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Analysis of the impact on the health care budget and consumers of the use of the preparation of omega-3 acid ethyl esters 90 in the treatment of patients with atherogenic dyslipidemia

Aim	To evaluate economic results of using omega-3 acid ethyl esters 90 for primary prevention of cardiovascular catastrophes in patients with residual hypertriglyceridemia (HTG).
Material and methods	The economic evaluation of using the medicine omega-3 acid ethyl esters 90 in the system of drug provision of the population of the Russian Federation was performed by analyzing the effect on the budget using a pharmacoeconomic model developed with the Microsoft Office Excel 2016 software. The effect of omega-3 acid ethyl esters 90 was evaluated in 555643 patients with residual HGT (Moscow). The study lasted for one year. Results of the meta-analysis by A. A. Bernasconi et al. (2020) were used as a source of efficacy data. The following direct and indirect medical expenses for treatment of cardiovascular complications of residual HTG were taken into account in this study: expenses for drug therapy; expenses for therapy and rehabilitation for nonfatal complications; expenses for fatal outcomes; state support for disability; foregone per capita gross domestic product resulting from losses of earnings due to temporary incapacity to labor by people of work-able age; and salary payments for temporary incapacity to work.
Results	Using omega-3 acid ethyl esters 90 in 555643 patients with residual HTG will allow preventing 1437 fatal ischemic cardiovascular complications (including 564 deaths from ischemic heart disease and 1128 cases of myocardial infarction (MI), including 558 fatal cases of MI). Furthermore, the difference in expenses compared to the high-dose statin treatment alone will be 359252253 rubles or 0.32%.
Conclusion	The results of this comprehensive pharmacoeconomical study showed that the use of omega-3 acid ethyl esters 90 in patients with residual HGT is an economically preferrable strategy compared to high-dose statin treatment alone and does not influence significantly the budgetary expenses as a part of the State Guarantee of Free Medical Care to the Citizens of the Russian Federation (increase in expenses by 0.32% compared to the current practice). At the same time, the use of omega-3 acid ethyl esters 90 results in a 10% decrease in the number of fatal ischemic cardiovascular complications.

Keywords	Dyslipidemia; residual hypertriglyceridemia; omega-polyunsaturated fatty acids; cost of disease; cardiovascular complications
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Introduction

Data accumulated over many decades supports the hypothesis that triglycerides (TGs) are directly involved in the pathogenesis of atherosclerosis [1]. Findings from population-based studies demonstrate that blood levels of TG are directly related to cardiovascular risk [2]. Post-hoc analysis of data obtained in statin efficacy studies suggests that TG blood levels are associated with cardiovascular events and coronary atherosclerosis progression during treatment regardless of the achieved low-density lipoprotein (LDL) cholesterol levels [3]. Hypertriglyceridemia often accompanies insulin resistance and associated risk factors, including hypertension, hyperglycemia, hypercoagulation, along with other common disorders associated with atherogenic dyslipidemia, which may increase cardiovascular risk [4]. Triglyceride-rich lipoproteins can directly affect vascular wall stiffness. Genetic studies have shown that polymorphism of factors regulating TG levels [5], including changes in the activity of apolipoprotein

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C–III and angiopoietin-like protein (ANGPLT) [6], were associated with higher TG levels and cardiovascular risk. Nonclinical studies have demonstrated the role of triglyceride-rich lipoproteins in stimulating inflammatory, oxidative, and thrombotic processes involved in the pathogenesis of atherosclerotic lesions in the vascular wall [7].

There has also been increasing emphasis on the need to control the entire range of atherogenic lipoproteins. Since statins cause a limited decrease in the TG blood levels, it makes sense that many patients require additional lipid-normalizing therapy in order to achieve the treatment goals [8]. Residual hypertriglyceridemia (TG>1.7 mmol/L during target-dose statin therapy) remains a major and common risk factor for fatal cardiovascular events regardless of the achieved LDL cholesterol levels [9].

However, it is clear that TG levels need to be corrected. For example, a recent systematic review and regression meta-analysis by Marston et al., based on data from 197,270 subjects of 24 randomized clinical trials (RCTs) with a mean follow-up period of 43.8 years, showed that a decrease in TG level by 0.45 mmol/L resulted in an 8% reduction in the incidence of cardiovascular events irrespective of lipid-lowering therapy [10].

Thus, the effect on TG levels is an essential factor for the optimal correction of atherogenic dyslipidemia. Hypertriglyceridemia can be corrected by two groups of drugs: fibrates and omega-3 polyunsaturated fatty acids [9]. Here, target levels of LDL cholesterol are achieved during the use of the maximum tolerated doses of statins for primary prevention following the current clinical guidelines [11]. The use of omega-3-acid ethyl esters 902–4 g/day is recommended at the TG levels of 1.7–2.3 mmol/L and in case of fibrate intolerability at higher TG levels. The only drug approved in the Russian Federation for the treatment of hypertriglyceridemia that contains sufficient eicosapentaenoic and docosahexaenoic acids (EPA/DHA) is an omega-3-acid ethyl ester 90 drug (Omacor; EPA/DHA 1.2/1840 mg). The assessment of clinical efficacy showed that the use of omega-3-acid ethyl esters 90 additionally reduced TG levels by 15%, even when combined with the maximum tolerated dose of rosuvastatin [12].

