RESEARCH ARTICLE

ISSN 2307-9266 e-ISSN 2413-2241

Scientific and Practical Journal
PHARMACY & PHARMACOLOGY
(ФАРМАЦИЯ И ФАРМАКОЛОГИЯ)

Clinical and economic benefits of using sonidegib in the 1-line therapy of patients with locally advanced basal cell carcinoma

O.I. Ivakhnenko[1], V.V. Ryazhenov[1], M.Yu. Frolov[2], V.A. Rogov[2]

[1] Sechenov First Moscow State Medical University (Sechenov University),
2 Trubetskaya Str., Bldg 8, Moscow, Russia, 119991
[2] Volgograd State Medical University,
1 Pavshikh Bortsov Sq., Volgograd, Russia, 400066

E-mail: oii@hta-expert.ru

Received 15 Jan 2025 After peer review 14 June 2025 Accepted 20 July 2025

One of the key factors in ensuring the availability of modern treatments and choosing the optimal therapy for patients is the clinical and economic characteristics of new medical technologies.

The aim: to assess the clinical and economic feasibility of using sonidegib in widespread clinical practice.

Materials and methods. General scientific research methods were used as a methodological basis. A "decision tree" model was developed to conduct a clinical and economic assessment. The clinical and economic assessment of the use of sonidegib was carried out from the perspective of the healthcare system of the Russian Federation: the costs of systemic drug therapy for the 1-line of patients with locally advanced basal cell carcinoma (laBCC) were taken into account.

Results. A comparative analysis of efficacy based on the progression-free survival (PFS) criterion revealed the advantage of sonidegib over vismodegib: the odds ratio (OR) of disease progression in patients with laBCC 12 months after the start of therapy was 0.27778 (95% CI 0.125–0.618; p=0.0017; Z=3.1423). The reduction in the risk of progression when using sonidegib compared to vismodegib was 59.1% (OR=0.409; 95% CI 0.229–0.732, p=0.0026, Z=3.013). The results of testing the hypothesis about the equality of the proportion of patients with laBCC without disease progression 12 months after the start of therapy also confirmed the presence of statistically significant differences in efficacy between the two treatments in favor of sonidegib (χ^2=9.2007, df=1, p=0.002419, 95% CI 0.09312–0.432132). The use of sonidegib in the 1-line of therapy, 2.53 million rubles per year will be required per 1 patient, which is 10.86% lower than the use of vismodegib, and corresponds to an absolute saving of 308.55 thousand rubles. The "cost-effectiveness" indicator (CER) for sonidegib was 114,627 rubles versus 220,295 rubles for vismodegib. The incremental cost-effectiveness ratio (ICER) is 175,050 rubles per additional month of PFS. Sensitivity analysis showed the stability of the results when changing key parameters.

Conclusion. Based on the results of the study, the hypothesis about the clinical and economic benefits of sonidegib in the treatment of laBCC was confirmed, and data were obtained on the clinical and economic feasibility of using sonidegib in widespread clinical practice.

Keywords: sonidegib; clinical and economic analysis; basal cell carcinoma; health technology assessment

Abbreviations: INN — an international nonproprietary name; GCM — general characteristic of medicines; VEM — list of vital and essential medicines; BCC — basal cell carcinoma; RCTs — randomized clinical trials; MSP — the maximum selling price; OV — overall survival; PFS — progression-free survival; OR — odds ratio; RR — relative risk.

For citation: O.I. Ivakhnenko, V.V. Ryazhenov, M.Yu. Frolov, V.A. Rogov. Clinical and economic benefits of using sonidegib in the 1-line therapy of patients with locally advanced basal cell carcinoma. *Pharmacy & Pharmacology.* 2025;13(3):184-201. **DOI:** 10.19163/2307-9266-2025-13-3-184-201

Для цитирования: О.И. Ивахненко, В.В. Ряженов, М.Ю. Фролов, В.А. Рогов. Клинико-экономические преимущества применения лекарственного препарата сонидегиб в терапии 1 линии пациентов с местно распространённым базальноклеточным раком кожи. *Фармация и фармакология.* 2025;13(3):184-201. **DOI:** 10.19163/2307-9266-2025-13-3-184-201

Научно-практический журнал
ФАРМАЦИЯ И ФАРМАКОЛОГИЯ
(PHARMACY & PHARMACOLOGY)

ОРИГИНАЛЬНАЯ СТАТЬЯ

DOI: 10.19163/2307-9266-2025-13-3-184-201

Клинико-экономические преимущества применения лекарственного препарата сонидегиб в терапии 1 линии пациентов с местно распространённым базальноклеточным раком кожи

О.И. Ивахненко[1], В.В. Ряженов[1], М.Ю. Фролов[2], В.А. Рогов[2]

[1] Федеральное государственное автономное образовательное учреждение высшего образования «Первый Московский государственный медицинский университет имени И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский университет), Россия, 119048, г. Москва, ул. Трубецкая, д. 8, стр. 2
[2] Федеральное государственное бюджетное образовательное учреждение высшего образования «Волгоградский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Россия, 400066, г. Волгоград, пл. Павших Борцов, д. 1

E-mail: oii@hta-expert.ru

Получена 15.01.2025 После рецензирования 14.06.2025 Принята к печати 20.07.2025

Одним из ключевых факторов доступности современных методов лечения и выбора оптимальной терапии для пациентов являются клинико-экономические характеристики новых медицинских технологий.

Цель. Оценка клинико-экономической целесообразности применения препарата сонидегиб в условиях широкой клинической практики.

Материалы и методы. В качестве методологической основы применялись общенаучные методы исследования. Для проведения клинико-экономической оценки была разработана модель по типу «дерева решений». Клинико-экономическая оценка применения препарата сонидегиб проведена с позиции системы здравоохранения РФ: учитывались затраты на системную лекарственную терапию 1 линии пациентов с местно распространённым базальноклеточным раком кожи (мрБКРК).

Результаты. Сравнительный анализ эффективности по критерию «выживаемость без прогрессирования» (ВБП) выявил преимущество сонидегиба над висмодегибом: отношение шансов (ОШ) прогрессии заболевания у пациентов с мрБКРК через 12 мес. с момента начала терапии составило 0,27778 (95% ДИ 0,125–0,618, p=0,0017, Z=3,1423). Снижение риска прогрессирования при использовании сонидегиба по сравнению с висмодегибом составило 59,1% (ОР=0,409; 95% ДИ 0,229–0,732, p=0,0026, Z=3,013). Результаты проверки гипотезы о равенстве долей пациентов с мрБКРК без прогрессии заболевания через 12 мес. после начала терапии также подтвердили наличие статистически значимых различий в эффективности между двумя методами лечения в пользу сонидегиба (χ^2=9,2007, df=1, p=0,002419, 95% ДИ 0,09312–0,432132). При использовании сонидегиба в 1 линии терапии потребуется 2,53 млн руб. в год в расчёте на 1 пациента, что на 10,86% ниже, чем при использовании висмодегиба, и соответствует абсолютной экономии в размере 308,55 тыс. руб. Показатель «затраты–эффективность» (CER) для сонидегиба составил 114 627 руб. против 220 295 руб. для висмодегиба. Инкрементальный показатель «затраты–эффективность» (ICER) равен 175 050 руб. за дополнительный месяц ВБП. Анализ чувствительности показал устойчивость результатов при изменении ключевых параметров.

Заключение. На основании результатов исследования была подтверждена гипотеза о клинико-экономических преимуществах сонидегиба при лечении мрБКРК и получены данные о целесообразности применения сонидегиба в условиях широкой клинической практики.

Ключевые слова: сонидегиб; клинико-экономический анализ; базальноклеточный рак кожи; оценка медицинских технологий

Список сокращений: ЛП — лекарственный препарат; МНН — международное непатентованное наименование; ОХЛП — общая характеристика лекарственного препарата; ЖНВЛП — перечень жизненно необходимых и важнейших лекарственных препаратов; БКРК — базально клеточный рак кожи; РКИ — рандомизированные клинические исследования; ПОЦ — предельная отпускная цена; ОВ — общая выживаемость; ВБП — выживаемость без прогрессирования; ОШ — отношение шансов; ОР — относительный риск.

INTRODUCTION

Basal cell carcinoma (BCC) is the most common type of skin cancer, originating from basal cells, which are located in the lower layer of the epidermis. BCC accounts for about 80% of all skin cancer cases. According to statistics, most countries, especially those with high insolation, are experiencing an increase in the incidence of BCC [1, 2]. According to the American Cancer Society (2023), more than 5 million cases of BCC are diagnosed annually in the United States [3].

