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(54) Title: METHOD FOR PROVIDING EARLY ONSET OF ACTION IN THE TREATMENT OF ROSACEA

(57) Abstract: A regimen is described for providing early onset of action in the therapeutic treatment of rosacea including topically applying a pharmaceutical composition to the skin of a subject in need of said treatment. The pharmaceutical composition includes about 1% to about 10% benzoyl peroxide as the only active ingredient, and a pharmaceutically acceptable carrier or excipient. The pharmaceutical composition is applied once daily for a period of at least about 2, 4, 8 or 12 weeks. Based on early onset of action, a primary measure of success is at least about 9%, primary measure of success being defined as a 2-grade improvement in IGA of clear or almost clear; and a secondary measure of success is at least about 40%, secondary measure of success being defined as mean inflammatory lesion count percent reduction from baseline, after at least about 2 weeks of treatment.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB 20/00119

A. CLASSIFICATION OF SUBJECT MATTER

IPC - C09K 3/00 (2020.01)

CPC - A61K 31/327, A61K 9/0014, A61P 17/10, Y10S 514/857, A61K 9/06, A61Q 19/00, A61P 17/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2014/0147396 A1 (SOL-GEL TECHNOLOGIES LTD.) 29 May 2014 (29.05.2014); the entire document, and more specifically: para [0005]-[0009], [0016]-[0017], [0019], [0022], [0024]-[0025], [0030]-[0032], [0038], [0040]-[0041], [0043]-[0045], [0051], [0059]-[0061], [0067]-[0070], [0185]-[0195], [0204]; abstract; claims 1, 3, 5 and 22; examples 3 and 5-7; tables 2 and 5; figures 1 and 3	1-4, 46-48 and 57-59
A	US 2014/0121188 A1 (FOAMIX LTD.) 1 May 2014 (01.05.2014); the entire document	1-4, 46-48 and 57-59
A	US 9,107,844 B2 (CLARK et al.) 18 August 2015 (18.08.2015); the entire document	1-4, 46-48 and 57-59
A	US 2017/0216282 A1 (GALDERMA LABORATORIES, L.P.) 3 August 2017 (03.08.2017); the entire document	1-4, 46-48 and 57-59
A	US 2004/0171561 A1 (POPP) 2 September 2004 (02.09.2004); the entire document	1-4, 46-48 and 57-59
E/A	US 2020/0261397 A1 (SOL-GEL TECHNOLOGIES LTD.) 20 August 2020 (20.08.2020); the entire document	1-4, 46-48 and 57-59

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"D" document cited by the applicant in the international application

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB 20/00119

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 5-15, 20-32, 36-45, 49-56 and 60-67
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I: Claims 1-4, 46-48 and 57-59, directed to a regimen for providing early onset of action in the therapeutic treatment of rosacea, where the 2-grade improvement in Investigator Global Assessment (IGA) of clear or almost clear is used for a primary measure of success.

Group II: Claims 16-19 and 33-35, directed to a regimen for providing early onset of action in the therapeutic treatment of rosacea, using reduction of lesion count for evaluation.

****please see the continuation at the end of this form****

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-4, 46-48 and 57-59

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

****continuation of Box III (Lack of Unity) ****

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features:

Group I requires a primary measure of success, wherein the primary measure of success is defined as a 2-grade improvement in Investigator Global Assessment (IGA) of clear or almost clear, not required by group II.

Group II requires using reduction of lesion count for evaluation, not required by group I.

Common Technical Features:

Groups I and II share the technical feature of a regimen for providing early onset of action in the therapeutic treatment of rosacea, the regimen comprising topically applying to the skin of a subject in need of said treatment a pharmaceutical composition, the pharmaceutical composition comprising about 1% w/w to about 10% w/w benzoyl peroxide as an active ingredient, and a pharmaceutically acceptable carrier or excipient, wherein the benzoyl peroxide is the only active ingredient in said pharmaceutical composition; wherein said pharmaceutical composition is applied once daily for a period of at least about 2, 4, 8 or 12 weeks; lesion count reduction.

