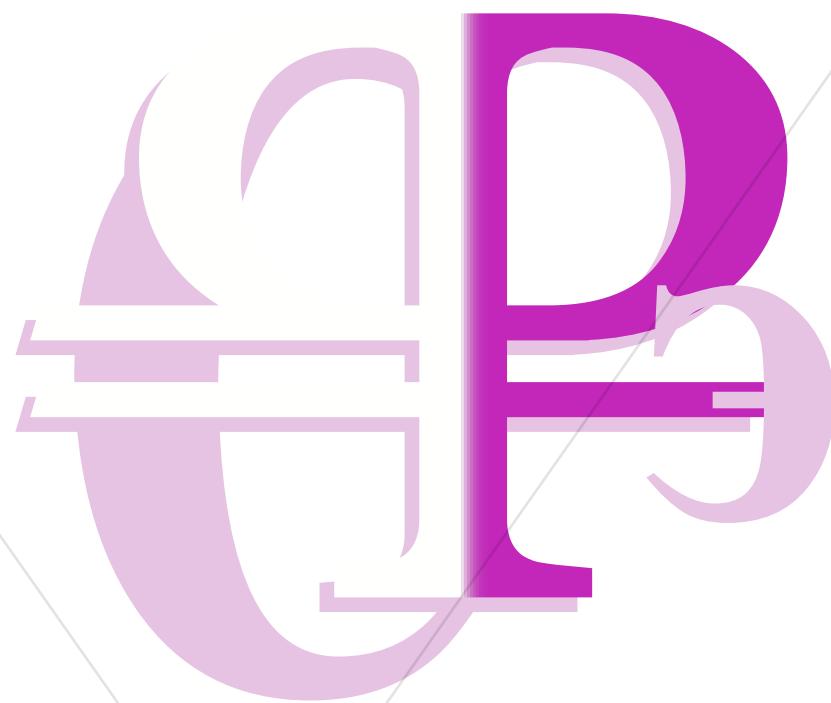


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# PHARMACOECONOMIC ANALYSIS TO COMPARE SUBCUTANEOUS VERSUS INTRAVENOUS MABTHERA® (RITUXIMAB) IN PATIENTS WITH FOLLICULAR LYMPHOMA

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**Abstract:** Follicular lymphoma is a disease requiring effective therapy that helps to improve a patient's quality of life. In this study, a comparative analysis of subcutaneous administration of MabThera versus intravenous MabThera was performed. Considering that the formulations are equally effective, a cost minimization analysis was carried out, which showed that transition from intravenous to subcutaneous MabThera resulted in savings of 35,847 rubles per one patient during the treatment course due to the decreased drug administration expenses, medical staff costs, and expenses for hospitalization or day-time staying.

The use of the subcutaneous formulation can also prevent economic damage caused by loss of the drug remaining in the vial with the use of the intravenous formulation where the dose depends on the body surface area.

**Key words:** rituximab, MabThera, follicular lymphoma, orphan disease, cost analysis, cost minimization analysis, budget impact analysis, subcutaneous injection, intravenous infusion, induction, supporting therapy.

## Introduction

Follicular lymphoma is a rare disease which, along with the introduction of more effective medicines, requires improvement of patient's quality of life. Considering that, an innovative medicine MabThera for subcutaneous (SC) injection was developed, which was earlier used in intravenous (IV) formulation.

With the introduction of the medicine that has comparable effectiveness but different formulation, a pharmacoeconomic analysis is needed to identify the most cost-effective therapy [12].

During the information retrieval, the main differences between SC MabThera and IV MabThera were identified. For example, SC injection requires less time and is easier to use compared to IV formulation. No less important is the fact that due to the decreased time of SC injection and reduced risk of developing serious adverse reactions, the procedure is carried out in outpatient settings, while IV MabThera requires hospitalization [1,17].

## Method

In this study, a pharmacoeconomic assessment of Non-Hodgkin's lymphoma treatment course consisting of induction (8 administrations) and supporting (12 administrations) therapies was performed. The first administration is always IV irrespective of the formulation used.

