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# SYSTEMIC RETINOIDS IN THE MANAGEMENT OF MODERATE TO-SEVERE ACNE: A CLINICAL CASE STUDY

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**Abstract**

**Introduction:** Acne vulgaris is a multifactorial inflammatory disorder affecting about 9% of the global population, most commonly in those aged 20–29 years. Its pathogenesis involves follicular hyperkeratinization, sebaceous hyperactivity, and immune activation, leading to inflammation and scarring, requiring targeted treatments like retinoids.

The **aim** of this study is to assess the clinical effectiveness of acnekutan in managing severe acne.

**Materials and Methods:** A retrospective case review was conducted using medical records from the dermatovenerology department of City Hospital No. 2, Abai region. The patient's condition was monitored in the CMIS from 2024 to 2025, following clinical guidelines approved by the Ministry of Health of Kazakhstan. Signed informed consent was obtained from both the clinic administration and the patient for publication.

**Results:** After transitioning a patient with severe acne to isotretinoin, a significant clinical improvement was observed. The treatment effectively reduced inflammatory lesions and prevented the formation of new acne elements. Clinical studies have demonstrated that acnekutan targets multiple pathogenic mechanisms of acne and enhances patients' quality of life. In our study, the patient experienced side effects such as skin dryness and a temporary increase in transaminase levels, consistent with global research findings.

**Conclusion:** Isotretinoin remains the preferred treatment for severe acne, ensuring high efficacy and prolonged remission. Careful monitoring and individualized dosing are essential for optimal patient management. Future research should focus on dosing optimization, combination therapies, and treatment resistance mechanisms.

***Keywords:*** *acne, isotretinoin, retinoids, inflammation, clinical case.*

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**Резюме**

# СИСТЕМНЫЕ РЕТИНОИДЫ В ЛЕЧЕНИИ СРЕДНЕТЯЖЕЛЫХ И ТЯЖЕЛЫХ ФОРМ АКНЕ: КЛИНИЧЕСКИЙ СЛУЧАЙ

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**Введение:** Обыкновенные угри - это многофакторное воспалительное заболевание, которым страдают около 9% населения земного шара, чаще всего в возрасте 20-29 лет. Его патогенез включает в себя гиперкератинизацию фолликулов, гиперактивность сальных желез и активацию иммунитета, что приводит к воспалению и образованию рубцов, требующих целенаправленного лечения, такого как системные ретиноиды.

**Цель:** оценить клиническую эффективность акнекутана в лечении тяжелой формы акне.

**Материалы и методы:** был проведен ретроспективный анализ случая на основе медицинской документации дерматовенерологического отделения Городской больницы №2 УЗ области Абай. Состояние пациента отслеживалось в медицинской информационной системе КМИС в период с 2024 по 2025 год в соответствии с клиническими рекомендациями, утвержденными Министерством здравоохранения Республики Казахстан и соблюдением этических норм.

**Результаты:** после перевода пациента с тяжелым акне на изотретиноин отмечено значительное клиническое улучшение. Препарат эффективно уменьшал воспалительные элементы и предотвращал появление новых высыпаний. Клинические исследования подтверждают, что акнекутан воздействует на основные звенья патогенеза акне и способствует улучшению качества жизни пациентов. В нашем исследовании пациент испытывал побочные эффекты, включая сухость кожи и временное повышение уровня трансаминаз, что соответствует данным мировых исследований.

**Заключение:** Изотретиноин остается предпочтительным методом лечения тяжелой формы акне, обеспечивая высокую эффективность и длительную ремиссию. Важную роль играет тщательный мониторинг побочных эффектов и индивидуальный подбор дозировки. Перспективы дальнейших исследований включают оптимизацию режимов дозирования, оценку комбинированной терапии и изучение механизмов устойчивости к лечению.

***Ключевые слова:*** *угревая болезнь, изотретиноин, ретиноиды, воспаление, клинический случай.*

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**Түйіндеме**

# БЕЗЕУДІҢ ОРТАША ЖӘНЕ АУЫР ТҮРЛЕРІН ЕМДЕУДЕГІ ЖҮЙЕЛІК РЕТИНОИДТАР: КЛИНИКАЛЫҚ ЖАҒДАЙ

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**Кіріспе:** кәдімгі безеу-бұл жер шарының шамамен 9% әсер ететін көп факторлы қабыну ауруы, көбінесе 20-29 жаста. Оның патогенезі фолликулалардың гиперкератинизациясын, май бездерінің шамадан тыс белсенділігін және иммунитетті белсендіруді қамтиды, нәтижесінде қабыну және жүйелі ретиноидтар сияқты мақсатты емдеуді қажет ететін тыртықтар пайда болады.

