$~ (Original)

* **IN THE HIGH COURT OF DELHI AT NEW DELHI**

Pronounced on 9th January 2023

\+ CS(COMM) 229/2019

NOVARTIS AG & ANR ..... Plaintiffs

Through: Mr. Hemant Singh, Ms. Mamta Jha, Mr. Ankit Arvind and Ms. Mamta Bhadu, Advocates.

Versus

NATCO PHARMA LIMITED ..... Respondent

Through: Mr J. Sai Deepak and Ms. Rajeshwari, Advocates.

CORAM:
HON'BLE MR. JUSTICE C. HARI SHANKAR

% J U D G M E N T
09.01.2023

I.A. 6384/2019 IN CS(COMM) 229/2019

1. The plaintiffs are the holders of Indian Patent IN 276026 ("IN'026"/"the suit patent"), titled "Novel Pyrimidine Compounds and Compositions as Protein Kinase Inhibitors", having been assigned rights, in respect of the said patent, by M/s IRM LLC, to whom the suit patent had been originally granted. The dispute relates to a Markush structure and to Ceritinib, claimed as Claims 1 , 4 and 5 in the suit patent.

2. The plaintiffs, who would collectively be referred to, singularly, as "Novartis" hereinafter, allege that the defendant Natco Pharma Limited (Natco), by manufacturing and selling Ceritinib tablets in the

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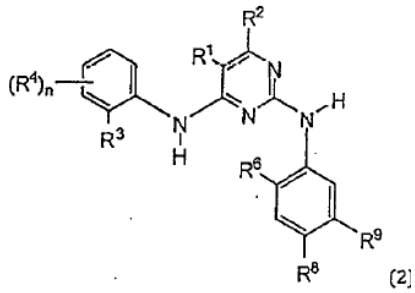
18:30:36

market, without obtaining a license from the plaintiff, is infringing the suit patent. Ceritinib is admittedly exemplified in Example 7 in the suit patent. A Markush formula, with suggested substitutions, by effecting select substitutions from which Ceritinib could be obtained is claimed as Claim 1 in the complete specifications of the suit patent. Ceritinib specifically is claimed in Claim 4.

3. For ready reference, Claims 1 and 4 and Example 7 in the suit patent may be reproduced thus:

"Claims 1 and 4

1. A novel pyrimidine compound of Formula (2):



(2)

or pharmaceutically acceptable salts thereof;
wherein $R^1$is halo or C_{1-6} alkyl;

R^2 is H;

R^3 is $(CR_2)_{0-2}SO_2R^{12}$,$(CR_2)_{0-2}SO_2NRR^{12}$,$(CR_2)_{0-2}CO_{1-2}R^{12}$, $(CR_2)_{0-2}$ $CONRR^{12}$ or cyano;

R^4 is C_{1-6}alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl; OR^{12}, $NR(R^{12})$, halo, nitro, SO_2R^{12}, $(CR_2)_pR^{13}$ or X; or R^4 is H;

R^6 is isopropoxy or methoxy;

one of R^8 and R^9 is $(CR_2)_qY$ and the other is C_{1-6} alkyl, cyano, $C(O)O_{0-1}R^{12}$, $CONR(R^{12})$ or $CONR(CR_2)_pNR(R^{12})$;

X is $(CR_z)_qY$, cyano, $C(O)O_{0-1}R^{12}$, $CONR(R^{22})$ $CONR(CR_z)_pNR(R^{12})$, $CONR(CR_z)_pOR^{12}$, $CONR(CR_z)_pSR^{12}$, $CONR(CR_2)_p S(O)_{1-2} R^{12}$ or $(CR_2)_{1-6}NR (CR_2)_p OR^{12}$;

Y is pyrrolidinyl, piperidinyl or azetidinyl, each of which is attached to the phenyl ring via a carbon atom;

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18:30:36

R^{12} and R^{13} are independently 3-7 membered saturated or partially unsaturated carbocyclic ring, or a 5-7 membered heterocyclic ring comprising N, O and/or S; aryl or heteroaryl; or R^{12} is H or C_{1-6} alkyl;

R is H or C_{1-6}alkyl;

n is 0-1;

p is 0-4; and

q is 0."
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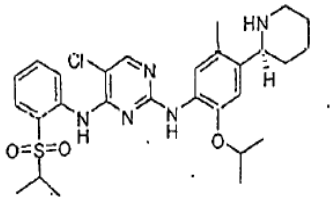
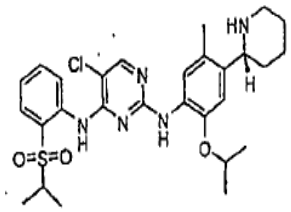
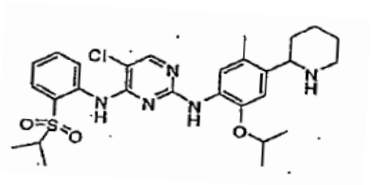
4. The novel pyrimidine compound as claimed in claim 1, wherein said compound is selected from the group consisting of



(S)-5-chloro-N2-(2-isopropoxy-5-methyl-4-(piperidin-2-yl)phenyl)-N4-(2-(isopropylsulfonyl)phenyl)pyrimidine-2,4-diamine;



(R)-5-chIoro-N2-(2-isopropoxy-5-methyl-4-(piperidin-2-yl)phenyl)-N4-(2-(isopropylsulfonyl)phenyl) pyrimidine-2,4-diamine;



5-chIoro-N2-(2-isopropoxy-5-methyl-4-(piperidin-2-yl)phenyl)-N4-(2-(isopropylsulfonyl)phenyl)pyrimidine-2,4-diamine;

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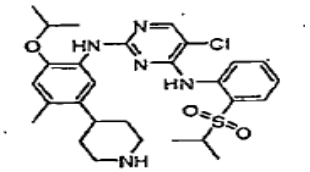
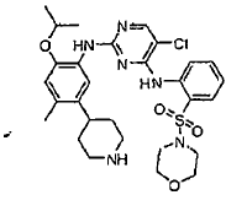
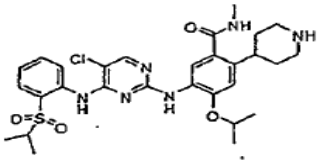
Signing Date:11.01.2023
18:30:36



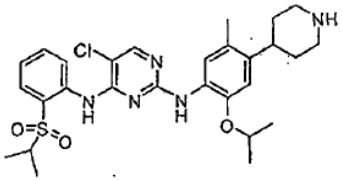
5-chloro-N2-(2-isopropoxy-4-methyl-5-(piperidin-4-yl)phenyl)-N4-(2-(isopropylsulfonyl)phenyl)pyrimidine-2,4-diamine;



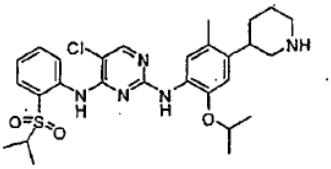
5-chloro-N2-(2-isopropoxy-4-merhyl-5-(piperidin-4-yl)phenyl)N4-(2(morpholinosulfonamido)phenyl)pyrimidine-2,4-diamine;



5-(4-(2-(isopropylsulfonyl)phenylamino)-5-chloropyrimidin-2-ylamino)-4-isopropoxy-N-methyl-2-(piperidin-4-yl)benzamide;



5-chloro-N2-(2-isopropoxy-5-methyl-4-(piperidin-4-yl)phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2,4-diamine; and



5-chloro-N2-(2-isopropoxy-5-meihyl-4-(piperidin-3-yl)phenyl)-N4-(2-(isopropyIsulfonyl)phenyl)pyrimidine-2,4-diamine;

or pharmaceutically acceptable salts thereof.

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Example 7

5-ChIoro-N^2-(2-isopropoxv-5-methyl-4-piperidin-4-yl-phenyl)-N^4-[2-(propane-2-sulfonyI)-phenyl]-pyrimidne-2,4-diaimine (66)

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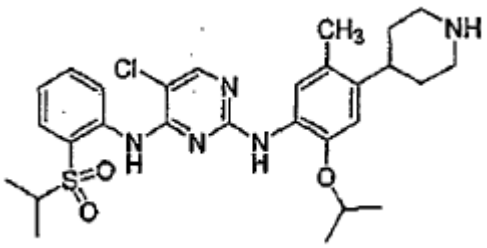
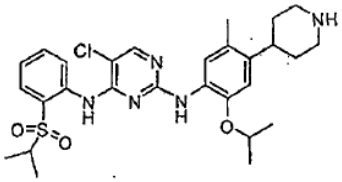
Signing Date:11.01.2023
18:30:36



Example 7 is Ceritinib. On that, there is no dispute. Among the molecules claimed in Claim 4, the following molecule is also, undisputedly, Ceritinib:



5-chloro-N2-(2-isopropoxy-5-methyl-4-(piperidin-4-yl)phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyriniidine-2,4-diamine "

Thus, Ceritinib stands specifically claimed in Claim 4 of the suit patent and exemplified in Example 7, whereas a Markush moiety, with suggested substitutions by effecting substitutions from which Ceritinib can be synthesised, is claimed as Claim 1. The plaintiff alleges infringement, by the defendant, of both Claim 1 and Ceritinib itself, as claimed in Claim 4 and exemplified in Example 7 in the suit patent.

Bibiolography of the suit patent

4. PCT International Application No. PCT/US/2007/085304, in respect of the inventions claimed in the suit patent was filed by IRM LLC on 20th November 2007 which, therefore, is the priority date for the suit patent in accordance with Section 2(1)(w)[1] read with Section

[1] **2. Definitions and interpretation**. –
(1) In this Act, unless the context otherwise requires, -
(w) "priority date" has the meaning assigned to it by Section 11;

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Signing Date:11.01.2023
18:30:36

11[2] of the Patents Act, 1970. The national phase application No. 3951/DELNP/2009, corresponding to the aforesaid PCT Application No. PCT/US/2007/085304, for "Compounds And Compositions As Protein Kinase Inhibitors" was filed before the Patent Office in India by IRM LLC on 16th June 2009. No pre-grant opposition was filed, opposing the grant of the suit patent. The suit patent was, therefore, granted by the Patent Office in favour of IRM LLC on 30th September 2016. It remains valid till 20th November 2027.

5. The compound exemplified in Example 7 of the suit patent IN'026 was assigned the International Non-Proprietary Name (INN) of "Ceritinib" by the World Health Organisation (WHO) in 2013. It is

[2] **11. Priority dates of claims of a complete specification.**—(1) There shall be a priority date for each claim of a complete specification. (2) Where a complete specification is filed in pursuance of a single application accompanied by—

(a) a provisional specification; or

(b) a specification which is treated by virtue of a direction under sub-section (3) of section 9 as a provisional specification, and the claim is fairly based on the matter disclosed in the specification referred to in clause (a) or clause (b), the priority date of that claim shall be the date of the filing of the relevant specification.

(3) Where the complete specification is filed or proceeded with in pursuance of two or more applications accompanied by such specifications as are mentioned in sub-section (2) and the claim is fairly based on the matter disclosed—

(a) in one of those specifications, the priority date of that claim shall be the date of the filing of the application accompanied by that specification;

(b) partly in one and partly in another, the priority date of that claim shall be the date of the filing of the application accompanied by the specification of the later date. 1

(3A) Where a complete specification based on a previously filed application in India has been filed within twelve months from the date of that application and the claim is fairly based on the matter disclosed in the previously filed application, the priority date of that claim shall be the date of the previously filed application in which the matter was first disclosed.

(4) Where the complete specification has been filed in pursuance of a further application made by virtue of sub-section (1) of section 16 and the claim is fairly based on the matter disclosed in any of the earlier specifications, provisional or complete, as the case may be, the priority date of that claim shall be the date of the filing of that specification in which the matter was first disclosed.

(5) Where, under the foregoing provisions of this section, any claim of a complete specification would, but for the provisions of this sub-section, have two or more priority dates, the priority date of that claim shall be the earlier or earliest of those dates.

(6) In any case to which sub-sections (2), (3), 1 (3A), (4) and (5) do not apply, the priority date of a claim shall, subject to the provisions of section 137, be the date of filing of the complete specification.

(7) The reference to the date of the filing of the application or of the complete specification in this section shall, in cases where there has been a post-dating under section 9 or section 17 or, as the case may be, ante-dating under section 16, be a reference to the date as so post-dated or ante-dated.

(8) A claim in a complete specification of a patent shall not be invalid by reason only of—

(a) the publication or use of the invention so far as claimed in that claim on or after the priority date of such claim; or

(b) the grant of another patent which claims the invention, so far as claimed in the first mentioned claim, in a claim of the same or a later priority date.

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Signing Date:11.01.2023
18:30:36

sold by the plaintiff in India (since May 2016) under the brand name SPEXIB and internationally (since 2014) under the brand name ZYKADIA. It functions as preferred first line therapy for treatment of adult patients suffering from anaplastic lymphoma kinase (ALK)-positive advanced non small cell lung cancer (NSCLC), who are intolerant to Crizotinib.

6. The Drugs Controller General of India (DCGI) granted approval for Ceritinib as a first line treatment for ALK-positive NSCLC on 3rd July 2015.

Proceedings after grant of suit patent

7. Post grant opposition, to the suit patent, was filed by Natco on 25th September 2017. The opposition board, constituted under Section 25(3)[3] of the Patents Act, read with Rule 56(4) of the Patents Rule recommended, on 18th May 2018, upholding of the validity of the suit patent.

8. While the post grant opposition filed by Natco was still awaiting decision by the Controller of patents, Natco launched its brand of Ceritinib in India on 29th March 2019 under the brand name NOXALK.

[3] (3) (a) Where any such notice of opposition is duly given under sub-section (2), the Controller shall notify the patentee.
(b) On receipt of such notice of opposition, the Controller shall, by order in writing, constitute a Board to be known as the Opposition Board consisting of such officers as he may determine and refer such notice of opposition along with the documents to that Board for examination and submission of its recommendations to the Controller.
(c) Every Opposition Board constituted under clause (b) shall conduct the examination in accordance with such procedure as may be prescribed.

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Signing Date:11.01.2023
18:30:36

9. Novartis, in these circumstances, instituted the present suit before this Court, alleging that Natco, thereby, infringed the suit patent. The suit, accordingly, seeks a decree of permanent injunction, restraining Natco and all others acting on its behalf from directly or indirectly dealing in any formulation containing Ceritinib either alone or in combination with any other active pharmaceutical ingredient (API) or other compound, as would infringe the suit patent IN '026.

10. *Vide* order dated 2nd May 2019, this Court, restrained Natco from manufacturing any fresh stock of pharmaceutical preparations containing the API Ceritinib, even while allowing Natco to sell the stock already manufactured and lying with it.

11. *Vide* order dated 16th August 2019, IN '026 was revoked by the controller on the ground that the suit patent lacked novelty. Novartis challenged the said order before the learned Intellectual Property Appellate Board ("the learned IPAB") *vide* Appeal No. OA/20/2019/PT/DEL.

12. Consequent on the said revocation, this Court, by order dated 28th August 2019, suspended further continuance of the earlier *ad interim* order dated 2nd May 2019, granting liberty to Novartis to seek appropriate orders from this Court in the event of any order favourable to Novartis being passed by the learned IPAB in the appeal preferred by Novartis before it.

13. *Vide* order dated 20th July 2020, the learned IPAB stayed the operation of the order dated 16th August 2019 passed by the learned Controller revoking the suit patent IN '026.

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Signing Date:11.01.2023
18:30:36

14. Consequent thereon, this Court, *vide* order dated 21st August 2020 passed in I.A. 6729/2020 restored the *ad interim* injunction granted by this Court on 2nd May 2019. The order continues to operate till date.

15. The present order, therefore, disposes of I.A. 6729/2020.

16. During the pendency of these proceedings, on 29th September 2020, the learned IPAB, *vide* a detailed judgment, set aside the order dated 16th August 2019 of the learned Controller, revoking the suit patent IN ’026 and, therefore, restoring the suit patent. WP (C) 9487/2020 has been preferred by Natco, challenging the said decision. The Writ Petition is however pending and no interlocutory orders have, till date, been passed thereon.

17. It is in this scenario that the present application has been argued and is being decided.

18. I have heard Mr. Hemant Singh, learned Counsel for the plaintiffs and Mr. J. Sai Deepak, learned Counsel for the defendant at length.

19. I may observe, even at this juncture, that, as the defence of Natco, to the suit, is almost entirely predicated on questioning the validity of the suit patent, and the learned IPAB has passed a final order holding the suit patent to be valid, a substantial *prima facie* case may be said, even on that score, to exist in favour of the plaintiff. The defendant would, therefore, have to make out a strong case to oppose the grant of interlocutory injunction to the plaintiff, as would

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Signing Date:11.01.2023
18:30:36

outweigh the effect of the judgement of the learned IPAB. Whether such a case has, or has not, been made out, therefore, has to be examined.

Rival Contentions

20. It would be profitable to juxtapose the rival contentions, on the relevant aspects of the dispute, against each other.

I. The Suit Patent and Inventive Step

21. Anaplastic Lymphoma Kinase (ALK) has, since long, been recognized as an oncogene which promotes progression and metastasis of lung cancer, specifically Non Small Cell Lung Cancer (NSCLC). Targeting of ALK, therefore, is one of the aims and objectives of NSCLC therapy. Treatment modules, towards this end, have had to constantly evolve, owing to repeated mutations in the ALK oncogene. As a result, considerable study evolved towards development and synthesis of ALK inhibitors.

22. One of the first ALK inhibitors developed was Crizotinib. Administration of Crizotinib, however, was found to result only in transient benefits. Moreover, Crizotinib was also found to be substantially toxic. Ceritinib, the compound forming subject matter of the suit patent, is claimed, by the plaintiffs, to be an oral second generation ALK inhibitor, which shows favourable responses in Crizotinib resistant ALK positive NSCLC as well as in ALK positive NSCLC which is otherwise resistant to treatment. Ceritinib is said to inhibit autophosphorylation of ALK, resulting in reducing

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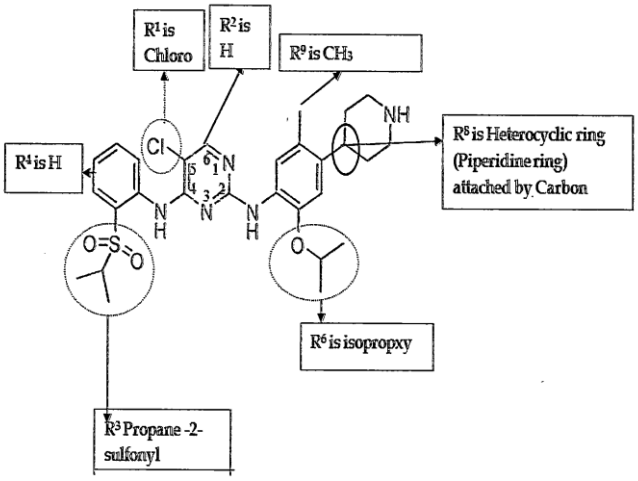
Signing Date:11.01.2023
18:30:36

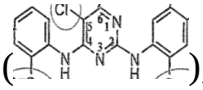
proliferation of ALK dependent cancer cells. Thus, the plaint asserts that Ceritinib was a marked improvement over existing therapies for ALK inhibitors, towards treatment of NSCLC.

23. The molecular formula of Ceritinib is $C_{28}H_{36}ClN_5O_{3S}$, and its chemical name, as per the publication of the World Health Organization (WHO) is 5-chloro-N^2-{5-methyl-4-(piperidin-4-yl)-2-[(propan-2-yl)oxy]phenyl}-N^4-[2-(propane-2-sulfonyl)phenyl]pyrimidine-2,4-diamine. The WHO recognized Ceritinib to be a New Chemical Entity (NCE) and assigned it the International Non-Proprietary Name (INN) in 2013.

24. The molecular structure of Ceritinib with its various constituent moieties is provided, in the plaint, thus:



25. Thus, the molecular structure of Ceritinib consists of the following features:

(i) There is a core pyrimidine moiety (), with three substitutions at positions 2, 4 and 5 of the moiety, of which the substitution at position 5 is of the chloro (Cl-) radical

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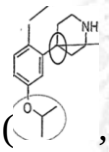
Signing Date:11.01.2023
18:30:36

whereas the substitution at positions 2 and 4 are of phenyl () rings, connected to the core pyrimidine moiety through amine (-NH-) linkages.

(ii) The phenyl ring substituted through the amino linkage at Position 4 (the N^4-phenyl ring) is bi-substituted, of which one of the substitutions is a propane-2-sulfonyl ()radical.