However, the primary prevention effects on clinical outcomes of EPA in combination with DHA remains unclear.

Cochrane meta-analysis carried out by Abdelhamid et al. [13] showed that omega-3-acid ethyl esters 90, when used for the primary prevention in patients with elevated TG levels, only reduced the statistically significant risk of developing cardiovascular events when treatment was longer than 2 years: odds ratio was 0.91 (95% confidence interval (CI) 0.86–0.96) for all-cause death, 0.94 (95% CI 0.88–0.99) for cardiovascular death, 0.79 (95% CI 0.69–0.90) for coronary artery disease (CAD), and 0.74 (95% CI 0.57–0.96) for non-fatal arrhythmias. This meta-analysis included the administration of nutritional recommendations and dietary supplements other than EPA/DHA. However, due to challenges involved in calculating doses and monitoring adherence to nutrition recommendations, which may have influenced the study results.

Bernasconi et al. [14] performed a meta-analysis of RCTs involving only omega-3-acid ethyl esters 90 medications and comprising a total of 40 studies and 135,267 subjects. The use of EPA/DHA was associated with reduced risk of myocardial infarction (MI) (OR 0.87, 95% CI 0.80–0.96), the number of patients needed to treat (NNT) to prevent one adverse outcome was 272 patients; ischemic complications (OR 0.90, 95% CI 0.84–0.97), NNT=192; fatal MI (OR 0.65; 95% CI 0.46–0.91), NNT=128; death due to CAD (OR 0.91, 95% CI 0.85–0.98), NNT=431. However, the decrease in cardiovascular mortality was not statistically significant (OR 0.95; 95% CI 0.90–1.00) [14] (Figure 1).

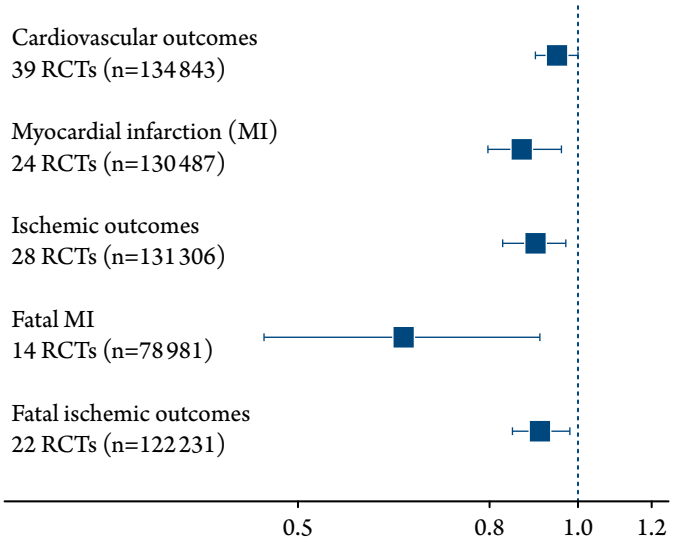
To determine whether EPA, DHA, or a combination of the two, are more effective in preventing CVD outcomes, the authors constructed a logit model to examine whether the effect depended on whether a combination of EPA and DHA or only EPA was used. The interaction did not differ significantly from zero for any of the outcomes. Thus, based on the available data, the authors concluded that there was no evidence confirming that the use of EPA alone was a more effective treatment for preventing CVDs than the combination of EPA and DHA.

Finally, the vital question arose as to whether the use of EPA/DHA was more effective for primary or secondary prevention of cardiovascular events. However, no response was received due to a lack of studies on primary prevention.

In a meta-analysis by Bernasconi et al. [14], the corresponding question was considered, whether the efficacy of EPA/DHA varies depending on the patient's initial risk. For each outcome, the corresponding risk was assessed in the placebo (no-treatment) group as an indicator of population risk. Most of the available RCTs were performed in high-risk groups (patients with documented CVDs, diabetes mellitus, or a history of cardiovascular events). It was found that EPA/DHA improved treatment efficacy only in patients at higher risk of MI compared to other risk groups and only following dose adjustment. Although the fact that the effect of EPA/DHA does not increase with a higher initial risk of cardiovascular events provides some reassurance that the efficacy findings can also be extrapolated to lower-risk patient groups, further clinical studies are required for definite confirmation.

Therefore, the objective of the present study is to estimate the economic consequences of using omega-3-acid ethyl esters 90 for the primary prevention of severe cardiovascular events in patients with residual hypertriglyceridemia.

Figure 1. Summary of meta-analysis of data on the efficacy of omega-3-acid ethyl ethers 90 in reducing the cardiovascular risk



The combined value of the odds ratio and 95% confidence interval, and the number of studies, and the total number of subjects are shown. RCT, randomized clinical trial.

