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Pharmacoeconomic Analysis of Treatment Regimens for Coronavirus Infection Coronavirus Disease-19

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Abstract

BACKGROUND: In March 2020, the coronavirus disease (COVID-19) infection was assigned the status of a pandemic. As of the beginning of 2021, the Russian Federation ranks fourth in terms of the prevalence of coronavirus infection. Over the period from March 2020 to February 2021, more than 84,000 fatal cases of the disease were recorded in Russia.

AIM: However, at the moment, there are no medications with proven effectiveness and safety against the novel coronavirus infection. In this regard, the purpose of our study was to conduct a pharmacoeconomic analysis of medications for etiotropic therapy of all forms of COVID-19 recommended by the Ministry of Health of the Russian Federation (clinical guidelines, version 10 dated February 8, 2021) to identify the best treatment option.

MATERIALS AND METHODS: In the course of the study, the "cost of illness" was determined for all forms of the disease in an outpatient and inpatient setting. The authors took into account the direct medical costs of medication therapy and diagnostic and treatment procedures. In terms of direct non-medical costs, they calculated the cost of a bed-day excluding medication treatment, and indirect costs included payments for temporary disability sheets. Costs for medications were calculated based on the active ingredient (AI) and the packages for treatment on an outpatient basis and in the case of the hospital setting based on the AI only. The cost of medical and diagnostic procedures was determined based on the Tariff Agreement for 2020 dated December 30, 2019. Next, a cost-effectiveness analysis was performed. Effectiveness criteria were selected based on published clinical trial results for the medications in question. Then, they performed a calculation of the cost-effectiveness coefficients and an incremental analysis.

RESULTS: Thus, in the course of the analysis of the cost of illness, the most economically profitable treatment regimens were the ones with hydroxychloroquine both for outpatient treatment (13,150.31 rubles: Mild form, 22,326.44 rubles: Moderate form excluding antibiotic therapy, and 21,513.76 rubles: Moderate form, taking into account antibacterial therapy) and for inpatient treatment (34,441.53 rubles).

CONCLUSION: As a result of the cost-effectiveness analysis, the use of favipiravir can be considered optimal (comparative effectiveness research = 17,607.14 rubles), and for the mild form, the optimal medication is umifenovir, since during the incremental analysis, it was found that for therapy with favipiravir, 100 people would need an additional allocation of 96.291 rubles, which, given the form of the disease, is not entirely appropriate.

Introduction

On December 31, 2019, an outbreak of coronavirus disease (COVID)-19 coronavirus infection was reported for the 1st time in Wuhan, China. Then, the prevalence of this disease took on a global scale, and on March 11, 2020, the World Health Organization (WHO) assigned COVID-19 the status of a pandemic. As of the beginning of 2021, the Russian Federation ranks fourth in terms of the prevalence of coronavirus infection. Over the period from March 2020 to February 2021, more than 84,000 fatal cases of the disease were recorded in Russia [1].

However, the information available at the moment about the results of therapy with existing medications does not allow us to draw an unambiguous conclusion about their effectiveness and safety for the treatment of COVID-19 novel coronavirus infection [2].

Therefore, it is required to assess the feasibility of using the medications proposed for the treatment of the disease from the standpoint of pharmacoeconomics and pharmacoepidemiology.

The purpose of our work is to conduct a pharmacoeconomic analysis of medications recommended by the Ministry of Health of the Russian Federation for the treatment of COVID-19 novel coronavirus infection on an outpatient basis and in an inpatient setting.

Materials and Methods

In the course of the study, the analysis of the cost of illness including complete treatment regimens in outpatient and inpatient settings was carried out, and

the analysis of the cost-effectiveness of medications for etiotropic therapy recommended by the Ministry of Health in clinical guidelines (version 10, dated February 8, 2021).

We identified the following cost categories: Direct medical, direct non-medical, and indirect.

Direct medical costs include the cost of medication therapy, the cost of diagnostic procedures, and the cost of providing services by medical professionals.

Direct non-medical costs are determined only for inpatients: Cost of a bed-day (excluding medication therapy costs).

In terms of indirect costs, payments for temporary incapacity for work were calculated.

On an outpatient basis, the cost of individual medications was estimated based on the average prices of pharmacies in the city of Moscow [3].

