# GEORGIAN MEDICAL MEWS

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# ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии საქართველოს სამედიცინო სიახლენი

# **GEORGIAN MEDICAL NEWS**

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

**GMN:** Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

# WEBSITE

www.geomednews.com

# К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

- 1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра. Используемый компьютерный шрифт для текста на русском и английском языках Times New Roman (Кириллица), для текста на грузинском языке следует использовать AcadNusx. Размер шрифта 12. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.
- 2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.
- 3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

- 4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).
- 5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи. Таблицы и графики должны быть озаглавлены.
- 6. Фотографии должны быть контрастными, фотокопии с рентгенограмм в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста в tiff формате.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

- 7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.
- 8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform\_requirements.html В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.
- 9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.
- 10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.
- 11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.
- 12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

# REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

- 1. Articles must be provided with a double copy, in English or Russian languages and typed or computer-printed on a single side of standard typing paper, with the left margin of 3 centimeters width, and 1.5 spacing between the lines, typeface Times New Roman (Cyrillic), print size 12 (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.
- 2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.
- 3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

- 4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.
- 5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles. Tables and graphs must be headed.
- 6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

- 7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.
- 8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform\_requirements.html http://www.icmje.org/urm\_full.pdf
- In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).
- 9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.
- 10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.
- 11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.
- 12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

## ᲐᲕᲢᲝᲠᲗᲐ ᲡᲐᲧᲣᲠᲐᲓᲦᲔᲑᲝᲓ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

- 1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში Times New Roman (Кириллица), ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ AcadNusx. შრიფტის ზომა 12. სტატიას თან უნდა ახლდეს CD სტატიით.
- 2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ,რუსულ და ქართულ ენებზე) ჩათვლით.
- 3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).
- 4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).
- 5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.
- 6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით tiff ფორმატში. მიკროფოტო-სურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სუ-რათის ზედა და ქვედა ნაწილები.
- 7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა უცხოური ტრანსკრიპციით.
- 8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.
- 9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.
- 10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.
- 11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.
- 12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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# EFFECTIVENESS AND TOLERABILITY OF APREMILAST IN TREATMENT OF A SAMPLE OF PATIENTS WITH PSORIASIS

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# Abstract.

**Aim**: Current study was aimed to appraise the effectiveness and tolerability of apremilast in psoriasis patients at AL-Diwaniyah province, Iraq.

Materials and Methods: This prospective cross-sectional study conducted at Dermatology Unit/ AL-Diwaniyah Teaching Hospital/ Iraq, during the period from January to October 2023. A total of 125 patients, 90 males and 35 females, were enrolled in this study. Patients who were eligible were treated for 6 months using apremilast at a dose of 30 mg/day. Psoriasis Area and Severity Index scoring system was used for assessment of patients' response to treatment. Data were analyzed using the Statistical Package for Social Sciences (version 26).

**Results:** Data from current study revealed that there was a significant reduction of mean PASI score from  $20.37 \pm 6.25$  at baseline to  $3.72 \pm 2.09$  after 6 months of treatment (p< 0.001).

**Conclusion:** Apremilast is effective in reducing PASI mean score with negligible adverse effects. However, multi-center studies are needed to establish its efficacy and safety in Iraqi patients with psoriasis.

**Key words.** Apremilast, psoriasis, psoriasis area and severity index, phosphodiesterase inhibitor, tumor necrosis factor alpha.

# Introduction.

Psoriasis is a widespread persistent inflammatory skin condition that mostly affects adults between the 2<sup>nd</sup> and 3<sup>rd</sup> decades of life although it may appear earlier. Moreover, it is characterized by thickened skin patches covered by silvery scales and is associated, in approximately 30% of patients, with arthropathy [1,2]. Even in patients with minimal skin involvement, the disease significantly lowers the quality of life of the affected individuals. The latter may be disproportionately affected by specific psoriasis area, such as the scalp, nails, palms and/or soles, and genital areas, where the disease manifests in highly visible or sensitive areas [3].