In Europe, the incidence rate varies from 20 to 200 cases per 100,000 population in different regions [2]. In Australia, keratinocyte carcinomas, including basal cell and squamous cell carcinomas, create a significant medical and financial burden for the population and the country's healthcare system [4]. According to the WHO, in 2022, skin cancer ranked 5th in terms of primary morbidity and 22nd in the structure of mortality due to oncopathology worldwide. In the Russian Federation, skin cancer (excluding melanoma) is among the oncopathologies that form 80% of the contingent of patients with malignant neoplasms (MNs). The absolute number of patients with skin MNs (ICD-10 C44) registered at the end of 2023 was 448,230 people. Since 2013, the prevalence of skin MN (excluding melanoma) has increased from 258.3 to 305.5 per 100,000 population. The proportion of patients with skin MNs (excluding melanoma) who were registered for 5 years or more in 2023 was 39.2%. In the overall structure of the contingent of patients with MNs registered for 5 years or more, its share was 7.2%. Skin MN (ICD-10 C44) are among the leading localizations and in the overall structure of MN morbidity — 13.6% in the general population, 11.2% among men and 15.6% among women. Over 10 years, the increase in age-standardized morbidity rates increased by 1.11% — from 25.14 in 2013 to 29.82 in 2023 per 100,000 population. In absolute terms, 91,867 people were registered with a diagnosis of skin MN (excluding melanoma) in 2023. The average age of patients with skin MN (excluding melanoma) is 70.2 years. At the same time, according to statistics, skin MN (excluding melanoma) are among the nosologies with the highest proportion in the age group from 30 to 59 years (8.3%), which determines the social significance of the disease among the economically active population of the Russian Federation. The proportion of skin MNs (excluding melanoma) detected at advanced stages in 2023 was 16.2%. BCC usually progresses slowly and rarely metastasizes, with mortality rates of less than 0.1% [3, 5]. Nevertheless, BCC causes serious complications, which, if not treated in a timely manner, can lead to significant changes in the skin and, as a result, to disability. Due to the heavy severity of the disease, BCC has high medical, social and economic significance and is characterised by a high burden on the healthcare system [6, 7].

The main methods of treatment for BCC are a surgical treatment and radiation therapy. In case of aggressive BCC with inoperable locally advanced or metastatic process or in case of ineffectiveness of previous methods of treatment, systemic drug therapy with Hedgehog signaling pathway inhibitors is recommended [7]. Currently, in the Russian Federation, there is only one non-alternative option for targeted therapy for such patients — vismodegib, which effectively blocks the Sonic Hedgehog (SHh) signaling pathway. In 2024, another Hedgehog inhibitor was registered in the Russian Federation — sonidegib.

One of the key factors in ensuring the availability of modern methods of treatment and choice an optimal therapy for patients is the clinical and economic characteristics of new medical technologies. In the Russian Federation, a pharmacoeconomic assessment of the sonidegib has not been previously conducted.

THE AIM of this study was to assess the clinical and economic feasibility of sonidegib in a wide clinical practice. To achieve this aim, the following objectives were solved:

- The characteristics of the new medical technology were determined: indications for use, administration regimen and dosage regimen, conditions of use in clinical practice;
- Modern approaches to the treatment of patients with BCC were studied to select alternative options for targeted therapy for conducting a clinical and economic assessment;
- A systematic search and review of papers on the comparative efficacy and (or) safety of sonidegib with selected alternatives was carried out to justify the choice of research method;
- Methods for accounting for direct medical costs and assessing clinical and economic indicators were developed;
- A mathematical model was developed for conducting a clinical and economic assessment of the use of sonidegib in the healthcare system of the Russian Federation.

MATERIALS AND METHODS

This study is based on the hypothesis of the clinical and economic feasibility of using the Hedgehog signaling pathway inhibitor — sonidegib — as part of the 1-line systemic therapy in patients with locally advanced BCC (laBCC). Developing the study design, general scientific methods were used to ensure a comprehensive and systematic approach to solving the objectives. To substantiate the hypothesis and develop the methodology for clinical and economic analysis, clinical guidelines for the diagnosis and treatment of patients with BCC, information from the State Register of Medicines, data on the comparative clinical efficacy

ОРИГИНАЛЬНАЯ СТАТЬЯ
DOI: 10.19163/2307-9266-2025-13-3-184-201

and safety of sonidegib with selected alternatives, and information from the State Register of Maximum Selling Prices were used. The regulatory framework of the study was formed on the basis of the current legislation of the Russian Federation in the field of regulation of medical care and drug provision, technical regulation norms for conducting assessments of medical technologies, clinical and economic studies and budget impact analysis, enshrined in the documents of the national standardisation system.

The clinical and economic assessment of the use of the sonidegib was carried out from the position of the healthcare system of the Russian Federation: the study took into account only direct medical costs for the 1-line systemic drug therapy of patients with BCC. To conduct a clinical and economic assessment it was developed "decision tree" model. The concept of the model was to assess the clinical and economic effectiveness of the 1-line systemic therapy of BCC depending on the chosen treatment (Fig. 1).

The determination of potential alternatives was carried out on the basis of an analysis of the current national clinical guidelines (CG) for the diagnosis and treatment of BCC, approved by the Scientific and Practical Council of the Ministry of Health of Russia, approved by the developers of the CG and posted in the clinical guidelines rubricator. The choice of research method and efficacy criteria for conducting a clinical and economic assessment was carried out based on the results of a systematic search and review of papers on the efficacy of sonidegib in comparison with alternative. The time horizon of the study was 1 year. The calculation of the costs of drug therapy was carried out on the basis of information on the method of administration and dosage regimen of the drug, indicated in the general characteristics of the medicines (GCM). When calculating the costs of therapy, the duration of 1 month was taken as 30.44 days in accordance with Federal Law of RF No. 107-FZ dated June 03, 2011 (as amended on April 14, 2023) "On the Calculation of Time". The basis for the development of the study design, the structure of the model and the determination of key parameters for calculations is the algorithm presented in Figure 2.

Methodology for determining the characteristics of medical technology

Registered indications for medical use for the proposed medicine, its administration regimen (method of administration, recommended dosage) are determined on the basis of an analysis of information from the GCM sonidegib[1] (Table 1).

Based on the results of the analysis, the following theses were determined, which formed the basis for the development of the clinical and economic study design:

Sonidegib is a Hedgehog signaling pathway inhibitor, indicated for use in adults for the treatment of laBCC that is not amenable to surgical treatment or radiation therapy;

The medicine is intended for oral administration, the recommended dose is 200 mg 1 time per day;

Duration of use of the drug — in clinical studies, treatment with sonidegib continued until disease progression or until unacceptable toxicity developed.

Methodology for studying existing approaches to the treatment of patients with basal cell skin cancer. Determination of alternatives for comparison

The provision of medical care, including drugs, in the Russian Federation is regulated by the provisions of Federal Law No. 323: medical care is carried out "in accordance with the procedure for the provision of medical care, on the basis of clinical guidelines and on the basis of standards of medical care approved by the authorized executive authority" (Article 37, Chapter 5, Federal Law No. 323)[2].

The choice of medicines for the formation of treatment regimens was carried out according to the following algorithm:

- first, modern approaches to the diagnosis and treatment of BCC were studied and then were selected alternatives for comparison;
- then, information from the State Register of Medicines of RF and the current list of vital and essential medicines (VEMs) was analysed;
- further, information from the GCM on the corresponding drugs selected as alternatives for comparison was studied.

According to the provisions of the CG, the choice of treatment tactics for patients with BCC is carried out individually, taking into account the prevalence of the tumor process, its localisation, prognostic factors (clinical form, localisation of BCC, the rate of the tumor process, etc.), the general condition of the patient, the presence of concomitant pathologies, and the expected

[1] The register of OHLP and LV in the EAEU. Sonidegib. Available from: https://lk.regmed.ru/Register/EAEU_SmPC

[2] Federal Law No. 323-FZ dated November 21, 2011 (as amended on December 28, 2024) On the Fundamentals of Public Health Protection in the Russian Federation" (as amended and supplemented, introduction in effective from March 01, 2025). Russian

life expectancy. The main goal of treatment for patients with BCC is the complete removal of the tumor (elimination of the tumor process) with maximum preservation of the functioning of the involved organ and the best cosmetic results[3].

Patients with laBCC who are not amenable to surgical treatment and radiation therapy, in the absence of contraindications (severe concomitant pathology and immunodeficiency states), are recommended to undergo systemic therapy with vismodegib until disease progression or intolerance to treatment[4]. Currently, this is the only treatment option in the 1-line therapy of patients with BCC. A summary characteristic of the information justifying the choice of the comparison medicine is presented in Table 2.

Vismodegib is used for the same indications and in the same clinical situation as sonidegib, is registered in the Russian Federation, is included in the current CG[5] and in the list of VEM[6], which allows it to be used as a comparison medicine for conducting a clinical and economic assessment of the use of sonidegib in a wide clinical practice.

Methodology for conducting a systematic search and review for the selection of a study method and the determination of key parameters for calculations

A systematic search for information on the comparative clinical efficacy of sonidegib and vismodegib was carried out in accordance with the Cochrane and the European Network for Health Technology Assessment (EUnetHTA). The following databases were used as sources of information when conducting a systematic search: PubMed/MEDLINE, National Institutes of Health, Cochrane Library.

Searching in the PubMed/MEDLINE database, the following keywords and logical operators were used: “advanced basal cell carcinoma” AND “therapy”. In the international register NIH, an advanced search was carried out using the following filters: condition OR disease — advanced basal cell carcinoma; status — completed; phase — phase 2 or 3; age group — adult. For the Cochrane Library, the following search strategy was used: MeSH descriptor: [advanced basal cell carcinoma] explode all trees and with qualifier(s): [therapy — TH]. When searching, restrictions on the language of scientific publications (English) were taken into account as filters. The time horizon of the search was not limited. The initial search for research results was carried out during the development of the study design and the development of the model (August 2024), an additional search was carried out at the validation stage in order to check for new data (October 2024).

The following criteria were taken into account when selecting studies: study design (comparative randomized clinical trials (RCTs), RCTs with a non-comparative design, non-randomized studies, indirect comparisons), description of the demographic characteristics of patients, allowing for an assessment of the comparability of groups between studies, the presence of Kaplan–Meier survival curves with data on progression-free survival (PFS). If there are results with PFS indicators for a longer observation period, current information on the efficacy for medical technologies included in the study was taken into account.

