The Controller of Patents

The Patent Office

Delhi

Date: 02nd September, 2022

Kind Attn.:

Dr Rajendra Lohiya

Ld. Asst. Controller of Patents & Designs

Dear Sir,

Re: **Pre-Grant Opposition under section 25(1) against-**

Patent Application **No. 4412/DELNP/2007** dated November 8th ,2006

(nationalization date: 08th June, 2007)

Patentee: **Novartis AG**

Opponent: **KETAKEE S. DURVE**

We submit herewith a written statement of pre-grant opposition U/S 25(1) of the Patents Act, 1970 read with Rule 55 of The Patents Rules, 2003. In-reference to this, we enclose herewith following documents:

i) Notice of Opposition on Form-7A,

ii) Representation of opposition under section 25(1) along with documents in support of written statement of representation.

iii) Power of Attorney.

Please grant a hearing in due course.

We request you to kindly take the opposition on record under intimation to us.

In accordance with the Rules, copies of the aforesaid documents are being sent to theApplicant's

Agent by post.

Yours Faithfully,

BEFORE THE CONTROLLER OF PATENTS

THE PATENT OFFICE

DELHI

PRE-GRANT OPPOSITION UNDER SECTION 25 (1) AGAINST PATENT APPLICATION No. (4412/DELNP/2007) dated November 8th, 2006

(nationalization date: June 8,2007)

Novartis AG having address at a corporation organized and existing under the laws of Switzerland, of Lichtstrasse 35, Ch4056, Basel, Switzerland

..... Applicant

And

KETAKEE S. DURVE, an Indian National having their address at C2/101, PUNYODAYA PARK, NEAR DON BOSCO SCHOOL, ADHARWADI JAIL ROAD, KALYAN WEST, 421301, MAHARASHTRA, INDIA

.....Opponent

FORM - 7A

THE PATENTS ACT, 1970 (39 OF 1970)

&

THE PATENTS RULES, 2003

NOTICE OF OPPOSITION

(See section 25 (1) and rule 55)

I, **KETAKEE S. DURVE**, an Indian National having their address at C2/101, PUNYODAYA PARK, NEAR DON BOSCO SCHOOL, ADHARWADI JAIL ROAD, KALYAN WEST, 421301, MAHARASHTRA, INDIA

hereby give notice of opposition under Section 25 (1) of the Indian Patent Act, 1970, against grant of patent in respect of patent application no. **4412/DELNP/2007** made by **Novartis AG.** and notified in the Journal on 24th August, 2007.

The impugned patent application is opposed on the following grounds:

a) **Section 25(1)(c): Prior claiming**

That the invention so far as claimed in any claim of the complete specification is clamed in a clam of a complete specification published on or after the priority date of the applicant's claim and filed in pursuance of an application for a patent India, being a claim of which the priority date is earlier than the applicant's claim.

b) **Section 25(1)(e): Obviousness/lack of inventive step**

that the invention so far as claimed in any claim of the complete specification is obvious and clearly does not involve any inventive step, having regard to the matter published as mentioned in clause (b) of Section 25(1) or having regard to what was used in India before the priority date of the applicant's claim.

c) **Section 25(1)(f) – Not an invention / Not patentable**

that the subject of any claim of the complete specification is not an invention within the meaning of this Act, or is not patentable under this Act;

d) **Section 25 (1) (h) – Breach of Section 8**

that the applicant has failed to comply with the requirements of Section 8 of the Patents Act.

Dated this 02nd day of September 2022

Name: KETAKEE S. DURVE

To

The Controller of Patents

The Patent Office,

At Delhi

BEFORE THE CONTROLLER OF PATENTS

THE PATENT OFFICE,

DELHI

IN THE MATTER of The Patents Act, 1970 as amended by The Patents (Amendment) Act 2005,

And

IN THE MATTER of The Patents Rules, 2003 (as amended till date)

And

IN THE MATTER of Indian Patent No. 4412/DELNP/2007 nationalized on June 8, 2007 from PCT Application No. PCT/US2006/043710 assigned to NOVARTIS AG., Lichtstrasse 35, CH-4056, Basel, Switzerland

..... Applicant

And

IN THE MATTER of opposition thereto U/S 25 (1) of the Patents Act, 1970 by,

KETAKEE S. DURVE, an Indian National of C2/101, PUNYODAYA PARK, NEAR DON BOSCO SCHOOL, ADHARWADI JAIL ROAD, KALYAN WEST, 421301, MAHARASHTRA, INDIA

.....Opponent

OPPOSITION UNDER U/S 25(1)

I, KETAKEE S. DURVE, an Indian National of C2/101, PUNYODAYA PARK, NEAR DON BOSCO SCHOOL, ADHARWADI JAIL ROAD, KALYAN WEST, 421301, MAHARASHTRA, INDIA (hereinafter called "Opponent") make the following representation under Section 25(1) of The Patents Act in opposing the grant of patent on the application indicated in the cause title

1. GROUNDS OF OPPOSITION

The Impugned patent application is opposed by the Opponent on the following grounds enumerated in Section 25 (1) of The Patents Act, 1970 (hereinafter referred to as the "Act"):

a. Section 25(1)(c): Prior claiming

That the invention so far as claimed in any claim of the complete specification is claimed in a claim of a complete specification published on or after priority date of the applicant's claim and filed in pursuance of an application for a patent in India, being a claim of which the priority date is earlier than that of the applicant's claim**;**

b. Section 25(1)(e): Obviousness/lack of inventive step

that the invention so far as claimed in any claim of the complete specification is obvious and clearly does not involve any inventive step, having regard to the matter published as mentioned in clause (b) of section 25(1) or having regard to what was used in India before the priority date of the applicant's claim.

c. Section 25(1)(f): Not an invention

that the subject of any claim of the complete specification is not an invention within the meaning of this Act, or is not patentable under this Act;

d. Section 25 (1) (h) – Breach of Section 8

that the applicant has failed to comply with the requirements of Section 8 of the Patents Act.