Since medications are presented on the pharmaceutical market in different forms and dosages, it is recommended to perform calculations based on the active ingredient (AI). However, it should be borne in mind that on an outpatient basis, a patient, as a rule, buys medicines for their own money, and in a pharmacy, medications are sold in whole packages, even if the consumer does not need the full number of units of the particular dosage form. Therefore, a calculation based on the number of packages is also necessary. We took most medications of a low price category and, if possible, with a minimum difference between the required number of units of a dosage form and their number in a real package [4], [5], [6].

The required amount of AI or packages for a full course for a specific medicinal product was determined based on the dosage regimens recommended by the Ministry of Health of Russia [2].

The cost of individual medications recommended for use in a hospital setting was calculated based on the state register of maximum selling prices (except for remdesivir, which is not included in it). At the same time, the marginal wholesale mark-up allowed for Moscow and the Moscow region, and the value-added tax was added to the indicated prices [7].

The price for remdesivir was obtained from the Rustekhprom distributor.

Since medications from the Vital and Essential Drugs list are presented in different forms and dosages, the calculation was carried out based on the AI [4], [5], [6].

If the treatment regimen assumed relatively equivalent alternative solutions for the medications of symptomatic, pathogenetic, and antibacterial therapies, then the price calculated based on the arithmetic mean was taken for them.

We made a complete list of direct non-medical costs based on the information provided in the temporary clinical guidelines for the diagnosis, prevention, and treatment of COVID-19 coronavirus infection [2].

The cost of each medical intervention was estimated under Appendices 11, 8.2, 6 to the Tariff Agreement for 2020 dated December 30, 2019 [7], [8], [9].

The required number of visits to a medical specialist or diagnostic procedures was also determined based on clinical guidelines and consultation with health professionals. In particular, to assess the length of stay of patients in a hospital, we proposed the following gradation depending on the severity of the disease:

- Mild: 7 days;
- Moderate: 10 days;
- Severe, cytokine storm: 16 days, then the patient switched to another form of the disease;
- Extremely severe: 5 days on a ventilator, then the patient goes into a serious condition.

Direct non-medical costs, in particular, the cost of a bed (excluding the cost of medication therapy), which amounted to 1500 rubles/day, were estimated based on the average value of the price lists of clinics in the Moscow region.

We also assumed that on average:

- With outpatient treatment and mild therapy in a hospital, the period of temporary disability (TD) will last 14 days;
- With a moderate form it will last 17 days;
- In severe or extremely severe forms, or with cytokine storm, it will last 30 days.

The further calculation was carried out according to the formulas presented in Table 1.

Table 1: Formulas

Direct costs	
1) By AI	2) By package
$Cost\ (Th)_a = Price\ (Th)_a * D\ (Th)_a * T\ (Th)$ (1) where $Cost\ (Th)_a$ is the cost of the medication course, calculated by the AI, rubles; $Price\ (Th)_a$ is the average cost of a unit of the AI of a medicinal product, rubles; $D\ (Th)_a$ is a single dose of a medication, AI units; T (Th) is the duration of the course of the medication (10).	$Cost\ (Th)_r = Price\ (Th)_r * D\ (Th)_r$ (2) where $Cost\ (Th)_r$ is the cost of the medication course, calculated by packages, rubles; $Price\ (Th)_r$ is the average cost of a medication package, rubles; $D\ (Th)_r$ is the course dose of the medication, packages (10).
Indirect costs	
1) The costs due to TD	
$Cost\ (TD) = (GDP_d+TD)*n$ (3) where Cost (TD) is the costs due to TD, rubles; GDP_D is GDP per capita per day, rubles; TD is the payment based on TD certificates, rubles; n is the number of days of TD [10].	
2) The average per capita GDP per year	3) The average per capita GDP per day
$GDP_P = GDP/P$ (4) where GDP is the total GDP for the year, rubles; GDP_P is the GDP per capita per year, rubles; P is the size of the able-bodied population, people [11].	$GDP_d = GDP_P/365$ (5) where GDP_D is GDP per capita per day, rubles; GDP_P is the GDP per capita per year, rubles; 365 is the number of days in a year [10].
4) Per capita income	5) Payments on TD sheets
$D_d = D_m/30$ (6) where D_d is the income per capita per day, rubles; D_m is the monthly income per capita, rubles; 30 is the number of days in a month [10].	$TD = D_d * (80/100)$ (7) where TD is the payment on TD sheets, rubles; D_d is the income per capita per day, rubles [10].