Psoriasis is a genetically predisposed skin condition that may develop unexpectedly or under the influence of a spectrum of predisposing factors (drugs, physical trauma, sunlight, bacterial infection, psychological stress) that stimulate the T lymphocytes and dendritic cells in the skin of genetically susceptible individuals. These activated immune cells produce inflammatory mediators that promote the proliferation of epithelial and endothelial cells in the skin to yield the pathological and clinical features of psoriasis [1,4,5].

Psoriasis is considered an autoimmune disease mediated by T-lymphocytes [4]. The latter, particularly CD8+ cells, infiltrate, in large numbers, through all the layers of epidermis [5]. In addition, other immune cells such as the dendritic cells also present in the epidermis, especially in its lower layers, and Langerhans cells are no longer showing a uniform distribution throughout the epidermis, instead of that, they tend to be more concentrated into the spinous layer of the epidermis [6]. Moreover, the stratum corneum is infiltrated by polymorph nuclear leukocytes.

The psychosocial impacts of psoriasis on patient's quality of life are comparable to those caused by cardiovascular or endocrine diseases such that patients with psoriasis have diminished physical and intellectual abilities, inefficient job performance; they encounter sexual problems and have impaired social communications [1,2,3].

Although the distinctive clinical presentation of psoriatic lesions is that of well-defined erythematous silver-scaly plaques with symmetric distribution, psoriasis shows variable degrees of severity, changeable course of clinical presentation and affects different body sites [7,8]. The latter may greatly influence the clinical presentation of psoriasis, for example, flexural psoriasis is characterized by redness and maceration, but scales are usually absent. Another example is that of nail involvement which is characterized by pitting, onycholysis, subungual hyperkeratosis and salmon patches [9-11].

On the other hand, it is essential to evaluate the effect of treatment on disease state (mild, moderate or severe disease) and one of the popular and objective instruments for this purpose, is the Psoriasis Area and Severity Index (PASI, 12). The latter's "score varies from 0 to 72, yet higher scores indicate severer conditions" [12].

Despite its pros and cons, "both the European Agency for the Evaluation of Medical Products and the Food and Drug Administration" consider PASI as valid and reliable instrument for evaluation of disease severity in psoriasis [13].

Traditionally, different categories of drugs (topical and systemic) have been used for treatment of psoriasis, yet some of them might be cost-ineffective and/ or associated with serious adverse effects [6,7].

However, a novel class of drugs known as small molecules which have a molecular weight of < 1 kD and work by influencing proinflammatory cytokines are becoming more and more popular as therapeutic options for inflammatory dermatosis apart from psoriasis because they are simple to use, have a good safety profile, and can be administered topically or orally. Among these, there is a growing interest in using apremilast due to its efficacy in treatment of inflammatory skin disorders [14].

The phosphodiesterase 4 (PDE4) inhibitor apremilast acts inside the cell by binding to the active site of PDE4 enzyme and inhibiting its activity. As a consequence, it raises the level of cAMP inside cells, which turns on PKA and phosphorylates the transcription factor Cyclic AMP-Response Element Binding

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protein (CREB). These changes result in an up-regulation of the anti-inflammatory cytokine (IL-10) and, through inhibiting the activity of NF-κB transcriptional factor, a down-regulation of inflammatory cytokines like TNF-α, IFN-γ, IL 23, and IL-17 [14]. Moreover, apremilast has a significant bioavailability (73%) following oral administration which, and the resultant efficacy, are not affected by food intake, however, hepatic-enzymes inducers (rifampicin and barbiturates) adversely affect the latter two pharmacological parameters. Furthermore, dose down-regulation may be needed in case of severe renal impairment.

Recently, the Iraqi Ministry of Health approved the use of apremilast in Iraqi hospitals. However, there are no published data concerning the efficacy and safety of apremilast in treatment of Iraqi patients with psoriasis.

Taken together, current study was aimed to appraise the effectiveness and tolerability of apremilast in psoriasis patients at AL-Diwaniyah province, Iraq.

# Patients and Methods.

A prospective cross-sectional study, that involved 125 patients (90 males and 35 females), was conducted at Dermatology Unit/ AL-Diwaniyah Teaching Hospital/ Iraq, during the period from January 2023 to October 2023. All participating patients provided written consents, and they were given apremilast at a dose of 30mg/day and continued for 6 months. Moreover, patients who included in the study were those:

- Adult patients (age  $\geq$  18 years).
- Patients were complaining of chronic plaque psoriasis.
- Patients with history of unsatisfactory response to previous conventional psoriasis medications such as topical steroids (with or without phototherapy) and methotrexate.