2. ANALYSIS OF SPECIFICATION OF THE IMPUGNED INVENTION

It is stated that the invention as disclosed in the impugned specification pertains to dual-acting compounds and combinations of angiotensin receptor blockers and neutral endopeptidase inhibitors (NEPi). In particular, these actives are linked via non-covalent bonding, or supramolecular complexes of the actives, also described as linked pro-drugs, such as mixed salts or co-crystals, as well as to pharmaceutical combinations containing such a dual-acting compound or combination, methods of preparing such dual-acting compounds and methods of treating a subject with such a dual-acting compound or combination.

The Opponent has learnt that the Applicant has filed an Indian National Phase Application No. 4412/DELNP/2007 (hereinafter also referred to as the "impugned application"), which is currently pending before the Patent Office. The said patent application is entitled "PHARMACEUTICAL COMBINATIONS OF AN ANGIOTENSIN RECEPTOR ANTAGONIST AND AN NEP INHIBITOR" and is drawn to a pharmaceutical formulation comprising of a dual-acting compound having a formula: [((S)-N-valeryl-N-{[2‟-(1-H-tetrazole-5-yl)-biphenyl4-yl]-methyl}-valine). [(2R,4S)-5-biphenyl-4-yl-4-(3-carboxy-propionylamino)-2- methyl-pentanoic acid ethyl ester) Na1-3.x H2O where x- 0-3, which is a combination of an angiotensin receptor antagonist valsartan and a neutral endopeptidase inhibitor (NEPi) (2R,4S)-5-biphenyl4-yl~5-(3-carboxypropionylamino)-2-methyl-pentanoic acid ethyl ester. The impugned application was filed on 8 June, 2007. It derives priority from 4 different applications being U.S. Provisional Application Nos. 60/735,093 dated November 9, 2005, 60/735,541 dated November 10, 2005, 60/789,332 dated April 4, 2006 and 60/822,086 dated August 11, 2006. The application was nationalized from PCT publication No. WO 2007056546 A1. The application originally contained a set of 29 claims which has now been amended to a set of 8 claims with the latest amendment's on its claims on 06th June,2020. It is stated that the First Examination Report (FER) was issued on January 30, 2015

3. CLAIMS OF THE IMPUGNED PATENT

The last amended set of 8 claims filed by the Applicant with its application seeking amendment as seen on the Patent Office website are the claims filed on June 6, 2020 by way of voluntary amendment in

Form 13 and reproduced below:

1. A compound comprising the Angiotensin Receptor Antagonist valsartan and the NEP Inhibitor (2R,4S)-5-biphenyl-4-yl-4-(3-carboxy-propionylamino)-2- methyl-pentanoic acid ethyl ester having the formula [((S)-N-valeryl-N-{[2'-(1 H-tetrazole-5-yl)-biphenyl-4-yl]-methyl}-valine) ((2R,4S)-5-biphenyl-4-yl-4-(3-carboxy-propionylamino)-2-methyl-pentanoic acid ethyl ester)]Na3 • x H2O, wherein x is 0 to 3.

2. The compound as claimed in claim 1, wherein x is 2.5.

3. The compound as claimed in claim 2, which is trisodium [3-((1S,3R)-1- biphenyl-4-ylmethyl-3-ethoxycarbonyl-1-butylcarbamoyl)propionate-(S)-3'- methyl-2'-(pentanoyl{2''-(tetrazol-5-ylate)biphenyl-4'-ylmethyl}amino)butyrate] Hemipentahydrate.

4. The compound as claimed in claim 1-3, wherein the compound is in crystalline form.

5. The compound as claimed in any one of claims 1 to 4 as and when used in a preparation of pharmaceutical composition or Medicament.

6. A method of preparing the compound as claimed in any of claim 1 to 4, said method comprising the steps of: (i) dissolving (S)-N-valeryl-N-{[2'-(1H-tetrazole-5-yl)-biphenyl-4-yl]- methyl}-valine or a salt thereof and (2R,4S)-5-biphenyl-4-yl-4- (3-carboxy-propionylamino)-2- methylpentanoic acid ethyl ester or a salt thereof in a suitable solvent; (ii) dissolving a basic Na compound in a suitable solvent; (iii) combining the solutions obtained in steps (i) and (ii); (iv) precipitation of the solid, and drying same to obtain the dualacting compound; or alternatively obtaining the compound by exchanging the solvent(s) employed in steps (i) and (ii) by (iva) evaporating the resulting solution to dryness; (va) re-dissolving the solid in a suitable solvent; (via) precipitation of the solid and drying same to obtain the compound.