The effectiveness criterion for cost-effectiveness analysis was determined based on the results of data

from clinical trials of medications for etiotropic therapy (umifenovir, remdesivir, and favipiravir) on the Internet, in particular, in PubMed, Clinical Trials, Cline Line, Cochrane and Library databases.

Hydroxychloroquine, which is used in Russia as a medication for etiotropic therapy, was recognized as ineffective against coronavirus infection in the framework of the Solidarity study initiated by the WHO. Therefore, it is not advisable to further evaluate it [12].

The main condition for inclusion in the analysis of clinical trials was the completeness of the data provided according to the following criteria: Study design, comparison medications, conditions of randomization, characteristics of participants, presented results, and at least complete information on the primary endpoint.

The list of clinical trials for the above medications with their brief characteristics is presented in Tables 2-4.

The cost-effectiveness ratio was calculated using the following formulas:

Comparative effectiveness research (CER) = Cost/Ef (8)

where CER is the cost-effectiveness ratio of the technology;

Cost is the costs associated with technology in monetary terms;

Ef is the clinical effectiveness of the technology, expressed in the appropriate units [11].

$$CER = ((DC1 + IC1) – (DC2 + IC2))/(Ef1 – Ef2) \quad (9)$$

Where, CER is an indicator of an increase in cost-effectiveness (demonstrating what additional investments are required to achieve one additional unit of effectiveness when using a more efficient technology);

DC1 is the direct costs when using technology 1;

IC1 is the indirect costs when using technology 1;

DC2 and IC2 are the direct and indirect costs for technology 2, respectively;

Ef1 and Ef2 are the treatment effects when using technologies 1 and 2, respectively [11].

Evaluation of the medications was carried out for a specific form of coronavirus infection, that is, for a

Table 2: List of clinical trials for the medication with the international non-proprietary name (INN) remdesivir

Source	Number of patients, age	Design of the study	Duration of the study	Comparison alternative	The severity of the disease	Primary endpoint
[13]	237 (158, 79), ≥18 years	Randomized, double-blind, placebo-controlled, multicenter trial	28 days	Remdesivir + lopinavir-ritonavir, interferons, corticosteroids, placebo + lopinavir-ritonavir, interferons, corticosteroids,	Severe form	Time of clinical improvement up to 28 days on a 6-point scale of clinical status (21 – remdesivir, 23 – placebo)
[14]	596 (197, 199, 200), ≥18 years	Phase 3 randomized open-label trial	28 days	Remdesivir for 5 days, remdesivir for 10 days, CT for 10 days	Moderate form	Clinical status on the 11th day on a 7-point scale: 68%: Remdesivir for 10 days, 74%: Remdesivir for 5 days, 64%L CT
[15]	1062 (521, 541), ≥18 years	Randomized, double-blind, placebo-controlled, multicenter trial	29 days	Remdesivir, placebo	Mild, moderate, severe	Recovery time: 10: Remdesivir, 15: Placebo
[16]	61, ≥18 years	Uncontrolled prospective observational study	28 days	Remdesivir	Severe	Clinical status on day 18 (improvement): 68%

Table 3: List of clinical trials for the medication with INN favipiravir

Source	Number of patients, age	Design of the study	Duration of the study	Comparison alternative	The severity of the disease	Main endpoints
[17]	89 (44, 45), ≥16 years	Multicenter open-label randomized trial	45 days	Favipiravir (immediate and delayed intake)	Mild	Virus elimination by day 6: 66.7%, 56.1%, elimination by day 10: 86.1%, 83.1%
[18]	80 (35,45), ≥16 years	Multicenter open-label randomized trial	28 days	Favipiravir+Interferon (IFN) — alpha, CT, lopinavir/ritonavir + + IFN-alpha, CT	Severe	Elimination of the virus on day 4: 22.86%, 17.78% Day 9: 56.25%, 35.55% Day 14: 91.43%, 62.22%
[19]	236 (116, 120), ≥18 years	Prospective, randomized, controlled, open-label, multicenter study	17 days	CT+Favipiravir CT+Umifenovir	Mild, moderate severity	Clinical recovery rates on the seventh day: 71/116; 62/120
[20]	168 (112; 56)	Multicenter, open, randomized, Phase III clinical trial with active control in outpatients and inpatients	28 days	Favipiravir Umifenovir+INF-alpha/ Hydroxychloroquine+INF — alpha	Mild, moderate severity	The median time to achieve elimination of the virus on day 3 is 71.40%, 57.10% On the 5th day: 81.20%, 67.90%