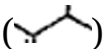
(iii) The phenyl ring joined to the core pyrimidine moiety through the amino group at Position 2 (the N^2-phenyl ring) is tri-substituted ( , the three substituents being as under:

(a) Substitution R^6 in the figure is of the isopropoxy () radical, and

(b) Of the substitutions R^8 and R^9,

(i) one substituent is a pyrrolidinyl, or a piperidinyl or an azetidinyl radical; in the example shown here, it is a piperidinyl () radical, and

(ii) the other substitution is of the methyl ($-CH_3$) radical.

(ii) The heterocyclic pyrollidinyl/piperidinyl/azetidinyl radical is linked to the phenyl ring by a carbon to carbon () linkage.

26. The defendant does not dispute the above factual position.

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Signing Date:11.01.2023
18:30:36

II. Infringement

27. Relying on the judgement of a Division Bench of this Court in ***F. Hoffmann-La Roche Ltd v. Cipla Ltd***[4] ("***Roche***", hereinafter), Mr Hemant Singh submits that the existence, or non-existence, of infringement only involves comparing the suit patent of the plaintiff with the product of the defendant. If the defendant is making or dealing in the product in respect of which the plaintiff has a valid and subsisting patent, infringement, he submits, *ipso facto* has taken place, within the meaning of Section 48[5] of the Patents Act. There is no dispute that Natco had, in fact, launched its NOXALK product, containing Ceritinib 150 mg/capsule, in the market. Infringement, therefore, according to him, is undisputed. Section 108(1)[6] of the Patents Act, submits Mr.Hemant Singh, entitles the patent holder to an injunction against an infringer.

28. Natco does not dispute the fact that it is manufacturing and marketing Ceritinib. Nor does it dispute the fact that Novartis has a subsisting patent for Ceritinib. Natco, however, contends that it has an absolute defence against any charge of infringement, under Section 107[7] read with Section 64(1)[8] of the Patents Act, as the suit patent is

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[4] **2016 (65) PTC l (Del) (DB)**

[5] **48. Rights of patentees**. – Subject to the other provisions contained in this Act and the conditions specified in Section 47, a patent granted under this Act shall confer upon the patentee –
(a) where the subject-matter of the patent is a product, the exclusive right to prevent third parties, who do not have his consent, from the act of making, using, offering for sale, selling or importing for those purposes that product in India;
(b) where the subject-matter of the patent is a process, the exclusive right to prevent third parties, who do not have his consent, from the act of using that process, and from the act of using, offering for sale, selling or importing for those purposes the product obtained directly by that process in India:

[6] **108. Reliefs in suits for infringement**. –
(1) The reliefs which a court may grant in any suit for infringement include an injunction (subject to such terms, if any, as the court thinks fit) and, at the option of the plaintiff, either damages or an account of profits.

[7] **107. Defences, etc. in suits for infringement**. –

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Signing Date:11.01.2023
18:30:36

vulnerable to revocation of several grounds envisaged in Section 64(1). Natco also denies having practised the suit patent of Novartis; rather, Natco's contention is that it is practising US patent No. US 7153964 (US '964) of AstraZeneca AB ("AstraZeneca") which, too, according to Natco, claims and discloses Ceritinib.

III. Novelty and inventive step; anticipation and obviousness

29. Of all the features enlisted in para 25 *supra*, the plaint asserts that the three inventive features of the claim in the suit patent, i.e. Ceritinib are

(i) the core novel pyrimidine moiety with two phenyl rings attached to the pyrimidine ring at its second and fourth position via amine groups,

(ii) the phenyl group attached to the pyrimidine ring at the second position being tri-substituted and

(iii) of the three substitutions, one of the substitutions (at R^8 and R^9 of the figure above) being a heterocyclic pyrrolidinyl,

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(1) In any suit for infringement of a patent, every ground on which it may be revoked under Section 64 shall be available as a ground for defence.

[8] **64. Revocation of patents**. –

(1) Subject to the provisions contained in this Act, a patent, whether granted before or after the commencement of this Act, may, be revoked on a petition of any person interested or of the Central Government or on a counter-claim in a suit for infringement of the patent by the High Court on any of the following grounds, that is to say, -

(a) that the invention, so far as claimed in any claim of the complete specification, was claimed in a valid claim of earlier priority date contained in the complete specification of another patent granted in India;

*****

(d) that the subject of any claim of the complete specification is not an invention within the meaning of this Act;

(e) that the invention so far as claimed in any claim of the complete specification is not new, having regard to what was publicly known or publicly used in India before the priority date of the claim or to what was published in India or elsewhere in any of the documents referred to in Section 13;

(f) that the invention so far as claimed in any claim of the complete specification is obvious or does not involve any inventive step, having regard to what was publicly known or publicly used in India or what was published in India or elsewhere before the priority date of the claim;

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Signing Date:11.01.2023
18:30:36

piperidinyl or an azetidinyl ring, linked to the phenyl ring by a carbon to carbon linkage.

The synthesis of Ceritinib from known prior art, therefore, submits the plaintiff, involves these "inventive steps", within the meaning of Section 2(1)(ja)[9] of the Patents Act.

30. Of these three inventive features, the plaint further goes on to assert that the most inventive feature, so to say the USP of Ceritinib, is the heterocyclic piperidinyl ring and its linkage to the N^2 phenyl group by a carbon-to-carbon bond. Elsewhere (in the replication filed in response to the written statement of the defendant), Novartis has identified the carbon-carbon bond whereby the heterocyclic ring is attached to the phenyl ring as the main inventive step in Ceritinib, as this carbon-to-carbon bond inhibits undesirable metobolic oxidation of the compound, thereby reducintg its toxicity. Novartis has, in the course of its pleadings, acknowledged that there may be other existing patents involving a core piperidine ring, with N^2 and N^4 phenyl ring substituents linked to the core piperidine ring via amine groups, and even having the N^2-phenyl ring being further tri-substituted, with one of the substitutions being of a heterocyclic ring. Even in such cases, according to the plaint, the linkage between the heterocyclic ring and the phenyl ring is not through a carbon-carbon bond. Formula 2 of the suit patent IN'026 specifically envisages such a carbon-to-carbon linkage between N^2-phenyl ring and the heterocyclic ring which is bonded to it. This carbon-to-carbon linkage, it is asserted, avoids metabolic oxidation of the compound and reduces toxicity. The

[9] (ja) "inventive step" means a feature of an invention that involves technical advance as compared to the existing knowledge or having economic significance or both and that makes the invention not obvious to a person skilled in the art;

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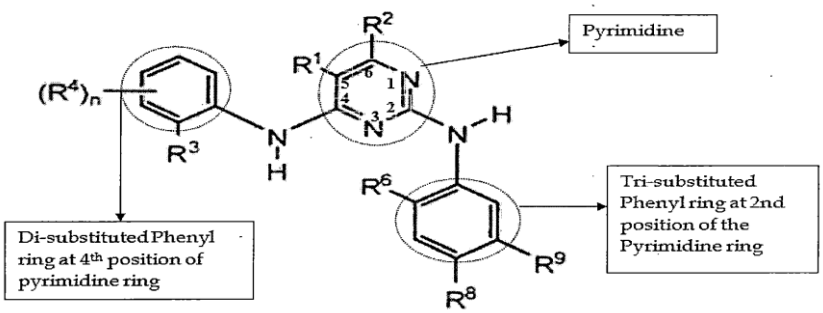
Signing Date:11.01.2023
18:30:36

assertions regarding the inventiveness of the suit patent and, specifically, Ceritinib, *vis-à-vis* existing patents is to be found in the following recitals in the plaint and the replication:

"Plaint

11.4 The present invention as claimed under suit patent being Indian Patent No. 276026, is the compound of Formula 2 or pharmaceutically acceptable salts thereof, as recited in claim 1 of the suit patent and illustrated as under:



(Markush structure of Formula 2 as per claim 1)

The invention claimed in suit patent is novel pyrimidine compounds having two phenyl rings attached to the pyrimidine ring at its 2nd and 4th position via amine groups wherein the phenyl group attached to pyrimidine ring at the 2-position is tri- substituted (i.e. R^6, R^8 and R^9 may not be hydrogen atom) and one of R^8 and R^9 is a heterocyclic ring of pyrrolidinyl, piperidinyl or azetidinyl, each of which is attached to the phenyl ring via a carbon atom. This combination of the tri-substituted phenyl ring and the heterocyclic group of either R^8 or R^9 attached to that phenyl ring via a carbon atom renders the compound of Formula 2 as per claim 1 novel and inventive.

CLAIMS:

11.5 Claim 1 of the suit patent, being Markush claim, encompasses a number of different compounds covered by formula (2). One of the compounds synthesized in accordance with formula (2) and specifically disclosed in the suit patent as Examples 7 and 66 is "Ceritinib" wherein R^1 represents Chloro, R^2 represents Hydrogen; R^3 represents isopropyl Sulfonyl; R^4 does not represent any functional group when n is zero/0; R^6 represents isopropoxy; R^8 represents Piperidinyl and R^9 represents Methyl. The said compound is specifically claimed in claim 4 and 5 in free form or

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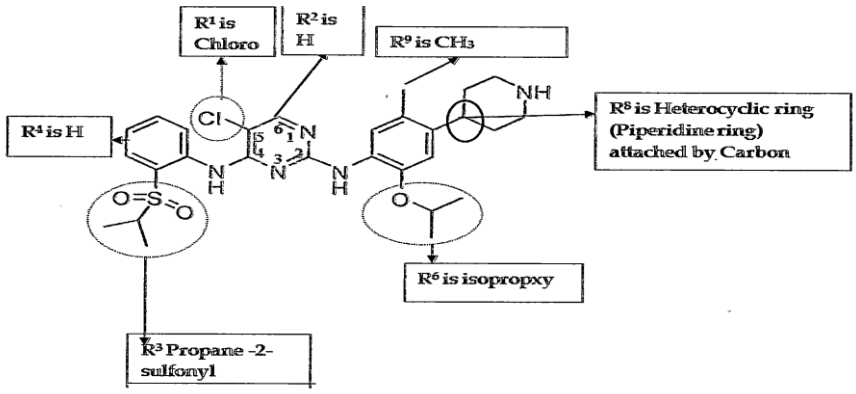
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

in form of a pharmaceutically acceptable salt. The structure of Ceritinib is derived from Markush structure of claim 1 and is illustrated as under:



Molecular structure of Ceritinib

5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl) N4[2-(propane-2-sulfonyl)-phenyl] -pyrimidine-2,4-diamine

*****

12. Ceritinib is a novel and inventive compound which has been given International Non-proprietary Name (INN) of Ceritinib being a New Chemical Entity (NCE). None of the prior arts discloses Ceritinib, subject matter of suit patent IN 276026. The claims in the suit patent are limited to pyrimidine compounds having two phenyl rings attached to 2nd and 4th position to the pyrimidine ring via amine groups wherein the phenyl group attached to Pyrimidine ring at the second position is tri-substituted (i.e. R^6, R^8 and R^9 may not be hydrogen atom) and one of R^8 and R^9 is pyrrolidinyl, piperidinyl or azetidinyl, each of which is attached to the phenyl ring via a carbon atom. This combination of tri-substituted phenyl ring and heterocyclic group attached to the phenyl ring via a carbon atom is one of the novel features of the presently claimed compound.

*****

14. PLAINTIFF'S PRODUCT- SPEXIB (Ceritinib):

14.1 The invented compound Ceritinib is marketed and sold under the brand SPEXIB in India and under the brand ZYKADIA for countries other than India. SPEXIB is a life extending prescription drug containing Ceritinib free base available in dosage strength of 150 mg capsules:

-as monotherapy for first line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non small cell lung cancer (NSCLC);

-for treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non small cell lung cancer (NSCLC) who have

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

progressed on or are intolerant to Crizotinib. The API in the said drug is the patented compound Ceritinib.

14.2 A single pack of SPEXIB (150 mg) box contains three boxes wherein each box has 5 strips of capsules and that each strip has 10 capsules. Therefore, a single pack of SPEXIB (150 mg) box contains 150 capsules. The recommended dose of SPEXIB for patients with NSCLC is 450 mg orally once a day with food at the same time each day. Treatment with SPEXIB is to be continued as long as the patient is deriving clinical benefit from this drug.

14.3 APPROVAL STATUS OF ZYKADIA/ SPEXIB:

ZYKADIA has been approved by USFDA as kinase inhibitor indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to Crizotinib in 2014.

Furthermore, Plaintiff No.2 secured import and marketing approval from Drug Controller General of India on 03rd July, 2015 for formulations containing Ceritinib in 150 mg dosage, 4, -for treatment of patients with anaplastic lymphoma kinase (ALK)- positive metastatic non small cell lung cancer (NSCLC) who have progressed on or are intolerant to Crizotinib and the same is marketed under the brand SPEXIB in India. Another import and marketing approval dated 28th December, 2017 was issued by Drug Controller General of India to Plaintiff No.2 for formulations containing Ceritinib in 150 mg dosage for first line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non small cell lung cancer (NSCLC). The aforementioned import and marketing approvals were subsequently transferred to another entity-M/s Sandoz Private Limited vide approvals dated 27th April, 2018 and 9th July, 2018. Copies of the said import and marketing authorizations in respect of Ceritinib in India are placed on record.

****

Replication

17. In its written statement and counter claim, the Defendant has also raised the issue of invalidity of the suit patent and has cited a handful of prior arts in an attempt to show that the suit patent is invalid. The entire contention of alleged invalidity of the claim of suit patent in respect of Ceritinib is based on misconceived plea of coverage and disclosure. It is submitted that *none of the cited prior arts, discloses Ceritinib. None of prior arts specifically identifies the particular set of substituents as claimed & disclosed in IN 276026 from the multitude of possible substituents disclosed in each patent. None of the prior arts cited by the Defendant disclose either the compound of Formula 2 or the new chemical entity-Ceritinib, subject matter of suit patent IN*

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

276026. Under the patent law, genus claims cover a large number of compounds, which either were prepared by the patentee or could be prepared according to the same method of preparation. It is now a settled position under the Patent law that genus claims technically cover any subsequent invention (species) in the form of compounds being prepared at a later stage and also falling within the genus and would necessarily involve infringement. However, a species claim would be entitled to an independent patent claim, if it can be shown that notwithstanding the existence of the disclosure of the patent having the genus claim, there was novelty and inventive step and the patent did not suffer from the afflictions of the prior art or obviousness. A genus claim may cover large number of compounds. However, in absence of specific examples or specific disclosure, any subsequent compound embraced or covered by a genus claim, but innovated and developed subsequently which is novel and inventive over the prior disclosure, is entitled to independent patent protection. Therefore, the absence of specific disclosure of the claimed compounds of suit patent in the prior arts, render such compounds as patentable being novel and inventive compounds, which compounds have advantageous and unexpected properties as active in inhibitors of ALK, FAK, ZAP-70 and IGFIR. *The prior art compounds that have heterocyclic ring linked to the phenyl ring via a carbon-hetero atom bond (e.g., carbon-nitrogen, carbon-oxygen, etc.) were likely to undergo metabolic oxidation that can lead to the formation of potentially toxic adducts, leading to potential toxicological liabilities/properties. In contrast, compounds within the scope of Formula 2 of IN 276026, including Ceritinib, are limited to compounds in which the N^2-phenyl is linked to a heterocyclic ring via a carbon-carbon bond that may not undergo undesirable metabolic oxidation. Avoiding the metabolic oxidation while maintaining ALK inhibition activity is the key advance of the invention claimed in the suit patent. Ceritinib, as one of the compounds disclosed in the suit patent, was subsequently developed as a drug and was found to be an effective ALK inhibitor without the toxicity observed with TAE684 and hence it renders the suit patent novel and inventive.* More so, on account of such settled law pertaining to distinction between genus patent and species patent, the Plaintiff No.l has been granted valid and subsisting patents corresponding to suit patent in several countries including in US for compound of Formula 2 and Ceritinib in particular as novel and inventive compounds. In support of the above submissions, the Plaintiffs seek to place reliance on the affidavit of Dr. Altenbach filed in the present proceedings."

(Emphasis supplied)

31. Natco contends that the suit patent is invalid on the ground of want of novelty or any inventive step, as it is obvious and anticipated by earlier existing prior art, in the form of other patents which had

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

been granted in India and elsewhere. In this context, the defendant cites

(i) the plaintiffs' own patents IN 252653 (IN'653) [corresponding to US 7964592 (US'592) and WO 2004/080980 (WO'980)] and IN 240560 (IN'560) [corresponding to US 7893074 (US'074) and WO 2005/016894 (WO'894)],

(ii) Astrazeneca's patent US'964, corresponding to WO 0164654 (WO'654) and

(iii) US Patent Nos. US 8188276 (US'276), US 8835430 (US'430, US 9416112 (US'112) and US 9018204 (US'204) of Rigel Pharmaceuticals Inc ("Rigel" hereinafter).

32. ALK mutation, resulting in exacerbation of NSCLC, submits Natco, was a known phenomenon, to combat lung cancer for which research was continually ongoing. Various ALK-inhibitors had been devised and patented and it was not, therefore, as if Novartis could claim any ingenious inventive step to its credit. By way of publications relating to ALK-inhibitors, Natco cites 'Detection of anaplastic lymphoma kinase (ALK and nucleolar protein nucleophosmin (NPM)-ALK proteins in normal and neoplastic cells with the monoclonal antibody ALK 1' by Pulford K, Lamant L, Morris SW, Butler LH, Wood KM, Stroud D, Delsol G, Mason DY and Blood, 1997 Feb 15; 89 (4):1394-404 and a work introduced in the November 2006 Conference of the ASH Annual Meeting.

33. Natco contends, in its written statement, thus:

> "It is denied that the combination of trisubstituted phenyl ring and the heterocyclic group or either R8 or R9 attached to that phenyl ring via carbon atom renders the compound of Formula 2 novel and inventive. Such trisubstituted

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

compounds have been made in the prior art and were found to provide anti-cancer effect."

WO'980 (US'592/IN'653), WO'894 (US'074/IN'560) of Novartis and WO'654 (US'964) of Astrazeneca have been cited as examples of "several patents in the prior art which provided such anti-cancer effect".

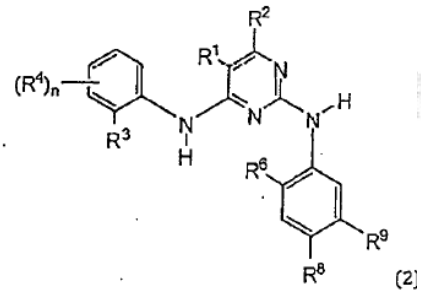
34. <u>*Vis-à-vis* IN'653 and IN'560</u>:

34.1 *Vis-à-vis* IN'653, Natco contends (in paras 35 and 36 of the written statement) that the Markush Claim 1 in the suit patent and Ceritinib itself, as Claim 4 in the suit patent, stand fully disclosed by the Markush Claim 1 in IN'653.

34.2 Claim 1 in the suit patent, in IN'653 and in IN'560, all being Markush claims, read thus:

<u>Claim 1 in the suit patent</u>

"1. A novel pyrimidine compound of Formula (2):



(2)

or pharmaceutically acceptable salts thereof;
wherein $R^1$is halo or C_{1-6} alkyl;

R^2 is H;

R^3 is $(CR_2)_{0-2}SO_2R^{12}$,$(CR_2)_{0-2}SO_2NRR^{12}$,$(CR_2)_{0-2}CO_{1-2}R^{12}$, $(CR_2)_{0-2}$ $CONRR^{12}$ or cyano;

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

R^4 is C_{1-6}alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl; OR^{12}, $NR(R^{12})$, halo, nitro, SO_2R^{12}, $(CR_2)_pR^{13}$ or X; or R^4 is H;

R^6 is isopropoxy or methoxy;

one of R^8 and R^9 is $(CR_2)_qY$ and the other is C_{1-6} alkyl, cyano, $C(O)O_{0-1}R^{12}$, $CONR(R^{12})$ or $CONR(CR_2)_pNR(R^{12})$;

X is $(CR_z)_qY$, cyano, $C(O)O_{0-1}R^{12}$, $CONR(R^{22})$ $CONR(CR_z)_pNR(R^{12})$, $CONR(CR_z)_pOR^{12}$, $CONR(CR_z)_pSR^{12}$, $CONR(CR_2)_p S(O)_{1-2} R^{12}$ or $(CR_2)_{1-6}NR (CR_2)_p OR^{12}$;

Y is pyrrolidinyl, piperidinyl or azetidinyl, each of which is attached to the phenyl ring via a carbon atom;

R^{12} and R^{13} are independently 3-7 membered saturated or partially unsaturated carbocyclic ring, or a 5-7 membered heterocyclic ring comprising N, O and/or S; aryl or heteroaryl; or R^{12} is H or C_{1-6} alkyl;

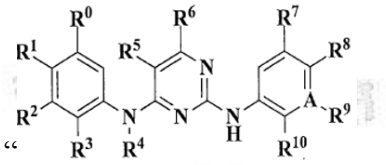
R is H or C_{1-6}alkyl;

n is 0-1;

p is 0-4; and

q is 0."