Based on the results of a systematic search and review, no direct comparative studies of the efficacy and safety of sonidegib and vismodegib were found. After studying the abstracts and removing duplicates of published research results, the following works were selected for further analysis: naive indirect adjusted comparison by Odom et al. (2017) [8] and published results of studies BOLT [9–11] and ERIVANCE [12–14].

In the study by Odom et al. (2017), the “matching-adjusted indirect comparison” (MAIC) method was used to adjust for differences in the baseline characteristics of patients between studies, taking into account two key factors — the proportion of patients who received previous radiation therapy and surgical treatment. After weighting, the objective response rates and median PFS in patients receiving sonidegib practically did not change (ORR: 56.1% before and 56.7% after weighting; PFS: 22.1 months before and after weighting). For vismodegib, the corresponding figures were 47.6% and 9.5 months. The authors noted the absence of a significant impact of the correction of individual patient data from the BOLT study on the efficacy of the drug according to the PFS criterion — the median PFS before and after correction was 22.1 months (95% CI 14.8–NE — not estimable / not amenable to assessment) [11]. This suggests that differences in populations did not have a statistically significant impact on absolute or relative effect indicators [15].

[3] Clinical Guidelines. Basal cell carcinoma of the skin; 2024.
[4] Ibid.
[5] Ibid.
[6] Decree of the Government of the Russian Federation dated October 12, 2019 No. 2406-r (as amended on January 15, 2025) On approval of the list of vital and essential medicines, as well as lists of medicines for medical use and the minimum range of medicines required for medical care. Russian

ОРИГИНАЛЬНАЯ СТАТЬЯ
DOI: 10.19163/2307-9266-2025-13-3-184-201

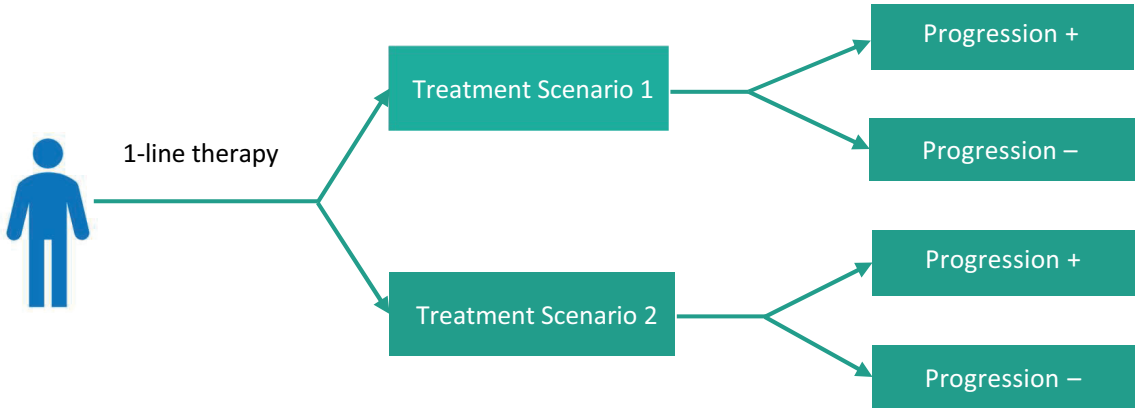

Figure 1 – Model diagram for conducting a clinical and economic assessment.

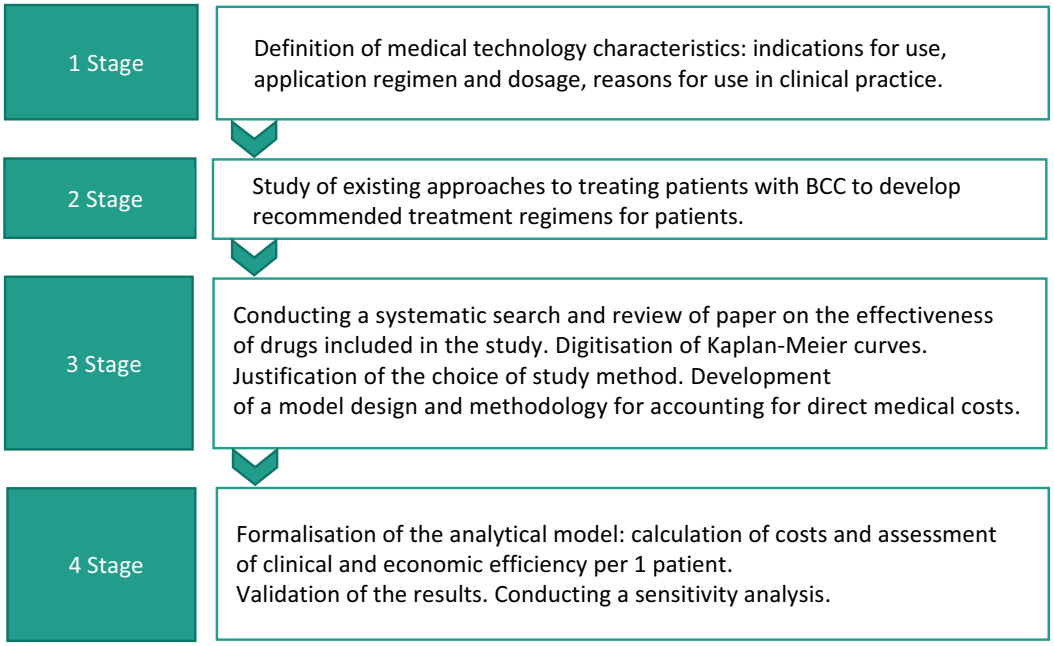

Figure 2 – Algorithm for developing the study design, the structure of the analytical model and determining key parameters for conducting a clinical and economic assessment.
Note: BCC — basal cell carcinoma.

Table 1 – Characteristics of the medical technology

INN / T	Characteristics	Medication elease form and dosage	Registration status of medicine in RF	Indications for use	Recommended dose and administration regimen
Sonidegib (Ozomdo)	ATC code: L01XJ02; PTG: antitumor agents, other antitumor agents; MA: Hedgehog signaling pathway inhibitors.	Capsules 200 mg, No. 30	LP-No. (006795)-(RG-RU) 05.09.2024	Sonidegib is indicated for use in adults for the treatment of locally advanced BCC that is not amenable to surgery or radiation therapy.	The recommended dose of sonidegib is 200 mg, orally, 1 time per day. Treatment should be continued until disease progression or unacceptable toxicity develops

Note: INN — international nonproprietary name; TN — trade name; PTG — pharmacotherapeutic group; ATC — Anatomical Therapeutic Chemical classification; MA — mechanism of action; BCC — basal cell carcinoma.

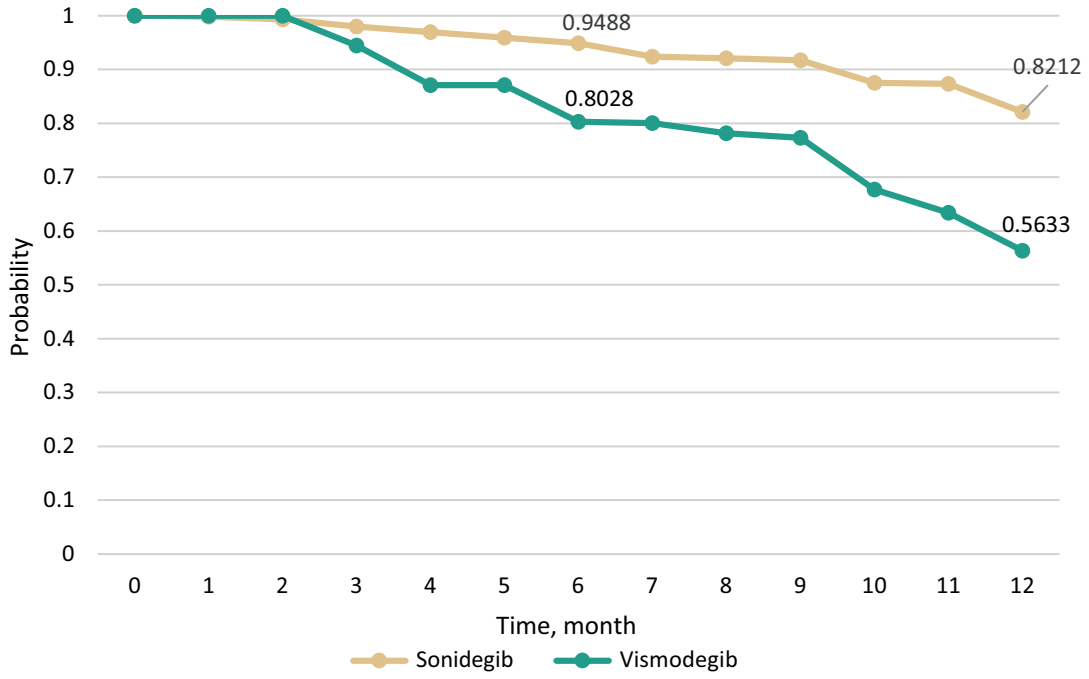

Figure 3 – Results of the restoration of individual patient data from studies (compiled by the authors according to the data from the BOLT [10] and ERIVANCE [12] studies).

Figure 4 – Change in cost–effectiveness (CER) values when varying the efficacy and prices of sonidegib and vismodegib within the sensitivity analysis compared to the results of basic calculations.
Note: PFS — progression-free survival; MSP — maximum selling prices.

