MAXEPA 1g, capsule
Box of 60 (CIP: 329 763-8)

Applicant: PIERRE FABRE MEDICAMENT

Natural fish oil containing at least 30% omega-3 polyunsaturated fatty acids, including 18% eicosapentaenoic acid (EPA) and 12% docosahexaenoic acid (DHA), alpha-tocopherol acetate.

Date of initial Marketing Authorisation: July 17, 1987, July 5, 2007 (latest revision of Marketing Authorisation)

Reason for request: Inclusion on the list of medicines reimbursed by National Insurance and approved for hospital use.

The laboratory is requesting MAXEPA’s inclusion only for the management of HIV-infected patients receiving antiretroviral polytherapy and with hypertriglyceridaemia.

Health Technology Assessment Division
1. CHARACTERISTICS OF THE MEDICINAL PRODUCT

1.1. Active ingredient
Fish oil with a high concentration of polyunsaturated fatty acids from the omega-3 series in their natural form as triglycerides: eicosapentaenoic acid (EPA: 18%) and docosahexaenoic acid (DHA: 12%) (See SPC: Pharmacodynamic properties).

1.2. Indication
Endogenous, isolated or predominant hypertriglyceridaemia in patients at risk of coronary heart disease and/or pancreatitis, supplementing a suitable, strict diet which, when prescribed on its own, has proven to be insufficient in terms of providing an adequate response.

1.3. Dosage
In adults: 6 capsules/day (2 capsules x3/day).

2. SIMILAR MEDICINAL PRODUCTS

2.1. ATC Classification
C: Cardiovascular system
C10: Serum lipid-reducing agents
C10A: Cholesterol and triglyceride reducing agents
C10AX: Other cholesterol and triglyceride reducing agents
C10AX06: Omega-3 triglyceride
2.2. Medicines in the same therapeutic category

2.2.1 Comparator medicines

The medicinal product OMACOR\(^1\), which is also composed of omega-3 triglycerides, has the following indications:
- endogenous, isolated or predominant hypertriglyceridaemia in patients at risk of coronary heart disease and/or pancreatitis, supplementing a suitable, strict diet which, when prescribed on its own, has proven to be insufficient in terms of providing an adequate response.
- adjuvant treatment for the secondary prevention of myocardial infarction, combined with reference treatments (including statins, platelet aggregation inhibitors, beta-blockers and ACE inhibitors).

NB: OMACOR is only reimbursed in its indication for cardiovascular prevention.

Reminder of composition of MAXEPA and OMACOR:
- MAXEPA: Natural fish oil, containing a minimum of 30% of omega-3 polyunsaturated fatty acids: 1 g includes: eicosapentaenoic acid (EPA): 18% docosahexaenoic acid (DHA): 12%. Excipients: alpha-tocopherol acetate (1.75 mg/caps). Capsule shell: gelatin, glycerol, purified water. Calibration: no. 20
- OMACOR: Omega-3 acid ethyl esters at 90%: 1 g (or in eicosapentaenoic acid ethyl esters [EPA: 46%] and docosahexaenoic acid [DHA: 38%]: 840 mg/caps), alpha-tocopherol (antioxidant): 4 mg. Excipients: Capsule shell: gelatin, glycerol, purified water.

2.3. Medicines with a similar therapeutic aim

- In the case of isolated hypertriglyceridaemia: fibrates (gemfibrozil, fenofibrate …).
- In the case of mixed types of dyslipidaemia, combined with hypertriglyceridaemia and hypercholesterolaemia: statins; NIASPAN LP (nicotinic acid).

\(^1\) The medicinal product OMACOR (composed of an 85% concentrate of polyunsaturated omega-3) belongs to the same therapeutic category as MAXEPA (medicinal product). Marketed by the PIERRE FABRE MEDICAMENT laboratories, it has the following indication:
- endogenous, isolated or predominant hypertriglyceridaemia in patients at risk of coronary heart disease and/or pancreatitis, supplementing a suitable, strict diet which, when prescribed on its own, has proven to be insufficient in terms of providing an adequate response and.
- adjuvant treatment for the secondary prevention of myocardial infarction, combined with reference treatments (including statins, platelet aggregation inhibitors, beta-blockers and ACE inhibitors).

The Committee considered that the actual benefit of OMACOR depended on the indication:
- in the treatment of hypertriglyceridaemia: insufficient to justify reimbursing the treatment cost
- as secondary prevention of myocardial infarction: substantial.