Material and Methods

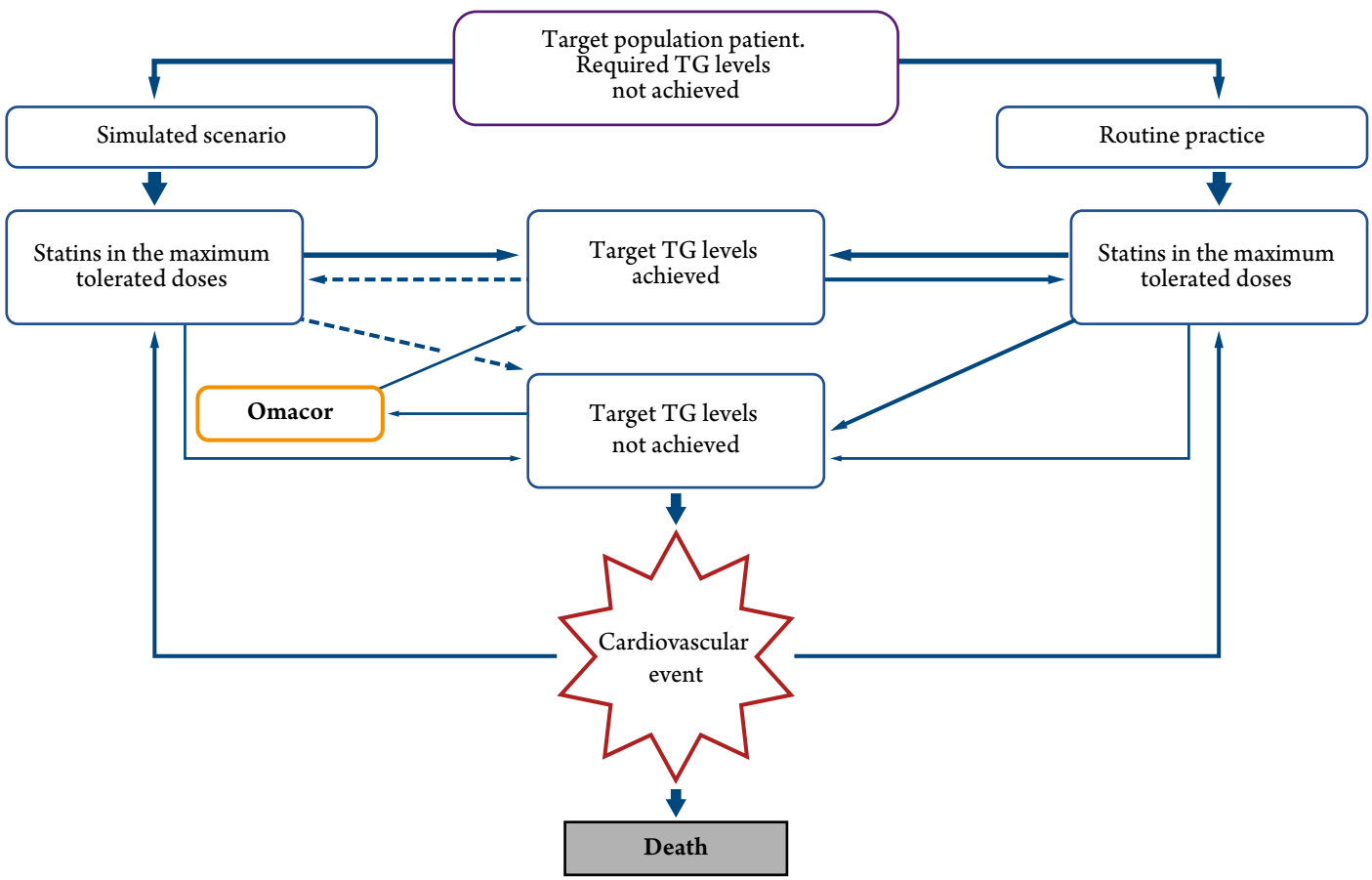
Comparative evaluation of omega-3-acid ethyl ester 90 (Omacor) therapy for primary prevention of cardiovascular events in patients with residual hypertriglyceridemia during high-dose statin therapy and high-dose statin monotherapy was conducted in the pharmacoeconomic model developed in Microsoft Office Excel 2016. This model can be used to calculate the cost of events in a cohort of patients with residual hypertriglyceridemia based on the efficacy indicators of the tactics of interest (Figure 2). The meta-analysis data by Bernasconi et al. were used as a source of efficacy data [14] (Table 1).

Given the 48-month median duration of RCTs included in the meta-analysis by Bernasconi et al. [14] and the findings on clinical efficacy for the corresponding period, the following formulas with an intermediate calculation of the event rates were used to calculate the annual probability of events [15]:

$$p=1-\exp^{-\lambda t},$$

$$\lambda=-\frac{1}{t}\ln(1-p),$$

Figure 2. Model structure



The model allows calculating the cost of events in a cohort of patients with residual hypertriglyceridemia based on the efficacy indicators of the tactics of interest.