Claim 1 in IN'653



Wherein

each of R^0, R^1, R^2 and R^3 independently is hydrogen, C_1-C_8alkyl, C_2-C_8 alkenyl, C_2-C_8alkinyl, C_3-C_8cycloalkyl, C_3-C_8cycloalkylC_1-C_8alkyl, C_5-C_{10}arylC_1-C_8alkyl, hydroxyC_1-C_8alkyl, C_1-C_8alkoxyC_1-C_8alkyl, aminoC_1-C_8alkyl, haloC_1-C_8alkyl, unsubstituted or substituted C_5-C_{10}aryl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1, 2 or 3 hetero atoms selected from N, 0 and S, hydroxy, C_1-C_8alkoxy, hydroxy C_1-C_8alkoxy, C_1-C_8alkoxyC_1-C_8alkoxy, haloC_1-C_8alkoxy, unsubstituted or substituted, C_5-C_{10}arylC_1-C_8alkoxy, unsubstituted

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

or substituted heterocyclyloxy or unsubstituted or substituted heterocyclyl C_1-C_8alkoxy, unsubstituted or substituted amino, C_1-C_8alkylthio, C_1-C_8alkylsulfinyl, C_1-C_8 alkylsulfonyl, C5-C_{10} arylsulfonyl, halogen, carboxy, C_1-C_8 alkoxycarbonyl, unsubstituted or substituted carbamoyl, unsubstituted or substituted sulfamoyl, cyano or nitro;

or R^0 and R^1, R^1 and R^2, and/or R^2 and R^3 form, together with the carbon atoms to which they are attached, a 5 or 6 membered carbocyclic or heterocyclic ring comprising 0, 1, 2 or 3 heteroatoms selected from N, O and S;

R^4 is hydrogen or C_1-C_8alkyl;

each of R^5 and R^6 independently is hydrogen, C_1-C_8alkyl, C_1-C_8alkoxy C_1-C_8alkyl, haloC_1-C_8alkyl, C_1-C_8alkoxy, halogen, carboxy, C_1-C_8alkoxycarbonyl, unsubstituted or substituted carbamoyl, cyano, or nitro;

each of R^7, R^8, R^9, and R^{10} independently is C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkinyl, C_3-C_8cycloalkyl, C_3-C_8cycloalkyl C_1-C_8alkyl, C_8-C_{10}arylC_1-C_8alkyl, hydroxyC_1-C_8alkyl, C_1-C_8alkoxy C_1-C_8alkyl, aminoC_1-C_8alkyl, haloC_1-C_8alkyl, unsubstituted or substituted C_5-C_{10}aryl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1, 2 or 3 hetero atoms selected from N, O and S, hydroxy, C_1-C_8 alkoxy, hydroxyC_1-C_8alkoxy, C_1-C_8alkoxyC_1-C_8alkoxy, haloC_1-C_8alkoxy, unsubstituted or substituted C_5-C_{10}arylC_1-C_8alkoxy, unsubstituted or substituted heterocyclyloxy, or unsubstituted or substituted heterocyclyl C_1-C_8 alkoxy, unsubstituted or substituted amino, C_1-C_8alkylthio, C_1-C_8alkylsulfinyl, C_1-C_8alkylsulfonyl, C_5-C_{10}arylsulfonyl, halogen, carboxy, C_1-C_8alkoxycarbonyl, unsubstituted or substituted carbamoyl, unsubstituted or substituted sulfamoyl, cyano or nitro; wherein R^7, R^8 and R^9 independently of each other can also be hydrogen.

or R^7 and R^8, R^8 and R^9 and/or R^9 and R^{10} form together with the carbon atoms to which they are attached, a 5 or 6 membered carbocyclic or heterocyclic ring comprising 0, 1, 2 or 3 heteroatoms selected from N, O and S;

A is C or N, most preferably C;

and salts thereof.

Claim 1 in IN'560

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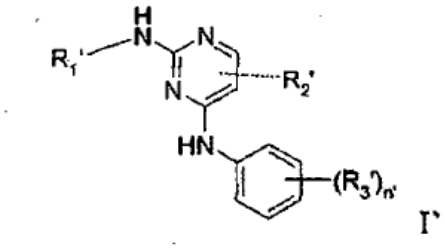
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

"A compound of formula 'I'



I'

in which:

n' is selected from 1 and 2;

R'2 is selected from hydrogen and halo;

R '3 is selected from – $S(O)_{0-2}NR'_5R'_6$, $-S(O)_{0-2}R'_6$, $-NR'_5S(O)_{0-2}R'_6$, and $-C(O)NR'_5R'_6$; wherein R'_5 is selected from hydrogen and C_{1-6} alkyl; and R'_6 is selected from hydrogen, C_{l-6}alkyl and C_{3-12} cycloalkyl, and R'_1 is selected from phenyl, pyridinyl, pyrazolyl and pyrimidinyl; wherein any aryl or heteroaryl of R'_1 is substituted by 3 radicals independently selected from ethoxy, ethyl, propyl, methyl, t-butyl, trifluoromethyl, nitrile, cyclobutyloxy, 2,2,2-trifluoroethoxy, isobutyloxy, t-butyloxy, isopropyloxy, methyl-amino-carbonyl, cyclopropyl-methoxy, dimethylamino-propyl-amino, methoxy-ethoxy, $-X'R'_4-C(O)R'_4$ and $-OX'R'_4$; wherein X' is a bond, methylene or ethylene; R'_4 is selected from piperazinyl, piperidnyl, pyrrolidinyl, morpholino, azepanyl and 1,4-dioxa-8-aza-spiro[4.5]dec-8-yl; wherein R'_4 is optionally substituted by 1 to 3 radicals independently selected from methyl, isopropyl, acetyl, acctyl-methyl-amino, 3- dimethylamino-2,2-dimethyl-propylamino, ethyl-methyl-amino-ethoxy, diethyl-amino-ethoxy, amino-carbonyl, ethyl, 2-oxo-pyrrolidin-l-yl, pyrrolidinyl, pyrrolidinyl-methyl, piperidinyl optionally substituted with methyl or ethyl, morpholino, dimethylamino, dimethylamino-propyl-amino- methyl-amino and ethyl-amino"

34.3 Alleged disclosure of Ceritinib in IN'653: From the suggested substitutions in Claim 1 in IN'653, if one were to substitute

(i) H for R^0,

(ii) H for R^1,

(iii) H for R^2,

(iv) the alkylsulfonyl radical for R^3,

(v) H for R^4,

(vi) the halogen radical for R^5,

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

(vii) H for R^6,

(viii) C_1-C_8 alkyl for R^7,

(ix) C_1-C_8 alkoxy for R^8,

(x) a 6-membered heterocyclyl group with 1 hetero-substitution for R^9 and

(xi) C for A,

the resultant product, submits Natco, would be Ceritinib. Thus, submits Natco, Claim 4 in the suit patent, which is Ceritinib, is also "disclosed by and falls within" the Markush claim in IN'653.

34.4 Alleged disclosure of the Markush Claim 1 in the suit patent in IN'653: Natco also contends, in para 35 of its written statement, that "a comparison of IN'653 and the claims of IN'026 (the suit patent) would reveal that the compounds claimed in the Markush structure of the impugned patent (claim 1) are encompassed and embraced by the Markush formula of claim 1 in IN'653". No clear elucidation of this contention is, however, forthcoming in the written statement which, prior thereto, merely reproduces, in a tabular format, Claim 1 in the suit patent and Claim 1 in IN'653 side by side.

34.5 Alleged disclosure of Ceritinib in IN'560: From the suggested substitutions in Claim 1 in IN'560, if one were to substitute

(i) a trisubstituted phenyl for R^1, with methyl, isopropyloxy and piperidinyl substitutions,

(ii) a halogen radical for R^2,

(iii) $S(O)_{0-2}R^6$ for R^3

(iv) R^6 being a selected C_{1-6} alkyl,

Ceritinib, contends Natco, would result.

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Signing Date:11.01.2023
18:30:36

34.6 It is also contended, in para 24 of the written statement, that Novartis claimed Ceritinib in IN'653 and in IN'560.

35. *Vis-à-vis* Astrazeneca's US'964/WO'654

35.1 US'964/WO'654 is also alleged, by Natco, to include a trisubstituted N^2-phenyl with anti-cancer properties. The disclosure of Ceritinib, in Claim 1 US'964 is sought to be demonstrated thus, in para 60 of the written statement:

"Claim 1 of US 984 (sic. US 964) reads:-

> l. A pyrimidine derivative of the formula (I):
> wherein:
>
> Q1 and Q2 are independently selected from aryl or carbon linked heteroaryl; and Q1 is substituted on a ring carbon by a sulphamoyl group, or one of Ql and Q2 or both Q1 and Q2 is substituted on a ring carbon by one group selected from N— (Cl-4alkyl)sulphamoyl (optionally substituted by halo or hydroxy), N,N-di-(Cl-4alkyl)sulphamoyl (optionally substituted by halo or hydroxy), Cl-4alkylsulphonyl (optionally substituted by halo or hydroxy) or a substituent of the formula (la) or (la'):
>
> wherein:
>
> Y is —NHS(O)2—, —S(O)2NH— or —S(O)2—;
>
> Z is RaO— RbRcN—, RdS—, ReRfNNRg—, C3-8cycloalkyl, phenyl or a heteroc wherein said phenyl, C3-8cycloalkyl or heterocyclic group are optionally substituted on a rig carbon by one or more groups selected from Rh; and wherein if said heterocyclic group contains an —NH— moiety that nitrogen may be optionally substituted by a group selected from Ri;
>
> Ra, Rb, Rc, Rd, Re, Rf and Rg are independently selected from hydrogen, Cl-4alkyl, C2-4alkenyl, phenyl, heterocyclic group and C3-8cycloalkyl; wherein said C1-4alkyI, C2-4alkenyl and C3-8cycloalkyl are optionally substituted by one or more groups selected from Rj;
>
> n is 0 or 1;

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

m is 1, 2 or 3, in addition m may be 0 when Z is C3-8cycloalkyl,
phenyl or a heterocyclic group;

Q3 is a nitrogen linked heterocycle; wherein said heterocycle is optionally substituted on a ring carbon by one or more groups selected from Rk; and wherein if said heterocyclic group contains an —NH— moiety that nitrogen may be optionally substituted by a group selected from Rm

G is —O—, —S— or —NR2—;

R2 is selected from hydrogen, Cl-6alkyl, C3-6alkenyl and C3-6alkynyl; wherein said Cl-6alkyl, C3-6alkenyl and C3-6alkynyl are optionally substituted by one or more groups selected from Rn;

R1 is selected from hydrogen, halo, hydroxy, amino, N—(Cl-3alkyl)amino, N,N-di-(Cl-3alkyl)amino, cyano, tidfluoromethyl, trichloromethyl, Cl-3alkyl [optionally substituted by 1 or 2 substituents independently selected from halo, cyano, amino, N—(Cl-3alkyl)amino, N,N-di-(Cl-3alkyl)amino, hydroxy and trifluoromethyl], C3-5alkenyl [optionally substituted by up to three halo substituents, or by one tidfluoromethyl substituent], C3-5alkynyl, Cl-3alkoxy, mercapto, Cl-3alkylsidphanyl, carboxy and Cl-3alkoxycarbonyl;

Q1 is optionally substituted on a ring carbon by one to four substituents independently selected from halo, mercapto, nitro, formyl, formamido, carboxy, cyano, amino, ureido, carbamoyl, Cl-4alkyl, C2-4alkenyl, C2-4alkynyl [wherein said Cl-4alkyl, G2-4alkenyl and C2-4alkynyl are optionally substituted by one or more groups selected from Ro], C1-4alkanoyl, Cl- 4alkoxycarbonyl, heterocyclic group, C1-4alkylS(0)a wherein a is 0 or 1 [optionally substituted by hydroxy], N'—(C1-4alkyl)ureido, N',N'-di-(C1-4alkyl)ureido, N'—(C1-4alkyl)-N—(C1-4alkyl)ureido, N',N'-di-(Cl-4alkyl)-N—(Cl-4alkyl)ureido, N—C1-4alkylamino, N,N-di-(C1-4alkyl)amino, N-Cl-4alkylcarbamoyl, N,N-di-(Cl-4alkyl)carbamoyl and Cl-4alkanoylamino;

and also independently, or in addition to, the above substituents, Q1 may be optionally substituted by one to two substituents independently selected from aryl, C3-8cycloalkyl and a heterocyclic group; wherein said aryl,

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

C3-8cycloalkyl or heterocyclic group may be optionally substituted on a ring carbon by one or more groups selected from Rp; and wherein if said heterocyclic group contains an —NH— moiety that nitrogen may be optionally substituted by a group selected from Rq;

and also independently, or in addition to, the above substituents, Q1 may be optionally substituted by one Cl-4alkoxy or by one hydroxy substituent;

Q2 is optionally substituted on a ring carbon by one to four substituents independently selected from halo, hydroxy, mercapto, nitro, formyl, formamido, carboxy, cyano, amino, ureido, carbamoyl, Cl-4alkyl, C2-4alkenyl, C2-4alkynyl, Cl- 4alkoxy [wherein said Cl-4alkyl, C2-4alkenyl, C2-4allcynyl and Cl-4alkoxy are optionally substituted by one or more groups selected from Rl], Cl-4alkanoyl, Cl-4alkoxycarbonyl, heterocyclic group, Cl-4alkylS(0)awherein a is 0 or 1 [optionally substituted by hydroxy], N'—(Cl-4alkyl)ureido, N',N'-di-(Cl-4alkyl)ureido, N'—(Cl-4alkyl)-N—(Cl-4alkyl)ureido, N',N',-di-(Cl-4alkyl)-N—(Cl-4alkyl)ureido, N—Cl-4alkylamino, N',N'-di-(Cl-4alkvl)amino, N-Cl-4alkylcarbamoyl, N,N-di-(Cl-4alkyl)carbamoyl, C1-4alkenyloxy, C2-4alkynyloxy and Cl-4alkanoylainino;

and also independently, or in addition to, the above substituents, Q2 may be optionally substituted by one to two substituents independently selected from aryl, C3-8cycloalkyl or a heterocyclic group; wherein said aryl, C3-8cycloalkyl or heterocyclic group may be optionally substituted on a ring carbon by one or more groups selected from Rs; and wherein if aid heterocyclic group contains an —NH— moiety that nitrogen may be optionally substituted by a group selected from Rt;

Rj, Rn, Ro and Rr are independently selected from hydroxy, halo, amino, cyano, formyl, formamido, carboxy, nitro, mercapto, carbamoyl, sulphamoyl, N—C1-4alkylamino, N,N-di-(C1-4alkyI)amino, Cl-4alkanoyl, Cl-4alkanoyloxy, Cl-4alkoxy, Cl-4alkoxycarbonyl, N—Cl-4alkylcarbamoyl, N,N-di-(Cl-4alkyl)carbamoyl, Cl-4alkanoylamino, Cl-4alkylS(0)a wherein a is 0 to 2, Cl-4alkylsulphonylamino, N—(Cl-4alkyl)sulphamoyl, N—(C1-4alkyl)2sulphamoyl, N—(C1-4alkyl)carbamoyl, N—(Cl-4alkyl)2carbamoyl, phenyl, phenylthio, phenoxy, C3-8cycloalkyl and a heterocyclic group; wherein said phenyl, phenylthio, phenoxy, C3-8cycloalkyl or heterocyclic group may be optionally substituted on a ring carbon by one or

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

more groups selected, from Ru; and wherein if said heterocyclic group contains an —NH— moiety that nitrogen may be optionally substituted by a group selected from Rv;

Rh, Rk, RpRs and Ru are independently selected from hydroxy, halo, amino, cyano, formyl, formamido, carboxy, nitro, mercapto, carbamoyl, sulphamoyl, Cl-4alkyl [optionally substituted by one or more groups selected from halo, cyano, amino, N—C1-4alkylamino, N,N-di-(Cl-4alkyl)amino or hydroxy], C2-4alkenyl [optionally substituted by one or more groups selected from halo], C2-4alkynyl, N—Cl-4alkylamino,N,N-di-(Cl-4alkyl)amino, Cl-4alkanoyl, Cl-4alkanoyloxy, Cl-4alkoxy [optionally substituted by one or more groups selected, from halo], Cl-4alkoxycarbonyl, N—Cl-4alkylcarbamoyl, N,Ndi-(Cl-4alkyl)carbamoyl, Cl-4alkanoylamino, Cl-4alkylS(O)a wherein a is 0 to 2, Cl-4alkylsulphonylamino, N—(Cl-4alkyl)sulphamoyl, N—(Cl-4alkyl)2sulphamoyl, phenyl, C3-8cycloalkyl and a heterocyclic group; and

Ri, Rq, Rt and Rv are independently selected from Cl-4alkyl, Cl-4alkanoyl, Cl-4alkylsulphonyl, Cl-4alkoxycarbonyl, carbamoyl, N—(C1-4alkyI)carbamoyl, N,N—(C1-4alkyl)carbamoyl, benzyl, benzyloxycarbonyl, benzoyl and phenylsulphonyl;

or a pharmaceutically acceptable salt or in vivo hydrolysable ester formed from an available carboxy or hydroxy group thereof

When the above substituents are made, the resultant product is ceritinib."

35.2 Additionally, para 61 of the written statement alleges that Ceritinib is "covered by and embraced by US'964" as

(i) Novartis had admitted, in para 13.2 of the plaint, that "amino pyrimidine compounds were subject of research by various companies such as Astrazeneca, who had applied for, and were granted, patents therefor, such as US'964", and had also admitted that "US'964 claimed various Markush

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

compounds, wherein Ceritinib would be generically disclosed and claimed",

(ii) it was for this reason that Novartis had obtained a "freedom to operate" licence from Astrazeneca,

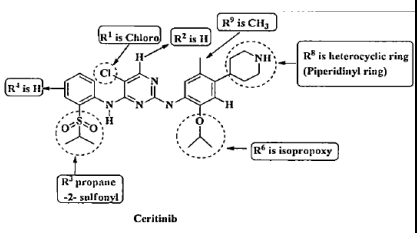
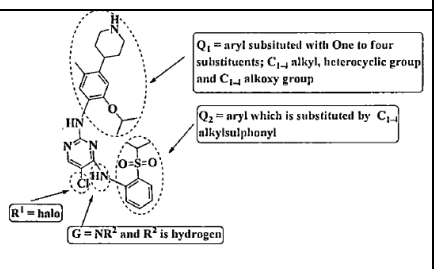
(iii) but for the said licence, the suit patent would be infringing US'964 and

(v) while listing relevant patents at the time of applying for approval to the US Food and Drug Authorities (USFDA), Novartis had also cited US'964.

35.3 Natco claims to be practising US'964 and, therefore, not to be infringing the suit patent.

35.4 Para 8 of the written statement asserts that Ceritinib, as claimed in the suit patent, as also Natco's product, is derived from, as well as claimed and covered by, US'964/WO'654. The paragraph reads thus:

> 8. That the Defendant submits that its product is a compound which is derived from the patent granted to Astra and published as WO 0164654 (WO'654). It is submitted that as admitted by the Plaintiff, the compound Ceritinib is claimed and covered by WO'654. The product manufactured and sold by the Defendant is squarely claimed and covered by the said patent. The same is illustrated as under:-

Suit Patent 276026	WO 2001/64654 (Astrazeneca)
 Ceritinib	 Ceritinib

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

36. Mr. Hemant Singh, appearing for Novartis, seeks to distinguish between the concepts of infringement and anticipation/obviousness/disclosure. He seeks, thereby, to explain the theory of genus patent and species patent. He submits that a genus patent may claim a Markush entity/formula with suggested substitutions which, if substituted onto the Markush moiety, may lead to a vast number of possible compounds, at times running into millions. All these compounds, he submits, would be within the coverage of the Markush moiety and, therefore, within the coverage of the genus patent. Any person who seeks to manufacture and market any compound which is one among the millions of compounds thus "covered" by the Markush moiety is, therefore, technically infringing the genus patent. There is, however, a distinction between "coverage" and "disclosure" of the genus patent. Only those moieties or compounds can be said to be "disclosed" by the genus patent, in respect of which sufficient teaching, to lead one to synthesize such a moiety or compound is available in the genus patent. In other words, the genus patent must teach the way to arrive at the species patent. Where such teaching is available at the genus patent, the specie patent would be vulnerable to revocation on the ground of want of novelty or inventive step and, consequently, therefore, as being anticipated and obvious from the genus patent. Where such teaching is not, however, forthcoming in the complete specifications of the genus patent, which merely provides suggested substitutions without leading a person, seeking to synthesize to make specific selections or choices from the suggested substitutions, the genus patent does not possess the requisite teaching, so as to show the person the way to teach the species patent. In such a situation, the person who arrives at the specie patent, even if

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

it is from the Markush moiety claimed in the genus patent, does so as a result of its own inventive skill. An inventive step is, therefore, involved, resulting in a patentable "invention". The specie patent, in such a case, cannot be said to be invalid as being obvious from the genus patent.