However, patients who excluded from the study were those:

- Pregnant or lactating women.
- Having other forms of psoriasis other than chronic plaque type.
- Patients who refused to be enrolled in the study.

As one of the researchers is dermatologist, the latter evaluated all participating patients, then data regarding their age, sex, body mass index, duration of disease, prior medications and therapeutic interventions as well as clinical characteristics were collected by both researchers and these data were employed for the calculation of Psoriasis Area and Severity Index (PASI; 14) at baseline and 6 months later. "In calculating the PASI, severity is determined by dividing the body into four regions: head (h), upper extremities (u), trunk (t) and lower extremities [1], that account for 10%, 20%, 30%, and 40% of the total body surface area, respectively. Each of these areas is assessed separately for erythema, induration, and scaling, which is rated on a scale of 0 (none) to 4 (very severe)" [14]. According to PASI scores, "extent of psoriatic involvement is graded as follows: 0 = no involvement, 1 = 1% to 9%, 2 = 10% to 29%, 3 = 30% to 49%, 4 = 50% to 69%, 5 = 70% to 89%, 6 = 90% to 100%.

The following formula is used to calculate the PASI score: PASI = 0.1 (Eh + lh + Sh) Ah + 0.2 (Eu + lu + Su) Au + 0.3 (Et + lt + St) At + 0.4 (El + ll + Sl) Al

Where E = erythema, I = induration, S = scaling, A = area, h = head score, u = upper extremities, t = trunk score, and l = lower extremities score" [14].

# Statistical analysis.

The Statistical Package for Social Sciences software (SPSS, version 26) was used for data analysis. Descriptive statistics were used for presentation of data. Continuous variables presented as mean $\pm$ standard deviation (SD), while categorical variables presented as number and percentage. The paired *t*-test was used to examine the difference between two means within the means of the analysis variables between two points in time within the same group. The level of significance was considered at P< 0.05.

# Results.

General characteristics of patients recruited in current study were presented in Table 1. The age of participants ranged from 18-55 years. In addition, there were 90(72%) male patients and 35(28%) females. Also, the BMI of participants ranged from 21.37 to 32.83 kg/m². The recruited patients had psoriasis for 3-11 years.

**Table 1.** General characteristics of enrolled patients with chronic plaque psoriasis.

Characteristic	Result
Age (year)	
Mean±SD	35.39±7.92
Range	18-55
Sex	
Male, number (%)	90 (72.0 %)
Female, number (%)	35 (28.0 %)
Body Mass Index (kg/m²)	
$Mean \pm SD$	27.57±8.07
Range	21.37-32.83
Disease duration (year)	
Mean ±SD	6.29±4.93
Range	3-11

SD: Standard Deviation

On the other hand, the mean Psoriasis Area and Severity Index (PASI) scores before and after treatment with apremilast were shown in Table 2. Data revealed a statistically significant reduction (P < 0.001) in the mean PASI score from  $20.37\pm6.25$  (at baseline) to  $3.72\pm2.09$  (after 6 months of treatment).

**Table 2.** Mean PASI score prior to, and following, apremilast treatment.

Characteristic	Baseline	6 months after treatment	P
PASI			
Mean ±SD	20.37±6.25	3.72±2.09	< 0.001
Range	6.8 -52.8	0-20	
DACI. Drawing Anna and Savanity Indox CD: Standard Daviation			

**PASI:** Psoriasis Area and Severity Index. **SD:** Standard Deviation.

### Discussion.

In 2015, the European Medicines Agency approved the isoform 4 of phosphodiesterase inhibitors "apremilast" for management of psoriatic patients with significant disease severity [15]. It exhibited its effectiveness and tolerability in those who had been treated with "systemic therapy" in phase 3 as well as 4 placebocontrolled clinical studies [15,16], in patients who had never received biologic therapy but had moderate-to-severe psoriasis [17] and in patients with moderate psoriasis who had never

received both systemic and biologic therapy [18]. Apremilast has just lately been available in our community, and there are conflicting reports regarding its effectiveness and safety in treating Iraqi patients with persistent psoriasis.