**Зерттеудің мақсаты**: безеудің ауыр түрін емдеудегі акнекутанның клиникалық тиімділігін бағалау.

**Материалдар мен әдістер**: Абай облысының № 2 ДСБ Қалалық ауруханасының дерматовенерологиялық бөлімшесінің медициналық құжаттамасы негізінде жағдайға ретроспективті талдау жүргізілді. Пациенттің жағдайы Қазақстан Республикасы Денсаулық сақтау министрлігі бекіткен клиникалық ұсынымдарға және этикалық нормалардың сақталуына сәйкес 2024-2025 жылдар аралығында ҚМИС медициналық ақпараттық жүйесінде бақыланды.

**Нәтижелер:** ауыр безеумен ауыратын науқасты изотретиноинге ауыстырғаннан кейін айтарлықтай клиникалық жақсару байқалды. Препарат қабыну элементтерін тиімді түрде азайтып, жаңа бөртпелердің пайда болуына жол бермеді. Клиникалық зерттеулер акнекутанның безеу патогенезінің негізгі буындарына әсер ететінін және пациенттердің өмір сүру сапасын жақсартуға ықпал ететінін растайды. Біздің зерттеуімізде пациент жанама әсерлерді, соның ішінде құрғақ теріні және трансаминазалардың уақытша жоғарылауын бастан кешірді, бұл әлемдік зерттеулерге сәйкес келеді.

**Қорытынды:** изотретиноин жоғары тиімділік пен ұзақ мерзімді ремиссияны қамтамасыз ететін ауыр безеуді емдеудің таңдаулы әдісі болып қала береді. Жанама әсерлерді мұқият бақылау және дозаны жеке таңдау маңызды рөл атқарады. Әрі қарайғы зерттеулердің болашағы дозалау режимдерін оңтайландыруды, аралас терапияны бағалауды және емдеуге төзімділік механизмдерін зерттеуді қамтиды.

***Түйінді сөздер**: безеу ауруы, изотретиноин, ретиноидтар, қабыну, клиникалық жағдай.*

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**Background**

Acne vulgaris is a polymorphic, multifactorial dermatological disorder primarily driven by inflammation of the pilosebaceous unit [6]. Epidemiological data indicate that approximately 9% of the global population is affected, with 80–85% of cases occurring in individuals aged 12 to 24 years [25]. In recent years, a growing body of research has highlighted a shift in the age distribution of acne, with an increasing prevalence among individuals aged 20–29 years [5]. Given its primary localization on the face and trunk, acne can significantly impair patients' quality of life, negatively affecting self-esteem and contributing to the development of anxiety and depressive disorders [3].

The classification of acne is based on disease severity, which is determined by the number and type of inflammatory lesions, including papules, pustules, and nodules [2]. The etiology and pathogenesis of acne involve a complex interplay of intrinsic and extrinsic factors, ultimately resulting in chronic inflammation [29]. One of the earliest pathogenic events is follicular hyperkeratinization, characterized by excessive proliferation and impaired desquamation of keratinocytes, the superficial skin cells. This dysregulated keratinization leads to the accumulation of keratinocytes within the sebaceous gland ducts, culminating in follicular obstruction and the formation of comedones - the primary lesions of acne [8]. Another key pathogenic mechanism is sebaceous gland hyperactivity, which leads to increased sebum production. Sebum, a lipid-rich substance that prevents skin dryness, is regulated by androgens. Elevated androgen levels stimulate sebaceous gland hypertrophy and excessive sebum secretion, which in turn contributes to follicular occlusion and provides a nutrient-rich environment for *Cutibacterium acnes* proliferation. *C. acnes* produces lipases that hydrolyze triglycerides in sebum into free fatty acids, which exert a pro-inflammatory effect on keratinocytes and activate the immune response [12].