7. The method as claimed in claim 6 wherein the suitable solvent in steps (i) and/or (iva) is acetone.

8. The method as claimed in claims 6 or 7, wherein the basic Na compound is NaOH, Na2CO3, NaHCO3, NaOMe, NaOAc or NaOCH.

4. PRIOR ART DOCUMENTS

i. D1: 1538/CHENP/2004: Indian Patent Document (US Priority: 17/01/2002) "Pharmaceutical Compositions Comprising Valsartan And Nep Inhibitors" published on 10/02/2006 [For prior claiming]

ii. D1A: PCT publication WO2003/059345 published on July 24, 2033 (corresponding to 1538/CHENP/2004: Indian Patent Document published on 10/02/2006) for other grounds.

iii. D2 (EP0498361A2): European Patent Document "Combination Of An Angiotensin II Antagonist Or Renin Inhibitor With A Neutral Endopeptidase Inhibitor" published on 12.08.92: Priority date: 06.02.91 (US)

iv. D3(EP0726072A2): European Patent Document" Composition For The Treatment Of Hypertension And Congestive Heart Failure, Containing An Angiotensin II Antagonist And An Endopeptidase Inhibitor" published on 14.08.1996

v. D4: Chinese patent document CN1443l76A, "Valsartan salts published on September 17, 2003.

vi. D5: WO2003074474- Multiple component solid phases containing at least one pharmaceutical active ingredient, published on 12th Sept 2003.

5. GROUNDS OF OPPOSITION

Ground I: Section 25(1)(c): That the invention so far as claimed in any claim of the complete specification is claimed in a claim of a complete specification published on or after priority date of the applicant's claim and filed in pursuance of an application for a patent in India, being a claim of which the priority date is earlier than that of the applicant's claim;

It is being stated that the disclosure D1 bearing Application 1538/CHENP/2004 related to "A pharmaceutical composition comprising (i) the AT 1-antagonist valsartan or a pharmaceutically acceptable salt thereof and (ii) N-(3-carboxy-1-oxopropyl)-(4S)-pphenylphenylmethyl)-4-amino-2R-methylbutanoic acid ethyl ester or N- (3-carboxy-1-oxopropyl)-(4S)-pphenylphenylmethyl)-4-amino-2Rmethylbutanoic acid or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier."

On the other hand the claims of the impugned invention pertains to "A compound comprising the Angiotensin Receptor Antagonist valsartan and the NEP Inhibitor (2R,4S)-5-biphenyl-4-yl-4-(3-carboxy-propionylamino)-2- methyl-pentanoic acid ethyl ester having the formula [((S)-N-valeryl-N-{[2'-(1 H-tetrazole-5-yl)-biphenyl-4-yl]-methyl}-valine) ((2R,4S)-5- biphenyl-4-yl-4-(3-carboxy-propionylamino)-2-methyl-pentanoic acid ethyl ester)]Na3 • x H2O, wherein x is 0 to 3."

From a comparative claim mapping of the claims of the two patent specification, it can be seen that the claims of the impugned invention are already claimed by the claims of the prior art D1 which has an earlier priority than that of the impugned application but a later publication date than the impugned application.

Furthermore, from a comparative analysis of both the claims it can be seen that both the claims disclose an antagonist in the form of valsartan in combination with an ethyl ester consisting of a carboxy propyl biphenyl methyl amino carboxylic acid comprising of 5 carbons.

All the elements of claim 1(independent claim of the impugned application is disclosed and claimed in the cited prior art D1. Further claim 4&5 of the impugned application mentions that the compound (in 1-3) exist in a crystalline form which is used in a pharmaceutical composition whereas in claim 1 of the cited prior art it states that the combination with valsartan should be a pharmaceutically acceptable salt.

In this regard it is being pointed out that as per page 15 of the complete specification of the prior art D1, it states that the active ingredient of the invention exists in the form of a hydrate or other solvents used for crystallization. Furthermore, as per page 7 para 5 and page 10 para 4 of the complete specification of the prior art, the use of sodium as preferred salts in regards to the NEPi has been clearly disclosed. It is pertinent to note that the impugned invention also discloses the combination of valsartan or with the NEPi in a sodium hydrate salt form. Furthermore, the elements of carboxyl group along with and amino group are also claimed in both the invention. It can be seen from a mere reading of claim 1 of the impugned application that it relates to a combination of an AT-antagonist valsartan in combination with a (2R,4S)-5-biphenyl-4-yl-4-(3-carboxy-propionylamino)-2- methyl-pentanoic acid ethyl ester. The claim 1 of the cited prior art D1 (1583/CHENP/2004) discloses a composition comprising an AT antagonist valsartan or a pharmaceutically acceptable salt thereof and (ii) N-(3-carboxy-1-oxopropyl)-(4S)-pphenylphenylmethyl)-4-amino-2R-methylbutanoic acid ethyl ester or N- (3-carboxy-1-oxopropyl)-(4S)-

pphenylphenylmethyl)-4-amino-2Rmethylbutanoic acid.

Moreover, it is being stated that this event of prior claiming w.r.t D1 in regards to the impugned invention is furthermore substantiated by the Applicant's submission is foreign jurisdictions.