37. Viewed thus, Mr. Hemant Singh would submit that the prior art cited by Mr. Sai Deepak in the form of the plaintiffs' IN'560 and IN'653, Astrazeneca's US'964, and Rigel's patents US 8188276, US 8835430 and US 9018204 and 9416112 patents do not disclose, much less claim, Ceritinib. At the highest, he submits, they only claimed only Markush moiety from which, using the teaching contained in the said patents and common general knowledge as existing at the time of the grant of the said patents, a person skilled in the art (who has, in some cases, been regarded as a "person ordinarily skilled in the art" often abbreviated as POSA), would not be able to arrive at the suit patent. As such, even if the suit patent may be regarded technically as infringing one or more of the said prior arts, because of the fact that Formula 2 in the suit patent, and Ceritinib itself, may fall within the broad coverage, or embrace of the prior art patents, none of them actually disclosed either Formula 2 in the suit patent or Ceritinib. There is, submits Mr. Hemant Singh, no disclosure, in any prior art, of all the three distinctive inventive features of Ceritinib as delineated in para 25 *supra*. Specifically, the plaintiffs aver that the heterocyclic ring which is attached to the N^2 phenyl ring via a carbon-carbon bond is a feature which is absent in prior art, or at the least, a feature to which the prior art does not specifically draw attention.

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

38. Mr. Hemant Singh does not dispute the fact that the prior art cited by Natco covers Ceritinib. However, he reiterates that coverage is not the same as disclosure and that disclosure in the prior art must be enabling in nature i.e. it must enable the person who seeks to synthesize the compound which forms subject matter of the suit patent from the prior art to know how to do so, from the teaching contained in the prior art itself, along with common general knowledge existing at the time. The prior art cited by the defendant, he submits, does not contain the said teaching. The manner in which the defendant has, in its written statement, arrived at Formula 2 in the suit patent and/or Ceritinib itself, is by hindsight analysis, by cherry-picking substituents from the various substitutions suggested in the Markush formulae contained in the prior art. The defendant has, in other words, been able to reach at the suit patent from the prior art only because of the foreknowledge, possessed, by the defendant, of the suit patent and its actual molecular structure. The teaching, for choosing the substituents, from the various substitutions in the Markush formulae contained in the prior art, so as to arrive at the suit patent, therefore, he submits, is contained in the suit patent and not in the prior art. Having with it foreknowledge of the actual molecular structure of the suit patent, Mr. Hemant Singh submits that the defendant has cherry-picked those substituents from the various substitutions suggested in the Markush formulae contained in the prior art, as would lead the defendant from the prior art Markush formula to the suit patent. Such an exercise, he submits, is completely impermissible in law, and cannot constitute the basis for an assertion that the suit patent is lacking in inventive step or is otherwise anticipated or obvious from the prior art.

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

39. "Disclosure", submits Mr Hemant Singh, has to be in the manner envisaged by Section 64(1)(e) of the Patents Act, for it to invalidate the specie patent. It has to be, therefore, "by exemplification, illustration, individualized description or use known publicly"[10]. In para 13 of the plaint, Novartis acknowledges that "compounds comprising a pyrimidine ring with substituted phenyl rings attached via amino groups were subject matter of Markush claims of prior arts", but asserts that "none of the prior arts disclosed the compound Ceritinib or the Markush formula included in the suit patent". Mr Hemant Singh, cites, in support,

(i) paras 75 to 80 and 90 to 94 of the decision of the UK High Court in ***Dr Reddy's Laboratories (UK) Ltd v. Eli Lilly & Co. Ltd***[11] ("***Dr Reddy-I***", hereinafter),

(ii) paras 27 to 30 and 33 of the decision of the Court of Appeal in ***Dr Reddy's Laboratories (UK) Ltd v. Eli Lilly & Co. Ltd***[12] ("***Dr Reddy-II***, hereinafter),

(iii) para 486 of the decision of the Supreme Court of the UK in ***The General Tire & Rubber Co. v The Firestone Tyre & Rubber Co. Ltd***[13] and

(iv) paras 1, 2, 7, 5 and 16 of the judgement of the High Court of Bombay in ***Farbewerke Hoechst Aktiengesellschaft Vormals Meister Lucius & Bruning a Corporation v. Unichem Laboratories***[14] (***"Hoechst v. Unichem***").

There is no jurisprudence, anywhere in the world, submits Mr Hemant Singh, which equates "coverage" and "disclosure". "Coverage determines the scope of the claim of the invention and determines the

[10] Refer Novartis' Written Submissions dated 23rd November 2020
[11] **[2008] EWHC 2345 (Pat); [2009] FSR (5) 271**
[12] **[2009] EWCA 1362; [2010] RPC 9**
[13] **[1972] RPC 457**
[14] **AIR 1969 Bom 255**

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

issue of infringement based on claim construction. A species of product may be covered by an earlier genus patent though not disclosed thereon."[10] He relies, for this purpose, on paras 18, 19 and 50.9 of the decision of a coordinate single bench of this Court in ***Eisai Co. Ltd v. Satish Reddy***[15] and paras 27, 29, 32, 37 and 39 of the decision, also of a learned Single Judge of this Court, in ***Astrazeneca AB v. Emcure Pharmaceuticals***[16]. There is no prior art, he submits, which discloses *all the three inventive features* of the suit patent, as delineated in para 25 *supra*.

40. Mr Hemant Singh also contends that the fact that, despite the alleged prior art having remained alive, Ceritinib could not be synthesized by any practitioner thereof, indicates that Ceritinib was a novel invention, involving an inventive step.

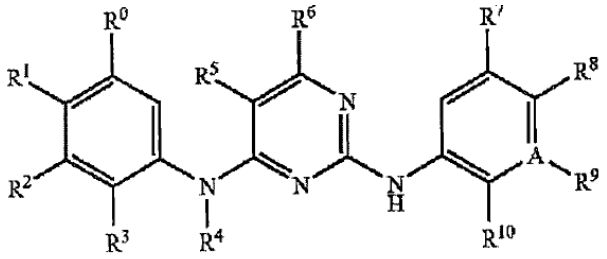
41. Specifically adverting to the prior art cited by Natco, Mr Hemant Singh submits that neither Formula 2 in the suit patent, nor Ceritinib, stands disclosed by any of the prior art patents cited by Natco, i.e. IN'653 and IN'560 of Novartis, US'964/WO'654 of Astrazeneca, or US'276, US'430, US'204 and US'112 of Rigel.

42. Apropos IN'653 and IN'560, Mr Hemant Singh submits that neither the Markush Formula 2 in the suit patent, nor Ceritinib, had been disclosed in either of these patents. TAE 684, one of the compounds disclosed in IN'560 and IN'653, was isolated for development studies. Though the compound inhibited the ALK

[15] **(2019) 79 PTC 568 (Del)**
[16] **(2020) 81 PTC 588 (Del)**

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

enzyme, it was found to be unacceptably toxic. Ceritinib achieved the same end without such toxicity. Apropos IN'653 specifically, Mr Hemant Singh submitted that IN'653 claimed the following Markush structure, which disclosed a broad genus of substituted pyrimidines, without any disclosure of Ceritinib:



Mr Hemant Singh pointed out that over 500 compounds were exemplified in IN'653, but Ceritinib was not one amongst them. None of the compounds contained a trisubstituted phenyl ring linked to the core piperidine ring by an amine group, with one of the substitutions on the trisubstituted phenyl ring having to be a pyrrolidinyl/piperidinyl/azetidinyl heterocyclic ring, linked to the phenyl ring by a carbon-to-carbon bond.

43. Neither IN'560, nor IN'653, therefore, taught or disclosed Formula 2 in the suit patent or Ceritinib, or the inventive feature in the suit patent, submits Mr Hemant Singh.

44. US'964/WO'654 of Astrazeneca, too, submits Mr Hemant Singh, claimed a Markush formula with a core 2,4-substituted pyrimidine ring, which inhibited CDK Kinase, but did not disclose Formula 2 in the suit patent, or Ceritinib. Paras 13.2 to 13.4 of the plaint aver, in this regard, thus:

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

"13.2 … One of such companies was Astrazeneca, which filed patent application in 2001 and obtained US Patent No. 7153964 in 2006. Aztrazeneca's US Patent No. 7153964 contained a Markush claim thereby claiming compounds having inhibitory activity on CDK Kinase. However, the said patent did not disclose either the compound of formula 2 or the new chemical entiry-Ceritinib, subject matter of the suit patent. … In addition, a license was obtained by the Plaintiff No. 1 from Astrazeneca under the previously referenced Astrazeneca patents. The purpose of taking a license under the Astrazeneca patents and resolving the litigation with Rigel was to obtain "freedom to operate" under the broad genus claims of the Astrazeneca and Rigel patents even though none of those patterns disclosed formula 2 of the suit patent or the compound Ceritinib within the scope of formula 2. Moreover, because AstraZeneca and Rigel patents did not disclose formula 2 of the suit patent or the compound Ceritinib within the scope of formula 2, Plaintiff No. 1 was able to obtain its own patent rights claiming the compounds of Formula 2 and Ceritinib including the suit patent in India, and in the U.S. and throughout the world.

13.3 Under the patent law, genus claims cover a large number of compounds, which either were prepared by the patentee or could be prepared according to the same method of preparation. Genus claims technically cover any subsequent invention (species) in the form of compounds being prepared at a later stage and also falling within the genus and would necessarily involve infringement. However, a species claim would be entitled to an independent patent claim, if it can be shown that notwithstanding the existence of the disclosure of the patent having the genus claim, there was novelty and inventive step and the patent did not suffer from the afflictions of prior art or obviousness. Therefore, the earlier patents either of Astrazeneca, Rigel or of the Plaintiff No. 1 itself may have genus claims but none of the said patents disclose the compound Ceritinib or any other compound disclosed and claimed in the suit patent.

13.4 As stated above, compounds of Formula 2 of the suit patent including Ceritinib are novel and inventive and not disclosed in any of the patents obtained by Astrazeneca or Rigel or the Plaintiff No. 1's earlier patents being patent IN 240560 and IN 232653 itself. A genus claim may cover a large number of compounds. However, in absence of specific examples or specific disclosure any subsequent compound embraced by a genus claim, but innovated and developed subsequently which is novel and inventive over the prior disclosure, is entitled to independent patent protection. There is no compound disclosed in any of the prior art wherein the phenyl group attached to Pyrimidine ring at the second position is trisubstituted (i.e. R^6, R^8 and R^9 may not he hydrogen atom) and one of R^8 and R^9 is pyrrolidinyl, piperidinyl or

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

azetidinyl, each of which is attached to the phenyl ring via a carbon atom."

Para 50 of the replication filed by the plaintiff reiterates this contention, thus:

"The contents of para 33 of the written statement are mere denials and merit no response except for the fact that the contention that the compound Ceritinib is disclosed by the prior patents. It is denied that Ceritinib is disclosed in any of the prior patents including IN 240560 and IN 232653. At the cost of repetition, it is submitted that compounds of Formula 2 of the suit patent including Ceritinib are novel & inventive and not disclosed in any of the patents obtained by Astrazeneca or Rigel of the Plaintiff No. 1's earlier patents being patent IN 240560 and IN 232653 itself. A Genus claim may cover large number of compounds. However, in absence of specific examples or specific disclosure, any subsequent compound embraced by a Genus claim, but innovated and developed subsequently which is novel and inventive over the prior disclosure, is entitled to independent patent protection. There is no compound disclosed in any of the prior art wherein the phenyl group attached to Pyrimidine ring at the second position is tri-substituted (i.e. R^6, R^8 and R^9 may not be hydrogen atom) and one of R^8 and R^9 is pyrollidinyl, piperidinyl and azetidinyl, each of which is attached to the phenyl ring via a carbon atom."

Specifically with reference to US'964/WO'654, the replication avers thus:

"It is submitted that the Astrazeneca Patent does not disclose Ceritinib. WO'654 discloses a broad genus of substituted pyrimidines. It is submitted that WO'654 contains a Markush claim thereby claiming compounds having inhibitory activity on CDK kinase. However, the said patent does not disclose either the compound of Formula 2 or the new chemical entity Ceritinib, subject matter of the suit patent. Furthermore, the structures of Formula 2 and Ceritinib are not disclosed in any manner in the Astrazeneca Patent. The AstraZeneca Patent does not specifically identify structural feature of a carbon-carbon bond between the N^2-phenyl ring and its heretocyclic substituent, as found in Ceritinib and the compounds of Formula 2 of IN 276026."

45. Novartis disclaims that the plea of obviousness, as urged by Natco, is based only on cherry-picking of select substituents from the

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

suggested substitutions in the alleged prior art Markush patents. The written submissions of Novartis urge, in this regard, as under:

> "**Obviousness.**
>
> The plea of obviousness is misconceived and untenable as the same is based on 'cherry picking' and 'hindsight analyses' of the suit patent which is not a permissible test of obviousness.
>
> All the prior art citations of the Defendant are for Markush class of compounds with laundry list of multiple substituents at variable positions. None can arrive at the equivalent from the teaching of such prior art. None of the prior art teaches the inventive step subject matter of the compound of suit patent stated hereinabove.
>
> The prior art class of compound do not make Ceritinib obvious to an unimaginative and uninventive person of ordinary skill in the art. There is no suggestion of motivation in the prior art citations to select a disubstituted Pyrimidine compound linked to phenyl ring via amino group at second position which is further trisubstituted with either Pyrrolidinyl or Piperidinyl or Azetidinyl linked to phenyl ring via carbon atom."

Mr Hemant Singh cites, in support,

(i) paras 25 and 26 of ***Bishwanath Prasad v. H.M. Industries***[17],

(ii) paras 139, 142, 144, 145 to 152, 154 to 156 and 158 of ***Roche***[4],

(iii) paras 112 and 113 of the judgement of a learned Single Judge of this Court in ***Merck Sharp & Dohme Corporation v. Glenmark Pharmaceuticals Ltd***[18] ("***Merck-I***" hereinafter),

(iv) paras 457 and 471 of the judgement of the Federal Court of Australia in ***Eli Lilly & Co. Ltd v. Apotex Pty Ltd***[19],

(v) paras 57, 64, 66 and 74 of ***Dr Reddy-II***[12],

(vi) ***Takeda Chemical Industries v. Alphapharm***[20],

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[17] **AIR 1982 SC 1444**
[18] **2015 (64) PTC 417 (Del)**
[19] **[2013] FCA 214**

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

(vii) para 36 of the judgment of a learned Single Judge of this Court in ***Bristol Myers Squibb Holdings Ireland Unlimited Company v. BDR Pharmaceuticals International Pvt Ltd***[21],

(viii) paras 353 to 355, 360 and 362 of the decision of the House of Lords in ***Technograph Printed Circuits Ltd v. Mills & Rockley (Electronics) Ltd***[22] and

(ix) the decision of the Court of Appeal in ***Windsurfing International Inc v Tabur Marine (Great Britain) Ltd***[23].

46. These submissions, therefore, apply *mutatis mutandis* to the Rigel patents US'276, US'430, US'204 and US'112 as well.

47. Answering Natco's reliance on the fact that Novartis had obtained licenses from Astrazeneca and Rigel for granting it "freedom to operate" their patents, Mr. Hemant Singh submits that the licenses were taken only because the patents of Astrazeneca and Rigel also contain a tri-substituted core pyrimidine ring with substitutions, via amine radicals at positions 2 and 4. He, however, reiterates that neither Formula 2 in the suit patent, nor Ceritinib was disclosed in any of the patents of Astrazeneca and Rigel. In fact, even to reach Ceritinib from the Markush structure at Formula 2 in the suit patent, Mr. Hemant Singh points out that there would have to be select substitutions at points R^1 to R^9, out of the several substitutions suggested in the Markush structure forming Formula 2. By effecting such select substitutions, he submits that Novartis was able to reach Ceritinib, also claimed in the suit patent as Claim 4.

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[20] **492 F. 3d. 1350 (2007)**
[21] **MANU/DE/0299/2020**
[22] **[1972] RPC 346**
[23] **[1985] RPC 59**

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

48. Learned Senior Counsel for Natco, needless to say, dispute these contentions. They contend that IN'653 clearly covers Claim 1 in the suit patent, and, for the purpose, have provided a side-by-side comparison of Claim 1 in IN'653 and Claim 1 in the suit patent in para 34 of the written statement.

49. They further contend that US'964/WO'654 also has a pyrimidine ring linked to a trisubstituted phenyl ring which displays anti-cancer properties. Para 31 of the written statement avers, in this context, as under:

> "… As admitted by the Plaintiff, many other entities such as Astrazeneca, Rigel and the Plaintiff themselves had obtained patents for compounds that have anticancer effect and which are structurally similar and/or identical to ceritinib. Ceritinib is squarely covered by the patent US 7153964, which is issued to Astrazeneca. It is pertinent to note that Astrazeneca has not filed any equivalent patent for the compounds covered by US'964 in India. This is a material fact and a very important fact, which is wilfully suppressed by the Plaintiff in the present suit. The averments in this paragraph made by the Plaintiff also make it clear that ceritinib is covered by US'276, US'430, US'204 and US'112. It is denied that the Rigel patents do not cover or disclose the compound ceritinib. Because, Rigel patents covered ceritinib, Rigel had filed suit for infringement against Novartis. Because, the patents granted to Astra and Rigel covered and claimed ceritinib, the Plaintiff was forced to seek license from these two entities, admitting that Plaintiff's product ceritinib is covered by the aforesaid patents. However, to cover up for such admission, the Plaintiff states that it got the licences for a 'freedom to operate'. The grant of patents to the Plaintiff despite the fact that Astra and Rigel patents were granted does not demonstrate its validity. In fact, these patents nor the act of the Plaintiff obtaining licenses was disclosed by the Plaintiff to any of the patent offices, which resulted in the Plaintiff obtaining three patents for the same compound, which is not countenanced by Indian law."

50. Relying on the judgement of the Supreme Court in ***Novartis AG v. U.O.I.***[24] ***(***hereinafter ***'Novartis-I')***, it is contended that "coverage"

[24] **(2013) 6 SCC 1**

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

cannot be distinguished from "disclosure". Inasmuch as Novartis has admitted coverage of Ceritinib, and of Formula 2 in the suit patent, by the prior art, Natco submits that, *ipso facto*, disclosure also stands admitted. Natco, therefore, pleads a Gillette defence[25], statutorily engrafted in Section 107 read with Section 64(1) of the Patents Act.

IV. The New Drug Application (NDA), listings in the Orange Book and the Patent Term Extension (PTE) Application of Novartis

51. Novartis sought patent term extension (PTE) for US'592 (which is the US equivalent of IN'653) under 35 U.S.C § 156[26], citing ZYKADIA as the "Approved Product". The relevant recitals, in the application, may be reproduced thus:

> "IN RE. U.S. PATENT NO. 7,964,592
>
> ISSUED: June 21, 2011
>
> INVENTORS: Garcia-Echeverria et al.

[25] derived from the following classic exposition of Lord Moulton in **Gillette Safety Razor Co. v. Anglo American Trading Co. Ltd, [1913] 30 RPC 465:**

> "I am of the opinion that in this case the defendant's right to succeed can be established without an examination of the terms of the specification of the plaintiff's letters patent. I am aware that such a mode of deciding a patent case is unusual, but from the point of view of the public it is important that this method of viewing their fights should not be overlooked. In practical life it is often the only safeguard to the manufacturer. It is impossible for an ordinary member of the public to keep watch on all the numerous patents which are taken out and to ascertain the validity and scope of their claims. But he is entitled to feel secure if he knows that that which he is doing differs from that which has been done of old only in non- patentable variations such as the substitution of mechanical equivalents or changes of material, shape or size. The defense that 'the alleged infringement was not novel at the date of the plaintiff's letters patent,' is a good defense in law, and it would sometimes obviate the great length and expense of patent cases if the defendant could and would put forth his case in this form, and thus spare himself the trouble of demonstration on which horn of the well-known dilemma the plaintiff had impaled himself, invalidity or non-infringement."

[26] § 156. **Extension of patent term –**

> (a) The term of a patent which claims a product, a method of using a product, or a method of manufacturing a product shall be extended in accordance with this section from the original expiration date of the patent, which shall include any patent term adjustment granted under section 154(b), if –
>
> *****
>
> (4) the product has been subject to a regulatory review period before its commercial marketing or use;
>
> *****
>
> The product referred to in paragraphs (4) and (5) is hereinafter in this section referred to as "the approved product".