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Table 1. Results of a meta-analysis of using of EPA/DHA in patients with residual hypertriglyceridemia

Number of studies	Study design	Number of events/patients		Effect	
		EPA / DHA	control	OR (95% CI)	AR (95% CI)
Cardiovascular events					
39	RCTs	7,963 / 67,746 (11.8%)	8,304 / 67,448 (12.3%)	0.95 (0.90–1.00)	6 events less per 1,000 patients (12–0)
Nonfatal MI					
24	RCTs	1,877 / 66,612 (2.8%)	2,115 / 66,401 (3.2%)	0.87 (0.80–0.96)	4 events less per 1,000 patients (6–1)
Ischemic events					
28	RCTs	4,224 / 67,210 (6.3%)	4,553 / 66,906 (6.8%)	0.90 (0.84–0.97)	7 events less per 1,000 patients (11–2)
Fatal MI					
14	RCTs	272 / 43,261 (0.6%)	363 / 43,081 (0.8%)	0.65 (0.46–0.91)	3 events less per 1,000 patients (5–1)
Death of CAD					
22	RCTs	1,728 / 63,790 (2.7%)	1,870 / 63,588 (2.9%)	0.91 (0.85–0.98)	3 events less per 1,000 patients (4–1)

EPA/DHA – eicosapentaenoic and docosahexaenoic acids; OR – odds ratio; CI – confidence interval; AR – absolute risk; RCT – randomized clinical trial; MI – myocardial infarction; CAD – coronary artery disease.

where p – probability of the event; t – time of the event; λ – rate of events.

Then, the economic evaluation of using omega-3-acid ethyl ester 90 drugs in the Russian pharmaceutical provision system was carried out using budget impact analysis (BIA). In this analysis, the calculations were made for Moscow based on the example of available epidemiological data.

Due to the lack of an official hypertriglyceridemia register in the Russian Federation, the prevalence of residual hypertriglyceridemia can only be evaluated according to the results of individual studies. In [16], the patient population was calculated based on the observational cross-sectional retrospective study of the prevalence of hypertriglyceridemia in Russia (PROMETHEUS). Although this study does not provide data on the prevalence of residual hypertriglyceridemia during high-dose statin therapy, analysis of the 2007–2014 NHANES registry [9] showed that statins had a minimal effect on the TG levels; for this reason, the PROMETHEUS data can be used to support an assumption to calculate the target patient population (Table 2).

According to the clinical guidelines [11], the resulting patient population included either patients who received high-dose statins and had TG levels of 1.7–2.3 mmol/L or those who received high-dose statins and had TG levels >2.3 mmol/L and fibrate intolerance. The estimated population of such patients in Moscow was 555,643.

The BIA was performed according to the generally accepted method and following the guidelines on the evaluation of the budget impact within the State Guarantee of Free Medical Care to the Citizens of the Russian Federation approved by order of the Center for Healthcare Quality Assessment and Control of the Ministry of Health of the Russian Federation No. 242-od as of December 29, 2018 [19].

The budget impact was calculated using the formula:

$$BIA\ (RUB)=C1-C0,$$
$$BIA\ (\%)=C1/(C0)-1,$$

where BIA (RUB) – difference in total costs between the current options of the drug therapy and the expected therapy (using the investigational drug) in rubles; BIA (%) – difference in total costs between the current option of the drug therapy and the expected therapy (using the investigational drug) in percent; C0 – total cost of therapy

Table 2. Number of patients requiring hypertriglyceridemia correction in Moscow

Parameter	Number of patients		Source
	n	%	
18 years and older	10,470,000	100	Russian Federal State Statistics Service [17]
Prevalence of dyslipidemia	3,141,000	30.0	[16]
Prevalence of atherogenic dyslipidemia (TG 1.7–2.3 mmol/L)	502,560	16	[16]
Prevalence of atherogenic dyslipidemia (TG >2.3 mmol/L)	408,330	13.0	[16]
Fenofibrate intolerance in patients with TG >2.3 mmol/L	53,083	4	[18]

TG, triglycerides.

for all patients at the baseline distribution; C1 – cost of treatment in case of a potential increase in the number of patients taking omega-3-acid ethyl ethers 90. The BIA horizon was equal to 1 year.

Types of costs taken into account and sources of information

The study considered direct and indirect medical costs of cardiovascular events in residual hypertriglyceridemia: costs of drug therapy; costs of treating non-fatal (acute cerebrovascular accident, MI) events in residual hypertriglyceridemia; costs of rehabilitation following non-fatal events in residual hypertriglyceridemia.

Costs of fatal cases

The dosing regimens as per drug labels were used to calculate the costs of drug therapy. Since the List of Vital and Essential Drugs includes only one drug for high-dose statin therapy (atorvastatin), the cost of annual treatment with atorvastatin 80 mg/day was calculated as the median value of all approved trademarks of this INN. The atorvastatin price was determined according to the State Register of Maximum Sale Prices (as of October 10, 2020). The calculation of the treatment cost, VAT (10%), and the expected wholesale premium (11.84%) according to the corresponding data of the Federal Antimonopoly Service of the Russian Federation (as of October 10, 2020) [20].

Thus, the cost of atorvastatin (80 mg/day) therapy was 10,840.5 rubles a year. The cost of one pack of Omakor (1000 mg, 28 capsules) was provided by the customer according to IQVIA as of 06.2020 and was equal to 1,642 RUB. Since in the meta-analysis by Bernasconi et al. [14], the mean dose of EPA/DHA was 1221 mg/day, with no dose-dependent effect for OR of non-fatal or fatal MI and death of CAD, the dose of 1000 mg/day was used, which corresponded to the dose for primary prevention according to the drug label [21]. The study used only data on full-dose treatment costs taking into account the assumption of an equal rate of treatment refusal.