ОРИГИНАЛЬНАЯ СТАТЬЯ
DOI: 10.19163/2307-9266-2025-13-3-184-201

Table 2 – Characteristics of medicines used for the 1-line of therapy of patients with metastatic and unresectable basal cell carcinoma who are not amenable to surgical treatment and radiation therapy

INN	Indications for use	Registration status in the Russian Federation	Availability of recommendations for use for the target indication in clinical guidelines	Availability in the lists of drugs for medical use
Vismodegib	Vismodegib is indicated for use in adults over 18 years of age for treatment of metastatic or locally advanced BCC: in case of recurrence after surgical treatment; if surgical treatment or radiation therapy is not advisable.	LP-No. (001355)-(RG-RU), 27.10.2022; original drug (TN: Erivedge®); LP-No. (004472)-(RG-RU), 01.02.2024, reproduced drug (TN: Vismodegib-Promomed).	Included in the CG, 1-line of therapy.	The drug vismodegib is included in the list of VEM: L01XX other antitumor medicine; capsule dosage form.

Note: INN — international nonproprietary name; TN — trade name; CG — clinical guidelines; VEM — list of vital and essential medicines.

Table 3 – Four-field contingency table for calculating the odds ratio of progression in patients with locally advanced basal cell carcinoma when using alternative therapeutic options

Alternative therapeutic options	Outcomes 12 months after the start of therapy		Total
	Progression+	Progression–	
Sonidegib	12	54	66
Vismodegib	28	35	63
Total	39	90	129

Table 4 – Results of calculating relative risk and odds ratio with confidence intervals, Z-statistics and p-values

Indicator	Assessment	95% CI lower limit	95% CI upper limit	*Z*	*p*
OR	0.278	0.125	0.618	–3.143	0.0017
RR	0.409	0.229	0.732	–3.013	0.0026

Note: OR — odds ratio; RR — relative risk; CI — confidence interval.

Table 5 – Results of testing the hypothesis on the equality of the proportions of patients with locally advanced basal cell carcinoma without disease progression 12 months after the start of therapy with compared medicines

Alternative therapeutic options	Number of patients with laBCC without disease progression 12 months after the start of therapy	Total patients in the sample [10, 12]	Proportion of patients with laBCC without disease progression 12 months after the start of therapy	Test results
Sonidegib	54	66	0,8212	χ^2=9.2007 df=1 *p*=0.002419 95% CI 0.09312–0.432132
Vismodegib	35	63	0.5633	

Note: laBCC — locally advanced basal cell carcinoma.

Table 6 – Price of drugs used when accounting for the costs of the 1st line drug therapy (base scenario)

INN	Release form	Administration regimen and dosage regimen	Maximum selling price of the manufacturer without VAT / with VAT, rubles, (USD)[7]	Price per 1 unit without VAT / with VAT, rubles.** (USD)[8]	Costs for 1 month of therapy with VAT, rubles.*** (USD)[9]
Vismodegib	Capsules 150 mg, No. 28	150 mg 1 time per day	198 051.61 / 217 856.77 (2 058.83 / 2 264.71)*	7 073.27 / 7 780.60 (73.53 / 80.88)*	236 817.11 (2461.81)*
Sonidegib	Capsules 200 mg, No. 30	200 mg 1 time per day	189 158.29 / 208 074.12 (1 966.38 / 2 163.02)*	6 305.28 / 6 935.80 (65.55 / 72.10)*	211 104.20 (2 194.52)*

Note: * The average value of the dollar exchange rate in relation to the ruble was used in the calculations: 96.1962 rubles per 1 USD for October 2024; **Costs per 1 administration, rubles;*** In the calculations, the duration of 1 month was taken as 30.44 days in accordance with Federal Law "On the Calculation of Time" dated June 3, 2011 N 107-FZ. INN — international nonproprietary name.

Table 7 – Price of medicines used when accounting the costs of the 1-line drug therapy when conducting a sensitivity analysis

INN	Base value of the maximum selling price without VAT / with VAT, rubles. (USD)*	Change in the maximum selling price of the manufacturer	Key parameters for calculating direct medical costs when conducting a sensitivity analysis*		
			Value of the MSP without VAT / with VAT rubles. (USD) within the SA	Price per 1 unit without VAT / with VAT, rubles (USD)	Costs for 1 month of therapy, rubles. (USD) with VAT**
Key parameters for calculating direct medical costs when changing the MSP for sonidegib and the base value of the MSP for vismodegig					
Visodegib	198 051.61 / 217 856.77 (2 058.83 / 2 264.71)	No changes	198 051.61 / 217 856.77 (2 058.83 / 2 264.71)	7 073.27 / 7 780.60 (73.53 / 80.88)	236 817.11 (2 461.81)
Sonidegib	189 158.29 / 208 074.12 (1 966.38 / 2 163.02)	Increase in the range from 5 to 20% with a step of 5% (+5%)	198 616.20 / 218 477.82 (2 064.70 / 2 271.17)	6 620.54 / 7 282.59 (68.82/ 79.22)	221 659.41 (2 304.24)
		+10%	208 074.12 / 228 881.53 (2 163.02 / 2 379.32)	6 935.80 / 7 629.38 (89.61/ 100.01)	232 214.62 (2 413.97)
		+15%	217 532.03 / 239 285.23 (2 261.34 / 2 487.47)	7 251.07 / 7 976.17 (110.41 / 120.80)	242 769.82 (2 523.70)
		+20%	226 989.95 / 249 688.94 (2 359.66 / 2 595.62)	7 566.33 / 8 322.96 (131.20 / 141.59)	253 325.03 (2 633.42)
Key parameters for calculating direct medical costs when changing the MSP for vismodegib and the base value of the MSP for sonidegib					
Vismodegib	198 051.61 / 217 856.77 (2 058.83 / 2 264.71)	Reduction of the base value of the MSP by 22.5% to the MSP for the generic vismodegib	161 605.16 (1 679.95)	5 771.61 / 6 348.77 (60.00 / 66.00)	193 129.71 (2 008.78)
Sonidegib	189 158.29 / 208 074.12 (1 966.38 / 2 163.02)	No changes	189 158.29 / 208 074.12 (1 966.38 / 2 163.019)	6 305.28 / 6 935.80 (65.55 / 72.10)	211 104.20 (2 194.52)
Key parameters for calculating direct medical costs when changing the MSP for sonidegib and vismodegib					
Vismodegib	198 051.61 / 217 856.77 (2 058.83 / 2 264.71)	Reduction of the base value of the MSP by 22.5% to the MSP for the generic vismodegib	161 605.16 (1 679.95)	5 771.61 / 6 348.77 (60.00 / 66.00)	193 236.84 (2 008.78)
Sonidegib	189 158.29 / 208 074.12 (1 966.38 / 2 163.02)	Reduction of the base value of the MSP by 10%	172 361.03 (1 791.77)	5 745.37 / 6 319.90 (59.73 / 65.70)	192 358.14 (1 999.64)

Note: * The calculations used the average exchange rate of the dollar against the ruble: 96.1962 rubles per 1 USD for October 2024. ** In the calculations, the duration of 1 month was taken as 30.44 days in accordance with Federal Law No. 107-FZ of June 3, 2011 "On the Calculation of Time". INN — international non-proprietary name; MSP — maximum selling price.

[7] The dynamics of the official exchange rate of a given currency: the US dollar from October 1, 2024 to October 31, 2024. The Bank of Russia. Available from: https://cbr.ru/currency_base/dynamics/

[8] Ibid.

[9] Ibid.

ОРИГИНАЛЬНАЯ СТАТЬЯ
DOI: 10.19163/2307-9266-2025-13-3-184-201

Table 8 – Costs of 1-line therapy per 1 patient with locally advanced basal cell carcinoma per year, rubles

INN	Application scheme	Price per 1 unit without VAT, rubles (USD)	Price per 1 unit with VAT, rubles (USD)	Costs per month, rubles (USD)	Therapy costs per year, rubles (USD)
Vismodegib	150 mg 1 time per day	7 073.27 (73.53)*	7 780.60 (80.88)*	236 817.11 (2 461.81)*	2 841 805,35 (29 541,76)*
Sonidegib	200 mg 1 time per day	6 305.28 (65.55)*	6 935.80 (72.10)	211 104.20 (2 194.52)*	2 533 250,35 (26 334,21)*
Difference in costs between medicines		768,00 (7,98)*	844.79 (8.78)*	25 712.92 (267.30)*	308 555.00 (3207.56)*
Percentage of cost deviation, %					10.86%

Note: * The calculations used the average exchange rate of the dollar against the ruble: 96.1962 rubles per 1 USD for October 2024. INN — international non-proprietary name.

Table 9 – Results of sensitivity analysis to changes in medicine prices

Alternative therapeutic options	Basic MSP value without VAT used in calculations, rubles (USD)*	Change in MSP without VAT within the sensitivity analysis, rubles (USD)*	Difference in costs, rubles (USD)*	Percentage of cost deviation, % / differences in costs for sonedigib compared to costs for vismodegib[10]
Scenario 1 of changes in drug prices: increase in MPC for sonidegib with the basic value of MPC for vismodegib				
Vismodegib	198 051.61 (2 058.83)	198 051.61 (2 058.83)	–	–
Sonidegib	189 158.29 (1 966.38)	198 616.20 (+5%) (2 064.70)	-181 892.48 (-1 890.85)	-6.40 % insignificant differences
		208 074.12 (+10 %) (2 163.02)	-55 229.96 (-574.14)	-1.94 % insignificant differences
		217 532.03 (+15%) (2 261.34)	+71 432.55 (742.57)	+2.51% insignificant differences
		226 989.95 (+20 %) (2 359.66)	+197 985.24 (2 058.14)	+6.97 % insignificant differences
Scenario 2 of changes in drug prices: decrease in MPC for vismodegib with the basic value of MPC for sonidegib				
Vismodegib	198 051.61 (2 058.83)	161 605.16 (1 679.95)	+214 289,33 (2 227,63)	9.25% insignificant differences
Sonidegib	189 158.29 (1 966.38)	189 158.29 (1 966.38)		
Scenario 3 of changes in drug prices: decrease in MPC for both medicines				
Vismodegib	198 051.61 (2 058.83)	161 605.16 (1 679.95)	-10 538.60 (109.55)	0.45% parity costs
Sonidegib	189 158.29 (1 966.38)	172 361.03 (1 791.77)		

Note: * The calculations used the average exchange rate of the dollar against the ruble: 96.1962 rubles per 1 USD for October 2024. INN — international non-proprietary name; MSP — maximum selling prices.