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Signing Date:11.01.2023
18:30:36

FOR: 2,4-DI (PHENYLAMINO) PYRIMIDINES USEFUL IN THE TREATMENT OF NEOPLASTIC DISEASES, INFLAMMATORY AND IMMUNE SYSTEM DISORDERS

PATENT TERM EXTENSION APPLICATION UNDER 35 U.S.C. § 156

Sir:

Pursuant to 35 U.S.C. § 156 and 37 C.F.R. § 1.710 *et seq*, Novartis AG ("Applicant"), a Corporation organized under the laws of Switzerland, hereby requests an extension of the patent term *due to regulatory review of U.S. Patent No. 7,694,592*, which was granted on June 21, 2011.

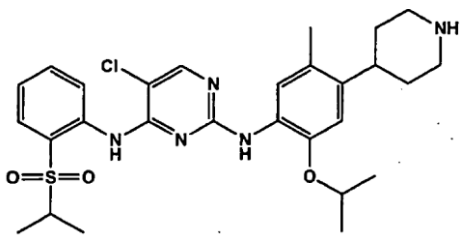
*****

In accordance with 35 U.S.C. § 156 and 37 C.F.R. § 1.740, Applicant provides the following information in support of its request for a patent term extension. The following sections are numbered analogously to 37 C.F.R. § 1.740.

1. Identification of the Approved Product

The approved product is ZYKADIA™ (generic name: ceritinib), a tyrosine kinase inhibitor for oral administration that is indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to Crizotinib. The active ingredient in ZYKADIA™, ceritinib, has a chemical name 5-chloro-N2-(2-isoproproxy-5-methyl-4-(piperidin-4-yl) phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2,4-diamine. An alternative chemical name is 5-chloro-N4-[2-[(1-methylethyl) sulfonyl] phenyl]-N2-[5-methyl-2-(1-methylethoxy)-4-(4-piperidinyl) phenyl0-2,4-pyrimidinediamine.

The molecular formula of ceritinib is $C_{28}H_{36}N_5O_3ClS$. The molecular weight of ceritinib is 55814 g/mole. The chemical structure of ceritinib is:



*****

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Signing Date:11.01.2023
18:30:36

6. Identification of Patent for which Extension is Sought

This application seeks to extend the term of U.S. Patent No. 7,964,592, which issued June 21, 2011 to Garcia-Echeverria et al, the term of which would otherwise expire on January 13, 2027.

*****

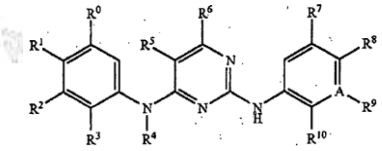
9. A statement that the patent claims the approved product, or a method of using or manufacturing the approved product, and a showing which lists each applicable patent claim and demonstrates the manner in which at least one such patent claim reads on: (i) the approved product, if the listed clais include any claim to the approved product; (ii) the method of using the approved product, if the listed claims include any claim to the method of using the approved product; and (iii) the method of manufacturing the approved product, if the listed claims include any claim to the method of manufacturing the approved product.

U.S. Patent No. 7,964,592 claims the approved product, a method of manufacturing the approved product, and a method of using the approved product. *Claims 1-4, 7-10, 14, and 15 read on the approved product. Claim 13 reads on a method of manufacturing the approved product. Claim 16 reads on a method of using the approved product*.

Approved product:

Claim 1. A compound of formula I

(I)



"each of R^0 or R^2 independently is hydrogen, C_1-C_8alkyl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, C_1-C_8alkoxy, unsubstituted or substituted heterocyclyloxy, unsubstituted or substituted, heterocyclyl C_1-C_8alkoxy, unsubstituted or substituted amino or halogen;

R^1 is hydrogen, C_1-C_8alkyl, haloC_1-C_8alkyl unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, C_1-C_8alkoxy, unsubstituted or substituted heterocyclyloxy, unsubstituted or substituted,

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

Heterocyclyl C_1-C_8alkoxy, unsubstituted or substituted amino or halogen;

R^3 is C_1-C_8alkylsulfinyl, C_1-C_8alkylsulfonyl, C_5-C_{10}arylsulfonyl or unsubstituted or substituted carbamoyl;

R^4 is hydrogen:
R^5 is chloro or bromo;
R^6 is hydrogen:

each of R^7 and R^9 independently is hydrogen, C_1-C_8alkyl, haloC_1-C_8alkyl, unsubstituted or substituted C_5-C_{10}aryl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, C_1-C_8 alkoxy, unsubstituted or substituted heterocyclyloxy, unsubstituted or substituted heterocyclyl, C_1-C_8alkoxy, unsubstituted or substituted amino, halogen, unsubstituted or substituted carbamoyl or unsubstituted or substituted sulfamoyl:

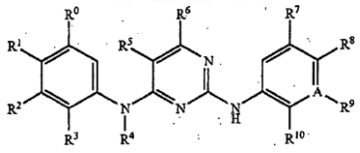
R^8 is C_5-C_{10}aryl: unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S: C_5-C_{10}aryloxy: unsubstituted or substituted heterocyclyloxy: or unsubstituted or substituted heterocyclyl C_1-C_8alkoxy: and

$R^{10}$is C_1-C_8alkyl, haloC_1-C_8alkyl, C_1-C_8alkoxy, unsubstituted or substituted heterocyclyl C_1-C_8alkoxy, unsubstituted or substituted amino, or halogen; and

A is C:

or salt thereof:*"*

Claim 1 *reads on* the approved product, *because ceritinib is the compound of claim 1 when, in formula (I)*:



"each of R^0 and R^2 is hydrogen;

R^1 is hydrogen;

R^3 is C_1-C_8alkylsulfonyl;

R^4 is hydrogen;

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

R^5 is chloro;

R^6 is hydrogen;

R^7 and R^9 are, respectively, C_1-C_8alkyl and hydrogen;

R^8 is unsubstituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S,

R^{10} is C_1-C_8alkoxy; and

A is C"

52. While applying for New Drug Approval (NDA) with the US FDA in accordance with 21 U.S.C. § 355(b)(1) for ZYKADIA, Novartis listed, in the cited patents, all the prior art, i.e. the plaintiff's US'592 and US'074 patents, Astrazeneca's US'964 patent and Rigel's US'276, US'430, US'204 and US'112 patents. The averment to this effect, as contained in para 13.5 of the plaint, reads thus:

> "13.5 The U.S. Food and Drug Administration ("FDA") publication, "Approved Drug Products with Therapeutic Evaluations, also known as the "Orange Book," lists FDA-approved drug products along with patent and regulatory exclusivity information. The patent information is provided by the entity filing a new drug application or "NDA" in accordance with 21 U.S.C. § 355(b)(1): "The applicant shall file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." Accordingly, applicants for new drug approval are required to submit information on patents having claims with respect to which a claim of patent infringement could be made against an unauthorized manufacturer, user, or seller of the drug. A patent claiming a genus of compounds encompassing the active molecule in an approved drug product can be listed in the Orange Book just as a patent that specifically claims the active molecule by its chemical structure or name. This is the case for the Orange Book entry for Zykadia (Ceritinib) which lists both (i) the Astra Zeneca and Rigel patents disclosing and claiming genera encompassing, but not describing, Ceritinib, and

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

(ii) the IRM/Plaintiffs patents specifically disclosing and claiming Ceritinib.

Under the U.S law, listing of patents in the Orange Book facilitates the resolution of patent disputes raised by generic applicants under 21 U.S.C. § 355(b)(2) for a "Paper NDA" or 21 U.S.C. § 355(j) for an abbreviated new drug application or "ANDA." In particular, generic applicants seeking FDA marketing approval prior to the expiration date of an Orange Book-listed patent are required to certify "that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted" and provide notice to the NDA owner of its certification, known as a "Paragraph IV" certification. § 355(b)(2)(A)(IV), § 355(j)(2)(A)(vii)(IV). If the NDA owner files an infringement action within 45 days of the receipt of such notice, FDA approval of the generic application is stayed for a period of 30 months while the patent dispute is litigated. § 355(c)(3), § 355(j)(5)(iii). This statutory mechanism provides for the litigation of both patents having only genus claims encompassing an active molecule and of patents which specifically disclose and claim the active molecule as both types of patents can be the subject of a claim of patent infringement by an NDA owner against an applicant seeking FDA approval to make a generic version of the NDA owner's drug product."

53. Natco, in its written statement, urges that, by having applied for PTE for US'592 citing Ceritinib to be the approved product, Novartis had acknowledged the fact that US'592 claims Ceritinib. Indeed, point out learned Senior Counsel for Natco, specific assertion to the effect that US'592 claims Ceritinib, is found at more than one place in the PTE application.

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

54. The written statement asserts, therefore, that the PTE application of Novartis "clearly identified and admitted that Ceritinib is covered by and forms part and parcel of US 7964592". Para 37 of the written statement reiterates this assertion thus:

> "37. As stated in the foregoing paragraph, the fact that ceritinib is covered by IN'653 is reinforced by the Plaintiffs own averments in the petition for term extension wherein the Plaintiff has sought extension of term on the basis and on the strength of the disclosure in IN'653 (US equivalent thereof being US 7964592)."

55. Para 28 of the written statement further asserts that Novartis had, in the Orange Book, listed listing the plaintiffs' US'592 and US'074 patents, Astrazeneca's US'964 patent and Rigel's US'276, US'430, US'204 and US'112 patents which constituted prior art and disclosed Ceritinib. By doing so, Novartis has, according to Natco, acknowledged, yet again, that the said prior art patents disclosed Ceritinib.

56. Novartis thus stands estopped, according to Natco, from contending that Ceritinib is not claimed or disclosed in IN'560 and IN'653 or in US'964, US'276, US'430, US'204 and US'112.

57. In its rejoinder, Novartis has, in respect of its PTE application for US'592, and the listing of the prior art patents by Novartis while seeking NDA approval and listing the patents in the Orange Book sought to clarify the position thus in its replication.

> "6. It is submitted that the Defendant has raised the issue in its written statement that the Plaintiff has identified that Ceritinib is covered by and forms part of US 7964592 (hereinafter referred to as '592) in the patent term extension (hereinafter referred to as PTE) filed by the Plaintiff for '592. It is submitted that the application for a PTE for the '592 Patent is not an admission that the '592 patent describes Ceritinib. Under the U.S. statute

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

providing for PTEs, 35 U.S.C. § 156(a), "the term of a patent which claims a product. . . shall be extended" if certain criteria are met. Accordingly, eligibility for a PTE is based on whether the claims of the patent "read on" or encompass the approved product, not whether the patent discloses or describes the specific compound.

7. It is submitted that the application for PTE filed with the USPTO for the '592 patent clearly demonstrates how the genus claims of that patent "read on" (i.e., encompass) Ceritinib, but only if certain specific substitutions are made out of vast multitude of substitutions disclosed in '592 patent. The application for PTE contains no admission that the '592 patent discloses or describes the molecule Ceritinib itself.

8. It is submitted that under U.S. law, although ultimately only one patent may receive a PTE for a regulatory review period for any product (35 U.S.C. § 156(c) (4); 37 C.F.R. § 1.785(a), it is permissible for a patentee to file PTE applications for more than one patent with claims that "read on" the same product. However, when the applications for PTE are eligible for grant, the patentee must ultimately select only one patent to receive the PTE. Reference is made to 37 C.F.R. § 1.785. The patentee may apply for PTE and select any patent that has a claim that "reads on" or encompasses the approved drug product or a method of using the approved drug product, regardless of whether the patent discloses the specific compound contained in the approved drug product. Thus, as discussed above, an application for PTE is only probative of the fact that a patent contains a claim that encompasses or "reads on" the approved product, not that the patent discloses the specific chemical molecule contained in that product, and mere filing of the PTE application is not any implication or admission of specific disclosure.

9. The specification of a U.S. patent may disclose subject matter specifically or via a genus that contains within the genus certain substitutions that are not otherwise specifically disclosed. In the U.S., a first patent that discloses a genus of significant size may be supported by a few specific examples that are related to one or more species within the scope of the genus and not have any specific disclosure with respect to other substitutions that are within the scope of the genus. A subsequent patent claiming a narrower range or "sub-genus" of substitutions that are not specifically disclosed in the first patent may perfectly well co exist and be valid as to such narrower sub-genus.

10. Under U.S. law, Novartis was required to list all the patents in the Orange Book and also permitted to apply for PTEs with respect to patents that "read on" or "encompass" or "cover"

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

> Ceritinib (1) by genus claims contained in patents though do not disclose Ceritinib itself and (2) by claims that specifically claim Ceritinib contained in patents that specifically disclose Ceritinib itself.
>
> 11. A claim of patent infringement could reasonably be asserted" against the unlicensed "manufacture, use, or sale of Ceritinib" because the genus claims of the '592 Patent, encompass or "read on" the compound Ceritinib, without specifically disclosing the compound Ceritinib. Thus, the application for PTE contains no admission that the '592 patent discloses or describes the molecule Ceritinib itself. In support of the above submissions, the Plaintiffs seek to place reliance on the affidavit of Mr. Irving Fishman, filed in the present proceedings."

58. Additionally, with respect to the application for PTE, para 22 of the replication avers as under:

> "22. The contents of Paragraph 5 of the written statement except that are matter of record are denied for being false and misleading. It is wholly misconceived and hence denied that in the application seeking extension of patent term of US 7964592, the Plaintiff has made any admission of Ceritinib being disclosed in US 7964592. It is submitted that the application for a PTE for the '592 Patent is not an admission that the '592 patent describes Ceritinib. Under the U.S. statute providing for PTEs, 35 U.S.C. § 156(a), "the term of a patent which claims a product…..shall be extended" if certain criteria are met. Accordingly, eligibility for a PTE is based on whether the claims of the patent "read on" or encompass the approved product, not whether the patent discloses or describes the specific compound. The extracts from the PTE and reliance thereof is out of context, misconceived and misleading. It is submitted that there is no bar in law to apply and protect a species patent which meets the criteria of patentability. The contents of the plaint and the preliminary submissions are reiterated herein and the same are not being repeated for the sake of brevity. Reference is also made to the affidavit Mr. Irving Fishman and the contents of the said affidavit may be read as part and parcel of reply to para under reply. The same are not repeated herein for the sake of brevity."

V. Patentability

59. Mr. Hemant Singh submits that patentability requires satisfaction of only three pre-requisites, namely, novelty, the existence of an inventive step and the capability of the invention to be put to an

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

industrial application. All these three criteria, he submits, stand satisfied in the case of the suit patent. He seeks to point out that, prior to the suit patent, Ceritinib was unknown and non-existent. As such, he submits that the defendant could not seek to contend that the suit patent was not vulnerable to revocation. Mr. Hemant Singh has also placed reliance, in this context, on Section 64(1) of the Patents Act, especially on Clauses (d), (e) and (f) thereof. It is only where one of the delimiting factors envisaged by Clauses (d), (e) and (f) of Section 64(1) would apply, submits Mr. Hemant Singh, that a suit patent could be held to be vulnerable to revocation. None of these circumstances, he submits, applies in the present case. Section 64(1)(d) does not apply, submits Mr. Hemant Singh, as Ceritinib satisfies the definition of "invention" as contained in Section 2(1)(j)[27], and is the product of an "inventive step" over prior art, within the meaning of Section 2(1)(ja)[9] of the Patents Act. Section 64(1)(e) would not apply, as the Markush Claim 1 in the suit patent, as well as Ceritinib, were novel *vis-à-vis* prior art. Section 64(1)(f) would not apply as neither Formula 2 nor Ceritinib could be said to be obvious from prior art, to a person's skilled in the art.

Analysis

60. The principles of law, with respect to the dispute and controversy are well settled. An authoritative pronouncement on the issue is to be found in the judgment of the Supreme Court in ***Novartis-I*** [24]. That decision has been considered in detail by this Court in its

[27] (j) "invention" means a new product or process involving an inventive step and capable of industrial application;

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

judgment in ***FMC Corporation v. Best Crop. Science LLP***[28] and ***Novartis AG v. Natco Pharma Limited***[29] (hereinafter "***Novartis-II***"). In fact, the issues in controversy, which arose for consideration in ***FMC Corporation***[28] and ***Novartis-II***[29], were more or less identical to those which arise in the present case, and the findings of this Court, in the said decisions – which remain undisturbed till date – cover the controversy herein.

A. Relevant statutory provisions

61. Section 6 of the Patents Act entitles any person, claiming to be the true and first inventor of an invention, to apply for a patent for an invention. A patent has, therefore, necessarily to be for an "invention".

61.1 "Invention" is defined, in Section 2(1)(j), as "a new product or process involving an inventive step and capable of industrial application". As such, Mr. Hemant Singh is correct in the submission that the three ingredients of an "invention" as envisaged by Section 2(1)(j) are (i) novelty, (ii) an inventive step and (iii) capability of industrial application.

61.2 The aspect of capability of industrial application need not detain us, not being one of the points on which the parties have chosen to join issue.

[28] **2021 SCC OnLine Del 3647**
[29] **2021 SCC OnLine Del 5340**

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

61.3 "Inventive step" is further defined in Section 2(1)(ja) as meaning "a feature of an invention that involves technical advance as compared to the existing knowledge or having economic significance or both and that makes the invention not obvious to a person skilled in the art". This definition, therefore, introduces the elements of "obviousness" and the "person skilled in the art". The judgment of the Division Bench of this Court in ***Roche***[4], clearly explained both these concepts, as has been noticed in detail by this Court in ***Novartis-II***[29]**.** In fact, several concepts, pivotal to the issue in controversy, stand clarified in the said decision. More detailed allusion, in this regard, is to follow.

61.4 From Section 11A, in Chapter IV, of the Patents Act commence the provisions dealing with the manner in which in which an application, seeking grant of a patent, is to be processed. Section 12 requires the application to be sent to the examiner for examination. Sub-sections (1) and (2) of Section 13[30] require the examiner to examine whether the patent is anticipated by prior publication or by prior claiming, is set out in Chapter IV of the Patents Act, comprising Sections Section 13 refers to the exercise to be undertaken by the examiner to whom an application for a patent is referred. The

[30] **13. Search for anticipation by previous publication and by prior claim**. –
(1) The examiner to whom an application for a patent is referred under Section 12 shall make investigation for the purpose of ascertaining whether the invention so far as claimed in any claim of the complete specification –
(a) has been anticipated by publication before the date of filing of the applicant's complete specification in any specification filed in pursuance of an application for a patent made in India and dated on or after the 1st day of January, 1912;
(b) is claimed in any claim of any other complete specification published on or after the date of filing of the applicant's complete specification, being a specification filed in pursuance of an application for a patent made in India and dated before or claiming the priority date earlier than that date.
(2) The examiner shall, in addition, make such investigation for the purpose of ascertaining whether the invention, so far as claimed in any claim of the complete specification, has been anticipated by publication in India or elsewhere in any document other than those mentioned in sub-section (1) before the date of filing of the applicant's complete specification.

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

examiner is required to investigate as to whether the invention claimed in the complete specification as set out in the application for grant of patent, is anticipated by prior publication or is anticipated by prior claiming. He has, in other words, to examine whether the invention has been anticipated by publication before the date of filing of the complete specification of the applicant or whether it has been claimed in any claim of any other complete specification published on or after the date of filing of the applicant's complete specification but of an earlier priority date. The report of the examiner, in terms of Section 13 has to be considered by the Controller of Patents under Section 14. If the Controller feels that the application does not comply with the requirements of the Patents Act or the Patents Rules, Section 15 empowers the Controller to refuse the application or require the application to be amended to his satisfaction. Sub-section (1)[31] of Section 18 deals with the procedure to be followed by the Controller where he feels that the claim in the suit patent is anticipated by prior publication, and sub-sections (2) and (3)[32] deal with the

[31] **18. Powers of Controller in cases of anticipation**. –

(1) Where it appears to the Controller that the invention so far as claimed in any claim of the complete specification has been anticipated in the manner referred to in clause (a) of sub-section (1) or sub-section (2) of Section 13, he may refuse the application unless the applicant –

(a) shows to the satisfaction of the Controller that the priority date of the claim of his complete specification is not later than the date on which the relevant document was published; or

(b) amends his complete specification to the satisfaction of the Controller.

[32] (2) If it appears to the Controller that the invention is claimed in a claim of any other complete specification referred to in clause (*b*) of sub-section (1) of Section 13, he may, subject to the provisions hereinafter contained, direct that a reference to that other specification shall be inserted by way of notice to the public in the applicant's complete specification unless within such time as may be prescribed, -

(a) the applicant shows to the satisfaction of the Controller that the priority date of his claim is not later than the priority date of the claim of the said other specification; or

(b) the complete specification is amended to the satisfaction of the Controller.

