



सत्यमेव जयते

GOVERNMENT OF INDIA
CENTRAL DRUGS STANDARD CONTROL
ORGANISATION (Headquarter)
(Directorate General of Health Services)
Ministry of Health & Family Welfare
FDA Bhavan
ITO, Kotla Road
New Delhi - 110002 (Delhi)
Phone No.: 91-11-23216367
Fax No.: 91-11-23236973
E-Mail : dci@nic.in

File No. CT/24/000056

To,

M/s. AstraZeneca Pharma India Limited,
Block N1, 12th Floor Manyata Embassy,
Business Park, Rachenahalli Outer Ring Road,
Bangalore, Karnataka (India) – 560045.

Sir,

With reference to your application No. GCT/CT04/FF/2024/42771 dated 05-Apr-2024, please find enclosed herewith the permission in Form CT-06 for conduct of clinical trial titled, **“A Randomized, Double-blind, Parallel Group, Multi-center, Phase III Study to Assess the Efficacy of Budesonide, Glycopyrronium, and Formoterol Fumarate Metered Dose Inhaler Relative to Glycopyrronium and Formoterol Fumarate MDI on Cardiopulmonary Outcomes in Chronic Obstructive Pulmonary Disease (THARROS)”** Protocol No.: D5989C00001 Version No. 2.0 dated 28 Jan 2024 and Local CSP Addendum IND-1: Version 1.0, dated 10 Jan 2024 with a total of up-to 65 subjects from India under the provisions of New Drugs and Clinical Trial Rules, 2019

The permission granted by the Central Licensing Authority to conduct clinical trial shall be subject to following conditions, namely:-

- (i) **Human biological samples i.e. Whole blood, urine, and plasma related to clinical trial shall be permitted to be exported for analysis subject to the clearance by port offices of CDSCO.**
- (ii) 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;
- (iii) 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;

- (iv) 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;

- (v) 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;
- (vi) 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;
- (vii) 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;
- (viii) 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;
- (ix) 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 electronically in the SUGAM portal;
- (x) 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;
- (xi) 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;
- (xii) in case of injury during clinical trial to the subject of such trial, complete medical management and compensation shall be provided in accordance with Chapter VI 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;
- (xiii) 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 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;
- (xiv) 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 authorised 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;
- (xv) 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;
- (xvi) the laboratory owned by any person or a company or any other legal entity and utilised 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 Licencing Authority and may be used for test or analysis of any drug for and on behalf of Central Licencing Authority;
- (xvii) 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;
- (xviii) the sponsor and the investigator shall maintain the data integrity of the data generated during clinical trial.
- (xix) Merely granting permission to conduct the **clinical trial** with the Investigational Drug Product does not convey or imply that, based on the **clinical trial study data** generated with the investigational drug, permission to market this drug in the country will automatically be granted to you;

(xx) The permission to initiate clinical trial granted under rule 22 in form CT-06 or automatic approval under rule 23 in Form CT 4A shall remain valid for a period of **two years** from the date of its issue, unless extended by the Central Licencing Authority.

Yours faithfully,

(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India) &
Central Licencing Authority
Stamp

FORM CT-06
(See rules 22,25,26,29 and 30)
**PERMISSION TO CONDUCT CLINICAL TRIAL OF NEW DRUG OR
INVESTIGATIONAL NEW DRUG**

1. The Central Licensing Authority hereby permits **M/s. AstraZeneca Pharma India Limited, Block N1, 12th Floor, Manyata Embassy Business Park, Rachenahalli, Outer Ring Road, Bangalore, Karnataka (India) - 560045** to conduct clinical trial of the new drug or investigational new drug as per **Protocol No.: D5989C00001 Version No. 2.0 dated 28 Jan 2024 and Local CSP Addendum IND-1: Version 1.0, dated 10 Jan 2024** in the below mentioned clinical trial sites [As per Annexure].
2. Details of new drug or investigational new drug and clinical trial site [As per Annexure].
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.

Place: New Delhi

Date _____

(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India) &
Central Licencing Authority
Stamp

Note: The permission to initiate clinical trial granted under rule 22 in form CT-06 shall remain valid for a period of **two years** from the date of its issue, unless extended by the Central Licencing Authority.

Annexure:

Details of new drug or investigational new drug:

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| Names of the new drug or investigational new drug | Budesonide++Glycopyrronium+ Formoterol fumarate (BGF) |
| Therapeutic class: | ICS (Inhaled corticosteroid) + LAMA (Long-acting muscarinic antagonist) LABA (Long-acting β 2-agonists) |
| Dosage form: | Inhalation aerosol (metered dose inhaler) |
| Composition: | Budesonide, micronized =160.0000 micrograms (μ g) In House Specification, Ph.Eur, Active Glycopyrronium bromide, micronised =9.0000 micrograms (μ g) In House Specification, Ph.Eur Active Formoterol fumarate dihydrate, micronised =5.0000 micrograms (μ g) In House Specification, Ph.Eur, Active |
| Indications: | Cardiopulmonary Outcomes in Chronic Obstructive Pulmonary Disease (COPD) |

Annexure:

Details of clinical trial site:

| Sr. No. | Names and address of clinical trial site | Ethics committee details | Name of investigator |
|----------------|--|--|------------------------------------|
| 1. | Topiwala National Medical College and B.Y.L Nair Charitable Hospital, Mumbai Central, Mumbai, Maharashtra - 400008 | Institutional Ethics Committee, TNMC Nair Hospital, Topiwala National Medical College Nair Hospital, Dr. A. L. Nair Road, Mumbai Central, Mumbai City, Maharashtra – 400008 ECR/22/Inst/Maha/2013/RR-19 | Dr Girish Chandrakant Rajadhyaksha |
| 2. | All India Institute of Medical Sciences, Ansari Nagar, New Delhi - 110029 | Institute Ethics Committee, All India Institute of Medical Sciences, Old OT Block, Room No.102, Ansari Nagar, New Delhi, 110029 ECR/538/Inst/DL/2014/RR-20 | Dr Anant Mohan |
| 3. | KLES Dr Prabhakar Kore Hospital & Medical Research Centre, Nehrunagar, Belagavi - 590010, Karnataka | Institutional Ethics Committee, KLE Dr PK Hospital and MRC, Nehru Naga, Belagavi, Karnataka – 590010 ECR/211/Inst/KA/2013/RR-19 | Dr. Jyothi Hattiholi |

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| 4. | Shri Mahant IndiresH Hospital, Patel Nagar, Dehradun - 248001, Uttarakhand | Institutional Ethics Committee, SGRR Institute of Medical Health Sciences IEC, Administrative Building, Patel Nagar, Dehradun, Uttarakhand – 248001 ECR/710/Inst/UK/2015/RR-21 | Dr Jagdish Rawat |
| 5. | Jawaharlal Nehru Medical College & Hospital, Aligarh Muslim University, Aligarh - 202002, Uttar Pradesh | Institutional Ethics Committee, Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Civil Line, Koil, Uttar Pradesh – 202002 ECR/1418/Inst/UP/2020 | Dr Mohammad Shameem |
| 6. | Institute of Chest Disease, Government Medical College, Kozhikode, Kerala - 673008 | Institutional Ethics Committee, Govt. Medical College, Kozhikode, 4th Floor, Golden Jubilee Annex, Institute of Maternal and Child Health, Kozhikode, Kerala – 673008 ECR/395/Inst/KL/2013/RR-20 | Dr Prejeesh B |
| 7. | Vinaya Hospital and Research Centre (A Unit of KIMS), Karangalpady, Mangaluru - 575003, Karnataka | Ethics Committee Vinaya Hospital, Vinaya Hospital and Research Center, Pintos Lane, Karangalpady, Mangaluru, Dakshina Kannada, Karnataka – 575003 ECR/664/Inst/KA/2014/RR-20 | Dr Hamsraj Alva |
| 8. | Department of Respiratory Medicine, Medical College and Hospital, Kolkata, 88, College Street, Kolkata - 700073, West Bengal | Institutional Ethics Committee for Human Research, Medical College Kolkata, 88, College Street, Kolkata, West Bengal – 700073 ECR/287/Inst/WB/2013/RR-19 | Dr Kaushik Saha |
| 9. | Kamineni Hospitals Private Limited, L.B Nagar, Hyderabad - 500068, Telangana | Kamineni Institutional Ethics Committee, Kamineni Hospitals Private Limited, L.B. Nagar, Hyderabad, Ranga Reddy, Telangana – 500068 ECR/58/Inst/AP/2013/RR-19 | Dr Ravindra Reddy Etikala |
| 10. | Imperial Multispecialty Hospital, Gat No.1193, Pingale Pride, Near Radha Swami Ashram, Chikhali, Pune - 411062, Maharashtra | Imperial Ethics Committee, Imperial Multispecialty Hospital, GAT No. 1193, Pingale Pride, Haveli, Pune Maharashtra – 411062 | Dr Rajkumar Gautam Nikalje |

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| | | ECR/1693/Inst/MH/2022 | |
| 11. | Post Graduate Institute of Medical Education and Research (PGIMER), Sector 12, PGIMER, Chandigarh - 160012 | Institutional Ethics Committee, Post Graduate Institute of Medical Education & Research (PGIMER), Room No 6006, Sixth Floor, P.N Chuttani Block, Chandigarh – 160012 ECR/25/Inst/CH/2013/RR-20 | Dr Sahajal Dhooria |
| 12. | Nil Ratan Sircar – NRS Medical College and Hospital, 138, AJC Bose Road, Kolkata, 700014, West Bengal | Ethics Committee N.R.S. Medical College, NRS Medical College and Hospital, 138, A. J. C. Bose Road, Kolkata, West Bengal – 700014 ECR/609/Inst/WB/2014/RR-20 | Dr Jaydip Deb |
| 13. | Eternal Hospital, (Unit of Eternal Heart Care Centre & Research Institute Pvt. Ltd), 3 A, Jagatpura Road, Near Jawahar Circle, Jaipur - 302017, Rajasthan | Eternal Heart Care Centre and Research Institute-IEC, 3 A Jagatpura Road, Near Jawahar Circle, Jaipur, Rajasthan – 302017 ECR/615/Inst/RJ/2014/RR-20 | Dr Krishna Kumar Sharma |
| 14. | Kusum Dhirajlal Hospital (KD) Hospital, Vaishnodevi Circle, S.G Highway, Ahmedabad - 382421, Gujarat | KD Hospital Institutional Ethics Committee, KD Hospital, Vaishnavdevi Circle, S G Highway Khodiyar, Dascroi, Ahmedabad, Gujarat – 382421 ECR/1294/Inst/GJ/2019 | Dr Tushar B Patel |
| 15. | All India Institute of Medical Sciences, Nagpur, Plot No.02, Sector 20, MIHAN, Nagpur, 441108, Maharashtra | Institutional Ethics Committee for Clinical Trial, All India Institute of Medical Sciences, Nagpur, M/S Director AIIMS, Plot No 2, Sector 20, 1st floor, OPD Building, MIHAN, Nagpur, Maharashtra, 441108 ECR/1392/Inst/MH/2020 | Dr Srikant Kashinath Malegaonkar |