Beyond direct lipid metabolism, *C. acnes* also triggers innate immune activation, promoting the secretion of pro-inflammatory cytokines such as interleukin-1 (IL-1), interleukin-8 (IL-8), and tumor necrosis factor-alpha (TNF-α). The recruitment of immune cells - including neutrophils, macrophages, and lymphocytes - into the affected follicular unit further amplifies local inflammation. This process ultimately weakens the follicular wall, leading to rupture and extrusion of its contents into the surrounding dermis. The resultant inflammatory cascade contributes to the formation of nodules and cysts, which are frequently associated with post-inflammatory scarring [32]. Acne inflammation can be exacerbated by both endogenous and exogenous factors [14]. Endogenous contributors include hormonal fluctuations, particularly elevated androgen levels, which stimulate sebaceous gland hypertrophy and increase sebum production. Exogenous factors, such as inadequate skincare, the use of comedogenic cosmetics, mechanical irritation, and environmental pollutants, may further exacerbate inflammatory processes [4].

A thorough understanding of these pathogenic mechanisms is essential for selecting an appropriate and effective therapeutic strategy. Retinoids, derivatives of vitamin A, are among the few pharmacological agents capable of targeting multiple pathways in acne pathogenesis [9]. These compounds modulate epidermal turnover, normalize keratinocyte differentiation, and reduce hyperkeratinization, thereby preventing microcomedone formation. Additionally, retinoids interact with nuclear receptors, including retinoic acid receptors (RARs) and retinoid X receptors (RXRs), altering gene expression and counteracting follicular occlusion. Moreover, retinoids exhibit potent anti-inflammatory properties, making them effective in treating inflammatory acne lesions. They also modulate sebum production, reducing its secretion and preventing follicular obstruction [24].

First-line medications for the treatment of acne include retinoids (e.g., tretinoin, adapalene), as well as benzoyl peroxide and azelaic acid, which are used as topical therapy. In more severe cases, systemic agents such as oral antibiotics, hormonal therapy, and isotretinoin are prescribed in combination with topical treatment [13]. The U.S. Food and Drug Administration (FDA) has approved isotretinoin for the treatment of moderate to severe acne vulgaris that is resistant to other therapeutic options [26].

**Objective of the study:** to evaluate the clinical efficacy of acnekutan in the treatment of patients with severe acne.

**Materials and Methods:**

A retrospective case review was conducted using a patient's medical records from the dermatovenerology department of City Hospital No. 2, which is part of the Abai region's Health Department. From 2024 to 2025, the patient's condition was tracked by the comprehensive medical information system (CMIS). The diagnostic and therapeutic interventions followed the clinical recommendations approved by the Republic of Kazakhstan's Ministry of Health (Order No. 24, dated June 29, 2017). Both the clinic administration and the patient provided signed informed consent to publish treatment outcomes.

**Case description.**

Patient A., 18 years old, presented with complaints of persistent eruptions on the face, chest, and back, associated with tenderness, inflammation, and residual scarring and hyperpigmentation. The patient reported excessive skin oiliness, occasional pruritus, and psychological discomfort.

**Medical history.** The initial onset of acne occurred at the age of 14, characterized by moderate inflammatory lesions. By the age of 16, the condition had worsened, with the development of deep, painful nodules and cysts prone to suppuration and scarring. Previous treatments included topical agents (benzoyl peroxide, azelaic acid, and antibiotics) and systemic therapy (doxycycline), but these provided limited efficacy.

**Life history.** The patient was born at term and experienced normal growth and development. There is no history of chronic diseases or severe infections. The allergic history is unremarkable. The patient's diet is irregular, with a preference for fast food. No harmful habits were reported.

**Physical examination.**

General condition satisfactory, height 176 cm, weight 71 kg (normosthenic body type). Lymph nodes not enlarged. Respiratory system vesicular breath sounds, no rales. Cardiovascular system heart sounds muffled but rhythmic. Abdomen soft, non-tender. Bowel and urinary function unremarkable. Edema absent.

**Status localis:**

The skin of the face, upper back, and chest exhibited erythema with pronounced seborrhea. Numerous inflammatory lesions were observed, including nodules, cystic formations (up to 1 cm), papules, and pustules. Post-inflammatory hyperpigmentation and atrophic scars were noted on the cheeks and forehead. Open and closed comedones were present, along with signs of post-inflammatory skin thickening in affected areas.