Calculation of direct medical costs for inpatient care

Input intensity indices (III) provided by the payment system according to the clinical and statistical groups (CSGs) [22] and the normal standard of financial cost of one admission to 24-hour hospital (24hH) 34,713,70 RUB or day hospital (DH) 20,454.40 rubles for scheduled and emergency hospitalizations following the Resolution of the Russian Federation Government No.1610 «On the State Guarantee of Free Medical Care to the Citizens of the Russian Federation for 2020 and the planned period of 2021 and 2022» as of December 7, 2019 [23].

The total cost of hospital treatment was calculated using the formula:

$$COIinp=CostNS2 \cdot III,$$

where COIinp is inpatient care costs; CostNS2 – normal standard of financial cost of one admission; III – input intensity index depending on CSGs.

In case of emergency hospitalization, the cost of an emergency call (2,314.00 RUB/call) was added to the costs [23]. The costs of subsequent cardiac rehabilitation of patients after MI and CABG (CSG #st25.012). It was assumed that patients received this service once within the year following the event.

Since the mean base rate of DH and 24hH in the Russian Federation differs from the normal standard of financial costs of one case of hospitalization due to the formation of fixed insurance spares in the territorial obligatory medical insurance funds and allocation of a part of funds for high-tech medical care [24] following the guidelines on comparative clinical and economic evaluation of a drug approved by order of the Center for Healthcare Quality Assessment and Control of the Ministry of Health of the Russian Federation No. 242-od as of December 29, 2018 [25], correction factors (CF) were used (0.65 for the DH base rate and 0.6 for the 24hH base rate). Thus, the calculation of the mean cost of the completed case of hospitalization included in the CSG in the medical organizations (their structural units) providing medical care under obligatory medical insurance was carried out using the following formula [25]:

$$C24hH=N24hH \times CF \times III,$$

where C24hH – mean cost of a completed case of hospitalization, included in the CSG, in medical organizations (their structural units) providing inpatient medical care at the expense of obligatory medical insurance; N24hH – mean normal standard for financial costs of one case of hospitalization in medical organizations (their structural units) providing inpatient medical care at the expense of obligatory medical insurance; CF – correction factor reflecting the lower base rate (the mean cost of the completed inpatient case included in the CSG) of the normal standard of financial cost; III – input intensity index of the CSG to which this hospitalization is referred.

The management coefficient and differentiation coefficient were equal to 1 due to their regional specificity, which can be considered a limitation to the study.

Analysis of direct non-medical costs

The state support for payments of disability allowance was based on the number of patients who became disabled

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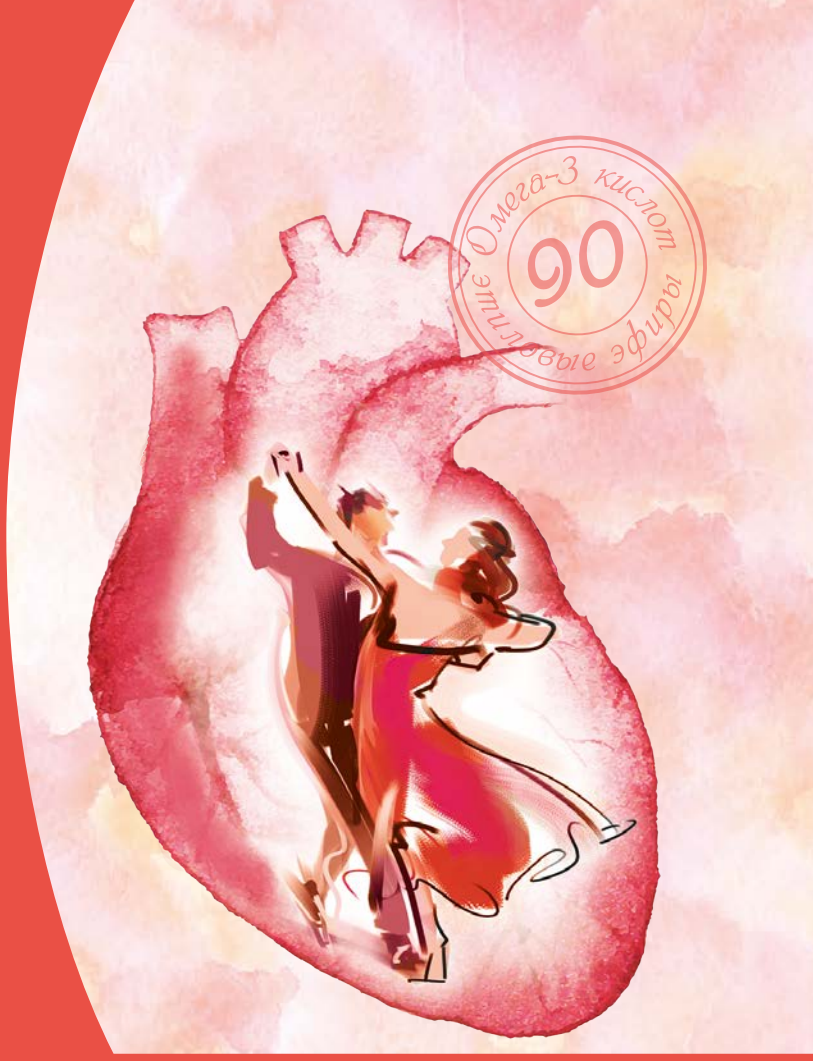
Abbott

- Способствует восстановлению клеток сердца*, 1, 2
- Снижает риск внезапной сердечной смерти на 45%*, 3
- Хорошо переносится при длительной терапии*, 4, 5



* У пациентов после инфаркта миокарда (в составе комбинированной терапии): в сочетании со статинами, антиагрегантными средствами, бета-адреноблокаторами, ингибиторами ангиотензинпревращающего фермента (АПФ).