(3) If it appears to the Controller, as a result of an investigation under Section 13 or otherwise,—

(a) that the invention so far as claimed in any claim of the applicant's complete specification has been claimed in any other complete specification referred to in clause (a) of sub-section (1) of Section 13; and

(b) that such other complete specification was published on or after the priority date of the applicant's claim,

then, unless it is shown to the satisfaction of the Controller that the priority date of the applicant's claim is not later than the priority date of the claim of that specification, the provisions of sub-section (2) shall apply thereto in the same manner as they apply to a specification published on or after the date of filing of the applicant's complete specification.

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

procedure to be followed where the invention is anticipated by prior claiming. These provisions are not strictly relevant for our purpose, since all patents in controversy are granted patents. What is relevant, therefore, is only the right of the Controller to refuse to grant an application for a patent on the ground that the patent is anticipated either by prior publication or by prior claiming.

61.5 Section 19[33] of the Patents Act is, however, of significance, as it permits patenting of an infringing patent. Infringement of an already existing patent is, not, therefore, a bar to registration. The applicant is only required to insert, in the patent, a reference to the earlier patent. This provision, therefore, underscores the difference between "infringement" and "obviousness" or "anticipation". Anticipation and obviousness are, therefore, inhibitors to registration, whereas potential infringement of an existing patent is not.

61.6 Chapter VI of the Patents Act deals with "anticipation", and comprises Sections 29 to 34. These provisions, however, do not explain "anticipation", or elucidate circumstances in which anticipation *takes place*, but, rather, stipulate, negatively,

[33] **19. Powers of Controller in case of potential infringement**. –
(1) If, in consequence of the investigations required under this Act, it appears to the Controller that an invention in respect of which an application for a patent has been made cannot be performed without substantial risk of infringement of a claim of any other patent, he may direct that a reference to that other patent shall be inserted in the applicant's complete specification by way of notice to the public, unless within such time as may be prescribed –
(a) the applicant shows to the satisfaction of the Controller that there are reasonable grounds for contesting the validity of the said claim of the other patent; or
(b) the complete specification is amended to the satisfaction of the Controller.
(2) Where, after a reference to another patent has been inserted in a complete specification in pursuance of a direction under sub-section (1) –
(a) that other patent is revoked or otherwise ceases to be in force; or
(b) the specification of that other patent is amended by the deletion of the relevant claim; or
(c) it is found, in proceedings before the court or the Controller, that the relevant claim of that other patent is invalid or is not infringed by any working of the applicant's invention,
the Controller may, on the application of the applicant, delete the reference to that other patent.

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

circumstances in which a patent would *not* be bad on account of anticipation. They are, therefore, in the form of negative covenants. Of these, Section 29[34] enumerates circumstances in which an invention would *not* be regarded as having been anticipated by prior publication. Clearly, none of the said extenuating circumstances applies to the present case.

61.7 Where the application for grant of a patent does not suffer from any of these disabilities, the patent is mandatorily to be granted, under Section 43(1)[35].

[34] **29. Anticipation by previous publication**. –

(1) An invention claimed in a complete specification shall not be deemed to have been anticipated by reason only that the invention was published in a specification filed in pursuance of an application for a patent made in India and dated before the 1st day of January, 1912.

(2) Subject as hereinafter provided, an invention claimed in a complete specification shall not be deemed to have been anticipated by reason only that the invention was published before the priority date of the relevant claim of the specification, if the patentee or the applicant for the patent proves –

(a) that the matter published was obtained from him, or (where he is not himself the true and first inventor) from any person from whom he derives title, and was published without his consent or the consent of any such person; and

(b) where the patentee or the applicant for the patent or any person from whom he derives title learned of the publication before the date of the application for the patent, or, in the case of a convention application, before the date of the application for protection in a convention country, that the application or the application in the convention country, as the case may be, was made as soon as reasonably practicable thereafter:

Provided that this sub-section shall not apply if the invention was before the priority date of the claim commercially worked in India, otherwise than for the purpose of reasonable trial, either by the patentee or the applicant for the patent or any person from whom he derives title or by any other person with the consent of the patentee or the applicant for the patent or any person from whom he derives title.

(3) Where a complete specification is filed in pursuance of an application for a patent made by a person being the true and first inventor or deriving title from him, an invention claimed in that specification shall not be deemed to have been anticipated by reason only of any other application for a patent in respect of the same invention made in contravention of the rights of that person, or by reason only that after the date of filing of that other application the invention was used or published, without the consent of that person, by the applicant in respect of that other application, or by any other person in consequence of any disclosure of any invention by that applicant.

[35] **43. Grant of patents**. –

(1) Where an application for a patent has been found to be in order for grant of the patent and either –

(a) the application has not been refused by the Controller by virtue of any power vested in him by this Act; or

(b) the application has not been found to be in contravention of any of the provisions of this Act,

the patent shall be granted as expeditiously as possible to the applicant or, in the case of a joint application, to the applicants jointly, with the seal of the patent office and the date on which the patent is granted shall be entered in the register.

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

61.8 Though it is not, in my view, strictly relevant to the issue at hand, Mr Hemant Singh, arguing for Novartis, also invoked Section 54(1)[36], which deals with "Patents of addition". The provision allows an applicant, who applies for a patent for improvement or modification of an invention already disclosed in prior art, to apply for a "patent of addition", of the already patented invention.

61.9 Section 64 deals with the circumstances, in which a granted patent may be revoked, and clauses (a), (d), (e) and (f) thereof, which alone are relevant, already stand extracted *supra*[8].

61.10 Chapter XVIII of the Patents Act deals with "Suits concerning Infringement of Patents", and comprises Sections 104 to 115. Of these, Section 107(1), which alone is relevant to the controversy at hand, allows every ground on which a granted patent may be revoked under Section 64 to be available as a ground for defence to a suit alleging infringement.

61.11 This, then, is the statutory scenario within which the present dispute peregrinates.

B. <u>The judgement in ***Roche***[4]</u>

62. The Division Bench in ***Roche***[4] held that, when examining patentability of a product, the authority was first required to apply

[36] **54. Patents of addition**. –
(1) Subject to the provisions contained in this section, where an application is made for a patent in respect of any improvement in or modification of an invention described or disclosed in the complete specification filed therefor (in this Act referred to as the "main invention") and the applicant also applies or has applied for a patent for that invention or is the patentee in respect thereof, the Controller may, if the applicant so requests, grant the patent for the improvement or modification as a patent of addition.

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

Section 3(d) to ascertain whether the product was prohibited from patentability under the said provision. If Section 3(d) did not apply, the product became entitled to be considered for grant of patent by applying Sections 2(1)(j) and (ja). It was not as though, therefore, by escaping Section 3(d), the product became, *ipso facto*, entitled to a patent. It had, thereafter, to be tested on the anvil of Section 2(1)(j) and (ja). Thus, held the Division Bench, Section 3(d) could not be regarded as an exception to Section 2(1)(j) or (ja).

62.1 ***Roche***[4] thereafter went on to explain the concept of an "active pharmaceutical ingredient" (API). It was held that APIs were the molecular entities that exerted the therapeutic effects of medicines and were biologically active. Patent protection was, ordinarily, granted to the API. Where the API was patented, any product of the API, in any form, stood protected. Any manufacture or marketing, by a third party, of such a product/derivative of the API would, therefore, infringe the patent granted to the API. Section 3(d), it was held, envisaged a variety of derivatives of known substances. Among these were (i) prodrugs, which were not active in themselves, but were metabolised in the body to form active drugs, (ii) compositions consisting of combinations of two or more APIs or a combination of a pharmaceutical carrier with a compound not used as a drug prior thereto and (iii) a drug delivery system, which was a composition which enabled its constituents to be administered in a particular way.

62.2 Claim construction, it was held, was pivotal to the examination of any infringement action. Having referred to various authorities, including ***Novartis-I***[24]**,** the judgement of a Division Bench of this

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

Court in ***Merck Sharp & Dohme Corportion v. Glenmark Pharmaceuticals***[37] ("***Merck-II***" hereinafter)**,** ***Edward H. Phillips* v. *AWH Corporation***[38], ***Pfizer* v. *Ranbaxy***[39] ("***Pfizer-I***", hereinafter) and ***Glaverbel SA* v. *British Coal Corporation***[40], the Division Bench enumerated the salient principles of claim construction with which, we, in the present case, need not be concerned, as no issue, regarding the manner of construction of the claims in question, is in controversy.

62.3 Additionally, the Division Bench held, relying on ***Merck-II*** and ***Glaverbel***, that the claim was required to be interpreted on its own language, and not by reference to subsequent conduct or prior material.

62.4 Examination of any infringement action would, it was held relying on ***Herbert Markman v. Westview***[41], require the Court, in the first instance, to determine the meaning and scope of the claims in the suit patent, applying the above principles of claim construction and, in the second, to compare the claim, thus deconstructed, with the allegedly infringing product or device. The Division Bench was at pains to observe that examination of an infringement claim involved a comparison of the product of the defendant with the claim of the plaintiff. What was required, therefore, was a product to patent comparison, and not a product-to-product comparison. In fact, the Division Bench held that one of the errors in the judgment of the learned Single Judge was that it proceeded on a product-to-product comparison, instead of a product-to-patent comparison.

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[37] **2015 (63) PTC 257 (Del) (DB)**
[38] **415. F. 3d. 1303**
[39] **457 F. 3d. 1284**
[40] **1995 RPC 255**
[41] **517 US 370 (1996)**

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

62.5 The Division Bench, thereafter, went on to comment on the usefulness of X-ray diffraction in examining patent infringement claims. In product patent infringement cases, it was held that X-ray diffraction was of little utility, as what was required was to compare the defendant's product with the plaintiff's patent, and the coverage of the latter. Had the suit patent claimed the polymorphic form of Erlotinib Hydrochloride, X-ray diffraction, it was observed, might have been of some use in estimating whether the polymorphic form which was marketed by Cipla was infringing the polymorphic form of Erlotinib Hydrochloride, in respect of which Roche held the patent, by comparing the defendant's product which the product disclosed in the suit patent. Where, however, the suit patent disclosed and claimed Erlotinib Hydrochloride *per se*, and infringement was alleged thereof, X-ray-diffraction, it was found, was of little utility. By concentrating on X-ray diffraction results, the Division Bench found that the learned Single Judge had erred in failing to apply the correct test, which was an examination of the scope of the suit patent IN 774, to ascertain whether it would encompass the product of the defendant.

62.6 As Cipla's product was a polymorphic form of Erlotinib Hydrochloride, which was claimed in the suit patent IN 774, the Division Bench held that Cipla had infringed the suit patent.

62.7 The decision thereafter went on to explain the principles of obviousness and the person skilled in the art.

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

62.8 On the aspect of obviousness, the Division Bench endorsed the following "triple test of obviousness", as postulated by the US Supreme Court in ***KSR International***[42]:

> "Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or non-obviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented."

62.9 Additionally, in paras 150 and 151 of the report, the Division Bench relied on ***Windsurfing***[23] and ***Eisai Co. Ltd***[43], thus:

> "150. In ***Windsurfing International Inc*** the Court of Appeals noted the four steps to answer the question of obviousness which were followed in ***Pozzoli SPA v. BDMO SA***[44] as under:—
>
> > "(i) identifying the inventive concept embodied in the patent;
> >
> > (ii) imputing to a normally skilled but unimaginative addressee what was common general knowledge in the art at the priority date;
> >
> > (iii) identifying the differences if any between the matter cited and the alleged invention; and
> >
> > (iv) deciding whether those differences, viewed without any knowledge of the alleged invention, constituted steps which would have been obvious to the skilled man or whether they required any degree of invention."
>
> 151. In ***Eisai Co. Ltd.***[43] the Board of Appeals of European Patent Office applying the problem solution approach which consists essentially in (a) identifying the closest prior art, (b) assessing the technical results (or effects) achieved by the claimed invention when compared with the closest state of the art established, (c) defining the technical problem to be solved as the object of the invention to achieve these results, and (d) examining whether or not a skilled person starting from the closest prior art

[42] **550 US 398 (2007)**
[43] **16 USPQ.2d 1897**
[44] **566 F.3d 999 (2009)**

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

> "would" arrive at something falling within claim by following the suggestion made in the prior art held that when deciding upon inventive step in relation to pharmacologically active compounds it is not essential whether a particular substructure of a compound could be replaced by another known isosteric one, but whether information was available on the impact of such a replacement on the pharmacological activity of the specific group of compounds concerned."

62.10 Even so, the Division Bench echoed the note of caution, sounded by the High Court of Bombay in ***F.H. & B. v. Unichem***[45], against regarding a patent as invalid on the ground of obviousness by resorting to hindsight analysis or reconstruction, using the teaching in the suit patent itself as a guide to reach the suit patent. The Division Bench also endorsed the observation in ***Pfizer Inc. v. Teva Pharmaceuticals***[46] ("***Pfizer-II***", hereinafter) that "a patent challenger however must demonstrate the selection of a lead compound based on its promising and useful properties, not a hindsight driven search for structurally similar compounds". These authorities, it was held, identified the following inquiries, which were required to be conducted while examining the claim of obviousness/lack of inventive steps:

> "Step No. 1 - To identify an ordinary person skilled in the art,
>
> Step No. 2 - To identify the inventive concept embodied in the patent,
>
> Step No. 3 - To impute to a normal skilled but unimaginative ordinary person skilled in the art what was common general knowledge in the art at the priority date.
>
> Step No. 4 - To identify the differences, if any, between the matter cited and the alleged invention and ascertain whether the differences are ordinary application of law or involve various different steps requiring multiple, theoretical and practical applications,

[45] **AIR 1969 Bom 255**
[46] **410 F. 3d. 1358**

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

> Step No. 5 - To decide whether those differences, viewed in the knowledge of alleged invention, constituted steps which would have been obvious to the ordinary person skilled in the art and rule out a hideside (*sic* hindsight) approach."

62.11 Thus, it was held, "to show obviousness besides structural similarity there should be a reason or motivation shown in the prior art to make the particular structural change in order to achieve the properties that the applicant was seeking". The following passages from the judgment of the Court of Appeals in ***Pfizer-II***[46] were cited, with emphasis:

> "The determination of obviousness is a legal conclusion based on underlying facts. ***Allergan, Inc. v. Sandoz Inc.***[47]. After a bench trial, we review the district court's factual findings for clear error and its conclusions of law de novo. ***Honeywell Int'l, Inc. v. United States***[48]. A patent claim is invalid for obviousness if "the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains." 35 U.S.C. § 103. The "underlying factual considerations in an obviousness analysis include the scope and content of the prior art, the differences between the prior art and the claimed invention, the level of ordinary skill in the art, and any relevant secondary considerations[,]" which include "commercial success, long-felt but unsolved needs, failure of others, and unexpected results." Allergan, 726 F.3d at 1290-91 (citations omitted). Patent invalidity must be established by clear and convincing evidence. ***Microsoft Corp. v. i4i Ltd. P'ship***[49]**,**.
>
> Whether a new chemical compound would have been prima facie obvious over particular prior art compounds follows a two-part inquiry under our precedent. First, the court determines whether a chemist of ordinary skill in the art would have selected the asserted prior art compound as a lead compound, or starting point, for further development. ***Eisai Co. v. Dr. Reddy's Labs., Ltd.,***. A lead compound is a compound in the prior art that would be "most promising to modify in order to improve upon its activity and obtain a compound with better activity." ***Takeda Chem. Indus., Ltd. v. Alphapharm Pty. Ltd..*** The selection analysis may

47 726 F.3d 1286, 1290-91 (Fed. Cir. 2013)
48 609 F.3d 1292, 1297 (Fed. Cir. 2010)
[49] 131 S.Ct. 2238, 2242 (2011)

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

> be guided by evidence of the compound's pertinent properties, such as chemical activity or potency. See ***Eli Lilly & Co. v. Zenith Goldline Pharm., Inc.***[50]**.** Mere structural similarity between a prior art compound and the claimed compound does not inform the lead compound selection**.** ***Otsuka Pharm. Co. v. Sandoz Inc.***[51]***;*** see ***Daichii Sankyo Co. v. Matrix Labs., Ltd.***[52]**.** Proof of obviousness of a chemical compound "clearly depends on a preliminary finding that one of ordinary skill in the art would have selected [a particular prior art compound] as a lead compound." *Takeda*, 492 F.3d at 1357. The second step of the obviousness analysis requires a showing that the prior art would have taught a skilled artisan to make "specific molecular modifications" to a lead compound so that the claimed compound may be made with a reasonable expectation of success. ***Id. at 1356-57.***"

62.12 ***Eli Lilly & Co.*** and ***Lilly Industries Ltd. v. Zenith Goldline Pharmaceuticals*** were cited, to reiterate the position that "to establish *a prima facie* case of obviousness based on a combination of elements in the prior art, the law requires a motivation to select the references and to combine them in the particular claimed manner to reach the claimed invention".

62.13 Having, thus, referred to earlier authorities on the point, the Division Bench concluded, on the aspect of obviousness, thus:

> "159**.** Thus though initially *'structural obviousness'* alone was deemed to create a presumption of unpatentability however the Courts expressing dissatisfaction with the Rule opined that the properties were also material to show unpatentability of new chemical and must be considered. Thus prior art disclosure should not merely be structurally similar compound but also at least to some degree demonstrate the same desired property which is relied on for the patentability of the new compound. In other words *'idea of new compounds is not separable from the properties that were sought by the inventor when making the compounds and structure and properties are essential compounds of the invention as a whole'.* (See In re: *Dillon*).

[50] 471 F.3d 1369, 1378 (Fed. Cir. 2006)
[51] 678 F3d 1280, 1292 (Fed. Cir. 2012)
[52] 619 F.3d 1346, 1354 (Fed. Cir. 2010)

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

> 160. Thus obviousness is a question of law based on facts and the burden to prove is on the party which alleges however after the party which alleges makes out a prima facie case of invalidity on the ground of obviousness, the burden shifts on the inventor to disprove obviousness."

62.14 In this context, the Division Bench also explained "the features of a person skilled in the art (as being) that of a person who practices in the field of endeavour, belongs to the same industry as the invention, possesses average knowledge and ability and is aware of what was common general knowledge at the relevant date".

62.15 The governing principle stands crystallized in the following brief exposition, as contained in para 24 of the report in ***Bishwanath Prasad***[17]:

> "24. The expression "does not involve any inventive step" used in Section 26(1)(e) of the Act and its equivalent word "obvious", have acquired special significance in the terminology of patent law. The "obviousness" has to be strictly and objectively judged. For this determination several forms of the question have been suggested. The one suggested by Salmond, L.J. in ***Rado v. John Two & Son Ltd.***[53] is apposite. It is: "Whether the alleged discovery lies so much out of the track of what was known before as not naturally to suggest itself to a person thinking on the subject, it must not be the obvious or natural suggestion of what was previously known."

In one breath, the decision in ***Rado***[53], as adopted with approval by the Supreme Court, identifies the crux of the enquiry into the aspect of obviousness of a patent *vis-à-vis* prior art, from the point or view of a person skilled in the art, as whether the specie patent is "the obvious or natural suggestion" *vis-à-vis* prior art, to "a person thinking on the subject". The person skilled in the art is, therefore, neither a dullard

[53] **[1967] RPC 297**

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

nor a genius. He is thinking on the subject, and, when thus thinking, the Court has to assess what would become "obvious or natural", to him, from the teachings in the known prior art.