[10] Decree of the Government of the Russian Federation dated August 28, 2014 No. 871 (as amended on July 25,2024) On Approval of the Rules for the Formation of Lists of medicines for medical use and the minimum range of medicines required for medical care. Russian

To assess the comparative efficacy according to the criterion "disease progression in patients with laBCC receiving therapy with sonidegib and vismodegib", the relative risk (RR) and odds ratio (OR) were calculated. The calculations were performed on the basis of digitised Kaplan–Meier curves from the BOLT [10] and ERIVANCE [12] studies. The digitization of Kaplan-Meier curves was carried out according to the method of Guyot et al. [16] using the Engauge Digitizer[11] utility, which allowed to restore individual patient data for subsequent analysis. The results of the restoration of individual patient data are presented in Figure 3.

The initial data for calculating RR and OR are presented in the form of a four-field contingency table, reflecting the number of events and the total number of patients in each group (Table 3).

To calculate OR, confidence interval (95% CI), *p-value* and *Z-score* and relative risk (RR), the R version 4.4.3 environment was used. The calculations were carried out according to generally accepted statistical formulas, standardly used in epidemiology and medical statistics[12].

OR 12 months after the start of therapy was 0.27778 (95% CI 0.125–0.618, p = 0.0017, Z = 3.143). The chances of progression on vismodegib therapy in patients were statistically significantly higher (OR < 1, 95% CI did not cross 1) compared to the use of sonidegib, which allows us to conclude that sonidegib is more effective according to the PFS criterion. The probability of progression in the sonidegib and vismodegib groups was 0.182 (18.2%) and 0.444 (44.4%), respectively, and the RR was 0.409 (95% CI 0.229–0.732, p = 0.0026; Z = 3.013). Thus, the reduction in the risk of progression when using sonidegib compared to vismodegib is 59.1%.

To confirm the presence of statistically significant differences in efficacy between sonidegib and vismodegib, a hypothesis test was also conducted on the equality of the proportions of patients with laBCC who did not have disease progression 12 months after the start of therapy. At the first stage, the null hypothesis (H0) was formulated: the proportions of patients without disease progression in the groups receiving sonidegib and vismodegib do not differ statistically significantly and any observed differences are due to random factors. The alternative hypothesis (H1) assumed the presence of a statistically significant difference in the efficacy of the two treatment methods, expressed in the difference in the proportions of patients without progression 12 months after the start of therapy. A significance level of $\alpha = 0.05$ was used to test the hypothesis.

Data analysis and assessment of the statistical significance of differences between proportions were carried out in the statistical environment R version 4.4.3 using the prop.test() function. This function implements a *z*-test for comparing proportions using statistics based on an approximation to the χ^2 distribution, taking as arguments the number of successful outcomes (number of patients without progression) and the total number of observations in each group. The prop.test() function also allows you to calculate the *p-value*, CI for the difference in proportions and the value of the test statistic, which provides a comprehensive assessment of the presence of statistically significant differences between groups. The results of the *z*-test for the equality of proportions are presented in Table 5.

The test results demonstrated statistically significant differences, which is consistent with the calculations of OR and RR and further confirms the advantage of sonidegib in efficacy according to the PFS criterion. Thus, the conclusions obtained justify the choice of the "cost–effectiveness" method for further clinical and economic assessment of the use of sonidegib.

Methodology for developing a model for conducting a clinical and economic assessment of the use of the sonidegib in a wide clinical practice

To analyze the economic consequences of the use of sonidegib in a wide clinical practice, a model was developed according to the "decision tree". A graphical diagram of the model is presented earlier in Figure 2. Based on the results of determining the characteristics of the new medical technology, studying existing approaches to the treatment of patients with BCC and selecting alternatives for comparison, a systematic search and review of data on the comparative efficacy of alternative technologies for selecting a research method, the model included 2 alternative scenarios for the treatment of patients with laBCC in the 1-line of therapy:

- Scenario 1 — the use of vismodegib in the 1-line of therapy of patients in the target population;
- Scenario 2 — the use of sonidegib in the 1-line of therapy of patients in the target population.

[11] Engauge Digitizer. Available from: http://digitizer.sourceforge.net/
[12] Medical and biological statistics [text]. Stanton gloss; Buzikashvili NE, Samoilova DV, editors; Moscow: Pravda; 1999. 459 p. Russian

ОРИГИНАЛЬНАЯ СТАТЬЯ
DOI: 10.19163/2307-9266-2025-13-3-184-201

The current national CG do not provide recommendations for the treatment of patients with laBCC after disease progression during therapy with SHh signaling pathway inhibitors. In this regard, when conducting a clinical and economic assessment, a conservative scenario was considered, i.e. only direct costs for the 1-line therapy were taken into account. However, it should be noted that in the practical recommendations of the Russian Society of Clinical Oncology, in case of ineffectiveness or intolerance of the 1st line targeted therapy, immune checkpoint inhibitors, or PD-1 inhibitors — cemiplimab, nivolumab, pembrolizumab are used as drugs of choice in the 2-line [7]. The lack of accounting for costs and efficacy in the 2-line may lead to an incomplete assessment of the clinical and economic efficacy of sonidegib, which is a limitation of this study.

Methodology for accounting for costs when conducting a clinical and economic assessment

The calculation of the costs of drug therapy for the interventions under consideration was carried out on the basis of information on the methods of administration and dosage regimens indicated in the GCM. Information on prices for vismodegib was used as a source of information on the current registered maximum selling price (MSP) of the manufacturer, posted in the State Register of Registered Prices for Medicines[13]. During 2024, the generic of the original vismodegib was not purchased at the expense of budgetary funds to ensure state and municipal needs. Nevertheless, to assess the potential impact of participation in the procurement of the original and reproduced medicine, the average registered MSP within the INN vismodegib was taken into account. Data on the MSP planned for registration for the medicine proposed for inclusion were provided by the manufacturing company. The duration of 1 month was taken as 30.44 days. The calculations took into account the allowances established by the legislation of the Russian Federation (VAT 10%). Key parameters for calculating the costs of conducting the 1st line therapy in the base scenario are given in Table 6.

Methodology for calculating clinical and economic indicators

The calculation of cost–effectiveness ratio (CER) indicators was carried out to the generally accepted methodology. Data on the clinical efficacy of alternative technologies and information on the costs of drug therapy depending on the chosen treatment scenario were used to calculate CER[14]:

$$CER_i = \frac{Cost_i}{Ef_i},$$

where CER_i — cost–effectiveness ratio when using therapy scenario i; $Cost_i$ — costs per 1 patient per course of therapy using scenario i; Ef_i — efficacy of therapy using scenario i.

The incremental cost–effectiveness ratio (ICER) was also calculated to assess the clinical and economic benefits of sonidegib in the population of patients continuing the 1-line therapy by the end of 1 year of treatment. To calculate ICER, data on the clinical efficacy of alternative technologies from the BOLT [10] and ERIVANCE [12] studies, and the costs of drug therapy in the case of using each of the options included in the study were used[15]:

$$ICER = \frac{\Delta Cost}{\Delta Ef},$$

where ICER — incremental cost–effectiveness ratio; ΔCost — the difference in the costs of therapy between alternative treatment scenarios in the 1-line of therapy; ΔEf — the difference in efficacy between alternative treatment scenarios in the 1-line of therapy.

Analysis of the sensitivity of the results to changes in input parameters

To study the stability of the results obtained to changes in the key parameters used in the calculations, a sensitivity analysis was carried out to changes in the MSP for medicine and efficacy indicators.

To assess the stability of the results obtained to changes in the efficacy of sonidegib, a one-factor analysis of the sensitivity was carried out to changes in the base value of the median PFS (22.1 months) within the confidence interval. To assess the stability of the results obtained to changes in the efficacy of vismodegib, a one-factor analysis of the sensitivity was carried out to changes in the base value of the median PFS within the CI.

To assess the stability of the results obtained to changes in the MSP for sonidegib and vismodegib, 3 variants of sensitivity analysis were carried out:

In the first variant analysis for sonidegib, the base

[13] The State register of marginal selling prices. Vismodegib. Available from: https:// grls.minzdrav.gov.ru/PriceLims.aspx

[14] Clinical and economic analysis; Vorobyev PA, Avksentieva MV, Yuryev AS, et al. Moscow: Newdiamed; 2004. 404 p. Russian

[15] Ibid.

value of the MSP was 189 158.29 rubles per package, varied in the range from +5 to +20% with a step of 5%. The initial value of the MSP for vismodegib did not change.

In the second variant base value of the MSP of sonidegib, the initial value of the MSP of vismodegib was reduced by 22.5% to the MSP for the reproduced drug.

The third variant assessed the stability of the results obtained when the MSP for vismodegib was reduced by 22.5% and the MSP for vismodegib was reduced by 10%.