From the patent database at the WIPO, the priority date and the priority application number from which the Indian patent application 1538/CEHNP/2004 is derived is mentioned as a US application no US 60/349,660 with a priority date of 17.01.2002. At the USPTO website based on reference to this particular priority application (relating to the cited prior art D1) it was observed that there existed four US patent application with Patent nos: 7468390, 8101659, 8404744 and 8796331 (annexed as US1, US2, US3 & US4 respectively). Furthermore, in the orange book database (annexed as Annexure A) it was found out that the said patents are listed under the drug composition comprising valsartan+sacrubital (NEPi) which is related to ENTRESTO. On the other hand, w.r.t to the impugned application no 4412/DELNP/2007, it has been observed that it is the Indian counterpart of the US patent application with patent Nos: 8877938 and 9388134 (annexed as US5 and US6 respectively). Interestingly, the very same patents with the patent nos: 8877938 and 9388134 were also noted as one of the patents covering the drug Entresto in US jurisdictions. Thus, this further substantiates that the claims of the impugned invention are already claimed by the prior art D1.

Ground II: Section 25(1)(e): That the invention so far as claimed in any claim of the complete specification is obvious and clearly does not involve any inventive step, having regard to the matter published as mentioned in clause (b) of section 25(2) or having regard to what was used in India before the priority date of the applicant's claim (obviousness/lack of inventive step)

D1A: PCT publication WO2003/059345 published on July 24, 2003 (corresponding to 1538/CHENP/2004: Indian Patent Document published on 10/02/2006)

It is being stated that D1A relates to a pharmaceutical composition comprising a combination of i the AT 1- antagonist valsartan or a pharmaceutically acceptable salt thereof and ii a NEP inhibitor or a pharmaceutically acceptable salt thereof and optionally a pharmaceutically acceptable carrier and to a method for the treatment or prevention of a condition or disease selected from the group consisting of hypertension, heart failure such as acute and chronic congestive heart failure, left ventricular dysfunction and hypertrophic cardiomyopathy, diabetic cardiac myopathy, supraventricular and ventricular arrhythmias, atrial fibrillation, atrial flutter, detrimental vascular remodeling, myocardial infarction and its sequelae, atherosclerosis, angina whether unstable or stable, renal insufficiency diabetic and non--diabetic, heart failure, angina pectoris, diabetes, secondary aldosteronism, primary and secondary pulmonary hypertension, renal failure conditions, such as diabetic nephropathy, glomerulonephritis, scleroderma, glomerular sclerosis, proteinuria of primary renal disease, and also renal vascular hypertension, diabetic retinopathy, the management of other vascular disorders, such as migraine, peripheral vascular disease, Raynaud's disease, luminal hyperplasia, cognitive dysfunction such as Alzheimer's, glaucoma and stroke, comprising administering a therapeutically effective amount of the pharmaceutical composition to a mammal in need thereof. As per the claims of the invention claims pharmaceutical composition, it comprises (i) AT 1-antagonist valsartan or its officinal salt and (ii) nep inhibitor or its officinal salt and pharmaceutically suitable carrier. The NEPi so claimed pertains to nep inhibitor which are N-(3-carboxyl-1-oxopropyl)-(4S)-right-phenyl methyl)-4-amino-2R-methylbutanoic acid ethyl ester via, its triethanolamine salt or its three (hydroxymethyl) aminomethane salt; Or N-(3-carboxyl-1-oxopropyl)-(4S)-right-phenyl methyl)-4-amino-2R-methylbutanoic acid or its officinal salt.

Furthermore, in the impugned invention the NEPi is said to exist in the form of sodium salt in a hemihydrate manner. Such a disclosure has also been made in the prior art D1 where it is stated that the NEPi is preferred in the form of a sodium salt. Also, the prior art D1 discloses that the active component or its official salt can also comprise the form that is crystalline other solvent with hydrate can be used. Such a hydrate form of reference w.r.t to the active components is also mentioned in the impugned application.

As mentioned previously, it is known that for establishing lack of inventive step, it's not necessary that all the elements of the impugned elements needs to be mentioned. However, the cited prior art must distinctly indicate a person skilled in the art to arrive at the impugned invention.

In light of this, the cited prior art D1A clearly and distinctly highlights all the essential features of the impugned invention. Further it is stated that the impugned application merely confirms the findings of the cited prior art D1A.

The primary inventive step of the cited prior art D1A lies in the combination of Angistensin II receptor antagonist in the form of valsartan and the NEPi which is preferred in hydrate form of a crystallized form for the purpose of providing a combination therapy to provide a treatment for entity for the treatment of patients with various cardiovascular and/or renal diseases. In its complete specification, the impugned application also states the same inventive step comprising same components. No specific technical advancement has been mentioned w.r.t D1A in this regard. A person skilled in the art can easily arrive at the impugned invention.