A moderate IAB (level III) was awarded in terms of therapeutic efficacy, taking into account the small reduction in mortality and its therapeutic use. Furthermore, the Committee pointed out that “secondary prevention of myocardial infarction leads to the prescription of 3 to 4 drugs per day (on average). The prescription of one additional drug may result in a reduction in compliance.” (Cf. opinion of March 20, 2002).

The medicinal product OMACOR has been included for reimbursement since 12/01/2005 only in its indication for cardiovascular prevention.
3. ANALYSIS OF AVAILABLE DATA

To support its request, the laboratory has submitted the results of a placebo-controlled comparative study of HIV patients with hypertriglyceridaemia. The results of a retrospective analysis have not been commented on in this opinion due to the potential methodological biases associated with this type of analysis.

3.1. Efficacy results

The objective of this study was to compare the progression of triglyceride levels in HIV patients being treated with antiretroviral triple therapy after treatment with MAXEPA or a placebo. The patients also had to have followed a diet for 1 month. This diet was continued during the study. The duration of the comparative phase was 8 weeks.

Design
It was a double-blind, randomised, placebo-controlled study, consisting of one hundred and twenty-two (122) outpatients, no younger than 18 years of age, of both sexes, carrying the HIV virus and stabilised by antiretroviral polytherapy for at least 2 months. They had a baseline triglyceride level of between 2 and 10 g/l after 1 month on the diet. Patients being treated with lipid-reducing agents or with a stroke history were not included.

Sixty patients were given 6 MAXEPA capsules per day (in three daily doses) for 8 weeks (2 months) and sixty-two patients were given a placebo.

NB:
- Ten patients with a triglyceride level above 10 g/l were given MAXEPA in an open-label phase.
- A 2-month non-comparative follow-up period took place.

The primary efficacy endpoint was the percentage of variation in the triglyceride level between the time of inclusion and the last measurement available.

NB: Statistical hypothesis: MAXEPA’s superiority over the placebo where a difference of at least 20% was highlighted between the two treatment groups.

- Numerous secondary efficacy endpoints were selected: in particular, the proportion of patients responding to treatment. The responders were defined as those patients whose triglyceride level was normalised (1st definition) or those whose triglyceride level dropped down to a lower category and was reduced by at least 20% (2nd definition). Three “categories” were defined: < 2g/l; ]2-4 g/l[; ]4-10 g/l[.

The assessment of the clinical signs of lipodystrophy was carried out by the investigator and the patient: circumference of the waist and hips, presence or absence of Bichat's fat pads, buffalo hump, lipomas, definition of the stage of lipodystrophy.
**Results**

The results were analysed in intention to treat (n = 120 ITT patients) and *per protocol* (n = 97). Only the results of the ITT analysis are presented below.

**Baseline patient characteristics**
- A majority (over 88%) were men. They had an average weight of 69 kg with a body mass index (BMI) of 22.7 kg/m².
- The patients had been HIV carriers on average for 11 years and had been receiving antiretroviral treatments for 7 years. At the time of inclusion in the study, almost 60% of them were at an asymptomatic primary infection stage and almost 30% were at an AIDS stage. The CD4 lymphocyte count was higher than 500/mm³ in almost 31% of patients and lower than 200/mm³ (22.4% in the MAXEPA group and 32.3% in the placebo group) in 27.5% of patients.

The antiretroviral triple therapy in progress at the time of inclusion involved the combination of nucleoside reverse transcriptase inhibitors and protease inhibitors for 47% of the patients in the MAXEPA group and for 53% of the patients in the placebo group. Almost a third of the patients did not receive any protease inhibitors.

- Their hypertriglyceridaemia condition had been evolving for over 3.1 years in the placebo arm and for 3.8 years in the MAXEPA arm. The concentration of triglycerides was 4.4g/l on average in the MAXEPA group and 4.7 g/l in the placebo group.

**Results**

58 patients were given MAXEPA and 62 a placebo.

After 8 weeks of treatment: the mean triglyceride level value was 3.4 g/l (CI<sub>95</sub>: 3.0 – 3.9 g/l) with MAXEPA and 4.8 g/l (CI<sub>95</sub>: 4.1 – 5.6 g/l) with placebo or an additional reduction of around 1.4 g/l (or -24.6% (-40.9%, - 8.4%)) in favour of MAXEPA, p= 0.0033.

