BEFORE THE CONTROLLER OF PATENTS
THE PATENT OFFICE BRANCH, MUMBAI

In the matter of:

Indian Patent 270765
Formerly 1863/MUMNP/2009
Date of Patent: 10.03.2009
Date of Grant: 18.01.2016

And

In the matter of:

Application for Compulsory Licence under Section 92(1) read with Section 92(3) of The Patents Act, 1970

By:

Natco Pharma Limited **…Applicant**
An Indian company of
NATCO House, Road No. 2, Banjara Hills
Hyderabad 500 034, Telangana State, India

The Applicant above-named respectfully submits as follows:

I. BACKGROUND TO THIS APPLICATION

1. The present application is being filed in the light of the grave and life threatening public health emergency which is currently prevailing in India due to the resurgence of the Covid-19 virus through a second wave since at least early February 2021.
2. Covid-19 was declared a pandemic in March 2020 and a national lockdown declared for a period of 25 days. The Central Government invoked its powers under the National Disaster Management Act and empowered the National Disaster Management Authority (NDMA) to take such measures as are necessary to ensure that the spread of this virus was limited/minimised. The NDMA declared the affliction of this virus a pandemic and has instituted various measures from March 2020 which are ongoing even as of now.
3. Reports in the public domain as of 03.05.2021 indicate that the number of people in India affected by Covid-19 is over 2 crore. The figures also state that while over 1.6 Crore people have recovered from Covid-19, over 34 lakh people continue to be afflicted, and

there are officially over 2 lakh deaths. Daily newspaper reports show an alarming rise not only in the number of cases, but also in the number of fatalities due to Covid-19.

4. All of the above are a matter of public record.

5. A significant reason for such high fatalities as well as the prolonged treatment regimen has been the lack of access to essential medicines for treatment of Covid – 19 partly due to lack of supply and also partly due to lack of affordability.

6. The graveness of the situation is such that all institutions in India, including the Hon'ble Supreme Court as well as various High Courts such as the Hon'ble High Court of Delhi are directly involved in evolving mechanisms by which the fundamental right to health of the residents of India is not just protected but also actively ensured with no discrimination based solely on lack of access inter alia, due to lack of availability of essential medicines or lack of affordability of such essential medicines.

7. For ease of reference, the interim Judgment of the Hon'ble Supreme Court of India in Suo Motu Writ Petition (C) 3/2021 dated 29.04.2021 is annexed herewith as **ANNEXURE – 1**. The Order of the Hon'ble Delhi High Court in Rakesh Malhotra v. GNCTD dated 20.04.2021 is annexed herewith as **ANNEXURE – 2**.

8. The seriousness of the situation can also be seen from the fact that the Drug Controller General of India as far back as 19.03.2020 issued a notification by which if any drug had received Emergency Use Authorisation for Covid -19 treatment, similar approval could be granted in India through a Special Regulatory Pathway involving inter alia waiver of/abbreviation/limitation of clinical studies etc. A copy of this notification is annexed herewith as **ANNEXURE – 3**.

II. ABOUT THE APPLICANT

9. The Applicant above-named is a company incorporated under The Companies Act, 1956 in 1981. It has its' registered office at NATCO House, Road No. 2, Banjara Hills, Hyderabad 500 034, Telangana Stage, India. The Applicant is in the business of research, development, manufacture and marketing of pharmaceutical substances and finished formulations for the Indian and international markets. The Applicant's underlying philosophy from its inception has been to make speciality medicines available for all. Natco set up its Research Center in 1997, and has consistently been at the forefront of making pharmaceutical products available at affordable prices.

10. The Applicant today has around 5000 employees, sister companies in several countries such as Canada, Brazil, Australia, and the US. It also partners, where required and appropriate, with other entities globally to ensure that the best of technologies and manufacturing practices are implemented and quality medicines are made available globally. Apart from its corporate vision of ensuring affordable medicines for all, the Natco family also works with equal vigour and dedication on issues such as ensuring medical care, education etc. in various parts of India. The background of the Applicant can be seen from the Annual Reports for the years 2018-2019 and 2019-2020 are annexed herewith as **ANNEXURE – 4 Colly**.

11. The Applicant has two facilities for manufacture of Active Pharmaceutical Ingredients (API's), and six facilities for manufacture of formulations which are spread across India. It also has a fully functional Research & Development Center in Sanathnagar in Hyderabad. The Applicant has approvals from various global regulatory authorities such as the US Food & Drug Administration (USFDA), the European Medicines Agency (EMEA), MFDS Korea, Infarmed-Brazil etc.