62.16 Section 3(d) of the Patents Act excludes new forms of non-substances from the scope of the expression "invention". It stipulates that a new form of non-substance, which does not possess enhanced efficacy *vis-à-vis* the efficacy of the non-substance would not be an "invention". The clause, as it exists today, was the result of the substitution, by the Patents (Amendment) Act, 2005 w.e.f. 4th April 2005, of the pre-existing Section 3(d) and, as has been held by the Supreme Court in ***Novartis-I***, was specifically engrafted in order to deal with pharmaceutical patents. The Explanation to Section 3(d) clarifies that "salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance" would be considered to be the same substance. The concept of "efficacy", in the context of Section 3(d) and especially in the context of pharmaceutical patents, was explained by the Supreme Court in ***Novartis-I***. Paras 157 and 158 of the report in ***Novartis-I*** explained the concept thus:

> "157. What is "efficacy"? "Efficacy" means "the ability to produce a desired or intended result" [*The New Oxford Dictionary of English*, Edn. 1998.]. Hence, the test of efficacy in the context of Section 3(*d*) would be different, depending upon the result the product under consideration is desired or intended to produce. In other words, the test of efficacy would depend upon the function, utility or the purpose of the product under consideration. Therefore, in the case of a medicine that claims to cure a disease, the test of efficacy can only be "therapeutic efficacy". The question then arises, what would be the parameter of therapeutic efficacy and what are the advantages and benefits that may be taken into account for determining the enhancement of therapeutic efficacy? With regard to the genesis of Section 3(d), and more particularly the circumstances in which Section 3(d) was amended

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

> to make it even more constrictive than before, we have no doubt that the "therapeutic efficacy" of a medicine must be judged strictly and narrowly. Our inference that the test of enhanced efficacy in case of chemical substances, especially medicine, should receive a narrow and strict interpretation is based not only on external factors but there is sufficient internal evidence that leads to the same view. It may be noted that the text added to Section 3(d) by the 2005 Amendment lays down the condition of "enhancement of the known efficacy". Further, the Explanation requires the derivative to "differ significantly in properties *with regard to efficacy*". What is evident, therefore, is that not all advantageous or beneficial properties are relevant, but only such properties that directly relate to efficacy, which in case of medicine, as seen above, is its therapeutic efficacy.
>
> 158. While dealing with the Explanation it must also be kept in mind that each of the different forms mentioned in the Explanation have some properties inherent to that form e.g. solubility to a salt and hygroscopicity to a polymorph. These forms, unless they differ significantly in property with regard to efficacy, are expressly excluded from the definition of "invention". Hence, the mere change of form with properties inherent to that form would not qualify as "enhancement of efficacy" of a known substance. In other words, the Explanation is meant to indicate what is not to be considered as therapeutic efficacy."

"Efficacy", when applied to a pharmaceutical product in the context of Section 3(d) of the Patents Act has, therefore, necessarily to be "therapeutic efficacy". The product must, therefore, demonstrate "enhanced therapeutic efficacy", if it is one to which Section 3(d) is otherwise attracted. "Therapeutic efficacy" cannot, additionally, relates to properties already possessed by the "known substance", as was made apparent by the Explanation to Section 3(d)."

C. Is the suit patent vulnerable on the ground of anticipation by prior claiming or prior disclosure, and obviousness?

63. The rival contentions in the present case throw into relief the concepts of "claim", "coverage" and "disclosure". Natco does not

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

dispute the fact that it is actually manufacturing and dealing in Ceritinib without obtaining a license from Novartis. Para 109 of ***Roche*** merely requires a comparison of the suit patent with the defendant's product in order to assess whether the infringement has, or has not, taken place. The suit patent is undisputedly in favour of Novartis and is in respect of, *inter alia*, Formula 2 and Ceritinib. It is also a matter of fact – and learned Senior Counsel for Natco has not been able to demonstrate otherwise – that Ceritinib, specifically, has not been claimed in any prior art. Perhaps, it would be more accurate to state that WHO has not accorded, to the invention in any prior art, the INN "Ceritinib". The entity claimed in Claim 4 and exemplified in Examples 7 and 66 of the suit patent is the first entity to have been accorded by the WHO.

63.1 Equally, the entity claimed in Claim 4 of the suit patent, and exemplified in Example 7, has not been claimed or exemplified in any prior art. Though Mr Sai Deepak, for Natco, did seek to contend, at one point, that Ceritinib has been claimed in prior art, neither is there any such admission by Novartis, nor has Natco drawn attention to any such claim. The plea of vulnerability, of the suit patent, to revocation on the ground of anticipation by prior claiming is, therefore, a plea without foundation.

63.2 The written statement of Natco, too, primarily alleges anticipation of Claims 1 and 4 in the suit patent by prior disclosure, via IN'653 and IN'560 of the plaintiff, US'964 of AstraZeneca and US'276, US'430, US'204 and US'112 of Rigel. It is required to be seen, therefore, whether, *prima facie*, the entity which forms subject

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

matter of the Markush Claim 1 and Claim 4 in the suit patent stands earlier claimed or disclosed in any prior art.

63.3 Mr. Hemant Singh does not dispute the fact that Ceritinib is covered by the prior art, to which learned Senior Counsel for Natco refers. He, however, submits that there is a difference between "coverage" and "disclosure". "Coverage", he submits, would envelope all compounds – which in many cases, as in the present, would run into hundreds of thousands – which fall within the broad embrace of the Markush claim in a patent.

63.4 While, therefore, a Markush claim in a genus patent may cover hundreds of thousands of compounds, it is only those compounds which could be "reached" by a person skilled in the art from the teachings in the Markush claim which the genus patent could be said to "disclose". "Disclosure", therefore, has to be enabling in nature. It must enable the person skilled in the art, having knowledge of the Markush formula, the suggested substitutions, the properties of the product that he desires to synthesize and armed with common general knowledge, to know how to reach the later from the former. In doing so, the person skilled in the art must not bring, to the exercise, *any creativity whatsoever*. *Obviousness* from prior art is, therefore, the determinative criterion, to assess disclosure and, therefore, anticipation. Where that teaching is present in the patent, the patent is contained an enabling disclosure. In that event, the synthesized compound stands disclosed in the genus patent.

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

63.5 If, in fact, the genus patent contains the requisite teaching to guide the person skilled in the art, to reach the compound claimed in the species patent, there is no reason why during the life of the genus patent, the said person skilled in the art has not been able to do so. The fact that the compound claimed in the species patent has, till the species patent was granted, not been synthesized in any earlier patent by any other person is, therefore, a strong indicator that the species patent is not invalid on the ground of anticipation by prior publication. Of course, that factor by alone is not determinative. It would always be open to a defendant in a suit to establish, from the genus patent that it contains the requisite teaching which would enable a person skilled in the art to synthesize the claim in the species patent from the claim in the genus patent.

63.6 The onus in that regard would, however, be on the person so asserting; classically, the defendant in a suit. That onus is very heavy. Anticipation by prior publication is not to be easily assumed. Where anticipation by prior publication is raised as a defence in a suit for infringement of a patent, the Court has to be mindful of the fact that the defendant is a person who has foreknowledge of the suit patent. He, therefore, is aware of the substitutions, from the substitutions in the genus patent, which are required to be effected in order to arrive at the species patent. The Court has, therefore, to be doubly satisfied that, in asserting that the suit patent is anticipated or obvious from the genus, the asserting defendant is not merely resorting to hindsight analysis by cherry-picking substituents from the various substitutions suggested in the genus patent, so as to arrive at the species patent. Such cherry-picking is completely impermissible in law.

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Signing Date:11.01.2023
18:30:36

63.7 Armed with above understanding of the law, all that is required to be seen is whether, applying these principles, the Formula 2 in the suit patent can be said to be anticipated by prior publication from any of the prior art patents on which Natco relies.

63.8 Novartis claims as the three inventive features that distinguish Formula 2 in the suit patent and, therefore, Ceritinib itself (i) a core tri-substituted pyrimidine ring, with phenyl ring substituted at Positions 3 and 4 through an amine linkage, (ii) the N^2 phenyl ring being tri-substituted, with one of the two constituents at R^8 or R^9 having necessarily to be a pyrrolidinyl, piperidinyl or azetidinyl radical and (iii) the linkage between N^2 phenyl ring and the said heterocyclic radical being via a carbon-to-carbon bond.

63.9 It is further contended that the carbon-to-carbon bond, which links the N^2 phenyl ring and the heterocyclic ring at R^8/R^9 imparts, to the claim in the suit patent, much less toxicity *vis-à-vis* prior art.

63.10 One may, therefore, examine whether the Markush Formula 2 constituting Claim 1 in the suit patent is or is not obvious from the various patents cited by Natco as prior art.

63.11 <u>*Vis-à-vis* IN'653 of Novartis</u>:

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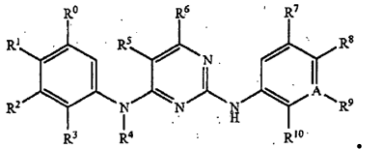
Signing Date:11.01.2023
18:30:36

63.11.1 The Markush Formula 1 in IN'653, from which Natco contends that Ceritinib is anticipated is  .

63.11.2 Comparing the Markush Formula 1 in IN'653 with Claim 1 in the suit patent, the following picture emerges (referring to the two phenyl rings, at Positions 2 and 4 as N^2- and N^4-phenyl respectively):

(a) the N^4 phenyl has four substitutions, designated as R^0, R^1, R^2 and R^3,

(b) to effect the substitutions R^0, R^1, R^2 and R^3, IN'653 offers two options, namely:

(i) each of R^0, R^1, R^2 and R^3 independently is

(a) hydrogen,

(b) C_1-C_8 alkyl,

(c) C_2-C_8 alkanyl,

(d) C_2-C_8 alkinyl,

(e) C_3-C_8 cycloalkyl,

(f) C_3- C_8 cycloalkyl C_1-C_8alkyl,

(g) C_5- C_{10}arylC_1-C_8alkyl,

(h) hydroxyC_1-C_8alkyl,

(i) C_1-C_8alkoxyC_1-C_8alkyl,

(j) aminoC_1-C_8alkyl,

(k) haloC_1-C_8alkyl,

(l) unsubstituted or substituted C_5-C_{10}aryl,

(m) unsubstituted or substituted 5 or 6 membered heterocyclyl comprising

(i) 1,

(ii) 2 or

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

(iii) 3 hetero atoms selected from

(i) N,

(ii) O and

(iii) S,

(n) hydroxyl,

(o) C_1-C_8 alkoxy,

(p) hydroxy C_1-C_8 alkoxy,

(q) C_1-C_8 alkoxy,

(r) C_1-C_8 alkoxy,

(s) halo C_1-C_8 alkoxy,

(t) unsubstituted or substituted C_5- C_{10} aryl C_1-C_8 alkoxy,

(u) unsubstituted or substituted heterocyclyloxy,

(v) unsubstituted or substituted heterocyclyl C_1-C_8 alkoxy,

(w) unsubstituted or substituted amino,

(x) C_1-C_8 alkylthio,

(y) C_1-C_8 alkylsulfinyl,

(z) C_5-C_{10} arylsulfonyl,

(aa) halogen,

(bb) carboxy,

(cc) C_1-C_8 alkoxycarbonyl,

(dd) unsubstituted or substituted carbamoyl,

(ee) unsubstituted or substituted I sulfamoyl,

(ff) cyano or

(gg) nitro, or

(ii) (a) R^0 and R^1, and/or

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

(b) R^1 and R^2, and/or

(c) R^2 and R^3 form,

together with the carbon atoms to which they are attached,

(a) a 5-membered, or

(b) a 6-membered

carbocyclic or heterocyclic ring comprising

(i) 0,

(ii) 1,

(iii) 2 or

(iv) 3 heteroatoms selected from

(a) N,

(b) O and

(c) S,

(c) of all these options available, Natco has selected

(i) H for R^0,

(ii) H for R^1,

(iii) H for R^2 and

(iv) the alkylsulfonyl radical for R^3,

(d) for R^4, IN'653 suggests either

(i) hydrogen or

(ii) C_1-C_8 alkyl,

out of which Natco has selected H,

(e) for each of R^5 and R^6, IN'653 suggests

(i) H,

(ii) C_1-C_8 alkyl,

(iii) C_1-C_8 alkoxy C_1- C_8 alkyl,

(iv) halo C_1-C_8 alkyl,

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

(v) C_1-C_8 alkoxy,

(vi) halogen,

(vii) carboxy,

(viii) C_1-C_8 alkoxycarbonyl,

(ix) unsubstituted or substituted carbamoyl,

(x) cyano, or

(xi) nitro,

out of which Natco has selected

(a) halogen substituent for R^5 and

(b) hydrogen for R^6,

(f) (i) for each of R^7, R^8, R^9 and R^{10}, IN'653 suggests

(a) C_1-C_8 alkyl,

(b) C_1-C_8 alkanyl,

(c) C_2-C_8 alkinyl,

(d) C_3-C_8 cycloalkyl,

(e) C_3-C_8 cycloalkyl C_1-C_8 alkyl,

(f) C_8-C_{10} aryl C_1-C_8alkyl,

(g) hydroxy C_1-C_8 alkyl,

(h) C_1-C_8 alkoxy C_1-C_8 alkyl,

(i) amino C_1-C_8 alkyl,

(j) halo C_1-C_8 alkyl,

(k) unsubstituted or substituted C_5-C_{10} aryl,

(l) unsubstituted or substituted 5 or 6 membered heterocyclyl comprising

(i) 1,

(ii) 2 or

(iii) 3 hetero atoms

selected from

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

(a) N,

(b) O and

(c) S,

(m) hydroxyl,

(n) C_1-C_8 alkoxy,

(o) hydroxyl C_1-C_8 alkoxy,

(p) C_1-C_8 alkoxy C_1-C_8 alkoxy,

(q) halo C_1-C_8 alkoxy,

(r) unsubstituted or substituted C_5-C_{10} aryl C_1-C_8 alkoxy,

(s) unsubstituted or substituted heterocyclyloxy,

(t) unsubstituted or substituted heterocyclyl C_1-C_8 alkoxy,

(u) unsubstituted or substituted amino,

(v) C_1-C_8 alkylthio,

(w) C_1-C_8 alkylsulfinyl,

(x) C_1-C_8 alkylsulfonyl,

(y) C_5-C_{10} arylsulfonyl,

(z) halogen,

(aa) carboxy,

(bb) C_1-C_8 alkoxycarbonyl,

(cc) unsubstituted or substituted carbamoyl,

(dd) unsubstituted or substituted sulfamoyl,

(ee) cyano or

(ff) nitro,

wherein R^7, R^8 and R^9 independently of each other can also be hydrogen or

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

(ii) R^7 and R^8, R^8 and R^9, and/or R^9 and R^{10} form together with the carbon atoms to which they are attached, a

(a) 5 or

(b) 6 membered

(i) carbocyclic or

(ii) heterocyclic ring

comprising

(a) 0,

(b) 1,

(c) 2 or

(d) 3 heteroatoms

selected from

(i) N,

(ii) O and

(iii) S,

out of which Natco has selected

(i) C_1-C_8 alkyl for R^7,

(ii) C_1-C_8 alkoxy for R^8, and

(iii) unsubstituted six membered heterocyclyl ring comprising one heteroatom for R^9, and

(g) A could be either

(i) C or

(ii) N,

out of which Natco has selected C.

63.11.3 It is plain that Natco has effected select substitutions from the various substitutions suggested in Claim 1 in IN'653 for the

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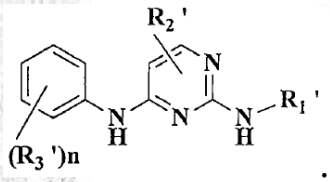
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

various radicals R^1 to R^8 and A (R^9 being hydrogen). The written statement does not contain any explanation or reasoning as to why Natco chose the said substituents out of the several substitutions suggested in Claim 1 in IN'653. Clearly, therefore, what Natco has merely cherry-picked select substituents out of the myriad substitutions provided in the Markush formula in Claim 1 in IN'653, in order to arrive at Ceritinib, having, with it, the foreknowledge of the exact molecular structure of Ceritinib. This is, therefore, a clear case of hindsight analysis.

63.12 *Vis-à-vis* IN'560 of Novartis:

63.12.1 The Markush Formula 1 in IN'560, from which Natco contends that Ceritinib is anticipated is 

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63.12.2 Comparing the Markush Formula 1 in IN'560 with Claim 1 in the suit patent, the following picture emerges:

(i) for R_1, Natco has selected phenyl substituted by

(a) methyl,

(b) isopropyloxy and

(c) piperidinyl,

out of suggested substitutions of

(a) phenyl, or

(b) pyridinyl, or

(c) pyrazolyl, or

(d) pyrimidinyl,

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

substituted, independently, by three radicals, out of

(i) ethoxy,

(ii) ethyl,

(iii) propyl,

(iv) methyl,

(v) r-butyl,

(vi) trifluoromethyl,

(vii) nitrile,

(viii) cyclobutyloxy,

(ix) 2,2,2,-trifluoroethoxy,

(x) Isobutyloxy,

(xi) t-butyloxy,

(xii) isopropyloxy,

(xiii) methyl-amino-carbonyl,

(xiv) cyclopropyl-methoxy,

(xv) dimethylamino-propyl-amino,

(xvi) methoxy-ethoxy, or

(xvii) X'R '4'-C(O)R'4,

(xviii) OX'R'4, wherein

(a) X is a

(i) methylene,

(ii) ethylene bond, and

(b) R'4 is selected from

(i) piperazinyl, or

(ii) piperidinyl, or

(iii) pyrollidinyl, or

(iv) morpholine or

(v) azepanyl or

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

(vi) 1,4-dioxa-8-azaspiro[4.5]dec-8-yl,

and is optionally substituted by

(i) 1, or

(ii) 2 or

(iii) 3

radicals, independently selected from

(i) methyl,

(ii) isopropyl,

(iii) acetyl,

(iv) acetyl-methyl-amino,

(v) 3-dimethylamino-2,2-dimethyl-propylamino,

(vi) ethyl-methyl-amino-ethoxy,

(vii) diethyl-amino-ethoxy,

(viii) amino-carbonyl,

(ix) ethyl,

(x) 2-oxo-pyrrolidinyl,

(xi) pyrrolidinyl,

(xii) pyrrolidinyl-methyl,

(xiii) piperidinyl,

optionally substituted by

(a) methyl, or

(b) ethyl-morpholino, or

(c) dimethylamino-propyl-amino-methyl-amino, or

(d) ethyl-amino**,**

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

(ii) for R_2, Natco has selected halogen out of a choice of hydrogen or halogen, and

(iii) for R_3, Natco selected $-S(O)_{0-2}R_6$, with C_{1-6} alkyl selected for R_6, where IN'560 suggests, for R_3,

(a) $-S(O)_{0-2}NR_5R_6$, or

(b) $-S(O)_{0-2}R_6$ or

(c) $-NR_5S(O)_{0-2}R_6$, or

(d) $-C(O)NR_5R_6$,

wherein R_5 could be

(i) H or

(ii) C_{1-6} alkyl and

R_6 could be

(i) H or

(ii) C_{1-6} alkyl or

(iii) C_{3-12} cycloalkyl.

63.12.3 Again, it is clear that, out of several suggested substitutions provided in the Markush formula in IN'560, Natco has cherry-picked substituents to attempt to arrive at the Markush Claim 1, and at Ceritinib, in the suit patent. There is nothing in IN'560 which can be said to teach the way the reach the suit patent, or select the substituents for that purpose. Nor, for that matter, is it so contended by Natco, either in its written statement or during oral arguments.

63.13 *Vis-à-vis* US'964/WO'654 of AstraZeneca

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Signing Date:11.01.2023
18:30:36

63.13.1 Para 60 of Natco's written statement, which purports to explain how the suit patent is anticipated or obvious from US'964, has been extracted in para 35.1 *supra*. A reading of the passage reveals that, but for reproducing the complete specifications and disclosure provided in Claim 1 of US'964, the paragraph does not explain how, by effecting substitutions on the Markush moiety claimed therein, a person skilled in the art would arrive either at the Markush Claim 1 in the suit patent or at Claim 4 therein, which is Ceritinib.

63.13.2 It becomes needless, therefore, to return any detailed finding in that regard. Suffice is to state that, from a bare reading of the suggested substitutions in Claim 1 in US'964, it becomes clear that, as in the case of IN'653 and IN'560, Natco – or anyone else – could arrive at the Markush claim, or at Claim 4, in the suit patent, only by cherry picking substituents from the substitutions suggested in US'964.

63.14 *In fact, Natco has, in its submissions, completely glossed over the most important query which it would have to answer, in order to set up even a credible challenge to the validity of the suit patent, vis-à-vis a Markush prior art. The suit patent could be said to be vulnerable to invalidity, vis-à-vis known Markush prior art, only if it is established, cumulatively, that*

(i) from the known prior art, it is possible to arrive at the suit patent, by effecting suggested substitutions in the Markush formula claimed in the prior art, from the substitutions suggested therein, and

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

(ii) the Markush prior art contains the requisite teaching, as would suggest the substitutions which are to be so made in order to arrive at the suit patent.

Where (ii) is absent, the exercise undertaken by the defendant, in questioning the validity of the suit patent, is merely hindsight analysis, by cherry-picking those substitutions, from the substitutions suggested in the prior art, as would enable it to arrive at the suit patent, the molecular structure of which is already known to it. The law completely discountenances such an exercise. Natco has not, in its submissions, indicated how the prior art, on which it places reliance, contains the requisite teaching, as to enable a person skilled in the art to reach either the Markush Claim 1 in the suit patent, or to Ceritinib. Natco's claim that the suit patent is anticipated or obvious from IN'653, IN'560 and US'964 cannot, therefore, sustain, prima facie.