It is further stated that at page 7, D1A discloses the surprisingly improved therapeutic effect of the combination than the administration of valsartan, ACE inhibitors or NEP inhibitors alone. It also discloses the lessening of adverse effects and prolonged duration of action on administration of the combination. It is stated that the alleged invention also seeks to provide an efficacious combination therapy which does not have deleterious side effects. Accordingly, the applicants have disclosed and claimed a supramolecular complex of valsartan and Page 13 NEP inhibitor being (2R,4S)-5-biphenyl-4-yl-4-(3-carboxy-propionylamino)-2- methyl-pentanoic acid ethyl ester having the formula as under. [((S)-N-valeryl-N-{[2‟‟-(1-H-tetrazole-5-yl)-biphenyl-4-yl]-methyl}-valine). [(2R,4S)-5-biphenyl-4-yl-4-(3-carboxy-propionylamino)-2-methyl-pentanoic acid ethyl ester) Na1-3.x H2O where x- 0-3. Thus, the mechanism

of action of these two active drugs and their metabolism were already known from D1A at the time of the invention and the applicant merely combined the actives to form a supramolecular complex.

D2 (EP0498361A2): European Patent Document "Combination of an angiotensin II antagonist or renin inhibitor with a neutral endopeptidase inhibitor" published on 12.08.92: Priority date: 06.02.91 (US)

It is stated that the invention of D2 (EP0498361A2) relates to a pharmaceutical composition for treating hypertension or congestive heart failure comprising an effective amount of a combination of a neutral endopeptidase inhibitor and either a renin inhibitor or an angiotensin II antagonist, in a pharmaceutically acceptable carrier. The use of a neutral endopeptidase (NMEP) inhibitor, in combination with either a renin inhibitor or an angiotensin II antagonist, for the preparation of a pharmaceutical composition useful in the treatment of hypertension or congestive heart failure. The NEP inhibitors are selected from a group of N-[N-[1(S)-carboxyl-3-phenylpropyl]-(S)-phenylalanyl]-(S)-isoserine; N-[N-[((1S)-carboxy-2-phenyl)ethyl]-(S)-phenylalanyl]-β-alanine; N-[2(S)-mercaptomethyl-3-(2-methylphenyl)propionyl]methionine. Thus, the alleged inventive step with respect to the impugned application which relates to a combination therapy where a complex of two active agents with different mechanisms of action, namely an angiotensin receptor antagonist and a neutral endopeptidase inhibitor, to form a molecular entity for treatment of patients with various cardiovascular and/or renal diseases, is known from D2. The angiotensin receptor antagonist that is being used is disclosed to be valsartan which is an Angiotensin II receptor antagonist. Moreover, in D2 as per para 0014 of the complete specification, mentions about preferred form of the angiotensin II receptor antagonist in the form of sodium salts. In this regard, the impugned invention disclosing an angiotensin receptor II antagonist in the form of valsartan as one of the active ingredients, is thus obviated by the disclosure of D2. The impugned invention does only as much to confirm this combination is effective w.r.t the specified therapy for treating hypertension or congestive heart failure. The teaching of the prior art D2 hints a person skilled in the art to arrive at the impugned invention. In relation to inventive step, it is known jurisprudence the prior art needn't disclose every aspect of the impugned invention, however the disclosure should be enough to hint a person skilled in the art to arrive at the present invention in absence of the knowledge

of the impugned invention.

D3 (EP0726072A2): European Patent Document "Composition for the treatment of hypertension and congestive heart failure, containing an angiotensin II antagonist and an endopeptidase inhibitor" published on 14.08.1996

It is further being stated that D3: EP0726072A2 discloses a combination therapy of Angiotensin I antagonist 2-butyl-6,7,8,9-tetrahydro-3-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1,3-diazaspiro[4.4]nonan-4-one and a selective neutral endopeptidase inhibitor or a dual acting neutral endopeptidase inhibitor. It is stated that the prior art D3 claims of angiotensin II antagonist 2-butyl-6,7,8,9-tetrahydro-3-[[2'-(1H-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl]methyl]-1,3-diazaspiro[4.4]-nonan-4-one or a pharmaceutically acceptable salt thereof and a selective neutral endopeptidase inhibitor or a dual acting neutral endopeptidase inhibitor for manufacturing a medicament for treating hypertension and/or congestive heart failure in a mammalian specie in need of such treatment. The element of angistenin II receptor antagonist in combination with the NEP inhibitor is the primary inventive step of the impugned application. In this regard, the mention of other elements such as existence of the complex in combination with sodium hemihydrate form is just yet another variation of the primary inventive concept. The impugned invention merely confirms the invention of prior art D3 while specifically providing an example of the angiotensin II receptor antagonist valsartan and the NEP inhibitor. The impugned invention is indicated by the prior art D3. The impugned claims as per claim 1 claims a compound comprising the Angiotensin Receptor Antagonist valsartan and the NEP Inhibitor (2R,4S)-5-biphenyl-4-yl-4-(3- carboxy-propionylamino)-2- methyl-pentanoic acid ethyl ester which exist in the form of a sodium hemihydrate. D3 discloses specific angiotensin II receptor antagonists and specific NEP proteins, a combination of enzyme inhibitors for the treatment of high blood pressure or congestive heart failure. Even though claim 1 replaces certain specific component of the prior art D3, the combination therapy using an angiotensin receptor II antagonist in combination with the NEPi remains the same. Further as per para 0008 of the complete specification of D3, it has been clearly stated that it is known in the state of art that the pharmaceutically acceptable form of these angiotensin II receptor antagonist is in the form of sodium or potassium salts. The existence of the compound in the form of a sodium salt is very much obvious to a person skilled in the art owing to the fact that another Angiotensin II receptor antagonist has been used in

the compound as one of the active ingredients.