Key parameters for conducting the analysis of the sensitivity according to the price criterion for drugs are given in Table 7.

Research period

The economic consequences of the proposed inclusion of the sonidegib were assessed within 1 year.

Discounting

As the modeling period was 1 year, discounting was not used to bring future cash income to the present moment.

RESULTS

Hedgehog (Hh) inhibitors are a key group of targeted medicines aimed to block the Hedgehog signaling pathway, which plays an important role in the pathogenesis of BCC [17, 18]. Hedgehog inhibitors are the only option for treating patients with progressive BCC when surgery or radiation therapy is not possible [19, 20].

The most studied and clinically significant representatives of this group are vismodegib and sonidegib. Vismodegib became the first Hedgehog signaling pathway inhibitor to be approved by the U.S. Food and Drug Administration (FDA) for the treatment of metastatic and locally advanced BCC that has recurred after surgery or when surgery or radiation therapy is not possible [21]. The efficacy and safety of vismodegib was studied in the international multicenter phase II ERIVANCE study, which included 104 patients with metastatic and locally advanced BCC. The primary endpoint of the study was to assess the objective response to therapy (reduction in tumor size). Secondary outcomes included objective response rate, duration of response to therapy, PFS, and overall survival (OS). According to the results of the study, in patients with locally advanced BCC and metastatic BCC who received vismodegib, the overall response rate (ORR) was 43% according to the assessment of an independent expert commission and 60% according to the assessment of local researchers for the cohort of laBCC, and for the cohort of metastatic BCC — 30 and 45%, respectively. The median duration of response was 7.6 months, and PFS was 9.5 months in both cohorts. After 39 months of follow-up, the ORR according to local investigators was 60.3% for the group of patients with laBCC and 48.5% for patients with metastatic BCC. The median duration of response was 26.2 months for laBCC and 14.8 months for metastatic BCC. The median OS could not be established in the cohort of laBCC, while in the cohort of metastatic BCC it was 33.4 months [12–14]. In 2015, the FDA and EMA approved another Hedgehog inhibitor, sonidegib (TN Odomzo®)[16], for the treatment of adult patients with laBCC, with recurrence after surgery or radiation therapy, or patients who are not candidates for surgery or radiation therapy. The efficacy and safety of the medicine was studied in an international multicenter double-blind randomized non-comparative phase II BOLT study involving 230 patients. The primary endpoint of the study was ORR, the proportion of patients with the best overall response. Secondary endpoints included response rate and duration, progression-free survival PFS OS, and safety. The ORR in patients with laBCC was 56% (95% CI 43–68). The median PFS was 22.1 months (95% CI not reached), the median duration of response to therapy was 26.1 months (95% CI not reached) when sonidegib was used at a dose of 200 mg once daily. Most adverse events were manageable and reversible with interruption of therapy or dose reduction. The median duration of sonidegib therapy was 11.0 months — 68% of patients took the drug for 8 months or more, 43% of patients — 12 months or more, 24% of patients — 20 months or more [9–11]. In the Russian Federation, the drug sonidegib became available in 2024.

To date, only one Hedgehog inhibitor, vismodegib, is included in the Formulary and the List of Vital and Essential Medicines. The medicine is recommended for use in the 1st line of therapy in adults over 18 years of age for the treatment of metastatic or locally advanced BCC with recurrence after surgical treatment or the impracticality of surgical treatment or radiation therapy.

[16] European Medicines Agency. Odomzo (Sonidegib). Available from: https://www.ema.europa.eu/en/ medicines/human/EPAR/odomzo#authorisation-details

ОРИГИНАЛЬНАЯ СТАТЬЯ
DOI: 10.19163/2307-9266-2025-13-3-184-201

No direct comparative studies of the efficacy and safety of sonidegib and vismodegib have been conducted. Based on our own calculations, the OR of disease progression in patients with laBCC receiving therapy with sonidegib and vismodegib after 12 months from the start of therapy was 0.27778 (95% CI 0.125–0.618; p = 0.0017; Z = 3.143). The probability of progression in the sonidegib and vismodegib groups was 0.182 and 0.444, respectively, and the OR was 0.409 (95% CI 0.229–0.732). Thus, the reduction in the risk of progression when using sonidegib compared to vismodegib was 59.1%. The results of data analysis and assessment of the significance of differences between the proportions of patients without disease progression when using sonidegib and vismodegib also made it possible to draw conclusions about significant differences in clinical outcomes between the analyzed technologies according to the PFS criterion — χ^2 = 9.2007, df = 1, p = 0.002419, 95% CI 0.09312–0.432132.

Based on the method of assessing direct costs, the cost of 1-line therapy per 1 patient when using vismodegib will be 2.84 million rubles per year, in the case of using sonidegib — 2.53 million rubles per year. The difference in costs between alternative treatment scenarios in absolute terms is 308.55 thousand rubles (or 10.86%) per 1 patient in favor of sonidegib (Table 8).

According to the data obtained, the use of sonidegib with greater efficacy requires lower costs. With the basic values of the median PFS for sonidegib and vismodegib of 22.1 and 12.9 months, respectively, the CER indicator was 114 626.71 rubles for sonidegib and 220 294.99 rubles for vismodegib, which indicates the clinical and economic advantages of sonidegib. Changes in the efficacy of sonidegib and vismodegib (median PFS) within the CI showed the stability of the results obtained in the study: the use of sonidegib remains the dominant technology in terms of CER when varying the values of the efficacy indicator and medicine prices (Fig. 4).

With a difference in efficacy according to the PFS criterion between the sonidegib and vismodegib of 9.2 months, the ICER for sonidegib was 175 050.21 rubles per 1 unit of additional efficacy — 1 month of PFS. With a decrease in the efficacy of sonidegib to the lower limit of the CI (PFS 14.8 months) and the basic value of the median PFS for vismodegib of 12.9 months, the ICER for sonidegib will be 36 527.03 rubles per 1 month of PFS with a difference in efficacy of 1.9 months. With an initial PFS value for sonidegib of 22.1 months and an increase in the efficacy of vismodegib to the upper limit of the CI (median PFS 14.8 months), the ICER for sonidegib will be 158 973.90 rubles per 1 month of PFS with a difference in efficacy of 7.3 months.

With statistically significant advantages in the efficacy of sonidegib, the percentage of cost deviation in the basic scenario was “-10.86%” in favor of sonidegib. In absolute terms, the savings per 1 patient was 308.55 thousand rubles per patient.

To interpret the results obtained regarding the difference in costs, we used the provisions of the rules for forming lists of medicinal products for medical use[17]. If the clinical efficacy of a medicine is statistically significantly higher compared to an alternative treatment option, and the difference in direct medical costs is more than 10%, then the use of such a drug is characterized by lower costs. Thus, we can say that the use of sonidegib is characterized by lower costs for therapy compared to vismodegib with statistically significantly greater efficacy according to the PFS criterion.

As part of the sensitivity analysis, it was shown that the economic feasibility of using sonidegib in the 1st line is maintained in the range of increasing MPC for the medicine from 5 to 20% with participation in procurement to ensure state and municipal needs for both the original and reproduced medicine within the INN vismodegib. With an increase in the price of sonidegib from 5 to 20%, a gradual decrease in the economic benefit of sonidegib is observed, however, even with the maximum price increase (+20%), the difference in costs is +6.97% and is considered “insignificant”[18]. This indicates that the results are resistant to changes in the price of sonidegib in this range.

With a decrease in the price of vismodegib to 161 605.16 rubles (the price of the reproduced drug) and the basic value of the price of sonidegib (189 158.29 rubles), the percentage of cost deviation between alternative treatment scenarios will increase to +9.25%, which also does not lead to a significant increase in direct costs when providing medical care to patients with laBCC[19]. A decrease in prices for both medicines leads to a decrease in the difference in

[17] Decree of the Government of the Russian Federation dated August 28, 2014 No. 871 (as amended on July 25,2024) On Approval of the Rules for the Formation of Lists of medicines for medical use and the minimum range of medicines required for medical care. Russian
[18] Ibid.
[19] Clinical Guidelines. Basal cell carcinoma of the skin; 2024.

costs (to parity of 0.45%). The results of the sensitivity analysis are shown in Table 9.

A comparative analysis of efficacy according to the PFS criterion revealed the advantage of sonidegib over vismodegib: OR of disease progression in patients with laBCC 12 months after the start of therapy 0.27778 (95% CI 0.125–0.618, p = 0.0017; Z = 3.1423). The reduction in the risk of progression when using sonidegib compared to vismodegib is 59.1% (OR = 0.409; 95% CI 0.229–0.732, p = 0.0026; Z = 3.013). The hypothesis about the equality of the proportions of patients with laBCC without disease progression 12 months after the start of therapy also made it possible to draw conclusions about the presence of statistically significant differences in efficacy between the two treatment methods in favor of sonidegib — χ^2 = 9.2007, df = 1, p = 0.002419, 95% CI 0.09312–0.432132.

The cost of the therapy with sonidegib for 1 year per 1 patient was 2.53 million rubles, which is 10.86% lower compared to vismodegib, which corresponds to an absolute savings of 308.55 thousand rubles per 1 patient. Thus, with greater efficacy, the use of sonidegib requires lower costs.