In view of the comparable effectiveness of the two formulations, in this study a cost minimization analysis was carried out, as a result of which the

following cost structure was identified:

- Pharmacotherapy with the respective MabThera formulation;
- Medical services;
- Drugs;
- Medical staff time;
- Bed-day [6,15,16].

## Cost analysis

The first step of the cost analysis was the calculation of MabThera cost per treatment course for both formulations. Dosage of IV formulation depends on the body surface area (BSA), which is equal to 1.82 m<sup>2</sup> on average. According to the instructions for use, infusion dose is 375 mg/m<sup>2</sup>, which is equivalent of 682.5 mg at average BSA. IV MabThera is available on the pharmaceutical market in two dosages, 100mg/10mL and 500mg/50mL and, consequently, average dose infusion requires 1 vial x 500 mg and 2 vials x 100 mg, at the cost of 63,628.98 rubles and 12,724.71 rubles (one vial), respectively. It follows, therefore, that the cost of one administration is 89,073.4 rubles, of induction therapy - 712,587 rubles, of supporting therapy - 1,068,881 rubles, and the total cost of one treatment course per patient is approximately 1,781,468 rubles. One of SC formulation advantages is fixed dosage where one vial with the drug is used for one injection. The price of SC MabThera pack consisting of one vial is 89,073.71 rubles which, in the cost calculation of Non-Hodgkin's lymphoma treatment course, gives the same costs as with the use of IV MabThera [1,2,10].

The next step of the cost analysis included the calculation of medical service (both treatment and diagnosis), using the formula below:

$$\text{Cost}(S) = \text{Price}(S) \times Q(S) \times F(S), \text{ где:} \quad (1)$$

*Cost(S) – is medical service expenses, rubles;*

*Price(S) – is the price of medical service, rubles;*

*Q(S) – is the average quantity of the medical service provided;*

*F(S) – is medical service frequency.*

The list of medical services, their average quantity and frequency were taken from the standard of care for patients with myeloid leukemia also reflecting the concomitant pharmacotherapy, which was calculated as follows:

**Cost(P) = Price(P) × Q(P) × F(P), where:**

(2)

*Cost(P) – is drug expenses, rubles;  
Price(P) – is the price of 1 mg of drug, rubles;  
Q(P) – is the course dose of drug;  
F(P) – is the frequency of drug administration.*

Information about the prices of medicines included in the Vital and Essential Drugs List was taken from the Vital and Essential Drugs List, and those of not included - from aptechka.ru (as of 27.12.2014) [8,9]. Prices of medical services were taken from the rates of the Federal Compulsory Medical Insurance Fund (FCMIF) [5].

The cumulative costs were similar for both formulations, amounting approximately to 1,100,108 rubles for medical services and 713,944 rubles for drugs included in the standard of care for patients with myeloid leukemia per one patient for a treatment course [4,8].

The next step of the cost analysis was the calculation of the drug administration cost, in which, according to FCMIF rates, the cost of IV infusion was estimated to be 76.98 rubles, and that of SC injection – 30.84 rubles, which is equivalent to 1,540 rubles and 663 rubles per treatment course, respectively [5].

There is also a difference observed in medical staff costs due to the reduced time of SC MabThera injection. It was assumed that the drug could be administered by both the physician and the nurse, and the time of IV infusion was 30.5 min, SC injection - 12.6 min. In view of the forgoing and taking into account average nurse and physician salaries, medical staff costs with the use of IV formulation per one patient for a treatment course were estimated to be approximately 3,275 rubles, and for SC formulation - 1,449 rubles.

Then the expenses per bed-day (arising from hospitalization or day-time staying) were calculated and the results were obtained as follows: 35,651 rubles per treatment course with IV MabThera and 1,783 rubles - with SC formulation [5].

#### Cost minimization analysis

In the cost analysis performed, the total cost of follicular lymphoma treatment course per one patient was 3,534,687 rubles for IV formulation and 3,498,840 rubles for SC formulation (Table 1).