Result for the secondary endpoints:
- There were more “responders” with MAXEPA than with placebo. As a result, the triglyceride level was more often normalised to less than 2g/l (22.4% vs. 6.5%, p =0.0126) and fell more often by at least 20% (37.9% vs. 17.7%, p = 0.0137 – ITT).
- The lipodystrophy was clinically stable in both groups: it remained at the same stage of severity in 74% of patients with MAXEPA and in 69% of patients with placebo.

**NB:**
For information, in the subgroup of 10 patients with a triglyceride level greater than 10 g/l, MAXEPA reduced the level without normalising it. The impact of the drop in the triglyceride level (biological effect) on the reduction in the risk of pancreatitis occurring (clinical effect) has not been established (see SPC for MAXEPA).

**Comments on the efficacy results**
- The duration of the diet was 1 month. Good practice guidelines in France² advocate a 3-month diet before introducing lipid-reducing medication.
- The patients could have benefited from the prescription of a fibrate (see Section 4.3 Therapeutic use).
- The size of MAXEPA’s effect as a triglyceride reducer in this subpopulation of patients is the same as that indicated for the general population.

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²“In the case of primary prevention, cardiovascular risk depends on the number of associated risk factors. Consequently, the overall cardiovascular risk should be assessed by listing the risk factors, the dyslipidaemia should be treated using diet and lifestyle measures for a minimum of 3 months, which after this period of time will be combined with drug treatment if the therapeutic objective has not been achieved. In the case of secondary prevention, cardiovascular risk is increased immediately.” Therapeutic management of patient with dyslipidaemia, Afssaps March 2005.
3.2. Adverse events

In the randomised, placebo-controlled study described above, there was no difference observed between the two arms in terms of adverse events after the 8 weeks of treatment during the comparative phase. The most common adverse events with MAXEPA were digestive problems. Taking MAXEPA had no influence on the progression of the HIV infection.

MAXEPA’s safety profile in HIV patients does not seem to differ from that known among the general population.

The MAXEPA SPC indicates that nausea and belching are rarely mentioned. There is one warning about the risk of bleeding when MAXEPA is combined with oral anticoagulants.

3.3. Conclusion

In a randomised, double-blind clinical study carried out on 122 HIV patients, receiving antiretroviral polytherapy and with a mean triglyceride level of 4.5 g/l after failing to comply with the dietary and lifestyle measures for 4 weeks, 6 capsules of MAXEPA per day were more effective than a placebo in reducing the triglyceride level after 2 months of treatment. The mean reduction in the triglyceride level was around -24.6% [-40.9%, -8.4%] in favour of MAXEPA (p = 0.0033), representing a drop of around 1.4 g/l. This triglyceride-reducing effect was achieved in combination with dietary measures.

The clinical relevance of MAXEPA’s triglyceride-reducing effect is not very well known, including in HIV patients. In fact, the short duration of this study and the choice of the placebo as a comparator means that it is not possible to assess the clinical benefit derived from MAXEPA in the case of extended treatment. As in the case of patients not infected with HIV, it is not demonstrated that the reduction in the triglyceride level achieved with MAXEPA can reduce the risk of pancreatitis or cardiovascular problems. In HIV-infected patients being treated with antiretroviral polytherapy, the impact of MAXEPA on the progression of lipodystrophy with an iatrogenic cause has not been established.

The safety profile of MAXEPA is known among the general population. This medicine is globally well tolerated (digestive problems reported). MAXEPA’s safety profile in HIV patients does not seem to differ from that known among the general population.

First-line drug treatment for hypertriglyceridaemia is based on the administration of fibrates, including for HIV-infected patients. No study has compared the efficacy and adverse effects of MAXEPA with those of fibrates. It has not been established that MAXEPA is effective in patients with a high level of hypertriglyceridaemia, which is resistant to properly followed dietary measures and treatment with fibrates, which would validate its benefit as an alternative treatment in these patients.

When hypertriglyceridaemia creates an immediate risk of pancreatitis, the role of MAXEPA and that of fibrates (or other triglyceride-reducing drugs) is not established.
4. TRANSPARENCY COMMITTEE CONCLUSIONS

4.1. Actual benefit

- The rise in the overall cholesterol level and the LDL cholesterol level, the fall in the HDL cholesterol level and hypertriglyceridaemia are risk factors in coronary heart disease and mortality of cardiovascular origin in France, as well as in other developed countries. Patients exposed to hypertriglyceridaemia are exposed in the short term to the risk of acute pancreatitis (in the case of hypertriglyceridaemia at a level of 10 g/l or more) and cardiovascular complications.