12. The Applicant has made critical contributions towards ensuring access to essential medicines available in an affordable manner across all sections of society. Some of these are outlined below:

    a. Teriflunomide and Glatiramer Acetate for treatment of multiple sclerosis;
    b. Posaconazole for antifungal treatment
    c. Apixaban for cardiovascular (specifically Deep Vein Thrombosis) treatment
    d. Oseltamivir monophosphate for Swine flu treatment
    e. Sofusbovir for Hepatitis C treatment
    f. Imatininb Mesylate for treatment of chronic myelogenous leukemia
    g. Erlotinib HCl for treatment of non-small cell lung cancer
    h. Regorafenib for treatment of colorectal cancer
    i. Sorafenib for treatment of kidney cancer
    j. Ticagrelor for treatment of Type II diabetes
    k. Liposomal Doxurubicin used in chemotherapy for treatment in breast cancer, Kapsi's sarcoma, lymphoma, and bladder cancer
    l. Daclatasvir for treatment of Hepatitis C

13. It is humbly submitted that the Applicant is the only entity which sought, fought, and secured a Compulsory License for Sorafenib for treatment of kidney cancer, thus making an otherwise unaffordable drug easily and readily accessible to the common person in India.

III. SUBJECT MATTER OF THE PRESENT APPLICATION

14. The present application for compulsory licence under Section 92 of the Act is in relation to a pharmaceutical product called Baricitinib.

15. Baricitinib is a selective and reversible Janus kinase inhibitor which works in respect of both JAK1 and JAK2 subtypes. Janus kinases which are tyrosine protein kinases have a significant role to play in the proinflammatory pathway signalling that is usually overactivated in autoimmune disorders such as rheumatoid arthritis. Baricitinib is reported to function by blocking the actions of JAK1 and JAK2 by disrupting the activation of downstream signalling molecules and proinflammatory mediators.

16. Baricitinib has been shown to have significant anti-inflammatory effect as well as preservation of bone and cartilage and with little or no detectable adverse hematologic effect in the treatment of rheumatoid arthritis. Baricitinib is reportedly approved for rheumatoid arthritis treatment in the European Union in 2017 and is believed to have received approval in India in 2018.

(i) BARICITINIB APPROVAL STATUS

17. Baricitinib was reportedly first approved in the European Union in February of 2017 as a second-line orally administered treatment for moderate to severe active rheumatoid arthritis in adults, either as a monotherapy or when combined with methotrexate. It is marketed under the trade name *Olumiant*.

18. Baricitinib is believed to have been approved in India sometime in 2018 for the same indication, namely second-line orally administered treatment for moderate to severe active rheumatoid arthritis in adults, either as a monotherapy or when combined with methotrexate.

19. A copy of the Olumiant leaflet is annexed herewith as **ANNEXURE – 5.**

(ii) BARICITINIB AND ITS USE FOR COVID-19 PATIENTS

20. As far back as 15.02.2020, the international renowned Journal *The Lancet* had reported that Baricitinib could be trialled for use in Covid-19 treatment pending development of

a vaccine. This was based on ai modelling and was predicated on the fact that Baricitinib could be effective to disrupt the AP2 associated protein kinase (AAK1) pathway which regulates endocytosis and could be useful in reducing viral entry and inflammation. This was followed by another article in April 2020 which reiterated the potential use of Baricitinib in Covid – 19 treatment using a combination of anti-viral and anti-inflammatory pathway regulation. Copies of the Articles from *The Lancet* are annexed herewith as **ANNEXURE – 6 Colly**.

21. In August 2020, the EMBO Molecular Medicine Journal reported that there was support in real time for the AI-predicted use of Baricitinib in Covid-19 treatment. The Journal reports that in a series of patients with bilateral COVID-19 pneumonia, Baricitinib treatment was associated with clinical and radiologic recovery, a rapid decline in SARS-CoV-2 viral load, inflammatory markers, and IL-6 levels. A Copy of the EMBO Molecular Medicine Article is annexed herewith as **ANNEXURE – 7**. This report also states that data supported further evaluation of the anticytokine and anti-viral activity of Baricitinib and further assessment in randomised clinical trials in hospitalised Covid-19 patients.

22. In December 2020, a report in the New England Journal of Medicine reported that Baricitinib + Remdesivir was superior to Remdesivir alone in reducing recovery time and accelerating improvement in clinical status among patients with Covid-19, notably among those receiving high-flow oxygen or non-invasive ventilation. The combination was also reported as being associated with fewer serious adverse events. A copy of this literature reference is annexed herewith as **ANNEXURE – 8**.