The CER indicator for sonidegib is lower (114 626.71 rubles) compared to vismodegib (220 294.99 rubles), which also indicates the clinical and economic advantages of sonidegib. Changes in key parameters for calculation within the sensitivity analysis did not affect the results. According to the CER indicator, the use of sonidegib remains the dominant technology even with a median PFS value of 14.8 months — CER for sonidegib is 171 165.56 rubles, which is lower than CER for vismodegib both at the initial efficacy values for the medicine and with an increase in the efficacy of vismodegib within the CI (192 013.87 rubles). With a difference in efficacy according to the PFS criterion between sonidegib and vismodegib of 9.2 months, the ICER for sonidegib was 175 050.21 rubles per 1 unit of additional efficacy — 1 month of PFS.

DISCUSSION

A clinical and economic assessment of the use of the sonidegib was carried out from the perspective of the healthcare system in the short term in this study. It seems appropriate to further study the clinical and economic characteristics of sonidegib in the long term in terms of its impact on overall survival rates and the achievement of the targets of the national project “Combating Oncological Diseases” [23, 24].

A promising direction for further analysis of the clinical and economic consequences of the use of sonidegib in widespread practice is also the use of more complex mathematical models. The results obtained by Purser et al. are of interest, for example [25]. The authors developed a partitioned survival model to analyze expected direct medical costs, life-years gained (LYG), and quality-adjusted life-years (QALY) within the time period of survival of patients with laBCC. According to the modeling results, LYG without discounting when using sonidegib and vismodegib was 3.89 years for both comparators. At the same time, the expected direct medical costs for sonidegib were lower compared to vismodegib and amounted to £108 037 and £129 435, respectively. The expected discounted QALY indicators for sonidegib and vismodegib were 2.58 and 2.46, respectively. Sensitivity analysis showed that the results are resistant to uncertainty and variability of key parameters used for calculations. According to the authors, sonidegib is the dominant technology in terms of QALY and lower costs. Thus, models based on partitioned survival are an effective tool for assessing the clinical and economic benefits of sonidegib in the long term.

Since clinical and economic models are limited by the availability and quality of source data, it is also advisable to take into account data from real clinical practice, which will allow taking into account a wider range of clinical outcomes and increase the accuracy of the assessment [25].

From a practical point of view and adaptation in relation to the conditions of real clinical practice, the results obtained in the study by García et al. are also of interest [26]. The authors conducted a comparative assessment of the efficacy and safety of sonidegib and vismodegib based on available data from the BOLT and ERIVANCE studies using effect size indicators: the number of patients who need to be treated to achieve a favorable effect (Number Needed to Treat — NNT), the number of patients who must be exposed to risk over a certain period so that one of them develops an adverse outcome (Number Needed to Harm — NNH), and the benefit-risk ratio when taking the medicine (Likelihood to be helped or harmed — LHH). The authors calculated the NNT indicator for sonidegib and vismodegib based on data on ORR. The NNH indicator was calculated using data on treatment discontinuation

ОРИГИНАЛЬНАЯ СТАТЬЯ
DOI: 10.19163/2307-9266-2025-13-3-184-201

due to adverse events and the frequency of adverse events. The LHH ratio was calculated as the ratio of the corresponding NNH to NNT values for each drug.

For sonidegib (dose 200 mg), the NNT indicator (the number of patients needed to treat to achieve one objective response, ORR) after 18 months was 1.65 (95% CI 1.35–2.01), while for vismodegib (150 mg) after 21 months — 2.10 (95% CI 1.65–2.82). The NNH indicator (the number of patients needed to observe one case of an adverse event leading to treatment discontinuation) was 1.9 (95% CI 1.6–2.5) for sonidegib and 1.8 (95% CI 1.4–2.2) for vismodegib. The LHH values (the ratio of the probability of benefit to the probability of harm) when treatment was discontinued due to adverse events were 1.14 for sonidegib and 0.84 for vismodegib, while when taking into account adverse events ≥ 3 degrees of severity — 1.41 for sonidegib and 0.85 for vismodegib. The NNT indicator reflects the efficacy of therapy and demonstrates how many patients need to be treated in order for one of them to achieve a clinically significant response. In this case, a lower NNT for sonidegib (1.65) indicates a higher probability of achieving a therapeutic effect compared to vismodegib (2.10). The NNH indicator characterizes the risk of adverse events leading to treatment discontinuation. The NNH values for sonidegib (1.9) and vismodegib (1.8) are close, which indicates a comparatively similar frequency of treatment discontinuations due to adverse effects. The LHH ratio integrates information about the benefit and harm of treatment, reflecting the probability of obtaining clinical benefit compared to the risk of developing adverse events. An LHH value greater than one (1.14 and 1.41 for sonidegib) indicates that sonidegib therapy is more likely to lead to a positive effect than to treatment discontinuation due to adverse events, while values below one (0.84 and 0.85 for vismodegib) indicate the opposite — the risk of harm exceeds the probability of benefit. Based on the results obtained, the authors concluded that these indicators confirm a more favorable benefit-risk profile for sonidegib compared to vismodegib. However, they conclude that the conclusions obtained require confirmation in clinical practice and/or in randomized direct comparative studies [26].

Limitations of the study

Due to the lack of direct comparative studies between the vismodegib and sonidegib, the choice of research method (justification of the research hypothesis) was carried out on the basis of our own calculations of OR and RR of disease progression in patients with laBCC receiving therapy with these medicines, 12 months after the start of treatment, and the results of testing the hypothesis about the equality of the proportions of patients with laBCC without disease progression 12 months after the start of therapy.

The study used a conservative scenario to assess the direct medical costs of systemic targeted therapy for patients with laBCC: accounting for costs only for the 1-line of therapy. The Russian Society of Clinical Oncology recommends the use of PD-1 inhibitors after disease progression while using Hedgehog inhibitors. In the 2-line of therapy, the cost of 1 administration, for example, for nivolumab, will be 205 104.24 rubles with a dosing regimen of 240 mg every 14 days and 341 840.40 rubles with a dosing regimen of 480 mg every 21 days [7] at an average price per 1 mg of 7 769.01 according to the Unified System of Cataloging of Medicines[20] and VAT of 10%. The cost of 1 month of treatment with Hedgehog inhibitors in the 1-line is 236 817.11 rubles when using vismodegib and 211 104.20 rubles in the case of using sonidegib. Reducing the risk of progression when using sonidegib in the 1st line potentially helps to reduce budget expenditures when patients with laBCC transition to the 2nd line of therapy.

Despite the objective assumptions and limitations of the study, even under a conservative assessment scenario, clinical and economic advantages of sonidegib were identified. Accumulation and analysis of real-world data on the management of patients with laBCC after progression while using Hedgehog inhibitors will allow further clarification and supplementation of the clinical and economic characteristics of sonidegib. Nevertheless, the results already obtained allow us to conclude that the medicine has a positive clinical and economic impact when used in widespread clinical practice.

CONCLUSION

Based on the results obtained in the study, the hypothesis about the clinical and economic advantages of sonidegib in the treatment of laBCC was confirmed, and data on the clinical and economic feasibility of using sonidegib in widespread clinical practice were obtained.

[20] Unified System of Cataloging of Medicines. Nivolumab. Available from: https://esklp.egisz.rosminzdrav.ru/esklp/smnn?smnn_gid=1ee6860a-bf5b-11e9-bd5d-93a13b914aa9&page=1&per_page=40

FUNDING

The study was supported by "Sun Pharmaceutical limited" (India). The sponsor had no influence on the selection of material for publication, data analysis and interpretation.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

Oksana I. Ivakhnenko — design development, collection and critical analysis of literature and regulatory legal documents, data collection and analysis, modeling and interpretation of results, writing, draft editing, final approval of the article; Vasily V. Ryazhenov — critical analysis of literature, making comments of intellectual content, draft editing; Maksim Yu. Frolov — critical analysis of literature, making comments of intellectual content, draft editing; Vladimir A. Rogov — critical analysis of literature, making comments on intellectual content, draft editing. All authors confirm that their authorship meets the international ICMJE criteria (all authors made a significant contribution to the development of the concept, conduct of the study and preparation of the article, read and approved of the final version before the publication).