HIV-infected patients are currently surviving longer and certain data would suggest they have an increased cardiovascular risk. Their condition and the treatments used for it encourage hyperlipidaemia, especially hypertriglyceridaemia, with levels which are sometimes very high. Fat distribution abnormalities (lipodystrophy: hypo and/or hypertrophy) are also observed in these patients.

- MAXEPA is slightly effective as a triglyceride-reduction agent versus placebo, but only very short term. The safety profile seems to be good. The efficacy/adverse effects ratio is modest in this population.

**Public health benefit in HIV-infected patients**

Hypertriglyceridaemia may expose these patients to the risks of acute pancreatitis (for concentrations at 10 g/l or higher) and cardiovascular disorders which are life-threatening. There is also an increase in the frequency of dyslipidaemia among the HIV-infected population, being treated with antiretroviral polytherapy. However, the burden represented by these patients is unknown: the frequency of pancreatitis due to hypertriglyceridaemia and the proportion of cardiovascular disorders attributable to hypertriglyceridaemia are not known for HIV-infected patients.

Improving the management of the HIV infection and preventing cardiovascular diseases are each one of the identified public health priorities (GTNDO³). Reducing cardiovascular risk is part of the management of HIV-infected patients.

It is not possible, based on the data available, to put forward a case for an impact in terms of morbi-mortality (pancreatitis, cardiovascular disorders) for MAXEPA in HIV-infected patients.

Therefore, there is no reason to think that MAXEPA can respond to the identified requirement.

Consequently, MAXEPA is not expected to benefit public health with regard to the population of HIV-infected patients.

- The management of these patients includes: a properly followed diet. The next step is, if possible, to replace the antiretroviral drug suspected of increasing the hypertriglyceridaemia. When the prescription of a triglyceride-reducing drug is considered, fibrates are the preferred first-line treatment.

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Taking into account the clinical data available, there is insufficient proof to indicate the benefit of prescribing MAXEPA:

- to recommend its prescription as a first-line treatment as an alternative to fibrates
- as a second-line treatment where fibrates are ineffective; there is no study available which has assessed the benefit of combining MAXEPA with a fibrate nor one concerning treatment with MAXEPA in patients with severe hypertriglyceridaemia, which is resistant to fibrates. MAXEPA’s efficacy in these situations remains to be established.
- as an alternative, when one of the fibrates available cannot be used, there are other drugs with a triglyceride-reducing effect (niacin or statins, for instance), which have better evidence of their long-term effect in preventing cardiovascular risk. In the case of hypertriglyceridaemia with high levels (> 10 g/l), with a potential risk of pancreatitis, no drug has proved to have a preventive effect.

- The effect of taking 6 MAXEPA capsules daily on the compliance of patients undergoing long-term antiretroviral polytherapy must also be taken into account.

In conclusion, the actual benefit of MAXEPA in HIV-infected patients is low, based on the clinical data available: a single randomised clinical study lasting 8 weeks; a moderate triglyceride-reducing effect compared to the placebo; no effect established in terms of preventing the risk of acute pancreatitis and cardiovascular risk; no clinical data available to prove the effect of MAXEPA in patients with a very high level of hypertriglyceridaemia (> 10 g/l), with these patients possibly being at risk of acute pancreatitis - taking into account the existence of other triglyceride-reducing drugs for which better evidence is available indicating their efficacy and safety when prescribed for several months/years.

4.2. Improvement in actual benefit

Not applicable.

4.3. Therapeutic use

Introduction
Screening for dyslipidaemia is based on investigating a lipid abnormality which determines the levels of total cholesterol, triglycerides, HDL and LDL cholesterol. Prescribing lipid-reducing drugs is not justified for numerous patients at a low cardiovascular risk. Treatment through diet is the basis for managing these patients. In France hypertriglyceridaemia is commonly associated with an excessive consumption of alcohol and the existence of a metabolic syndrome.

The role of an isolated increase in triglyceride levels as an independent cardiovascular risk factor remains controversial, even if certain studies suggest that the increase in the triglyceride level is an independent cardiovascular risk factor. However, there is no intervention study indicating that a drop in triglyceride levels leads to a significant reduction in cardiovascular morbidity. It is possible however to suggest that an increase in triglyceride levels is a marker of cardiovascular risk as it is often associated with carbohydrate metabolism problems, excess weight or obesity and/or a low HDL cholesterol level.
4.3.1. Reminder of management of hypertriglyceridaemia in general population

According to the 2005 recommendations for managing dyslipidaemia (which can be accessed from the Afssaps website):

Managing dyslipidaemia must be combined with the management of other cardiovascular risk factors.