23. To avoid prolix, the Applicant relies on the contents of the above documents in support of the undeniable fact that Baricitinib is an essential medicine for Covid-19 treatment as an adjunct to Remdesivir prescription, particularly in patients requiring oxygen support and non-invasive ventilation.

24. The United States Food & Drug Administration granted Emergency Use Authorisation of Baricitinib in combination with Remdesivir for the treatment of COVID-19 on 19.11.2020. A copy of this USFDA Communication is annexed herewith as **ANNEXURE – 9**. The relevant portion of the USFDA Emergency Use Authorisation is reproduced hereinbelow:

> ***"I. Criteria for Issuance of Authorization***
> *I have concluded that the emergency use of baricitinib for the treatment of COVID-19 when administered as described in the Scope of Authorization (Section II) meets*

the criteria for issuance of an authorization under Section 564(c) of the Act, because:
1. SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;

2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that baricitinib, in combination with remdesivir, may be effective in treating suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or ECMO, and that, when used under the conditions described in this authorization, the known and potential benefits of baricitinib when used in combination with remdesivir to treat COVID-19 in such patients outweigh the known and potential risks of such product; and

3. There is no adequate, approved, and available alternative to the emergency use of baricitinib, in combination with remdesivir, for treatment of suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or ECMO."

25. The Applicant is informed that physicians now regularly prescribe Baricitinib as a stand alone or in combination with Remdesivir for treatment in Covid-19 patients. The prescribed dosage is one tablet per day for a maximum of 14 days.

(iii) PATENT POSITION REGARDING BARICITINIB

26. The Applicant's search has shown up one granted patent for Baricitinib, viz. Indian Patent 270765 (IN'765). A copy of the E-Register of IN'765 is annexed herewith as **ANNEXURE – 10**. A copy of IN'765 as granted (as per records of the IPO on IPAIRS) is annexed herewith as **ANNEXURE – 11**. The Applicant is not disputing the fact that IN'765 covers Baricitinib.

27. The patent is owned as of 05.07.2018 by Incyte Holdings Corporation. While there is a reference in the E-Register to a licence having been granted to an entity called Eli Lilly & Co., and having been recorded in July 2019, (a) firstly this was done after assignment was recorded in 2018, and (2) a copy of such licence is unavailable for public inspection.

28. The Forms 27 filed on IN'765 for the calendar years 2019 and 2020 respectively are annexed herewith as **ANNEXURE – 12 Colly**.

29. It is submitted that the relevance and criticality of Baricitinib in treatment of Covid-19 has also been recognised and noted by the Hon'ble High Court of Delhi through its Order dated 20.04.2021 in *Rakesh Malhotra v. GNCTD* (supra).

IV. CONDITIONS FOR APPLICATION OF SECTION 92 OF THE ACT

i. Existence of a national public health emergency

30. The Applicant submits that this is an undisputed position – that there is in fact a grave national public health emergency. In support of this position, reliance is placed on the declaration of a pandemic by the NDMA as referred to above, which has not been withdrawn. Reliance is also placed on the DCGI/CDSCO Notification of 19.03.2020 which is operative across all drugs useful for Covid-19 treatment.

31. Reliance is also placed on the Judgments of the Hon'ble Supreme Court of India dated 29.04.2021 and of the Hon'ble Delhi High Court of 20.04.2021 referred to above.

32. It is submitted that the above trigger the operation of Section 92, and in particular Section 92(1) and 92(3) of the Act for the reasons as given hereinbelow:

a. The National Disaster Management Authority declares a pandemic in March 2020 which continues to operate as of date;

b. On 19.03.2020, the Central Drugs Standard Control Organisation through the DCGI, which operates under the direction and control of the Ministry of Health & Family Welfare, Government of India, issued a pan-India and drug-agnostic notification declaring that in the light of the prevailing Covid-19 pandemic, any drug approved anywhere in the world for Emergency Use Authorisation would be entitled to the same status i.e. Emergency Use Authorisation through a Special Regulatory Pathway in India;

c. On 19.11.2020, the USFDA notified and approved Baricitinib for Emergency Use Authorisation in the USA under Section 564 of the Federal Food, Drug & Cosmetics Act of USA as amended or added by the Pandemic and All-Hazards Preparedness Reauthorisation Act of 2013 (PAHPRA), which is pari materia with Section 92 of The Patents Act, 1970;

d. The CDSCO/DCGI ahs through its letters of 29.04.2021 recognised that there is a public health emergency due to Covid 19 pandemic and that there is an unmet medical need and has approved such Emergency Use Authorisation for manufacture of Baricitinib API and 1 mg, 2mg and 4mg tablets for Emergency Use in Covid-19 pandemic. Copies of such letters are annexed herewith as **ANNEXURE – 13 Colly**.