ОМАКОР ДЕЛО ЖИЗНИ

ДЛЯ ВТОРИЧНОЙ ПРОФИЛАКТИКИ ПОСЛЕ ИНФАРКТА МИОКАРДА*, 6

Омакор. Регистрационный номер: ЛС-000559. **Международное непатентованное или группировочное наименование:** Омега-3 кислот этиловые эфиры 90. **Лекарственная форма:** капсулы, 1000 мг. **Фармакологические свойства*.** Полиненасыщенные жирные кислоты класса омега-3 – эйкозапентаеновая кислота (ЭПК) и докозагексаеновая кислота (ДГК) – относятся к незаменимым (эссенциальным) жирным кислотам (НЭЖК). Результаты клинического исследования GISSI-Prevenzione, полученные за 3,5 года наблюдений, показали существенное снижение относительного риска смертности от всех причин, нефатального инфаркта миокарда и нефатального инсульта на 15 % ([2-26] p=0,0226) у пациентов после недавно перенесенного инфаркта миокарда, принимавших препарат Омакор по 1 г в сутки. Дополнительно, относительный риск смерти по причине сердечно-сосудистой патологии, нефатального инфаркта миокарда и нефатального инсульта снижался на 20 % ([5-32] p=0,0082). Результаты клинического исследования GISSI-Heart Failure, в котором пациенты с хронической сердечной недостаточностью получали препарат Омакор по 1 г в сутки в среднем в течение 3,9 лет, показали снижение относительного риска смертности от всех причин на 9 % (p=0,041), снижение относительного риска смертности от всех причин и госпитализации по причине сердечно-сосудистых патологий на 8 % (p=0,009), снижение относительного риска первичной госпитализации по причине желудочковых аритмий на 28 % (p=0,013). **Показания к применению.** Гипертриглицеридемия: эндогенная гипертриглицеридемия IV типа по классификации Фредериксона (в монотерапии) в качестве дополнения к гиполипидемической диете при ее недостаточной эффективности; эндогенная гипертриглицеридемия IIb или III типа по классификации Фредериксона в комбинации с ингибиторами ГМГ-КоА редуктазы (статинами), когда концентрация триглицеридов недостаточно контролируется приемом статинов. Вторичная профилактика после инфаркта миокарда (в составе комбинированной терапии): в сочетании со статинами, антиагрегантными средствами, бета-адреноблокаторами, ингибиторами ангиотензинпревращающего фермента (АПФ). **Противопоказания.** Повышенная чувствительность к действующему веществу, сое, арахису или любому из вспомогательных веществ, входящих в состав препарата. Возраст до 18 лет (эффективность и безопасность не установлены). Беременность и период грудного вскармливания. Омакор не следует применять у пациентов с экзогенной гипертриглицеридемией (гиперхиломикронемией I типа). **С осторожностью.** Установленная гиперчувствительность или аллергия на рыбу; возраст старше 70 лет; нарушения функции печени; одновременный прием с пероральными антикоагулянтами; геморрагический диатез; пациенты с высоким риском кровотечений (вследствие тяжелой травмы, хирургической операции); вторичная эндогенная гипертриглицеридемия (особенно при неконтролируемом сахарном диабете). **Применение при беременности и в период грудного вскармливания*.** Назначать Омакор беременным следует с осторожностью, только после тщательной оценки соотношения риска и пользы, когда польза для матери превышает потенциальный риск для плода. Препарат не должен применяться в период грудного вскармливания. **Способ применения и дозы*.** Внутрь, независимо от приема пищи. Во избежание развития возможных нежелательных явлений со стороны желудочно-кишечного тракта (ЖКТ) препарат Омакор может приниматься во время приема пищи. Гипертриглицеридемия. Начальная доза составляет 2 капсулы в сутки. В случае отсутствия терапевтического эффекта возможно увеличение дозы до максимальной суточной дозы – 4 капсулы. Вторичная профилактика инфаркта миокарда. Рекомендуется принимать по 1 капсуле в сутки. **Побочное действие*.** Желудочно-кишечные расстройства (в том числе вздутие живота, боль в животе, запор, диарея, диспепсия, метеоризм, отрыжка, гастроэзофагеальная рефлюксная болезнь, тошнота или рвота). *Перечень всех побочных действий представлен в инструкции по медицинскому применению.* **Передозировка.** Особые указания отсутствуют. Должна быть проведена симптоматическая терапия. **Взаимодействие с другими лекарственными средствами*.** При одновременном применении препарата Омакор с пероральными антикоагулянтами или другими препаратами, влияющими на систему гемостаза (например, ацетилсалициловая кислота или НПВП), наблюдалось увеличение времени свертывания крови. При этом геморрагических осложнений не наблюдалось. Ацетилсалициловая кислота: пациенты должны быть проинформированы о возможном увеличении времени свертывания крови. Совместное применение препарата Омакор с варфарином не приводило к каким-либо геморрагическим осложнениям. Однако необходим контроль соотношения протромбинового времени/международного нормализованного отношения (ПТВ/МНО) при совместном применении препарата Омакор с другими препаратами, влияющими на соотношение ПТВ/МНО, или после прекращения терапии препаратом Омакор. **Особые указания*.** Омакор должен применяться с осторожностью у пациентов с установленной гиперчувствительностью или аллергией на рыбу. В связи с умеренным увеличением времени свертывания крови (при приеме в высокой дозе, т.е. 4 капсулы в сутки) требуется наблюдение за пациентами, имеющими нарушения со стороны свертывающей системы крови или получающими антикоагулянтную терапию или другие препараты, влияющие на систему гемостаза (например, ацетилсалициловую кислоту или НПВП); при необходимости, доза антикоагулянта должна быть скорректирована. Необходимо учитывать увеличение времени свертывания крови у пациентов с высоким риском развития кровотечения. При терапии препаратом Омакор снижается уровень образования тромбоксана А2. Существенного влияния на уровень других факторов свертывания крови не наблюдалось. У некоторых пациентов наблюдалось небольшое, но достоверное повышение активности АСТ и АЛТ (в пределах нормы), при этом отсутствуют данные, указывающие на повышенный риск приема препарата Омакор пациентами с нарушением функции печени. Необходим контроль активности АСТ и АЛТ у пациентов с любыми признаками нарушения функции печени (в частности, при приеме в высокой дозе, т.е. 4 капсулы в сутки). Опыт применения препарата для лечения экзогенной гипертриглицеридемии (гиперхиломикронемии типа 1) отсутствует. Опыт применения препарата при вторичной эндогенной гипертриглицеридемии ограничен (особенно при неконтролируемом сахарном диабете). **Влияние на способность управлять транспортными средствами, механизмами*.** Ожидается, что препарат не оказывает или оказывает несущественное влияние на способность управлять транспортными средствами и работать с механизмами. **Условия хранения.** Хранить при температуре не выше 25 °С. Не замораживать. Хранить в недоступном для детей месте! Условия отпуска. Отпускают по рецепту.