D4: Chinese patent document CN1443l76A, published on September 17, 2003

The invention of D4 relates to new salts of valsartan or crystalline, also partly crystalline and amorphous salts of valsartan, the respective production and usage, and pharmaceutical preparations containing such a salt. Moreover claim 12 of D4 discloses of dual angiotensin-converting enzyme/neutral endopeptidase (ACE/NEP) inhibitor or its pharmacologically acceptable salt. Furthermore, claim 1 of D4 discloses of a sodium salt of valsartan. Moreover claim 4, 5, 7 & 9 of D4 discloses the existence of a hydrate form of the valsartan sodium salt. Furthermore, in the complete specification it has been mentioned that – there is a need of valsartan more stable form, for example crystalline form, that are easier to handle during drying or in the final step of chemical preparation process and in the step of preparing drug formulations, and be easier to processing. Thus, the feature of valsartan existing is a crystallized form to better stability of valsartan or for easier processing which enhances its usefulness in drug formulations is also clearly disclosed. The specification of the prior art D4 also discloses the preference of a sodium hydrated salt of valsartan in a crystalline form. In this regard claim 1 of the impugned application is obvious over D4. Even though it doesn't disclose the exact chemical formula of an NEPi, it howsoever teaches that as per claim 12 of the prior art D4, it states that the pharmaceutical preparation is composed of the described sodium valsartan and a dual angiotensin-converting enzyme/neutral endopeptidase (ACE/NEP) inhibitor. The composition of valsartan in the form of a sodium hydrate along with an NEPi is distinctly taught in D4. Hence D4 is obvious to a person skilled in the art in regards to the impugned application.

D5: WO200374474 (D5) recognizes the unmet goal of predictable crystal structure from crystal engineering. The D5 document relates to the concepts of crystal engineering to design new pharmaceutical compounds. In particular, it relates to multiple-component solids that contain more than one molecular components, such as two active pharmaceutical ingredients, so as to achieve crystalline assemblies (in the form of supramolecular synthons) having improved drug solubility, dissolution rate, stability and bioavailability. It may be emphasized that D5 document particularly, states that "Pharmaceutical molecules or ions are inherently predisposed for such crystal engineering studies since they already contain molecular recognition sites that bind selectively to biomolecules, and they are prone to supramolecular

self-assembly". D5 illustrates the groups commonly found in active pharmaceutical ingredients, and which are capable of forming supramolecular synthons include, but are not limited to, acids, amides, aliphatic nitrogen bases, unsaturated aromatic nitrogen bases (e.g. pyridines, imidazoles), amines, alcohols, halogens, sulfones, nitro groups, S-heterocyles, N-heterocycles (saturated or unsaturated), and O-heterocycles. Other examples include ethers, thioethers, thiols, esters, thioesters, thioketones, epoxides, acetonates, nitrils, oximes, and organohalides. D5 teaches that the supramolecular complex may be formed of an active pharmaceutical ingredient (API) and co- crystal former which can also be an API.

A person of skilled in the art reading the document D1A and D5 would have sufficient incentive to try to make the supramolecular complex of sacubitril and valsartan. **D5 document** undoubtedly teaches or motivates to make such complex with a reasonable expectation of success. It is stated that person skill in the art would be naturally inclined in the course of routine research to try various crystalline forms, including supramolecular complex of sacubitril and valsartan.

Furthermore, in this regard, it is being mentioned that those skilled in the art know that there are combination drugs with synergistic effects in the field of hypertension treatment. In this case the idea of combining an Angiotensin II receptor antagonist along with a Nep inhibitor is known in the state of art. Also, the type of NEPi used in the impugned application is obvious in regards to the teachings of D1, D2 & D3 since the compounds mentioned in these teachings as NEPi are same or derivatives of those mentioned in the prior art. The compound of the impugned application states that it exhibits a certain blood pressure lowering effect, but it cannot be confirmed that a synergistic effect or technical advancement is obtained in this regard since the blood pressure lowering effect of valsartan was already known in the state of art and so was the blood pressure lowering effect of combination of an Angiotensin II receptor antagonist (which in this case is valsartan) and an NEPi. Any significant contribution of the showing any technical advancement isn't exhibited in this case. The composition in this impugned application only has a certain blood pressure lowering effect, and it cannot be confirmed that a synergistic effect is obtained. Looking for a specific treatment based on D2 in the case of a composition for hypertension, one of skill in the art would be able to envision a combination of a blood pressure lowering compound that inhibits neutral endopeptidase and antagonizes angiotensin II receptors. Afterwards, the

composition can still exhibit a certain blood pressure lowering effect as a whole on the basis of each exerting a blood pressure lowering effect. From the specific compounds enumerated, as well as the blood pressure lowering compounds known in the art to be NEP inhibitors and angiotensin II receptor antagonists, those skilled in the art can easily expect that it can solve the technical problem actually solved by this patent. Therefore, those skilled in the art are motivated to combine the two specific compounds, angiotensin II receptor antagonists and NEP inhibitors disclosed in the technology, and so the blood pressure-lowering effect of the pharmaceutical combination compound obtained by the combination compound disclosed in claim 1 of impugned application does not possess an inventive step. Moreover, since claim(s) 2-8 are dependent on claim 1, they are also obvious and lacks inventive step, owing to the fact that the claim 1 is not inventive over the prior arts D1- D5.