33. In the light of the above, the first requirement, namely the recognition by the Central Government of the existence of a national emergency due to public health concerns as well as extreme urgency is satisfied, and in particular in relation to Baricitinib.

ii. Unmet need in India

34. The Applicant submits that there is an unmet need for Baricitinib both due to lack of supply as well as lack of affordability of even what is or has been supplied under the brand Olumiant by Eli Lilly

35. In this connection, the Applicant respectfully submits as follows:

a. Admittedly, the use of Baricitinib with remdesivir reduces hospital time, increases chances of survival and also has minimal adverse events associated therewith.

b. According to the Forms 27 filed on IN'765 for calendar years 2019 and 2020, the amount of Baricitinib tablets introduced in India are as follows:

2019:

2mg tablets:	263 at a total value of INR 849569.00
4mg tablets:	7997 at a total value of INR 25832709.00
Physician's samples:	810 at a total value of INR2616543.00

The total number of tablets are 8870 at an average cost per tablet of INR 3230.00 per tablet.

2020: (when pandemic continued to be ongoing)

2mg tablets:	1627 at a total value of INR 5255698.00
4mg tablets:	5763 at a total value of INR 18616219.00
Physician's samples:	995 at a total value of 3214149.00

The total number of tablets are 8385, again at an average cost per tablet of INR 3230.00 per tablet. Indeed the number of tablets appears to have reduced from 2019 to 2020 calendar years.

c. Olumiant is not manufactured in India but is only imported as per the Forms 27.

d. The total number of Covid-19 patients currently undergoing treatment is over 34 lakhs, and the numbers are only increasing on a daily basis.

e. A large number of such patients are prescribed Remdesivir injection.

f. The Baricitinib course regimen for Covid -19 is for a period of upto 14 days.

g. The tablets of Olumiant imported through 2020 by Lilly would serve at best to meet the needs of only approximately 600 patients.

iii. Unmet need to due to lack of supply

36. This firstly shows that there is a significant lack of access in terms of availability of such medicine to patients across India – even assuming only 25% of the Covid-19 patients are prescribed Remdesivir injection, and therefore can also avail of the benefit of co-treatment with Baricitinib, this in itself works out a patient population of approximately 8.5 lakh patients. The actual numbers are likely to be significantly higher – and will be known only after detailed studies regarding prescription of remdesivir and Baricitinib become available.

iv. Unmet need due to price/lack of affordability

37. Even if Eli Lilly undertakes to meet the full requirement, a significant barrier to access remains the price of the product. The per tablet cost is INR 3230.00. For a 14-day treatment regimen the price works out to INR 45220.00 per patient. As is self-evident this is not only more than the median average income of most families, it is actually more than the monthly income of even most qualified professionals across India. Simply put, this is classic price gouging and in itself reduces access to a very limited and extremely affluent section of Indian population.

v. Conditions of Section 92(3) satisfied

38. Critically, as stated hereinabove, it is an admitted position that Eli Lilly only imports the tablets and that too in limited quantities. Eli Lilly itself has a very narrow distribution network and it is inconceivable that it will ever be able to service the needs of the Indian population for Baricitinib in times of Covid-19 pandemic. Of necessity, any baricitinib product imported by Lilly will be limited in access to at best a few urban centers such as Delhi or Mumbai, if at all.

vi. Additional Factors

39. The Hon'ble High Court of Delhi in Rakesh Malhotra supra itself recognised that there is a need to invoke provisions such as Section 92 in relation inter alia to Baricitinib. The need to invoke compulsory licensing provisions under Section 92 and Government use provisions under Seciton 100 has also been noted by the Hon'ble Supreme Court in its judgment of 29.04.2021. One of the drugs under discussion and consideration during the hearing on 29.04.2021 before the Hon'ble Court was Baricitinib.

40. Thus, the above factors all show that the Learned Controller is not only empowered, but is also required to exercise discretion under Section 92(3) of the Act and issue a

compulsory licence in relation to IN'765 for Baricitinib for the period that the Covid-19 pandemic continues to subsist in India.