However, these shared technical features do not represent a contribution over prior art, because the shared technical feature is being obvious over US 2014/0147396 A1 to Sol-Gel Technologies Ltd. (hereinafter Sol-Gel). Sol-Gel teaches a regimen for providing therapeutic treatment of rosacea (abstract; para [0185]; example 7; The present invention relates to pharmaceutical compositions for topical use (including also dermatological compositions), for treating skin conditions and afflictions, such as rosacea and symptoms and conditions associated there from. Further, a multi-center, double-blind, randomized, vehicle-controlled, dose-range study was performed. Study duration was 12 weeks on mild to severe facial rosacea patients using encapsulated benzoyl peroxide gel, 1% (as described in Example 6) and 5% (as described in Example 3), and vehicle gel (as described in Example 5) once daily.), the regimen comprising topically applying to the skin of a subject in need of said treatment a pharmaceutical composition (claims 1 and 22; para [0017], [0019]; A method for the topical treatment of rosacea, comprising, topically administering to a patient in need an effective amount of the composition. Accordingly, the present invention provides a composition comprising benzoyl peroxide for topical use in the treatment of rosacea. The term topical use is meant to encompass the topical administration of a composition of the invention by formulating said composition in any way known in the art, or in formulations disclosed herein, which are compatible with the skin, mucous membranes and/or the integuments.), the pharmaceutical composition comprising about 1% w/w to about 10% w/w benzoyl peroxide as an active ingredient (claims 1 and 22; para [0017], [0019]; A method for the topical treatment of rosacea, comprising, topically administering to a patient in need an effective amount of the composition. Accordingly, the present invention provides a composition comprising benzoyl peroxide for topical use in the treatment of rosacea. The term topical use is meant to encompass the topical administration of a composition of the invention by formulating said composition in any way known in the art, or in formulations disclosed herein, which are compatible with the skin, mucous membranes and/or the integuments.), and a pharmaceutically acceptable carrier (claim 1; para [0043], [0045], [0051]; A pharmaceutically acceptable topical vehicle, wherein said vehicle is an oil-in-water emulsion comprising a polyoxystearate, a glycerystearate and at least one fatty alcohol.), wherein the benzoyl peroxide is the only active ingredient in said pharmaceutical composition (para [0025]; claim 1; The present invention discloses pharmaceutical compositions, including dermatological compositions, comprising benzoyl peroxide as a single pharmaceutical active agent in the solid form. And, as the sole pharmaceutical active agent, benzoyl peroxide [is] in solid form.),

wherein said pharmaceutical composition is applied once daily for a period of at least about 2, 4, 8 or 12 weeks (para [0185]-[0187]; example 7; A multi-center, double-blind, randomized, vehicle-controlled, dose-range study was performed. Study duration was 12 weeks on mild to severe facial rosacea patients using encapsulated benzoyl peroxide gel, 1% (as described in Example 6) and 5% (as described in Example 3), and vehicle gel (as described in Example 5) once daily. The investigator performed the Investigator Global Assessment (IGA) and inflammatory lesion (papules and pustules) counts at Screening, Baseline, and Weeks 4, 8, and 12 (end of study).). Sol-Gel does not specifically teach that the regimen is for providing early onset of action in the therapeutic treatment of rosacea. However, it would have been obvious to one ordinary skilled in the art to provide the regimen at different stages of treatment of rosacea, with routine experimentation; such as for example: the regimen is for providing early onset of action in the therapeutic treatment of rosacea; in order to evaluate the efficiency of the treatment (para [0188]-[0192]). Further, in order to provide treatment of the disease, its symptoms and associated conditions, in a safe and effective manner, that show improved efficacy in the treatment of rosacea, that impart greater tolerance to the active principles and that do not have the side effects described in the prior art (para [0016]).

As the shared technical features were known in the art at the time of the invention, they cannot be considered common technical features that would otherwise unify the groups. Therefore, Groups I-II lack unity under PCT Rule 13.

Note: claims 5-15, 20-32, 36-45, 49-56 and 60-67 are unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).