**Table 1.** Total cost of one follicular lymphoma case treatment

Costs	IV			SC		
	Induction	Support	Treatment course	Induction	Support	Treatment course
Medical services, rubles	534 278	465 830	1 000 108	534 278	465 830	1 000 108
Drugs, rubles	356 972	356 972	713 944	356 972	356 972	713 944
MabThera, rubles	712 587	1 068 881	1 781 468	712 587	1 068 881	1 781 468
Administration, rubles	616	924	1 540	293	370	663
Medical staff, rubles	790	1 186	1 976	385	490	874
Bed-day, rubles	14 260	21 391	35 651	1 783	0	1 783
<b>TOTAL</b>	<b>1 619 504</b>	<b>1 915 183</b>	<b>3 534 687</b>	<b>1 650 543</b>	<b>1 968 524</b>	<b>3 619 729</b>

Therefore, the use of SC MabThera can reduce the costs by 35,847 rubles due to the difference in drug administration expenses, medical staff costs and payment for a bed-day per one patient during the treatment course [7].

#### Budget impact analysis

Budget impact analysis allows to suggest how the new treatment regimen will influence the costs associated with the treatment of the specific disease [13]. The use of budget impact analysis also involves assessment of all types of expenditure associated with the introduction of a new treatment regimen in relation to all types of expenditure associated with the already existing treatment regimen. Costs were calculated according to the following formula:

**BIA = Cost1 - Cost2, where**

(3)

*BIA is the result of the budget impact analysis (rubles);  
Cost1 is the total cost of the first treatment option (rubles);  
Cost2 is the total cost of the second treatment option (rubles).*

For the detailed budget impact analysis it was found that there were approximately 425 patients with follicular lymphoma in Moscow. For this population, the total cost of using IV MabThera was estimated to be 1,502,241,933 rubles, and that of SC MabThera – 1,487,007,082 rubles (Table 2) [3,14].

**Table 2.** Total cost of the treatment course in the population of patients with follicular lymphoma

	Induction	Support	Treatment course
IV MabThera	688 289 194	813 952 738	1 502 241 933
SC MabThera	682 676 354	804 330 727	1 487 007 082

Finally, the results of the budget impact analysis showed that, with the use of SC MabThera compared with IV MabThera, savings would be 15,234,851 rubles per treatment course in the population of Moscow.

#### Drug loss

It is important to note that SC MabThera is used in the fixed dose while the dose of IV MabThera depends on patient's BSA. Therefore, drug volume often remains in the vial so it cannot be further used because the formulation loses its sterility. This results in the drug loss which, in monetary terms, amounts to 15,906 rubles per treatment course of one patient, and 6,760,000 rubles for the population.

#### Time saving

The results, including those obtained in Russia, were described in the Time and Motion study that included 700 patients in 330 centers of 27 countries. This study examined the time spent for the use of IV and SC formulations by both the medical staff and patients. It was found that the time spent by the healthcare professional on a patient in the treatment room was 30.5 min for IV MabThera and 12.6 min for SC MabThera. When the time spent by the patient at the healthcare facility was measured, it was found that IV MabThera infusion required 383.9 min, and SC injection took 123.1 min [17].

The obtained results allow for the conclusion that the use of SC MabThera significantly reduces the time spent by the healthcare professional on a patient, while also shortening the time of patient's stay at the healthcare facility, which has an effect on the quality of his life.

#### Discussion

In this study, the cost analysis was performed for the treatment of follicular lymphoma using IV MabThera in comparison with SC MabThera treatment regimen consisting of induction and supporting therapies. It was assumed that the drug can be administered by both the physician in 50% of cases and the nurse in the remaining cases. The same ratio was assumed for the distribution of hospitalization and day-time staying cases.

#### Conclusions

On the basis of the pharmacoeconomic analysis performed it can be concluded that the transition from IV MabThera to SC formulation:

- Provides savings in the amount of 35,847 rubles per treatment course of one patient and 15,234,851 rubles for the population.
- Prevents economic damage in the amount of approximately 15,906 rubles per treatment course of one patient and 6,760,000 for the population, with no loss of the drug in the fixed dose of SC formulation;
- Shows time savings which, in monetary terms, amount to 1,826 rubles per treatment course of one patient and 776,050 rubles for the population.

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