**Laboratory findings.**

Complete blood count (05.02.2024): hemoglobin: 142 g/L, erythrocytes $4.5\times10^{12}$/L, leukocytes $5.1\times10^{9}$/L, lymphocytes 20%, monocytes 4%, eosinophils 3%, band neutrophils 3%, segmented neutrophils 72%, ESR 10 mm/h. Conclusion: Mild signs of inflammation. Blood test for syphilis (RW, 05.02.2024) negative. Urinalysis (05.02.2024): color straw yellow, pH acidic, specific gravity 1014, transparency, protein negative, glucose negative, epithelial cells 1–2 per field of view, leukocytes negative, bacteria negative. Conclusion: no pathology. Biochemical blood analysis (05.02.2024): total protein 87 g/L, urea 8.6 mmol/L, creatinine 84 μmol/L, bilirubin 14.80 μmol/L, cholesterol 4.13 mmol/L, glucose 4.3 mmol/L, AST 18.10 U/L, ALT 14.30 U/L, Conclusion: no pathology. Hormonal panel (12.02.2024): (TSH, Free T4, Testosterone, DHEA-S) within normal limits. Microbiological examination for demodicosis and fungal infection: negative.

**Clinical Diagnosis:** Severe Acne. Post-acne (atrophic scars, hyperpigmentation).

**Treatment Plan and Management:** Systemic therapy: isotretinoin (acnekutan) initiated at 0.5 mg/kg/day, with a gradual increase to 1 mg/kg/day. The total treatment duration is planned for 5–6 months, with mandatory monitoring of liver function and lipid levels every four weeks. Adjunctive skin care: Hydrating skincare with hypoallergenic creams to restore the hydrolipidic barrier. Use of broad-spectrum sunscreen (SPF 50+). Avoidance of aggressive cosmetic procedures (chemical peels, mechanical extractions, laser treatments). Dietary modifications: Reduction of fatty and spicy foods. Increased intake of protein and vegetables.

**Follow-up visits:** monthly assessments to evaluate treatment efficacy and adjust the dosage if necessary. Treatment outcomes are presented in Figure 1.

**Discussion**.

Isotretinoin is one of the most effective drugs for the treatment of severe acne, as confirmed by numerous clinical studies [7]. The results of our study demonstrated the high efficacy of isotretinoin in a patient with severe acne. The patient exhibited a significant reduction in inflammatory lesions, decreased sebum production, and an overall improvement in skin condition. These findings are consistent with the study by Layton et al. (2021), in which 80% of patients receiving isotretinoin at a dose of 0.5–1 mg/kg/day for 20–24 weeks achieved significant clinical improvement [20]. Furthermore, *Zaenglein et al.* (2018) reported that isotretinoin outperforms conventional treatment regimens, including antibiotics and topical retinoids, both in terms of efficacy and remission duration [31]. Similar conclusions were drawn in a meta-analysis by Huang et al. (2020), which reported a significant reduction in acne recurrence following isotretinoin treatment compared to antibiotic therapy [15]. Major clinical studies on the use of retinoids in acne therapy are summarized in Table 1.

Despite its high efficacy, isotretinoin therapy is associated with several adverse effects, including skin and mucosal dryness, dyspeptic disorders, and potential elevations in liver enzyme and blood lipid levels [27]. In our study, the patient experienced adverse effects such as skin dryness and transient elevation of transaminase levels, which aligns with the findings of Kaur et al. (2019), where similar side effects were observed in 70–80% of patients [17].

Isotretinoin is highly teratogenic, making its use strictly contraindicated during pregnancy. It is essential to thoroughly inform patients about the associated risks and the necessity of reliable contraception during treatment and for at least one month after its completion [1].

Another important aspect is the risk of recurrence after treatment discontinuation. In a study by Dréno et al. (2019), 20% of patients experienced a relapse within the first year after isotretinoin withdrawal, highlighting the need for individualized dosage selection and treatment duration [10].