In the present study, the efficacy of apremilast was obvious since it was able to reduce the mean PASI score form 20.37±6.25 to 3.72±2.09. findings from current study were in agreement with those from previous studies. For example, a European study involved 50 patients with chronic plaque psoriasis who were treated with apremilast reported that the mean PASI score was reduced from 6.2±8.7 at treatment initiation to 3.1±5.2 after 6 months of treatment [3]. In addition, the APPRECIATE cross sectional, multinational, retrospective study [19] reported the similar finding with respect to efficacy of Apremilast. In the later APPRECIATE study, 480 patients with chronic plaque psoriasis were enrolled and their responses to Apremilast were collected form hospital records. The study shown that PASI score was reduced from 13.1 to 4.6.

The work of Shah et al. [20] has paved the way for further research regarding effectiveness and tolerability of Apremilast alone in managing psoriatic disease of significant severity in India as they showed that this approach resulted in significant improvement of PASI score in 80 Indian patients treated for 24 weeks. Other studies conducted in other region of the World also shed light on the effectiveness of apremilast in treatment of psoriasis [18,19,21-24].

With respect to adverse effects associated with the use of apremilast, those usually reported include nausea, vomiting, diarrhoea, dyspepsia and/ or abdominal. However, less frequently reported adverse effects include insomnia, headache and/ or mode disturbances [25].

Current study reported no serious adverse effects with the exception of nausea and vomiting by minority of participating patients. Moreover, none of them withdrew from the study due to adverse effects of the drug. These findings agreed with those reported by previous studies [17,26,27].

One important limitation of current study is that it is a single center study, and this sheds light on the need for further multi-center studies in the future to make clear the safety and efficacy of this drug in psoriasis patients in Iraq. In addition, the assessment of effectiveness by long-term follow-up might be another limitation of this study due to poor patients' compliance.

# Conclusion.

Apremilast is effective in reducing PASI mean score with negligible adverse effects. However, multi-center studies are needed to establish its efficacy and safety in Iraqi patients with psoriasis.

**Conflict of interest:** None.

Funding of study: Self-funded Study.

**Ethical approval:** It is obtained from Research Ethics Committee at the College of Medicine/ University of AL-Qadisiyah, AL-Diwaniyah Province, Iraq.