Table 4: List of clinical trials for the medication with INN umifenovir

Source	Number of patients, age	Design of the study	Duration of the study	Comparison alternative	The severity of the disease	Main endpoints
[19]	236 (116, 120), ≥18 years	Prospective, randomized, controlled, open-label, multicenter study	17 days	CT+Favipiravir CT+Umifenovir	Mild, moderate severity	Clinical recovery rates on the seventh day: 71/116; 62/120
[21]	86 (34, 35, 17), ≥18 years	A single-center randomized controlled trial	21 days	Lopinavir+Ritonavir, Umifenovir No therapy	Mild, moderate severity	Elimination of the virus on day 7: 35.3%, 37.1%, 41.2% On day 14: 85.3%, 91.4%, 76.5%
[22]	50 (34, 16), ≥18 years	Single-center randomized controlled trial	38 days	Lopinavir/Ritonavir, Arbidol	Moderate severity	Elimination of the virus on day 14: Arbidol: 100%, lopinavir/ritonavir: 56.4%

mild degree, a comparison of umifenovir and favipiravir is required, and for moderate and severe forms, favipiravir is compared with remdesivir.

Results and Discussion

The cost of illness analysis

The cost of medication therapy on an outpatient basis and in a hospital setting is indicated in Tables 5 and 6, respectively.

As can be seen from Table 5, in most cases, the cost of complete medication therapy is higher when calculated by the number of packages, which justifies our estimate of costs by the number of packages. Exceptions can be explained by the fact that there is a significant difference between the minimum and maximum prices for medications.

Direct medical costs (except for medication therapy) included in the outpatient setting included: Blood draw from a vein, bleeding; study of the erythrocyte sedimentation rate; study of the level of platelets in the blood; blood processing, including registration, an appointment with the district general practitioner (diagnostic, primary, and at home); an appointment with the district general practitioner (diagnostic, repeated, and outpatient visit); test of a blood smear for the analysis of abnormalities in the morphology of erythrocytes, platelets, leukocytes, performing the blood count, pulse oximetry, and polymerase chain reaction (PCR) diagnostics. In addition, for treatment regimens with hydroxychloroquine, electrocardiogram and determination of aspartate transaminase and alanine aminotransferase were taken into account. Furthermore, with a moderate degree, as a rule, an ambulance was called, and computed tomography of one anatomical region was performed in adults (without contrast).

In the hospital setting, for all forms, we took into account the ambulance visit, PCR diagnostics, pulse oximetry, computed tomography, general blood analysis, and consultation with a general practitioner in a hospital. For the moderate form, a coagulogram study is additionally carried out, and a study of the level of protein C, ferritin in the blood, and a biochemical blood test (11 indicators) are performed; for a severe form, consultations of narrow specialists are needed, for an extremely severe form, membrane oxygenation is taken into account.

The level of direct non-medical costs was calculated depending on the severity of the disease:

Mild form: 1500 * 7 = 10,500 rubles.

Moderate form: 1500 * 10 = 15,000 rubles.

Severe form: 1500 * 21 = 31,500 rubles.

Based on statistical data, it was found that the working-age population was 82.264 thousand people, the total GDP per year amounted to 185,534 billion rubles, and the monthly income per capita was 24,381.1 rubles [21].

Therefore, GDP_p=85,534*10^6/82.264*
10^3 = 2,255,348.63 rubles.

GDP_d = 2,255,348.63/365 = 6179.04 rubles.

D_d = 24,381.1/30 = 812.70 rubles.

TD = 812.70 * 0.8 = 650.16 rubles.

650.16 * 14 = 9102.24 rubles.

650.16 * 17 = 11,052.72 rubles.

650.16 * 30 = 19,504.80 rubles.

Thus, the total costs of outpatient and inpatient therapy are presented in Tables 7 and 8, respectively.

Thus, it can be concluded that, in an outpatient setting, for all forms of the disease, treatment regimens with hydroxychloroquine will be the most beneficial from the economic point of view. The most expensive medication from the consumer's point of view is favipiravir.