***Полная информация представлена в инструкции по медицинскому применению.**

СИП от 27.09.2019 на основании ИМП от 29.08.2019.

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Информация предназначена для медицинских и фармацевтических работников.

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due to cardiovascular events, residual hypertriglyceridemia, and the disability annuity amount, which was 167,850.00 RUB group I, 93,245.76 RUB for group II, and 77,721.00 RUB for group III in 2019 [26]. The percentage of patients who received a primary disability status following the development of cardiovascular events was retrieved from the literature: it is assumed that primary disability developed in 22% of patients after ST-segment elevation MI: disability of group I in zero patients, group II in 31.1%, and group III in 11.5% of patients [27, 28].

Calculation of indirect costs

The following indirect costs due to complications of residual hypertriglyceridemia were identified: calculation of the foregone GDP per capita due to loss of earnings for the incapacity of working-age citizens; incapacity pay.

Foregone GDP arising as loss of earnings due to the incapacity of working-age citizens, which is a lost benefit of GDP for the state and society as a whole, was calculated based on the number of days of incapacity of the employed working-age individuals in the past year multiplied by the mean daily GDP of 2,041, 28 RUB/day (GDP per capita in 2019 was 745,067.30 RUB) [29].

When calculating incapacity pay, the mean national accrued salary for 2019 multiplied by the number of days of incapacity due to cardiovascular events according to the medical care standards for the corresponding disease [30, 31]. In 2019, the mean salary in the Russian Federation was 46,324 RUB/month or 1,235.3 RUB [32].

The cost of death was taken as the minimum «cost» of life from the point of view of the person's «utility» for the country and his or her family in 2018 according to the data of the Finance University under the Government of the Russian Federation [33].

Results

The use of omega-3-acid of ethyl esters 90 was evaluated in 555,643 patients with residual hypertriglyceridemia in Moscow, to whom the drug was administered following the clinical guidelines [11]. By extrapolating the available efficacy data to an assumed cohort of high-risk patients in Moscow who had achieved the target levels of LDL cholesterol during treatment with the maximum tolerated doses of statins, but who still had residual hypertriglyceridemia, the number of preventable cases of cardiovascular events can be obtained (death of CAD, acute MI, or acute coronary syndrome) by using omega-3-acid ethyl ethers 90 for 1 year following the clinical guidelines (Table 3).

The economic analysis of the comprehensive pharmacological study of using omega-3-acid ethyl ethers 90 in patients with residual hypertriglyceridemia showed no statistically significant impact on budget expenditures under the State Guarantee of Free Medical Care to the Citizens of the Russian Federation. And the use of omega-3-acid ethyl esters 90 allows the number of cardiovascular events to be significantly reduced (by 10%), which correlates with the available data on the contribution of hypertriglyceridemia correction to the reduction of cardiovascular risk [10] (Table 4).