# REFERENCES

1. Raharja A, Mahil SK, Barker JN. Psoriasis: a brief overview. Clin Med (Lond). 2021;21:170-173.

- 2. Kimmel GW, Lebwohl M. Psoriasis: Overview and Diagnosis. Evidence-Based Psoriasis. 2018;1-16.
- 3. Cetkovská P, Dediol I, Šola M, et al. Apremilast Use in Severe Psoriasis: Real-World Data from Central and Eastern Europe. Adv Ther. 2023;40:1787-1802.
- 4. Dand N, Mahil SK, Capon F, et al. Psoriasis and genetics. Acta Derm Venereol. 2020;100:adv00030.
- 5. Budu-Aggrey A, Brumpton B, Tyrrell J, et al. Evidence of a causal relationship between body mass index and psoriasis: A mendelian randomization study. PLoS Med. 2019;16:e1002739.
- 6. Feldman SR, Goffe B, Rice G, et al. The challenge of managing psoriasis: unmet medical needs and stakeholder perspectives. Am Health Drug Benefits. 2016;9:504-513.
- 7. Lebwohl MG, Bachelez H, Barker J, et al. Patient perspectives in the management of psoriasis: results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis Survey. J Am Acad Dermatol. 2014;70:871-881.
- 8. Rachakonda TD, Schupp CW, Armstrong AW. Psoriasis prevalence among adults in the United States. J Am Acad Dermatol. 2014;70:512-516.
- 9. Parisi R, Symmons DP, Griffiths CE, et al. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Invest Dermatol. 2013;133:377-385.
- 10. Parisi R, Iskandar IYK, Kontopantelis E, et al. National, regional, and worldwide epidemiology of psoriasis: Systematic analysis and modelling study. BMJ. 2020;369:m1590.
- 11. Alobaidi A.H, Alsamarai A.M, Salih M.A. Psoriasis Beyond Local Skin Disease. Medico-legal Update, January-March. 2021;21:1409-1417.
- 12. Fredriksson T, Pettersson U. Severe psoriasis Oral therapy with a new retinoid. Dermatologica. 1978;157:238-244.
- 13. Schmitt J, Woze Gl. The Psoriasis Area and Severity Index Is the Adequate Criterion to Define Severity in Chronic Plaque-Type Psoriasis. Dermatology. 2005;210:194-199.
- 14. Papp K, Reich K, Leonardi CL, et al. Apremilast, an oral phosphodiesterase 4 (PDE4) inhibitor, in patients with moderate to severe plaque psoriasis: Results of a phase III, randomized, controlled trial (Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis [ESTEEM] 1). J Am Acad Dermatol. 2015;73:37-49.
- 15. Paul C, Cather J, Gooderham M, et al. Efficacy and safety of apremilast, an oral phosphodiesterase 4 inhibitor, in patients with moderate-to-severe plaque psoriasis over 52 weeks: a phase III, randomized controlled trial (ESTEEM 2). Br J Dermatol. 2015;173:1387-1399.
- 16. Reich K, Gooderham M, Green L, et al. The efficacy and safety of apremilast, etanercept and placebo in patients with moderate-to-severe plaque psoriasis: 52-week results from a phase IIIb, randomized, placebo-controlled trial (LIBERATE). J Eur Acad Dermatol Venereol. 2017;31:507-517.
- 17. Stein Gold L, Bagel J, Lebwohl M, et al. Efficacy and Safety of Apremilast in Systemic- and Biologic-Naive Patients With Moderate Plaque Psoriasis: 52-Week Results of UNVEIL. J Drugs Dermatol. 2018;17:221-228.
- 18. Augustin M, Kleyn CE, Conrad C, et al. Characteristics and outcomes of patients treated with apremilast in the real world: results from the APPRECIATE study. J Eur Acad Dermatol Venereol. 2021;35:123-134.

- 19. Shah BJ, Mistry D, Chaudhary N, et al. Real-world Efficacy and Safety of Apremilast Monotherapy in the Management of Moderate-to-severe Psoriasis. Indian Dermatol Online J. 2020;11:51-57.
- 20. Ighani A, Georgakopoulos JR, Zhou LL, et al. Effectiveness and safety of apremilast monotherapy for moderate to severe psoriasis: Retrospective study. J Cutan Med Surg. 2018;22:290-296.
- 21. Papadavid E, Rompoti N, Theodoropoulos K, et al. Real-world data on the effectiveness and safety of apremilast in patients with moderate-to-severe plaque psoriasis. J Eur Acad Dermatol Venereol. 2018;32:1173-1179.
- 22. Vujic I, Herman R, Sanlorenzo M, et al. Apremilast in psoriasis A prospective real-world study. J Eur Acad Dermatol Venereol. 2017;32:254-259.
- 23. Wong TH, Sinclair S, Smith B, et al. Real-world, single-centre experience of apremilast for the treatment of moderate to severe psoriasis. Clin Exp Dermatol. 2017;42:674-685.

- 24. Mayba JN, Gooderham MJ. Real-world experience with apremilast in treating psoriasis. J Cutan Med Surg. 2017;21:145-151.
- 25. Edwards CJ, Blanco FJ, Crowley J, et al. Apremilast, an oral phosphodiesterase 4 inhibitor, in patients with psoriatic arthritis and current skin involvement: a phase III, randomised, controlled trial (PALACE 3). Annals of the Rheumatic Diseases. 2016;75:1065-1073.
- 26. Ohata C, Ohyama B, Kuwahara F, et al. Real-world data on the effectiveness and safety of apremilast in Japanese patients with plaque psoriasis. J Dermatolog Treat. 2018;8:1-4.
- 27. Bai W, Sun X, Qiu B, et al. Pharmacokinetics and Bioequivalence of Apremilast Tablets in Chinese Healthy Subjects Under Fasting and Postprandial States. Drug Des Devel Ther. 2024;18:2273-2285.