REFERENCES

1. McDaniel B, Steele RB. Basal Cell Carcinoma. [Updated 2024 Mar 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
2. Peris K, Fargnoli MC, Kaufmann R, Arenberger P, Bastholt L, Seguin NB, Bataille V, Brochez L, Del Marmol V, Dummer R, Forsea AM, Gaudy-Marqueste C, Harwood CA, Hauschild A, Höller C, Kandolf L, Kellerners-Smeets NWJ, Lallas A, Leiter U, Malvehy J, Marinović B, Mijuskovic Z, Moreno-Ramirez D, Nagore E, Nathan P, Stratigos AJ, Stockfleth E, Tagliaferri L, Trakatelli M, Vieira R, Zalaudek I, Garbe C; EADO"A, EDF"B, ESTRO"C, UEMS"D and EADV"E. European consensus-based interdisciplinary guideline for diagnosis and treatment of basal cell carcinoma-update 2023. Eur J Cancer. 2023;192:113254. DOI: 10.1016/j.ejca.2023.113254
3. Kim DP, Kus KJB, Ruiz E. Basal Cell Carcinoma Review. Hematol Oncol Clin North Am. 2019;33(1):13–24. DOI: 10.1016/j.hoc.2018.09.004
4. Janda M, Olsen CM, Mar J, Cust AE. Early detection of skin cancer in Australia – current approaches and new opportunities. Public Health Res Pract. 2022;32(1):3212204. DOI: 10.17061/phrp3212204
5. Orlova KV, Martynova MV, Petenko NN, Nazarova VV, Demidov LV. Basal cell skin carcinoma: Epidemiology of locally advanced and metastatic forms based on the data of the N.N. Blokhin National Medical Research Center of Oncology: A retrospective study. Journal of Modern Oncology. 2025;27(1):14–8. DOI: 10.26442/18151434.2025.1.203188
6. Petenko NN, Demidov LV. Basal cell cancer treatment. Therapeutic experience with vismodegib therapy. Medical Council. 2018;(10):42–8. DOI: 10.21518/2079-701X-2018-10-42-48
7. Utyashev IA, Orlova KV, Zinov'ev GV, Trofimova OP, Petenko OP, Nazarova VV, Mudunov AM, Kramchaninov MM. Practice guidelines for medical management of malignant non-melanoma skin tumors (basal cell skin cancer, squamous cell skin cancer, Merkel cell carcinoma). Practice guidelines RUSSCO. 2022;12:672–96. DOI: 10.18027/2224-5057-2022-12-3s2-672-696
8. Odom D, Mladsi D, Purser M, Kaye JA, Palaka E, Charter A, Jensen JA, Sellami D. A Matching-Adjusted Indirect Comparison of Sonidegib and Vismodegib in Advanced Basal Cell Carcinoma. J Skin Cancer. 2017;2017:6121760. DOI: 10.1155/2017/6121760
9. Lewis K, Dummer R, Farberg AS, Guminski A, Squittieri N, Migden M. Effects of Sonidegib Following Dose Reduction and Treatment Interruption in Patients with Advanced Basal Cell Carcinoma During 42-Month BOLT Trial. Dermatol Ther (Heidelb). 2021;11(6):2225–34. DOI: 10.1007/s13555-021-00619-4
10. Lear JT, Migden MR, Lewis KD, Chang ALS, Guminski A, Gutzmer R, Dirix L, Combemale P, Stratigos A, Plummer R, Castro H, Yi T, Mone M, Zhou J, Trefzer U, Kaatz M, Loquai C, Kudchadkar R, Sellami D, Dummer R. Long-term efficacy and safety of sonidegib in patients with locally advanced and metastatic basal cell carcinoma: 30-month analysis of the randomized phase 2 BOLT study. J Eur Acad Dermatol Venereol. 2018;32(3):72–381. DOI: 10.1111/jdv.14542
11. Migden MR, Guminski A, Gutzmer R, Dirix L, Lewis KD, Combemale P, Herd RM, Kudchadkar R, Trefzer U, Gogov S, Pallaud C, Yi T, Mone M, Kaatz M, Loquai C, Stratigos AJ, Schulze HJ, Plummer R, Chang AL, Cornélis F, Lear JT, Sellami D, Dummer R. Treatment with two different doses of sonidegib in patients with locally advanced or metastatic basal cell carcinoma (BOLT): a multicentre, randomised, double-blind phase 2 trial. Lancet Oncol. 2015;16(6):716–28. DOI: 10.1016/S1470-2045(15)70100-2
12. Sekulic A, Migden MR, Basset-Seguin N, Garbe C, Gesierich A, Lao CD, Miller C, Mortier L, Murrell DF, Hamid O, Quevedo JF, Hou J, McKenna E, Dimier N, Williams S, Schadendorf D, Hauschild A; ERIVANCE BCC Investigators. Long-term safety and efficacy of vismodegib in patients with advanced basal cell carcinoma: final update of the pivotal ERIVANCE BCC study. BMC Cancer. 2017;17(1):332. DOI: 10.1186/s12885-017-3286-5. Erratum in: BMC Cancer. 2019;19(1):366. DOI: 10.1186/s12885-019-5568-6
13. Chang AL, Arron ST, Migden MR, Solomon JA, Yoo S, Day BM, McKenna EF, Sekulic A. Safety and efficacy of vismodegib in patients with basal cell carcinoma nevus syndrome: pooled analysis of two trials. Orphanet J Rare Dis. 2016;11(1):120. DOI: 10.1186/s13023-016-0506-z

ОРИГИНАЛЬНАЯ СТАТЬЯ
DOI: 10.19163/2307-9266-2025-13-3-184-201

14. Sekulic A, Migden MR, Oro AE, Dirix L, Lewis KD, Hainsworth JD, Solomon JA, Yoo S, Arron ST, Friedlander PA, Marmur E, Rudin CM, Chang AL, Low JA, Mackey HM, Yauch RL, Graham RA, Reddy JC, Hauschild A. Efficacy and safety of vismodegib in advanced basal-cell carcinoma. N Engl J Med. 2012;366(23):2171–9. DOI: 10.1056/NEJMoa1113713
15. Goryajnov SV, Rebrova OYu. Indirect comparisons in health technology assessment. Pediatric pharmacology. 2012;9(2):6–9. DOI: 10.15690/pf.v9i2.237
16. Guyot P, Ades AE, Ouwens MJ, Welton NJ. Enhanced secondary analysis of survival data: reconstructing the data from published Kaplan-Meier survival curves. BMC Med Res Methodol. 2012;12:9. DOI: 10.1186/1471-2288-12-9
17. Bossi P, Ascierto PA, Basset-Seguin N, Dreno B, Dummer R, Hauschild A, Mohr P, Kaufmann R, Pellacani G, Puig S, Moreno-Ramírez D, Robert C, Stratigos A, Gutzmer R, Queirolo P, Quaglino P, Peris K. Long-term strategies for management of advanced basal cell carcinoma with hedgehog inhibitors. Crit Rev Oncol Hematol. 2023;189:104066. DOI: 10.1016/j.critrevonc.2023.104066
18. Paradisi A, Mannino M, Brunetti F, Bocchino E, Di Stefani A, Peris K. Advanced Basal Cell Carcinoma: A Narrative Review on Current Systemic Treatments and the Neoadjuvant Approach. J Pers Med. 2025;15(6):226. DOI: 10.3390/jpm15060226
19. Kubanov AA, Saytburkhanov RR, Plakhova XI, Kondrakhina IN. Non-surgical treatments for basal cell skin cancer. Vestnik dermatologii i venerologii. 2021;97(6):20–32. DOI: 10.25208/vdv1294
20. Patel S, Armbruster H, Pardo G, Archambeau B, Kim NH, Jeter J, Wu R, Kendra K, Contreras CM, Spaccarelli N, Dulmage B, Pootrakul L, Carr DR, Verschraegen C. Hedgehog pathway inhibitors for locally advanced and metastatic basal cell carcinoma: A real-world single-center retrospective review. PLoS One. 2024;19(4):e0297531. DOI: 10.1371/journal.pone.0297531
21. Lavasidis G, Tzamalis A, Tsinopoulos I, Ziakas N. Exploring vismodegib: A non-surgical breakthrough in the management of advanced periocular basal cell carcinoma. Cancer Treat Res Commun. 2024;39:100796. DOI: 10.1016/j.ctarc.2024.100796
22. Casey D, Demko S, Shord S, Zhao H, Chen H, He K, Putman A, Helms W, Keegan P, Pazdur R. FDA Approval Summary: Sonidegib for Locally Advanced Basal Cell Carcinoma. Clin Cancer Res. 2017;23(10):2377–81. DOI: 10.1158/1078-0432.CCR-16-2051
23. Ryazhenov VV, Orlov SV, Ivakhnenko OI. Assessment of the impact of the use of durvalumab for the treatment of advanced small cell lung cancer on the achievement of the target “reduction in mortality from neoplasms”. Journal of Modern Oncology. 2022;24(1):30–40. DOI: 10.26442/18151434.2022.1.201498
24. Ivakhnenko OI, Ryazhenov VV, Falaleeva NA. Clinical and economic implications of using daratumubab with lenalidomide in the 1st and 2nd lines of therapy for multiple myeloma patients. FARMAKOEKONOMIKA. Modern Pharmacoeconomics and Pharmacoepidemiology. 2024;17(1):5–21. DOI: 10.17749/2070-4909/farmakoekonomika.2024.237
25. Purser M, Mladsi D, Kaye JA, PCN130 – Cost-Efffectivenes of Sonidegib Versus Vismodegib for The Treatment of Patients with Locally Advanced Basal Cell Carcinoma Not Amenable to Surgery or Radiotherapy. Value in Health. 2016;19(7):A731. DOI: 10.1016/j.jval.2016.09.2204.
26. García Ruiz AJ, García-Agua Soler N, Herrera Acosta E, Zalaudek I, Malvehy J. Benefit-risk assessment of sonidegib and vismodegib in the treatment of locally advanced basal cell carcinoma. Drugs Context. 2022;11:2022-1-2. DOI: 10.7573/dic.2022-1-2

AUTHORS

Oksana I. Ivakhnenko — Assistant of the Department of Regulatory Relations in the field of circulation of medicines and medical devices of the Sechenov First Moscow State Medical University (Sechenov University); Master of Law. ORCID ID: 0000-0002-9483-3171. E-mail: oii@hta-expert.ru

Vasily V. Ryazhenov — Doctor of Sciences (Pharmacy), Head of the Department of Regulatory Relations in the Field of Circulation of Drug Products and Medical Devices of the Sechenov First Moscow State Medical University (Sechenov University). ORCID ID: 0000-0002-1278-5883. E-mail: 5052568@mail.ru

Maxim Yu. Frolov — Candidate of Sciences (Medicine), Assistant Professor of the Department of Pharmacology and Pharmacy of the Volgograd State Medical University. ORCID ID: 0000-0003-2679-7524. E-mail: clinpharmrussia@yandex.ru

Vladimir A. Rogov — Candidate of Sciences (Pharmacy), Senior lecturer of the Department of Pharmacy Management and Economics, Medical and Pharmaceutical Commodity Science of the Volgograd State Medical University. ORCID ID: 0000-0002-2164-2323. E-mail: varogov@volgmed.ru