V. THE APPLICANT'S PREPAREDNESS FOR LAUNCH OF BARICITINIB

41. The Applicant had applied for Emergency Use Authorisation on 02.12.2020 before the DCGI/CDSCO.

42. On 11.12.2020, the Applicant wrote to the patentee seeking a voluntary licence and offering to pay a royalty of 7% on net profits. A copy was also marked to the purported licensee Eli Lilly. A copy of this communication is annexed as **ANNEXURE – 14**.

43. Till date there has been no response from the patentee. Instead communications were received on behalf of the licensee demanding certain confidential details to which the licensee is neither entitled to nor has any justification been shown as to why such information was being requested by Lilly. Simply put, a purported licensee cannot demand confidential information where the patentee itself has remained signally silent. Nothing was shown that Eli Lilly was in fact even authorised by Incyte Holdings Corporation to address such communications.

44. The Applicant respectfully submits that it is prepared to manufacture and launch Baricitinib in three separate dosage forms 1 mg, 2 mg and 4 mg tablets immediately for the purpose of co-treatment in Remdesivir treatment as per approvals granted by the CDSCO/DCGI for Emergency Use Authorisation.

45. The Applicant is devoting its existing facilities for production and its pan-India distribution network for this purpose. For example, Baricitinib product will be made available across India to hospitals directly on prescriptions issued by Registered Medical Practitioners to patients in critical care and under conditions approved by the Regulatory Authorities.

46. The Applicant stipulates that it has received such Emergency Use Authorisations. As can be seen from such authorisations, the DCGI itself has recognised that not only is there an emergency, there is an unmet medical need.

47. The Applicant 's products pricing details are as below:

    4 mg tablet: INR 30.00 per tablet, i.e. INR 420.00 for a maximum 14 day course

    2 mg tablet: INR 20.00 per tablet, i.e. INR 280.00 for a maximum 14 day course

    1 mg tablet: INR 15.00 per tablet, i.e. INR 210.00 for a maximum 14 day course

(Note: actual prices may vary due to factors such as GST etc., and any local variations. However, the Applicant is dedicated to ensuring that the variations are kept to a minimum).

48. As can be seen from the above, the pricing is structured not from the motive of profit at any cost, but access at any cost.

49. The Applicant has performed bioequivalence studies which were submitted to the regulatory authorities and the Applicant's product has been found to be bioequivalent to the reference product Olumiant. A synopsis of such studies is filed herewith as **ANNEXURE – 15**.

50. A detailed statement regarding the Applicant's baricitinib manufacturing capacity will be filed shortly. It is undisputed that that the Applicant has the capability – the total quantum over time details will be submitted shortly. In addition, the Applicant will be using its well established distribution network to ensure supply of its Baricitinib product to hospitals, Government facilities for treatment of Covid-19 etc.

51. In addition to the above, the Applicant had also filed an intervention application on 23.04.2021 before the Hon'ble Supreme Court of India in Suo Motu Writ Petition No. 3/2021 seeking inter alia the following directions:

    a. A direction that its application for Emergency Use Authorisation in relation to Baricitinib which had been filed as far back as 02.12.2020 be heard and disposed of expeditiously on merits by the regulatory authority. This has now been rendered moot due to the approvals granted on 29.04.2021;

    b. A direction that any application for compulsory licence be heard and disposed off expeditiously by the concerned authorities. This prayer is currently under consideration of the Hon'ble Supreme Court.

52. The Applicant is moving the present application on an urgent basis and reserves the right to file additional supporting documents and material as may be necessary in support of its case. The Applicant also undertakes to file any additional information as may be required by the Learned Controller subject only to conditions of confidentiality.

PRAYER

53. In the light of the above, the Applicant respectfully prays that the Learned Controller be pleased to exercise the duty mandated under Section 92(1) read with 92(3) of the Act

and grant the Applicant the Compulsory Licence requested and on the following terms and conditions:

a. Recognise the right of the Applicant to manufacture and market Baricitinib both as bulk API and 1 mg, 2 mg, and 4mg tablets as approved by the DCGI/CDSCO;
b. The compulsory licence will be with respect to Covid-19 indication only;
c. The compulsory licence will be limited to the territory of India, and till such time as the prevailing pandemic situation continues;
d. Payment of 7% royalty on net profits;
e. Preference is to be given to patients in the economically weaker sections, government (both central and state government) welfare schemes and in remoter areas of the Country;
f. In deserving cases, the product will be made available free of cost to patients.

54. The Applicant requests that no adverse decision be taken without providing the Applicant an opportunity of being heard in the matter.

Most respectfully submitted

Dated this the 3rd day of May 2021.

For Natco Pharma Limited

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