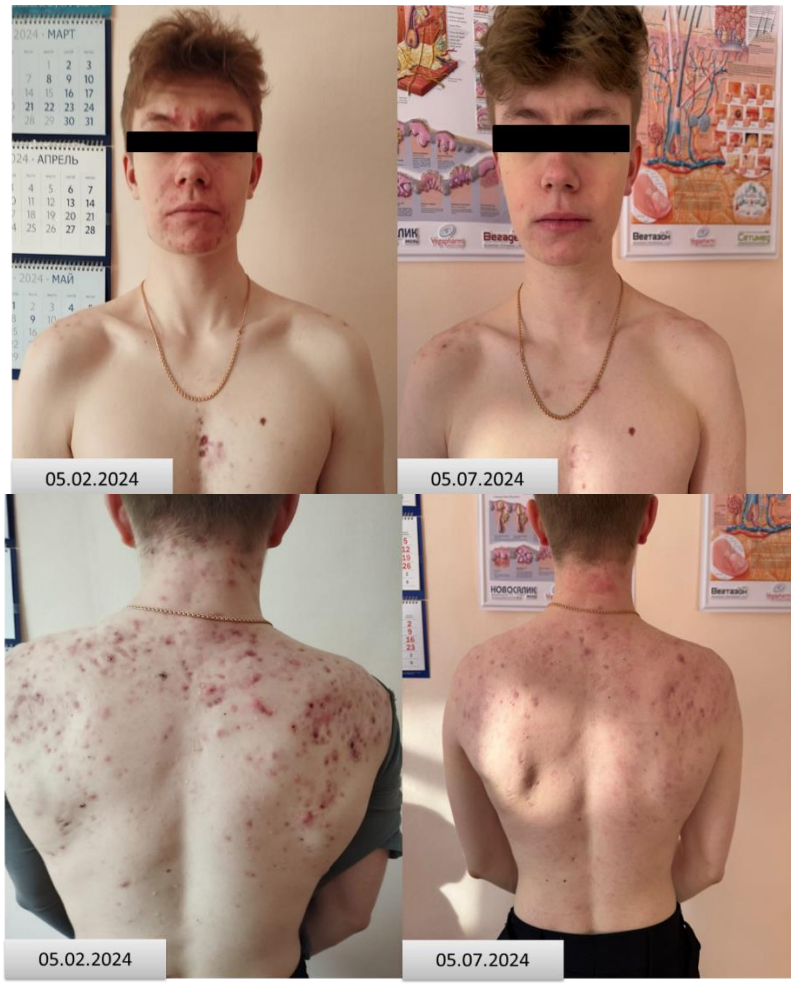


**Figure 1. Patient status localis Before and After treatment.**

*Table 1.* **The key studies of the last decade highlighting the efficacy of retinoids in acne treatment**

| Authors (Year of publication) | Publication Type | Retinoid type | Acne Type | Significance |
|---|---|---|---|---|
| Tan J. et al. (2016) [29] | Systematic Review | Oral | Severe inflammatory acne | Widely regarded as increasing remission potential |
| Zaenglein A.L. et al. (2016) [31] | Clinical guideline | Topical | Mild acne | A topical retinoid alone or in combination with antibiotic and/or BPO* is first-line therapy |
| Leyden J. et al. (2017) [22] | Review | Topical | Noninflammatory and inflammatory acne | Topical retinoids should be considered the foundation of acne therapy |
| Thiboutot D.M.et al. (2018) [30] | Clinical recommendations | Topical | Inflammatory and/or comedonal acne | A topical retinoid plus BPO* is first-line therapy |
| Kolli S.S. et al. (2019) [18] | Systematic review | Topical | Acne vulgaris | Should be used in combination with BPO* to optimize results in patients |
| Leung A.K. et al. (2021) [21] | Review | Topical/Systemic | - Mild-to-moderate acne vulgaris<br>- Moderate-to-severe acne | - Topical retinoids are the drugs of choice<br>- Systemic retinoids for refractory acne to topical therapies |
| Latter G. et al. (2021) [19] | Review | Topical/Systemic | - Mild-to-moderate acne vulgaris<br>- Severe acne | - Topical retinoid as a first-line treatment<br>- Oral retinoid for severe cystic acne |
| Eichenfield D.Z. et al. (2021) [11] | Review | Topical/Systemic | - Mild-to-moderate acne vulgaris<br>- Severe acne | - Topical retinoids are first-line therapies<br>- Systemic retinoids for severe cases |
| Mavranezouli I. et al. (2022) [23] | Systematic review and network meta-analysis | Systemic | Moderate-to-severe acne | Oral pharmacological – isotretinoin of total cumulative dose ≥ 120 mg kg−1 per single course |
| Huang C.Y. et al. (2023) [16] | Network Meta-Analysis | Systemic | Acne vulgaris | Oral isotretinoin is more effective than triple therapies containing a topical retinoid, BPO*, and an antibiotic |

***BPO – benzoyl peroxide**

**Conclusion.**

Thus, isotretinoin remains the treatment of choice for severe acne, providing high clinical efficacy and prolonged remission. However, the need for side effect monitoring and individualized dosing underscores the importance of a comprehensive approach to patient management. Future research directions include optimizing dosing regimens, evaluating combination therapies, and investigating the molecular mechanisms underlying treatment resistance.

***Conflict of Interest.*** *The authors declare that they have no conflict of interest.*

***Contribution of authors.*** *All authors were equally involved in the writing of this article.*

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