hospitalization for HF. Further research would be required to establish the treatment effect of IPE on HF incidence or hospitalization for HF in an appropriate population.

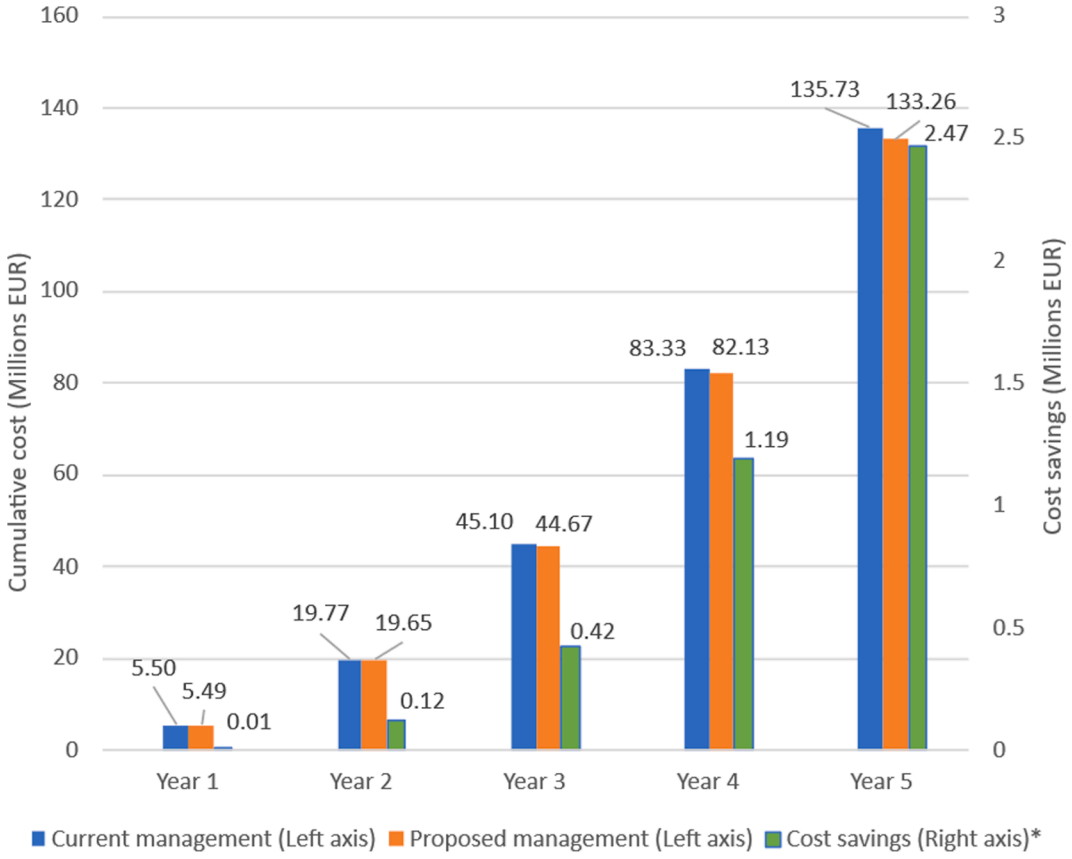
Second, similarly, the percentage of patients developing stroke/thromboembolism, arrhythmia, or CV death as a complication of HF included in the model is informed by the published literature, as the REDUCE-IT trial did not collect these data.

Third, the market share inputs for IPE in years 4 and 5 of the model are based on assumptions regarding uptake. If these market share values are lower in practice, IPE is still likely to be cost-saving, but savings may be lower.

Fourth, there has been some controversy surrounding the validity of the results of the REDUCE-IT trial, following the publication of data from the Long-Term Outcomes Study to Assess Statin Residual Risk with Epanova in High Cardiovascular Risk Patients with Hypertriglyceridemia (STRENGTH) trial, which showed less favorable results for a similar omega-3 fatty acid treatment in preventing CV events.[33,34] Nevertheless, there are substantial differences between the investigational medicinal products tested in each trial (REDUCE-IT, 4 g per day of ≥96% pure EPA ethyl ester versus STRENGTH, 4 g per day of omega-3-carboxylic acids, with at least 850 mg of polyunsaturated fatty acids, including multiple omega-3 fatty acids, EPA, and docosahexaenoic acid being the most abundant). To inform the clinical efficacy of IPE in our cost-offset model, it is considered most appropriate to use the results of the REDUCE-IT trial, following which, IPE was granted its marketing authorization in Spain and other European countries by the European Medicines Agency.[35] It has also been suggested that the treatment effect of IPE may have been overestimated in the REDUCE-IT trial because of the use of mineral oil in the placebo arm, which may have increased the risk of CV.[33] To account for this uncertainty, a conservative approach was taken by applying a 1.5% reduction to the treatment effect versus BSC in preventing CV events.

One of the key strengths of this cost-offset analysis is that it provides an estimate of the cost-benefit of introducing IPE in the adult population at very high risk for CV[36] with established CVD treated with statins by reducing incident HF, and outlines the cost-savings this would bring.

Figure 2. Base case results over the 5 years captured in the model. *As the budget impact of introducing IPE was negative, reflecting a cost saving in each year of the model, the scale on the right axis represents cost-savings as opposed to net budget impact.



IPE indicates icosapent ethyl.

It should also be noted that this model does not consider societal losses or impact on patients' quality of life (QoL). HF has a severe detriment on patients' QoL, as symptoms such as fatigue, shortness of breath, sleeping difficulties, chest pain, and depression can have negative impacts on patients' psychological well-being and ability to function independently.[37] Therefore, through preventing HF cases, IPE is likely to have an additional benefit in terms of improving the QoL of patients at high risk of CV events. Similarly, the cost estimate of the analysis did not include productivity loss, despite evidence that suggests that the costs of productivity loss may exceed the direct costs of HF itself.[38] Consequently, IPE would be likely to have additional benefits from a societal perspective by decreasing HF incidence.

Conclusions

IPE is an orally administered treatment composed of a highly purified and stable ethyl ester of the omega-3 fatty acid EPA. It is indicated in Europe to reduce the risk of CV events in adult statin-treated patients with elevated triglycerides at high risk of CV events, and results of the REDUCE-IT trial demonstrated that IPE significantly decreased the risk of nonfatal MI, nonfatal stroke, unstable angina, coronary revascularization, and CV death in this population. The premise of this study was that IPE would also reduce the risk of subsequent HF in patients who experienced nonfatal MI by reducing the risk of nonfatal MI. The reduction in HF risk with the introduction of IPE was demonstrated in this study to be associated with a reduction in hospital visits associated with HF, which resulted in cost-savings outweighing the treatment acquisition costs for IPE.

Author Disclosures

Author disclosure forms can be accessed below in the Supplemental Material section.

Supplemental Material

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.vhri.2025.101500.

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