Table 5: Costs for a full course of medication therapy per one person on an outpatient basis

Form	Medications	Costs-1 (by number of packages)	Costs-2 (by AI)	The difference in the value of costs (1 vs. 2), %
Mild				
Treatment regimen 1	Favipiravir, INF-alpha (intranasal), paracetamol	11,476.50 12,702.38	10,360.00 13,080.00	10.78 −2.89
Treatment regimen 2	Hydroxychloroquine, INF-alpha (intranasal), paracetamol	1401.45	1440.00	−2.68
Treatment regimen 3	Umifenovir, INF-alpha (intranasal), paracetamol	2153.27	2352.00	−8.45
Moderate (without pneumonia)				
Treatment regimen 1	Favipiravir, INF-alpha (intranasal), paracetamol, Rivaroxaban OR Apixaban	14,841.81 16,067.69	13,080.25 15,800.25	13.47 1.69
Treatment regimen 2	Hydroxychloroquine, INF-alpha (intranasal), Paracetamol, Rivaroxaban OR Apixaban	4766.76	4160.25	14.58
Antibacterial therapy (according to indications)	Amoxicillin + clavulanic acid OR amoxicillin OR azithromycin OR levofloxacin OR moxifloxacin OR clarithromycin	812.68	803.85	1.10
Moderate with pneumonia				
Treatment regimen 1	Favipiravir, rivaroxaban OR apixaban, dexamethasone OR prednisolone OR methylprednisolone	14,574.09 15,799.97	12,467.15 15,187.15	16.90
Treatment regimen 2	Hydroxychloroquine, rivaroxaban OR apixaban, dexamethasone OR prednisolone OR methylprednisolone	4499.04	3547.15	4.04
Antibacterial therapy (according to indications)	Amoxicillin + clavulanic acid OR amoxicillin OR azithromycin OR levofloxacin OR moxifloxacin OR clarithromycin	812.68	803.85	26.84

In a hospital setting, for mild-to-moderate forms, the use of hydroxychloroquine is also the least expensive alternative. The most expensive medication is the medication with INN remdesivir.

For severe and extremely severe forms, only one treatment regimen with INN is presented (favipiravir).

Regimens for the treatment of cytokine storms cannot be unambiguously compared, since their use is largely determined by the individual characteristics of the patient.

Cost-effectiveness analysis

To evaluate favipiravir and umifenovir, study No. 3 from Table 3 was selected since there is a direct comparison of these medications. The criterion of effectiveness is the frequency of complete elimination of the virus on day 7 (Tables 9 and 10).

The effectiveness coefficient is calculated according to formula 8, presented in the Materials and methods section.

If we focus only on the CER value, then the use of umifenovir is the most profitable in terms of cost-effectiveness ratio, since fewer costs are required to treat one person. However, the study found that the favipiravir contributed to the complete elimination of the virus in a larger number of people, therefore, incremental analysis is required to assess the increment of the cost-benefit unit according to formula 9:

CER = (986,000 – 119,381)/(61 – 52) = 96,291

The resulting number is, therefore, the added cost of increasing the number of recoveries per 100 people/week using favipiravir.

To evaluate favipiravir and remdesivir, no studies were conducted that were completely identical in design and endpoints, therefore, based on the maximum possible similarity of endpoints, study No. 2 and No. 2 from Tables 2 and 3, respectively, were selected.

The effectiveness criterion is the frequency of complete virus elimination on day 11 in the remdesivir group and the frequency of complete virus elimination on day 9 in the favipiravir group (Tables 11 and 12).

The effectiveness coefficient is calculated according to formula 1 presented in section 2.1.

Table 6: Costs for a full course of medication therapy per one person in a hospital setting