63.15 *Besides, neither IN'560 nor US'964, even in the substitutions provided in the Markush claims therein, "teach" the linkage of the heterocyclic ring with the N^2-phenyl by a carbon-carbon bond, which is one of the most distinguishing features of the suit patent.*

63.16 *Vis-à-vis* US'276, US'430, US'204 and US'112 of Rigel

63.16.1 The written statement of the defendant does not elucidate how either Claim 1 or Claim 4 in the suit patent is obvious, anticipated, or disclosed in any of the Rigel patents. I have, nonetheless, examined the Complete Specifications of the Rigel patents, to satisfy myself on this score. The "Summary of the

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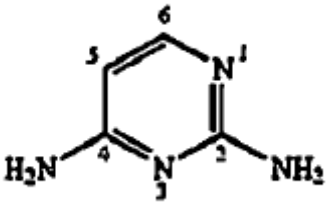
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

Invention" in all the aforesaid four Rigel patents is identical, and reads thus:

> "In one aspect, the present invention provides novel 2,4-pyrimidinediamine compounds that, as will be discussed in more detail below, have myriad biological activities. The compounds generally comprise a 2,4-pyrimidinediamine "core" having the following structure and numbering convention.
>
> 
>
>
> The compounds of the invention are substituted at the C2 nitrogen (N2) to form a secondary amine and are optionally further substituted at one or more of the following positions:
> the C4 nitrogen (N4), the C5 position and/or the C6 position. When substituted at N4, the substituent forms a secondary amine. The substituent at N2, as well as the optional substituents are the other positions, may range broadly in character and physic-chemical properties. For example, the substituent(s) may be a branched, straight-chained or cyclic alkyl, a branched, straight-chained or cyclic heteroalkyl, a mono- or polycyclic aryl a mono- or polycyclic heteroaryl or combinations of these groups. These substituent groups may be further substituted, as will be described in more detail below.
>
> The N2 and/or N4 substituents may be attached directly to their respective nitrogen atoms, or they may be spaced away from their respective nitrogen atoms via linkers, which may be the same or different. The nature of the linkers can vary widely, and can include virtually any combination of atoms or groups useful for spacing one molecular moiety from another. For example, the linker may be an acyclic hydrocarbon bridge (e.g. a saturated or unsaturated alkyleno such as methano,ethano, etheno, propane, prop[1]eno, butane, but[1]eno, but [2]eno, buta[1,3]dieno, and the like), a monocyclic or polycyclic hydrocarbon bridge (e.g.,[1,2]benzene,[2,3]naphthalene, and the like), a simple acyclic heteroatomic or heteroalkyldiy] bridge (e.g., — O—, —S—, —S—O—. —NH—, —PH—, —C(O) —, —C(O)NH—, —S(O) —. —$S(O)_2$—, —S(O)NH—, —$S(O)_2$NH—, —O—CH_2—. —CH_2—O—CH_2—, —O—CH—CH—CH_2—, and the like), a monocyclic or polycyclic heteroaryl bridge (e.g.,[3,4] furano, pyridine, thiopheno, piperidino, piperazino, pyrazidino, pyrrolidino, and the like) or combinations of such bridges.

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

> The substituents at the N2, N4, C5 and/or C6 positions, as well as the optional linkers, may be further substituted with one or more of the same or different substituent groups. The nature of these substituent groups may vary broadly. Non-limiting example of suitable substituent groups include branched, straight-chain or cyclic alkyls, mono- or polycyclic arysls, branched, straight-chain or cyclic heteroalkyls, mono- or polycyclic heteroaryls, halos, branched, straight-chain or cyclic haloalkyls, hydroxyls, oxos, thioxos, branched, straight-chain or cyclic alkoxys, branched, straight-chain or cyclic haloalkoxys, trifluoromethoxys, mono- or polycyclic aryloxys, mono- or polycyclic heteroaryloxys, ethers, alco-hols, sulfides, thioethers, sulfanyls (thiols), imines, azos, azides, amines (primary, secondary and teritiary), nitriles (any isomer), cyanates (any isomer), thiocyanates (any isomer), nitrosos, nitros, diazos, sulfoxides, sulfonyls, sulfonic acids, sulfamides, sulfonamides, sulfamic esters, aldehydes, ketones, carboxylic acids, esters, amides, amidines, formadines, amino acids, acetylenes, carbamats, lactones, lactams, glucosides, gluconurides, sulfones, ketals, acetals, thioketals, oximes, oxamic acids, oxamic esters, etc. and combinations of these groups. Substituent groups bearing reactive functionalities may be protected or unprotected, as is well-known in the art."

63.16.2 A bare reading of the aforesaid Markush claim in the Rigel patents makes it apparent that there are myriad suggested radicals by which substitutions could be made on the core Markush moiety. Assuming, *arguendo*, that, by making select substitutions from those suggested in the Rigel patents it were at all possible to reach either the Markush Claim 1 in the suit patent or Ceritinib, the complete specifications of the Regel patents do not contain the requisite teaching whereby a person skilled in the art could reach either.

63.17 The mere fact that Novartis may have obtained licenses from Astrazeneca or Rigel, or that the suit instituted by Rigel against Novartis may have been settled, cannot seriously affect the dynamics of the issue in controversy. The suit of Rigel against Novartis was an infringement suit. The fact that an infringement suit might have been

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

settled cannot constitute a basis to urge that Novartis was obvious or anticipated from the Rigel patents.

63.18 Natco's submission that the suit patents are vulnerable to revocation on the ground of obviousness, as being anticipated from prior art, therefore, has necessarily to fail.

D. "Coverage" versus "disclosure"

64. Mr Sai Deepak, for Natco, submitted, relying on the judgement of the Supreme Court in ***Novartis-I***, that there is no conceptual difference between "coverage" and "disclosure" and that, once Novartis had admitted coverage of the claims in the suit patent by the cited prior art, *ipso facto* the claims also stood disclosed thereby. Disclosure of the claims in prior art, he submits, renders the claims vulnerable to revocation on the ground anticipation by prior claiming as well as anticipation by prior disclosure.

64.1 I have already noted that Claim 1 and Claims 4 and 5 (Ceritinib) in the suit patent have not been claimed in any prior art. Sans a bare submission to that effect, no substantial material has been cited, by Natco, to indicate to the contrary.

64.2 The submission that the Supreme Court has, in ***Novartis-I***, equated "coverage" and "disclosure" has been addressed, at length, by this Court, in its decisions in ***Novartis-II*** and in ***F.M.C. Corporation***. ***Novartis-I*** does not equate "coverage" with "disclosure". It merely holds that a "wide gap" between coverage of a patent, and what is

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Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

disclosed therein, was not to be encourage, as it would enable circumnavigation of prior art, artfully handled. What matters, at all times, is disclosure. If the claim in a specie patent is disclosed in the genus patent, the specie patent stands invalidated thereby. Disclosure must be enabling; it must enable a person skilled in the art to reach the invention claimed in the specie patent *from the teachings in the genus patent*. I venture to state that, where this end is achieved *before* the publication of the specie patent, and before the invention claimed in the specie patent is made known to the public, it would be a far easier task for the claimant contesting the validity of the specie patent to so assert. Where, however, the claim to invalidity is made *after* the claim in the specie patent has been made known to the public, the challenger becomes a person armed with foreknowledge of the specie patent, so that the task of establishing that the derivation of the claim in the specie patent, from the claim in the genus patent, is actually guided by the teachings in the genus patent, and not by hindsight analysis and cherry-picking of substituents from the suggestion in the genus patent, becomes far more arduous. Where the genus patent is a Markush moiety, the difficulty of the task multiplies manifold. Thus does the "disclosure" in the genus patent attain significance.

64.3 Mr Hemant Singh has not contested the "coverage", of Claim 1 in the suit patent, of indeed even of Ceritinib, by the cited prior art. In doing so, he submits that every molecule of the millions which, theoretically, would result, by effecting the substitutions suggested in the Markush prior art at the suggested sites in the Markush moiety, are "covered" thereby. Theoretically, the synthesis of any such molecule, and its dissemination, without a license from the holder of the prior art

Signature Not Verified
Digitally Signed
By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

patent, would infringe prior art. That the claim in the suit patent, thus empirically seen, stands "covered" by and, in that sense, even infringes, prior art, he submits, does not indicate that it is *disclosed* in prior art. No person skilled in the art can, without hindsight analysis and cherry-picking of suggested substitutions, reach the suit patent from the cited prior art. Ergo, he submits, the prior art does not contain the requisite *teaching*, or *disclosure*, as would *enable* the person skilled in the art to reach the specie patent. The specie patent, i.e. the suit patent in the present case, is not, therefore, anticipated, or obvious, from the cited prior art.

64.4 I agree.

E. *F.M.C. Corporation* and *Novartis-II*

65. Indeed, the controversy in the present case is fully covered by the earlier decisions of this Bench in ***F.M.C. Corporation*** and ***Novartis-II***. The Court is, once again, being asked to plough the same field, which arose before this Court – indeed, this Bench – between the same parties and, one may add, the same redoubtable learned Counsel, in ***F.M.C. Corporation*** and ***Novartis-II***. Indeed, the facts in ***F.M.C. Corporation*** practically mirror those in the present case. Save for the identity of the suit patents and the cited prior art, the grounds of challenge by the defendants in that case are the very same as those urged in the present. This Court has, in the said decision, attempted to analyze the law on the subject threadbare, especially in view of the judgement of the Supreme Court in ***Novartis-I***. Even for the reasons cited in the said decisions, therefore, which would apply *mutatis*

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

mutandis to the present case, Novartis would, in the present case, too, be entitled to interlocutory relief.

65.1 Most of the judicial authorities that enlighten on the issues in controversy have been considered by this Court in these decisions. I have not, therefore, deemed it necessary to burden this judgment by any reference to case law beyond that which stands cited, though the reliance of learned Counsel thereon has been noted earlier in this judgement.

65.2 I may also note, here, that several of the decisions that have been cited at the Bar pertain to foreign jurisdictions. While, in patent law, overseas judgements are undoubtedly relevant, as the law continues to develop, and is yet to reach full adulthood, nearly all these decisions have been examined by Courts in this country in one decision or the other.

F. <u>"Invention" and "inventive step" and Section 3(d)</u>

66. Novartis has, in the plaint, asserted that the claims in the suit patent possess distinct pharmaceutical advantage over prior art. Among other things, it is contended that Ceritinib has the advantage of lower toxicity *vis-à-vis* earlier known ALK inhibitors. The pharmaceutical utility of the claim in the suit patent, *vis-à-vis* prior art, also stands thus distilled, in the recital regarding "Background Art" as contained in the complete specifications in the suit patent:

> "[0003] Anaplastic lymphoma kinase (ALK), a member of the insulin receptor superfamily of receptor tyrosine kinases, has been implicated in oncogenesis in hematopoietic and non-hematopoietic tumors. The

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

aberrant expression of full-length ALK receptor proteins has been reported in neuroblastomas and glioblastomas; and ALK fusion proteins have occurred in anaplastic large cell lymphoma. The study of ALK fusion proteins has also raised the possibility of new therapeutic treatments for patients with ALK-positive malignancies. (Pulford et al.. Cell. Mol. Life Sci. 61:2939-2953 (2004)).

[0004] Focal Adhesion Kinase (FAK) is a key enzyme in the integrin-mediated outside-in signal cascade (D. Schlaepfer et al., Prog Biophys Mol Bid 1999, 71,43578). The trigger in the signal transduction cascade is the autophosphorylation of Y397. Phosphoiylated Y397 is a SH2 docking site for Src family tyrosine kinases; the bound c-Src kinase phosphorylates other tyrosine residues in FAK. Among them, phsophorylated Y925 becomes a binding site for the SH2 site of Grb2 small adaptor protein. This direct binding of Grb2 to FAK is one of the key steps for the activation of dovra stream targets such as the Ra5-ERK2/MAP kinase cascade,

[0005] Zeta-chain-associated protein kinase 70 (ZAP-70), a member of the protein tyrosine kinase family, is of potential prognostic importance in chronic lymphocytic leukemia (CLL). ZAP-70, known to be of importance in T and NK cell signaling but absent in normal peripheral B cells, is expressed in the majority of the poorer prognosis unmutated CLL and absent in most cases with mutated IgVH genes. ZAP-70 is also expressed in a minority of other B ceil tumors. (Orchard et al., Leuk. Lymphoma 46:1689-98 (2005)).

[0006] InsuHn-Iike growth factor (IGF-1) signaling is highly implicated in cancer, with the lGF-1 receptor (IGF-1 R) as the predominating factor. IGR-IR is important for tumor transformation and survival of malignant cells, but is only partially involved in normal cell growth. Targeting of IGF-IR has been suggested to be a promising option for cancer therapy. (Larsson et al., Br. J, Cancer 92:2097-2101 (2005)).

[0007] Because of the emerging disease-related roles of ALK, FAX, ZAP-70 and IGF-IR, there is a continuing need for compounds which may be useful for treating and preventing a disease which responds to inhibition of ALK, FAX, ZAP-70 and/or IGF-IR."

66.1 Novartis contends that the unique inventive step, in synthesizing Ceritinib *vis-à-vis* known prior art, is in the trisubstituted N^2-phenyl ring (linked to the core pyrimidine moiety by an amine linkage) in which one of the substitutions at R^8 or R^9 (as suggested in the Markush formula) is the pyrrolidinyl, or piperidinyl, or azetidinyl ring, linked to the N^2-phenyl ring by a carbon-carbon bond. The cited

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

prior art does not disclose any such linkage; neither do the written statement filed by Natco, or the written submissions tendered to the Court, so urge. The principal submission of Natco, in this regard, is that study on ALK-inhibitors as NSCLC therapy is a subject matter of ongoing study, and that there are earlier patents which claim inventions that are useful in that regard. That, by itself, in my opinion, is insufficient to discredit the claim to inventive step, as urged by Novartis. The horizons of pharmaceutical therapeutic knowledge, especially in oncotherapy, which remains a challenging arena, are ever-expanding. Each added benefit, of a drug, improves on the existing prior knowledge.

66.2 One may also, in this context, refer to common knowledge that a principal challenge, in chemotherapy for treating cancer, is suppression of adverse side effects. The commonly understood notion that, even where the cancer has regressed, oftentimes the chemotherapy proves fatal, is not altogether unjustified. Titration of the need to address the underlying carcinogenic malady, *vis-à-vis* the adverse effects of chemotherapy – or, for that matter, of radiation – remains a challenge even to the most erudite of oncologists. The suppression of an adverse chemotherapeutic side effect, in cancer therapy is, therefore, a marked advancement over the state of existing knowledge. Even by itself, therefore, this would constitute an "inventive step" within the meaning of Section 2(1)(ja) of the Patents Act.

66.3 The mere contention that ALK-inhibition therapy is subject matter of earlier patented inventions cannot, therefore, serve to

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

discredit Novartis' contention that the claims in the suit patent, and Certinib in particular, constitute advancement, denoting an "inventive step", over prior knowledge. The only other drug which achieved a similar effect, submits Novartis, is Crizotinib, and Certinib has a clear advantage over Crizotinib as it acted in Crizotinib-resistant cases as well, and also exhibited much longer effect duration than Crizotinib, which was seen to result in reproliferation of the cancer after some time. These undoubtedly represent therapeutic advancement over Crizotinib. The defendant has not sought to question, on fact, these assertions by reference to any material that would indicate otherwise.

66.4 Besides, as Mr Hemant Singh correctly submits, the fact that, despite the cited prior art having remained in existence since long, Ceritinib was never synthesized by anyone else, including Natco, also indicates that it is an "invention" within the meaning of Section 2(j) of the Patents Act. The fact that Ceritinib has been granted NDA approval and has also been recognized as a NPE by the WHO which has assigned, to it, the INN 'Ceritinib', also substantiates, *prima facie*, the claim to inventiveness as asserted by Novartis.

66.5 It would not be out of place to mention, here, that there are concurrent findings, by the learned Controller of Patents in his order dated 28th September 2016 as well as in the order 29th November 2021 of the learned IPAB, that the suit patent was novel. A reading of the order dated 29th November 2021 of the learned IPAB reveals, indeed, that, to substantiate its stand that Ceritinib exhibited reduced toxicity on account of reduced reactive adduct formation, Novartis relied on the 2013 publication of the Journal of Medical Chemistry. Accepting

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

this, the learned Controller the claims in the suit patent were "novel and inventive and the compound claimed (was) absolutely novel and there (was) no nearest prior art compound that (was) structurally and functionally similar for comparing with the presently claimed molecule". This finding was also upheld by the learned IPAB in appeal. Though the decision of the learned IPAB is presently subject matter of challenge before this Court in WP (C) 9487/2020, it remains undisturbed, and no interlocutory orders interdicting its operation have been passed till date.

66.6 *Prima facie*, therefore, the claims in the suit patent, specifically Claim 1 and Claims 4 and 5 (Ceritinib) are novel and inventive, and satisfy clauses (j) and (ja) of Section 2 of the Patents Act.

66.7 Natco also contends, in its written submissions, that Novartis was bound to disclose the X Ray diffraction pattern of the claims in the suit patent and of Ceritinib, to enable a full disclosure thereof, relying, for the purpose, on ***Roche***. The submission, as urged, stands discountenanced by the subsequent decision of the Division Bench of this Court in ***Merck*** which also holds at, at the stage of consideration of the application for interlocutory injunction under Order XXXIX Rules 1 and 2 of the CPC, the Court could not examine X-ray diffraction patterns. This objection of Natco has, therefore, necessarily to be rejected.

G. PTE, NDA, disclosure, the Orange Book

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

67. Natco emphasized the fact that, in its PTE application for US'592, Novartis had stated that US'592 claimed Ceritinib.

67.1 That, however, would, in my opinion, be a truncated manner of reading the PTE application. While it has been stated, at one point in the application, that US'592 claimed Ceritinib, a holistic reading of the application indicates that Novartis had said so *because by effecting substitutions using select suggested substituents from those disclosed in the prior art, one could reach Ceritinib.* This, therefore, merely amounted to an acknowledgement that Ceritinib was *covered* by US'592, within the broad parameters of the Markush structure claimed therein.

67.2 Apropos the inclusion of the cited prior arts in the patents mentioned in the NDA application filed for ZYKADIA, Mr Singh has drawn attention to U.S.C. § 355(b)(1)[54], which requires the applicant to file, with the application, the number and expiry dates of all patents with respect to which the holder of the prior art could maintain a claim for infringement if the drug, for which NDA was being sought, was manufactured or sold by anyone without obtaining a license from the holder of such prior art patent. As such, Novartis included, in its NDA applications, the cited prior art, which merely covered Ceritinib, as well. The interpretation accorded by Mr. Hemant Singh to U.S.C. § 355(b)(1) may not be textually in accordance with U.S.C. § 355(b)(1), as the provision requires the applicant to file with the application the details of any patent which *claims* the drug for which

[54] The applicant shall file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.

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By:SUNIL SINGH NEGI
Signing Date:11.01.2023
18:30:36

the application has been filed. However, it goes on to use the expression "and with respect to which a claim for patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use or sale of the drug". If the word "claims", as used in the earlier part of the provision, is to be interpreted literally, it would render this latter stipulation otiose, as every genus patent which claims the invention in the specie patent would inevitably be infringed by the specie patent. A harmonious construction would, therefore, justify Mr Hemant Singh's submission that, while applying for NDA for a drug claimed in a specie patent, the applicant would be required to include reference to all genus patents which "cover" the claim in the specie patent and which, therefore, would be infringed thereby. All such genus patents could not, however, be cited as *disclosing* the specie patent; nor could it be alleged that the specie patent is *anticipated in* or *obvious from* the genus patent.

67.3 Ergo, the inclusion of the AstraZeneca and Rigel patents in the NDA application filed by Novartis for ZYKADIA cannot estop Novartis from contesting that, *vis-à-vis* prior art, Ceritinib was a novel and inventive invention, entitled to a patent.

Conclusion

68. Novartis is the holder of the suit patent, which claims Claim 1/Formula 2 and Ceritinib (in Claims 4 and 5). The suit patent continues to subsist till date. Natco has, without obtaining any license from the plaintiff, commenced manufacture and dealing in Ceritinib

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Signing Date:11.01.2023
18:30:36

under its own brand NOXALK. The defence of Natco, solely predicated on questioning the suit patent as vulnerable to challenge, cannot be treated as "credible" in view of the above discussion. Novartis is, therefore, entitled to an injunction as sought.

69. In view of the above discussion, the defendant Natco, its directors, associates, licensees, franchisees, agents, distributors and others acting on its behalf are restrained from dealing in the infringing product NOXALK and/or any Active Pharmaceutical Ingredient, pharmaceutical product or formulation containing Ceritinib alone or Ceritinib in combination with any other compound or API, as would infringe the suit patent IN 276026 of Novartis.

70. IA 6384/2019 stands allowed accordingly.

C.HARI SHANKAR, J

JANUARY 09, 2023
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18:30:36