

Application no.
ND/CT04/FF/2020/22453

F. No. ND/CT/20/000108

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Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(New Drugs Division)

FDA Bhawan, Kotla Road,
New Delhi-110002

Dated: 05 FEB 2021

To

M/s. Mylan Laboratories Limited,
Plot No. 564/A/22, Road No. 92, Jubilee Hills,
Hyderabad -500096, Telangana, India

05 FEB 2021

Sub.: Application for permission to conduct Phase IV Clinical Trial entitled "Randomized Trial to evaluate the Effectiveness and Safety of various doses of Linezolid in combination with Bedaquiline and Pretomanid in Adults with Extensively Drug-Resistant (XDR), pre-XDR or Non-responsive Multidrug-Resistant (MDR) Pulmonary Tuberculosis in India" - Reg.

Sir,

With reference to your application no. ND/CT04/FF/2020/22453 dated 10.11.2020; please find enclosed herewith the permission in **Form CT-06, No. CT/ND/06/2021** to conduct the subject mentioned clinical trial under the provisions of New Drugs and Clinical Trial Rules, 2019.

This permission is subject to the conditions, as mentioned below.

Yours faithfully



(Dr. V. G. Somani)
Central Licensing Authority

Condition of permission

- (i) Clinical trial at each site shall be initiated after approval of the clinical trial protocol and other related documents by the Ethics Committee of that site, registered with the Central Licensing Authority under Rule 8;
- (ii) Where a clinical trial site does not have its own Ethics Committee, clinical trial at that site may be initiated after obtaining approval of the protocol from the Ethics Committee of another trial site; or an independent Ethics Committee for clinical trial constituted in accordance with the provisions of Rule 7:

Provided that the approving Ethics Committee for clinical trial shall in such case be responsible for the study at the trial site or the centre, as the case may be:

Provided further that the approving Ethics Committee and the clinical trial site or the bioavailability and bioequivalence centre, as the case may be, shall be located within the same city or within a radius of 50 kms of the clinical trial site;

- (iii) In case an ethics committee of a clinical trial site rejects the approval of the protocol, the details of the same shall be submitted to the Central Licensing Authority prior to seeking approval of another Ethics Committee for the protocol for conduct of the clinical trial at the same site;
- (iv) The Central Licencing Authority shall be informed about the approval granted by the Ethics Committee within a period of fifteen working days of the grant of such approval;
- (v) Clinical trial shall be registered with the Clinical Trial Registry of India maintained by the Indian Council of Medical Research before enrolling the first subject for the trial;
- (vi) Clinical trial shall be conducted in accordance with the approved clinical trial protocol and other related documents and as per requirements of Good Clinical Practices Guidelines and the provisions of these rules;
- (vii) Status of enrolment of the trial subjects shall be submitted to the Central Licencing Authority on quarterly basis or as appropriate as per the duration of treatment in accordance with the approved clinical trial protocol, whichever is earlier;
- (viii) Six monthly status report of each clinical trial, as to whether it is ongoing, completed or terminated, shall be submitted to the Central Licencing Authority;
- (ix) In case of termination of any clinical trial the detailed reasons for such termination shall be communicated to the Central Licencing Authority within thirty working days of such termination;
- (x) Any report of serious adverse event occurring during clinical trial to a subject of clinical trial, shall, after due analysis, be forwarded to the Central Licencing Authority, the chairperson of the Ethics Committee and the institute where the trial has been conducted within fourteen days of its occurrence as per Table 5 of the Third Schedule and in compliance with the procedures as specified in Chapter VI of the New Drugs and Clinical Trials Rules, 2019;
- (xi) In case of injury during clinical trial to the subject of such trial, complete medical management and compensation shall be provided in accordance with the Chapter VI of the said Rules and details of compensation provided in such cases shall be intimated to the Central Licencing Authority within thirty working days of the receipt of order issued by Central Licencing Authority in accordance with the provisions of the said Chapter;
- (xii) In case of clinical trial related death or permanent disability of any subject of such trial during the trial, compensation shall be provided in accordance with the Chapter VI and details of compensation provided in such cases shall be intimated to the Central Licencing Authority within thirty working days of

receipt of the order issued by the Central Licencing Authority in accordance with the provisions of the said Chapter;