Form	Medications		Costs
Mild	Treatment regimen 1	Favipiravir, INF-alpha (intranasal), enoxaparin sodium	14,234.37
			16,654.37
	Treatment regimen 2	Hydroxychloroquine, INF-alpha (intranasal), enoxaparin sodium	5965.01
	Treatment regimen 3	Umifenovir, INF-alpha (intranasal), enoxaparin sodium	6958.17
Moderate	Treatment regimen 1	Favipiravir, baricitinib OR tofacitinib, enoxaparin sodium	47,714.80
			50,134.80
	Treatment regimen 2	Remdesivir, baricitinib OR tofacitinib, enoxaparin sodium	149,244.80
	Treatment regimen 3	Hydroxychloroquine, baricitinib OR tofacitinib, enoxaparin sodium	39,445.44
	Treatment regimen 4	Favipiravir, olokizumab OR levilimab, enoxaparin sodium	65,645.00
			68,065.00
	Treatment regimen 5	Remdesivir, olokizumab OR levilimab, enoxaparin sodium	167,175.00
	Treatment regimen 6	Hydroxychloroquine, olokizumab OR levilimab, enoxaparin sodium	57,375.64
Severe (pneumonia with respiratory insufficiency (RI) or acute respiratory distress syndrome (ARDS))	Treatment regimen 1	Favipiravir, tocilizumab OR sarilumab, enoxaparin sodium	163,981.46
Cytokine storm	Treatment regimen 1	Methylprednisolone, tocilizumab OR sarilumab, enoxaparin sodium	156,382.38
	Treatment regimen 2	Dexamethasone, tocilizumab OR sarilumab, enoxaparin sodium	155,733.18
	Treatment regimen 3	Dexamethasone, canakinumab, enoxaparin sodium	2,403,397.23
	Treatment regimen 4	Methylprednisolone, canakinumab, enoxaparin sodium	2,404,046.43
	Treatment regimen 5	Methylprednisolone OR dexamethasone, enoxaparin sodium	5370.18
	Treatment regimen 6	Tocilizumab OR sarilumab OR canakinumab, Enoxaparin sodium	155,511.46
			2,403,175.51

Table 7: The results of the cost of illness analysis per one person in an outpatient setting

Form	Medications		Costs
Mild	Treatment regimen 1	Favipiravir, INF-alpha (intranasal), enoxaparin sodium	14,234.37
			16,654.37
	Treatment regimen 2	Hydroxychloroquine, INF-alpha (intranasal), enoxaparin sodium	5965.01
	Treatment regimen 3	Umifenovir, INF-alpha (intranasal), enoxaparin sodium	6958.17
Moderate	Treatment regimen 1	Favipiravir, baricitinib OR tofacitinib, enoxaparin sodium	47,714.80
			50,134.80
	Treatment regimen 2	Remdesivir, baricitinib OR tofacitinib, enoxaparin sodium	149,244.80
	Treatment regimen 3	Hydroxychloroquine, baricitinib OR tofacitinib, enoxaparin sodium	39,445.44
	Treatment regimen 4	Favipiravir, olokizumab OR levilimab, enoxaparin sodium	65,645.00
			68,065.00
	Treatment regimen 5	Remdesivir, olokizumab OR levilimab, enoxaparin sodium	167,175.00
	Treatment regimen 6	Hydroxychloroquine, olokizumab OR levilimab, enoxaparin sodium	57,375.64
Severe (pneumonia with RI, ARDS)	Treatment regimen 1	Favipiravir, tocilizumab OR sarilumab, enoxaparin sodium	163,981.46
Cytokine storm	Treatment regimen 1	Methylprednisolone, tocilizumab OR sarilumab, enoxaparin sodium	156,382.38
	Treatment regimen 2	Dexamethasone, tocilizumab OR sarilumab, enoxaparin sodium	155,733.18
	Treatment regimen 3	Dexamethasone, canakinumab, enoxaparin sodium	2,403,397.23
	Treatment regimen 4	Methylprednisolone, canakinumab, enoxaparin sodium	2,404,046.43
	Treatment regimen 5	Methylprednisolone OR dexamethasone, enoxaparin sodium	5370.18
	Treatment regimen 6	Tocilizumab OR sarilumab OR canakinumab, enoxaparin sodium	155,511.46
			2,403,175.51

Table 8: The results of the cost of disease analysis in a hospital setting for one person