Therefore, it is stated that the claims 1 to 8 warrants rejection for being obvious to a person skilled in the art and for want of an inventive step.

The impugned application ought to be rejected on this ground alone.

Ground III - Section 25(1)(f): Not patentable subject matter / Not an invention:

The subject-matter of the claims 1 to 8 of the impugned application is not an invention within the meaning of this Act or is not patentable under this Act, based on the following grounds:

Section 2(1)(j) - The Opponent states that the claim 1 to 8 of the impugned application are not an invention as they are devoid of an inventive step for reasons stated in paragraphs under the preceding grounds of obviousness/lack of inventive step. The submissions are not being reiterated for the sake of brevity. Therefore, it is stated that the claims of the impugned application warrant rejection for failing to meet the requirements of Section 2(1)(j).

Section 2(1)(ja)- The Opponent states that the claim 1 to 8 of the impugned application are not an invention as they are devoid of an inventive step for reasons stated in preceding paragraphs under the ground of obviousness/lack of inventive step, which are not reiterated for the sake of brevity. Therefore, it is stated that the claims of the Impugned application warrant rejection for failing to meet the Section 2(1)(ja). The Opponent humbly submits that the said provision is an object of the Patents Act and the attempt to breach

the provision by the Applicant would tantamount to breach of the very object of the Patents Act and therefore the impugned application ought to be rejected.

Section 3(d) The Applicant states that claims 1 to 8 being in respect of pharmaceuticals must also pass the threshold of Section 3(d), but unfortunately the claims do not comply the threshold of Section 3(d). D1: PCT publication WO2003/059345 published on July 24, 2033 (corresponding to 1538/CHENP/2004: Indian Patent Document published on 10/02/2006), which is of the Applicant itself, discloses that the combination of valsartan with sacubitril is known and that the same is efficacious. The Applicant has purposely not shown any enhanced efficacy over D1 and it trying to mislead about the same. The Opponent humbly submits that the said provision is an object of the Patents Act and the attempt to breach the provision by the Applicant would tantamount to breach of the very object of the Patents Act and therefore the impugned application ought to be rejected.

The Opponent states that the impugned Patent ought to be revoked in to-to on this ground.

GROUND IV- Section 25 (1) (h) – Breach of Section 8

According to Section 8(1) of the Patents Act

(1) Where an applicant for a patent under this Act is prosecuting either alone or jointly with any other person an application for a patent in any country outside India in respect of the same or substantially the same invention, or where to his knowledge such an application is being prosecuted by some person through whom he claims or by some person deriving title from him, he shall file along with his application or subsequently within the prescribed period as the Controller may allow— (a) a statement setting out detailed particulars of such application; and (b) an undertaking that, up to the date of grant of patent in India, he would keep the Controller informed in writing, from time to time, of detailed particulars as required under clause (a) in respect of every other application relating to the same or substantially the same invention, if any, filed in any country outside India subsequently to the filing of the statement referred to in the aforesaid clause, within the prescribed time.

According to Section 8(2) of the Patents Act

(2) At any time after an application for patent is filed in India and till the grant of a patent or refusal to grant of a patent made thereon, the Controller may also require the applicant to furnish details, as may be prescribed, relating to the processing of the application in a country outside India, and in that event the applicant shall furnish to the Controller information available to him within such period as may be prescribed.

The applicant has not complied with Section 8 requirements. For instance, the applicant has willfully suppressed the details of invalidation proceeding in corresponding patent in China (application no. 200680001733.0), wherein an invalidation action was filed in Nov 2019 and a decision came in Jun 2021

(annexed herewith as Annexure B). Even though the decision was in favour of applicant, still the applicant did not inform about the same. The applicant also did not informed about the opposition proceedings against corresponding Peruvian patent application which was initiated long back in Dec 2007 and a decision was issued in Oct 2019. The applicant has not acted in good faith and has not discharged the duty of disclosure as per Section 8 of the Patents Act, by not submitting the documents related to corresponding foreign patent proceedings.

6. RELIEF SOUGHT

The Opponent prays for the following reliefs:

1. Take on record the present opposition;
2. Leave to make further submissions and evidence;
3. Grant of hearing;
4. Refusal of the application.

Dated this the 02nd September, 2022

for KETAKEE S. DURVE

(Opponent)

(Chirag Tanna, IN/PA-1785)