The sensitivity analysis results revealed that the analysis results were most resistant to fluctuations in the cost and efficacy of the drug being analyzed (Figure 3).

Table 3. Results of using omega-3-acid ethyl ester 90 (Omacor) in patients with residual hypertriglyceridemia in Moscow

Parameter	Ischemic events		MI	
	Total	Of those, death of CAD	Total	Of those fatal MI
Number of events per 1 year (atorvastatin), %	3.46	1.46	1.61	0.40
Number of events per 1 year (Omacor + atorvastatin), %	3.20	1.36	1.41	0.30
Number of events per 1 year, atorvastatin	19,224	8,116	8,963	2,227
Number of events per 1 year, Omacor + atorvastatin	17,787	7,553	7,834	1,669
Difference, events	**–1,437***	**–564***	**–1,128***	**–558***
Direct costs (atorvastatin), RUB	917,440,778	80,349,356,867	1,410,068,503	22,047,642,670
Direct costs (Omacor+atorvastatin), RUB	848,864,936	74,769,823,374	1,232,548,301	16,527,422,563
Difference, direct costs, RUB	–68,575,842	–5,579,533,493	–177,520,202	–5,520,220,108
Indirect costs (atorvastatin), RUB	1,177,306,658		607,928,012	
Indirect costs (Omacor+atorvastatin), RUB	1,087,672,927		541,910,296	
Difference, indirect costs, RUB	–89,633,730		–66,017,716	
Cost of drugs (atorvastatin), RUB	6,023,446,857			
Cost of drugs (Omacor+atorvastatin), RUB	17,884,200,201			
Difference, cost of drugs, RUB	11,860,753,343			

* – number of prevented cardiovascular events.

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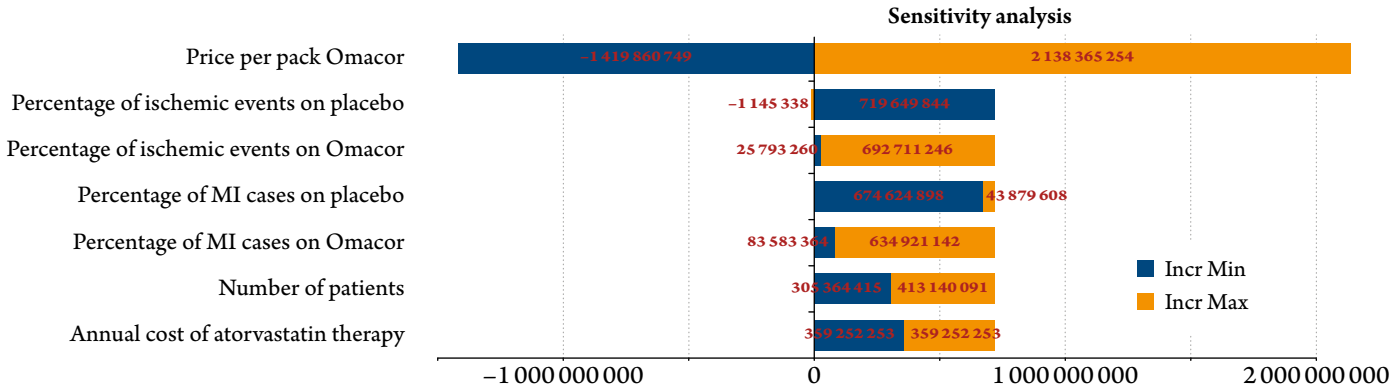
Table 4. Analysis of economic implications of using omega-3-acid ethyl ester 90 (Omacor) in patients with residual hypertriglyceridemia in Moscow

Indicator, RUB	Omacor+ atorvastatin 80 mg	Atorvastatin 80 mg	Difference	
			n, RUB	%
Costs of the health care system in case of cardiovascular events in hypertriglyceridemia, RUB	95,008,242,397	106,509,743,488	–11,501,501,090	–11
Direct costs, RUB	93,378,659,174	104,724,508,818	–11,345,849,644	–11
Indirect costs, RUB	1,629,583,223	1,785,234,669	–155,651,446	–9
Treatments costs, RUB	17,884,200,201	6,023,446,857	11,860,753,343	197
Total, RUB	112,892,442,598	112,533,190,345	359,252,253	0.32
Number of cardiovascular events	34,844	38,530	–3,686	–10

Figure 3. Sensitivity analysis, RUB



Incr Max – value of saving in the maximum value of the corresponding parameter;
Incr Min – value of saving in the minimum value of the corresponding parameter (according to the authors).

Conclusion

The results of the comprehensive pharmacoeconomic study suggest that the use of omega-3-acid ethyl ethers 90 (Omacor) in patients with residual hypertriglyceridemia is an economically advantageous tactic as compared to high-dose statin monotherapy, which does not have a statistically significant affect on the budget expenditure under the State Guarantee of Free Medical Care to the Citizens of the Russian Federation (0.32% increase in costs compared to the current practice), while allowing for a 10% decrease in the number of severe ischemic cardiovascular events.

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