Form	Treatment regimen	Cost category	Costs, rubles	Total costs, rubles
Mild	Treatment regimen 1 (with favipiravir)	Direct medical	24,123.35	55,103.47
		Direct non-medical	10,500.00	
		Indirect	9102.24	
	Treatment regimen 2 (with hydroxychloroquine)	Direct medical	14,839.29	34,441.53
		Direct non-medical	10,500.00	
		Indirect	9102.24	
	Treatment regimen 1 (with umifenovir)	Direct medical	15,637.15	35,239.39
		Direct non-medical	10,500.00	
		Indirect	9102.24	
Moderate	Treatment regimen 1 (with favipiravir + kinase inhibitor)	Direct medical	62,507.42	88,560.14
		Direct non-medical	15,000.00	
		Indirect	11,052.72	
	Treatment regimen 2 (with remdesivir + kinase inhibitor)	Direct medical	162,827.42	188,880.14
		Direct non-medical	15,000.00	
		Indirect	11,052.72	
	Treatment regimen 3 (with hydroxychloroquine + kinase inhibitor)	Direct medical	53,223.36	79,276.08
		Direct non-medical	15,000.00	
		Indirect	11,052.72	
	Treatment regimen 4 (with favipiravir + monoclonal antibodies [MAs])	Direct medical	81,647.62	107,700.34
		Direct non-medical	15,000.00	
		Indirect	11,052.72	
	Treatment regimen 5 (with remdesivir + MA)	Direct medical	180,757.62	206,810.34
		Direct non-medical	15,000.00	
		Indirect	11,052.72	
	Treatment regimen 6 (with hydroxychloroquine + MA)	Direct medical	71,153.56	97,206.28
		Direct non-medical	15,000.00	
		Indirect	11,052.72	
Severe	Treatment regimen 1 (with favipiravir)	Direct medical	199,114.96	250,119.76
		Direct non-medical	31,500.00	
		Indirect	19,504.80	
Extremely severe	Treatment regimen 1 (with favipiravir)	Direct medical	623,137.09	674,141.89
		Direct non-medical	31,500.00	
		Indirect	19,504.80	
Cytokine storm	Treatment regimen 1	Direct medical	188,322.67	239,327.47
		Direct non-medical	31,500.00	
		Indirect	19,504.80	
	Treatment regimen 2	Direct medical	187,673.47	238,678.27
		Direct non-medical	31,500.00	
		Indirect	19,504.80	
	Treatment regimen 3	Direct medical	2,435,337.52	2,486,342.32
		Direct non-medical	31,500.00	
		Indirect	19,504.80	
	Treatment regimen 4	Direct medical	2,435,986.72	2,486,991.52
		Direct non-medical	31,500.00	
		Indirect	19,504.80	
	Treatment regimen 5 (in case of contraindications to genetically engineered medications)	Direct medical	37,310.47	88,315.27
		Direct non-medical	31,500.00	
		Indirect	19,504.80	
	Treatment regimen 6 (in case of contraindications to hyaluronic acid (HA))	Direct medical	187,451.75 (MA) 2,435,115.80 (Canakinumab)	238,456.55 2,486,120.60
		Direct non-medical	31,500.00	
		Indirect	19,504.80	

Table 9: Required information on the clinical trial for the umifenovir and favipiravir medications

Medication	Number of people	Observed effect, %	The cost of the medication for one person, rub
Favipiravir	116	71/116, 61.2%	9860.00
Umifenovir	120	62/120, 51.67%	1193.81

Therefore, in this case, the cheapest and most effective alternative is favipiravir. Therefore, incremental analysis is not required.

Table 10: Results of the cost-effectiveness analysis for umifenovir and favipiravir

Medication	Number of people	Observed effect (out of 100 people)	CER
Favipiravir	100	61	986,000/61 = 16,163.93
Umifenovir	100	52	119,381/52 = 2295.79

Conclusion

In the course of the cost of illness analysis, calculations and estimates of direct medical, direct non-medical, and indirect costs were carried out. As a result of this study, it was found that the most

Table 11: Required information on the clinical trial for remdesivir and favipiravir

Medication	Number of people	Observed effect, %	The cost of the medication for one person, rub
Remdesivir	199	49.24%	110,000
Favipiravir	80	56.25%	9860.00

appropriate from an economic point of view is the use of hydroxychloroquine for the treatment of mild and moderate forms of infection.

Table 12: Results of the cost-effectiveness analysis for remdesivir and favipiravir

Medication	Number of people	Observed effect (out of 100 people)	CER
Favipiravir	100	56	986,000/56 = 17,607.14
Remdesivir	100	49	11,000,000/49 = 224,489.79

However, the cost-effectiveness analysis found that the use of this medication as an etiotropic therapy is not justified. Therefore, according to the results of the study, the most effective medication for the treatment of moderate and severe forms is favipiravir. When conducting a similar analysis for the

mild form, an ambiguous result was obtained: The most effective medication is also favipiravir, and umifenovir, which has lower effectiveness, but at the same time a lower price, has the lowest cost-effectiveness ratio, which is more appropriate from the point of view of pharmacoeconomical studies.

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