Authorized Patent Agent for the Opponent

To

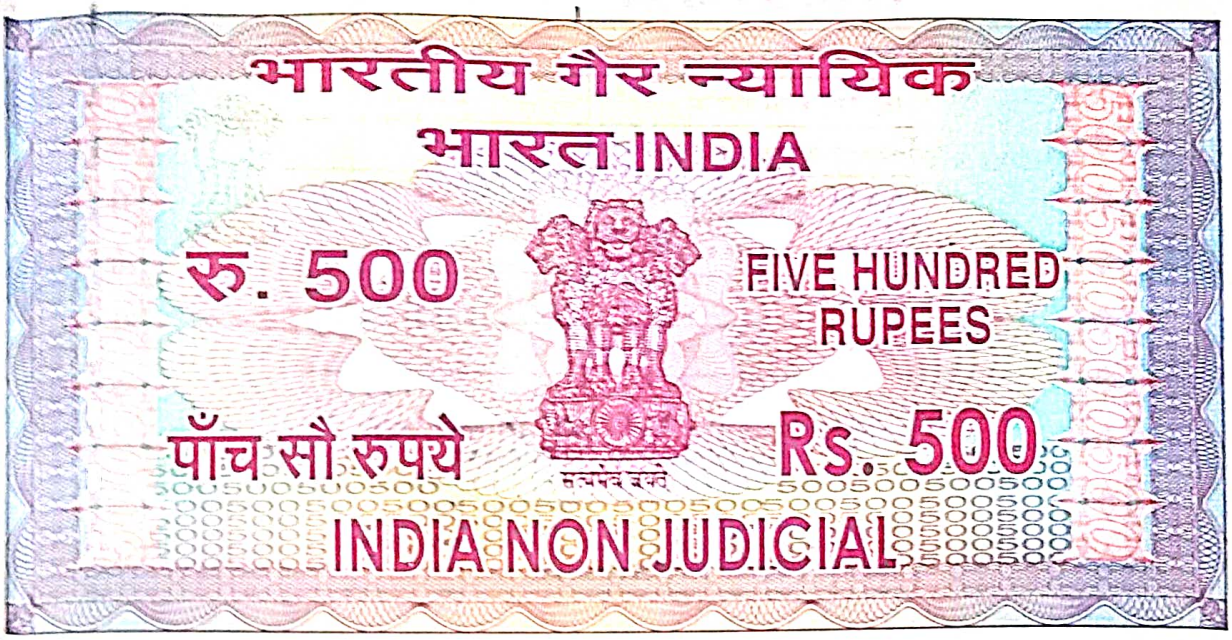
The Controller of Patents

The Patent Office

Delhi

Annexures:

- D1 – prior art
- D1A– prior art
- D2– prior art
- D3– prior art
- D4– prior art (English translation followed by CN original document)
- D5- prior art
- Annexure A – orange book patent list
- Annexure B- Corresponding CN Decision English translation followed by Chinese version
- US1 –copy of US7468390
- US2- copy of US8101659
- US3- copy of US 8404744
- US4- copy of US8796331
- US5- copy of US8877938
- US6- copy of US9388134



महाराष्ट्र MAHARASHTRA ◐ 2021 ◐ BM 422731

उप कोषागार अधिकारी
कल्याण
20 JUL 2022

FORM 26

THE PATENT ACT, 1970

(39 of 1970)

FORM OF AUTHORISATION OF PATENT AGENT

IN A MATTER OR PROCEEDING UNDER THE ACT

(See Sections 127 and 132; Rule 135)

I, KETAKEE S. DURVE, AN INDIAN NATIONAL HAVING THEIR ADDRESS AT C2/101, PUNYODAYA PARK, NEAR DON BOSCO SCHOOL, ADHARWADI JAIL ROAD, KALYAN WEST, 421301, MAHARASHTRA, INDIA

hereby authorise CHIRAG TANNA [Regn. No. IN/PA-1785], an Indian national, Registered Patent Agent of **INK IDÉE**, Trade Marks & Patents Attorneys, B-72, 62, 73 PEREIRA NAGAR NO. 7, KHOPAT, THANE (W) 400 601, MAHARASHTRA, INDIA, to act on my/our behalf in connection with filing applications, filing oppositions, responding to oppositions, sending notices, responding to notices, acting on and attending proceedings, filing petitions, filing renewals and maintenances, rectifications; to represent and sign all forms and documents under the PATENTS ACT and RULES on my behalf and appoint on my behalf and request that all notices, requisitions and communications relating thereto may be sent to such person at the above address unless otherwise specified.

I authorize CHIRAG TANNA to appoint substitute patent agents on his behalf to represent me.

I hereby revoke all previous authorizations, if any, in respect of same matter or proceeding.

I hereby assent to the action already taken by the said person in the above matter.

Dated this 28th day of July, 2022

28/07/2022

KETAKEE S. DURVE

To

The Controller of Patents,

The Patent Office at MUMBAI, DELHI, KOLKATA, CHENNAI

जोडपः २

मुद्रांक विक्री नोंदही अनु.क्रमांक / दिनांक :	1927 | 28.07.2022
दस्ताचा प्रकार :	२५ करारनामा
दस्त नोंदणी करणार आहेत का :	होय / नाही
मिळकतीचे थोडक्यात वर्णन :	—
मुद्रांक विकत घेणाऱ्याचे नांव व सही :	केतकी मुल - डुवे
हस्ते असल्यास त्यांचे नाव व पत्ता व सही :	कल्याण
दुसऱ्या पक्षकाराचे नांव :	चिराग पन्ना
मुद्रांक शुल्क रक्कम :	500 | —
परवानाधारक मुद्रांक विक्रेत्याची सही व परवाना क्रमांक : तसेच मुद्रांक विक्रीचे ठिकाण / पत्ता :	सौ. उषा किशोर वागळे 1206016 वागळे टि.स्टॉल, अहिल्याबाई चौक, कल्याण (प.), जि.ठाणे.

ज्या कारणासाठी त्यांनी मुद्रांक खरेदी केला त्यांनी त्याच कारणासाठी मुद्रांक खरेदी केल्यापासून ६ महिन्यात वापरणे बंधनकारक आहे.

28/07/2022