- (xiii) The premises of the sponsor including his representatives and clinical trial sites, shall be open for inspection by officers of the Central Licencing Authority who may be accompanied by officers of the State Licencing Authority or outside experts as authorized by the Central Licencing Authority, to verify compliance of the requirements of these rules and Good Clinical Practices Guidelines, to inspect, search and seize any record, result, document, investigational product, related to clinical trial and furnish reply to query raised by the said officer in relation to clinical trial;
- (xiv) Where the New Drug or Investigational New Drug is found to be useful in clinical development, the sponsor shall submit an application to the Central Licencing Authority for permission to import or manufacture for sale or for distribution of new drug in India, in accordance with Chapter X of these rules, unless otherwise justified;
- (xv) The Laboratory owned by any person or a company or any other legal entity and utilized by that person to whom permission for clinical trial has been granted used for research and development, shall be deemed to be registered with the Central Licensing Authority and may be used for test or analysis of any drug for and on behalf of Central Licensing Authority;
- (xvi) The Central Licencing Authority may, if considered necessary, impose any other condition in writing with justification, in respect of specific clinical trials, regarding the objective, design, subject population, subject eligibility, assessment, conduct and treatment of such specific clinical trial;
- (xvii) The sponsor and the investigator shall maintain the data integrity of the data generated during clinical trial.
- (xviii) Informed Consent Documents (ICD) viz. Patient Information Sheet (PIS) and Informed Consent Form (ICF) complete in all respect & must be got approved from the respective Ethics committee and submitted to CDSCO before enrolling first subject at the respective site.
- (xix) **Undertaking of all the Investigator as per Table 4 of the New Drugs & Clinical Trial, 2019 of all the proposed clinical trial sites should be submitted to CDSCO before the initiation of the trial.**
- (xx) **Firm should constitute DSMB as per requirements.**
- (xxi) **Firm should submit the interim data analysis report after review by DSMB to CDSCO for review by the committee.**

FORM CT-06

(See rules 22, 25, 26, 29 and 30)

**PERMISSION TO CONDUCT CLINICAL TRIAL OF NEW DRUG OR INVESTIGATIONAL
NEW DRUG**

The Central Licensing Authority hereby permits **M/s. Mylan Laboratories Limited, Plot No. 564/A/22, Road No. 92, Jubilee Hills, Hyderabad -500096, Telangana, India** to conduct clinical trial of the new drug as per **Protocol No. nil, Version:1.3, Dt. 23.09.2020** in the below mentioned clinical trials sites.

2. Details of new drug or investigational new drug and clinical trial site: -

Names of the new drug or investigational new drug:		Pretomanid
Therapeutic class:		Antituberculosis
Dosage form:		Tablet
Composition:		Each tablet contains: Pretomanid 200mg
Indications:		Pretomanid Tablets 200mg is indicated as part of a combination regimen with bedaquiline and linezolid, in adults for the treatment of pulmonary extensively drug resistant (XDR), or treatment intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis (TB).
Details of clinical trial sites-		
Sr. No.	Name of Principal Investigator & Trial Sites	Ethics Committee Name/ Registration Number
1.	Dr. Vikas Oswal Shatabti Centenary Hospital, Govandi, Mumbai, Maharastra	D Y Patil University - School of Medicine 11, Ayyappa Rd, Dr D Y Patil Vidyanagar, Sector 7, Nerul, Navi Mumbai, Maharashtra 400706, ECR/195/Inst/MH/2013/RR-19
2.	Dr. (Prof.) Suryakant King Georges Medical University Shahmina Road, Chowk, Lucknow Lucknow Uttar Pradesh - 226003	Institutional Ethics Committee, King Georges Medical University Shahmina Road, Chowk, Lucknow Lucknow Uttar Pradesh - 226003 ECR/262/Inst/UP/2013/RR-19
3.	Dr. (Prof.) Santosh Kumar S N Medical College Raja Mandi Near Agra College Agra Central Library, Moti Katra Mantola Agra Agra Uttar Pradesh – 282003	Institutional Ethics Committee S N Medical College Raja Mandi Near Agra College Agra Central Library, Moti Katra Mantola Agra Agra Uttar Pradesh – 282003 ECR/1409/Inst/UP/2020

4.	Dr. Rajesh Solanki BJ Medical College, Civil Hospital Office of Medical Superintendent Civil Hospital Ahmedabad, Gujarat	Institutional Ethics Committee B.J. Medical College and Civil Hospital Office of Medical Superintendent Civil Hospital Ahmedabad ECR/72/Inst/GJ/2013/RR-19
5.	Dr. Parul Vadagama Govt. Medical College, Surat, Gujarat	Human Research Ethics Committee Government Medical College, Majura Gate Surat Gujarat - 395001 ECR/42/Inst/GJ/2013/RR-19
6.	Dr. Neeta Singla National institute for Research in Tuberculosis and Respiratory Diseases, New Delhi Sri Aurobindo Marg Near Qutub Minar New Delhi	Ethics Committee, National Institute of TB and Respiratory Diseases Sri Aurobindo Marg Near Qutub Minar New Delhi, Delhi - 110030 India ECR/315/Inst/DL/2013/RR-19
7.	Dr. Prabhakaran Rathinam Govt. Rajaji Hospital, Madurai Medical College, Panagal Road Madurai, Tamil Nadu - 625020 India	Institutional Ethics Committee Madurai Medical College and Govt. Rajaji Hospital Panagal Road Madurai, Madurai Tamil Nadu - 625020 India ECR/1365/Inst/TN/2020

3. This permission is subject to the conditions prescribed in part A of Chapter V of the New Drugs and Clinical Trials Rules, 2019 under the Drugs and Cosmetics Act, 1940.

New Delhi

Date:

05 FEB 2021

(Dr. V. G. Somani)
Central Licensing Authority
Stamp

Dr. V. G. SOMANI
Drugs Controller General (India)
Dte. General of Health Services
Ministry of Health and Family Welfare
FDA Bhawan, Kotla Road, I.T.O.
New Delhi-110002