If dietary treatment is properly followed this can help to avoid introducing treatment using drugs in a large number of cases. In order to achieve this, it must be introduced with sufficient motivation on the part of the prescriber and patient.
The basic aim of making dietary changes is to reduce the consumption of animal fats (saturated fatty acids) and to lose weight, if necessary. These measures must be presented in a positive light.

Among the suitable dietary recommendations available, it would seem vital however to insist on the following specific points:
- stopping the consumption of alcohol and restricting the intake of fruit (cross-sensitivity between fructose and alcohol); carrying out a diagnosis test to confirm the abstention from alcoholic drinks for 5 to 7 days assesses how susceptible triglyceride levels are to the consumption of alcoholic drinks
- distinct restriction in the consumption of monosaccharides
- restriction in calorie intake if patients are overweight.

In the case of mixed types of hyperlipidaemia, certain measures which must be insisted on in particular are the adjustment of excess weight when there is any and carrying out regular physical exercise of a moderate intensity.

Dietary modification is proposed to all patients failing to achieve optimum concentrations defined by treatment targets determined according to the risk factors present. This will be continued for as long as possible.

*Consumption of fish oils as part of the diet is beneficial*

Oils derived from cold-water fish (rich in DHA and EPA fatty acids) have triglyceride-reducing properties. The consumption of EPA and DHA reduces the occurrence of plasma triglycerides and, to a lesser extent, the HDL cholesterol level. EPA and DHA also reduce blood pressure and the occurrence of arrhythmias, while also improving haemostasis. Eating fish regularly (2 to 3 times a week) is recommended. These objectives are achieved by partially substituting animal fats (butter, cheese, fatty meat, pork products, processed foods) with vegetable fats (oils rich in mono and/or polyunsaturated fatty acids, soft margarines) and fish.

*Managing hypertriglyceridaemia with drugs depends on its level.*

According to the guidelines, treatment using a lipid-reducing drug usually starts with the smallest dosage. If the condition has not been assessed adequately, the use of high doses and even of treatment combinations must be discussed on a case by case basis. It must not be initiated at the expense of safety and adherence to the treatment. Monitoring of the efficacy and safety begins between 1 and 3 months after the start of treatment.
- If there is an increase in the triglyceride blood level of between 2 g/l (2.25 mmol/L) and 4 g/l (4.5 mmol/L), this requires mainly specific dietary treatment based on stopping the consumption of monosaccharides and alcohol, along with reducing calorie intake in the case of associated excess weight.
- Above 4 g/l (4.5 mmol/L), if these measures do not help to achieve a reduction in the triglyceride level, resorting to prescribing medication may be justified in order to limit the risk of acute pancreatitis, which is a particular concern with a level of 10 g/l (11.25 mmol/L), even though no specific study has proved its efficacy.
Fibrates are the only medicinal products which can be used in this situation. The benefit of fish rich in omega-3 polyunsaturated fatty acids has not been established in this situation.

4.3.2. Managing hypertriglyceridaemia in the particular case of HIV-infected patients (according to the company's request to include only these patients for the reimbursement of the costs for MAXEPA):

According to the YENI report published in 2006, lipid abnormalities observed during antiretroviral treatment are frequent, whether in the form of hypertriglyceridaemia (TG > 1.5 or 2 g/l) or total hypercholesterolaemia, linked to an increase in LDL cholesterol (> 2.2 g/l, or 5.7 mmol/l) associated or not with a reduction in HDL cholesterol (< 0.35 g/l, or 0.9 mmol/l). These abnormalities caused by the drugs vary according to the antiretroviral drugs used, the patient's age, nutritional state, immunosuppressive state and level of chronic inflammation. There is very likely a link between lipid metabolism problems and lipodystrophic syndrome. In addition, every class of antiretroviral drug, except for enfuvirtide, may modify lipid parameters. Confirming the individual liability of each drug is made difficult by the fact that antiretroviral drugs are combined according to different regimens from one study to another.

The general principles for managing these patients are as follows.

First stage: dietary treatment.
Dietary treatment is proposed to all patients who do not have an optimum concentration corresponding to the treatment goal determined according to the risk factors present, and will be continued for as long as possible.

Changes in diet involve 4 categories of measures:

- restriction in the intake of saturated fatty acids (animal fats) in favour of mono and polyunsaturated fatty acids
- increased consumption of omega-3 polyunsaturated fatty acids (fish)
- increased intake of dietary fibre and natural micronutrients (fruits, vegetables, cereal products)
- restriction in dietary cholesterol or even the intake of foods supplemented in plant sterols.
- on top of these recommendations, there is the need to limit alcohol consumption, keep weight under control and change an excessively sedentary lifestyle.

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5 “Nutritional guidelines which have proved their contribution in cardiovascular prevention: oils derived from cold-water fish (rich in DHA and EPA fatty acids) have triglyceride-reducing properties. The consumption of EPA and DHA reduces the occurrence of plasma triglycerides and the HDL cholesterol level, to a lesser extent. They also reduce blood pressure and the occurrence of arrhythmias, while also improving haemostasis. Eating fish regularly (2 to 3 times a week) is recommended. These objectives are achieved by partially substituting animal fats (butter, cheese, fatty meat, pork products, processed foods) with vegetable fats (oils rich in mono and/or polyunsaturated fatty acids, soft margarines) and fish.”
Second stage: **modification of antiretroviral treatment.**
(Refer to principles defined in the YENI report.)

Third stage: **initiation of treatment with lipid-reducing drugs**.
The main objective of lipid-reducing treatment is to reduce cardiovascular risk. It is therefore necessary to estimate this risk with regards to other risk factors.

Management depends on the level of hypertriglyceridaemia.
- Severe, isolated hypertriglyceridaemia (> 4 g/l): treatment will be initiated with a fibrate [fenofibrate (Lipanthyl®) or gemfibrozil (Lipur®)], while regularly monitoring the liver profile and muscular enzymes due to the risk of rhabdomyolysis occurring, even though there is no proven interaction between fibrates and antiretroviral drugs.

At a dose of 1g per day, fish oils (long-chain omega-3 fatty acids: EPA and DHA) have indicated a beneficial effect with a reduction in the number of sudden deaths among patients not infected with HIV as a secondary prevention. When administered at high doses (3 to 4 g/day) in the form of supplements (MAXEPA, Omacor), fish oils have triglyceride-reducing effects (~25 to ~30 p. 100).

Using these products for HIV+ patients with major hypertriglyceridaemia which is resistant to dietary measures and other drug treatments may be considered, with the knowledge that their clinical benefit (prevention of pancreatitis and cardiovascular diseases) has not been demonstrated.

- Hypertriglyceridaemia with level above 15-20 g/l: there is a major risk of pancreatitis, which must be managed in a specific manner.

4.3.3 Management of lipodystrophy in HIV-infected patients

According to the YENI report (2006), there is no single treatment for lipodystrophy. Three levels of intervention may be differentiated: firstly, a modification of the antiretroviral treatment; secondly, corrective intervention (surgery, medical techniques based on filling products); thirdly, drug treatments. The prescription of MAXEPA is not an option considered.

4.4. **Target population**

Not applicable.

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6 Initiating lipid-reducing treatment (fibrates, statins) is not without risk for HIV patients, due to the possible interactions (cytochrome P450 3A4), aggravating the frequency of adverse events caused by the lipid-reducing drugs (rhabdomyolysis, hepatitis) and making the antiretroviral drugs metabolised by CYP450 less effective. The number of lipid-reducing drugs available is not very high and their lipid-reducing property varies from one class to another. The choice of lipid-reducing drug therefore depends on the lipid parameters to be modified. Combinations of drugs are possible, but it is preferable to have a specialist opinion. A statin-fibrate combination is likely to increase the risk of rhabdomyolysis.
4.5. Recommendations of the Transparency Committee

The Transparency Committee recommends against the request for the inclusion of MAXEPA on the list of medicines reimbursed by National Insurance and the list of products for hospital use for the management of HIV-infected patients receiving antiretroviral polytherapy and with hypertriglyceridaemia.

Reminder: The Transparency Committee issued an opinion7 in 1998 as part of a request for the reinclusion MAXEPA on the list of reimbursed products: “Hypertriglyceridaemia occurs most often against the background of complex metabolic problems which must be remedied through dietary and lifestyle measures as a first-line treatment. Omega-3 polyunsaturated fatty acids have a certain degree of efficacy in reducing triglyceride levels. This effect is very much lower than that achieved through the use of fibrates. The actual benefit of MAXEPA in the general population is inadequate compared to that of fibrates.” (Opinion of Transparency Committee of 05/01/2000). No new clinical data has been submitted in the non-infected population.

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7 See opinions concerning MAXEPA’s reinclusion of February 4th and 24th 1998.