Tele No.011-23236965
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F. No. ND/CT/24/000088
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(New Drugs Division)

FDA Bhawan, Kotla Road,
New Delhi-11 0002

To
M/s Bristol-Myers Squibb India Pvt. Ltd.,
6th Floor, Tower 1, One International Center
Senapati Bapat Marg, Elphinstone (West)
Mumbai (India) - 400013

Subject: Application for grant of permission to conduct Phase-IV Clinical trial titled- "A Phase 4, Single-Arm, Open-Label Study to Evaluate Safety, Tolerability, and Efficacy of Mavacamten in Adults with Symptomatic Obstructive Hypertrophic Cardiomyopathy in India (ROVER)"Protocol no. CV0271146 Dated: 01-Jul-2024 -regarding.

Sir,

With reference to your application no. **ND/CT04/FF/2024/46030 dated 30-OCT-2024**; please find enclosed herewith the permission in **Form CT-06, vide No. CT/ND/01/2025** 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

RAJEEV SINGH RAGHUVANSHI

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(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India)

Conditions 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 Licencing 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) The Informed Consent Document including ICF and Patient Information Sheet should clearly mention in understandable language about the details of the drug therapy that the patient may or may not receive.

FORM CT-06

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

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

CT Permission No. CT/ND/01/2025

The Central Licensing Authority hereby permits **M/s Bristol-Myers Squibb India Pvt. Ltd., 6th Floor, Tower 1, One International Center, Senapati Bapat Marg, Elphinstone (West), Mumbai (India) - 400013 Telephone: 022-66288600, Fax: 022- 66288700,022-66288701 E-Mail: NISHAGABRIEL.FERNANDES@BMS.COM** to conduct clinical trial of the new drug as per **Protocol no. CV0271146, dated: 01-Jul-2024** 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:~~	**Mavacamten capsules 2.5 mg, 5 mg,10 mg and 15 mg**
Therapeutic class:	**Cardiovascular drug Myosin inhibitor**
Dosage form:	Capsules for Oral Use
Composition:	**Mavacamten capsules 2.5 mg** Each Hard Gelatin Capsule contains: Mavacamten…….2.5mg Excipients: q.s Colour in capsule shell: Iron oxide black, Iron oxide red **Mavacamten capsules 5 mg** Each Hard Gelatin Capsule contains: Mavacamten…….5mg Excipients: q.s Colour in capsule shell: Iron oxide yellow **Mavacamten capsules 10 mg** Each Hard Gelatin Capsule contains: Mavacamten…….10 mg Excipients: q.s Colour in capsule shell: Iron oxide red **Mavacamten capsules 15 mg** Each Hard Gelatin Capsule contains: Mavacamten…….15mg Excipients: q.s Colour in capsule shell: Iron oxide black
Indications:	Mavacamten is indicated for the treatment of symptomatic (New York Heart Association, NYHA, class II-III) obstructive hypertrophic cardiomyopathy (oHCM) in adult patients.

Details of clinical trial sites-

Sr. No.	Name of Principal Investigator & Trial Sites	Ethics Committee Name/ Registration Number
1.	**Dr Johny Joseph** (Caritas Hospital and Institute of	Ethics Committee-Caritas Hospital

	Health Sciences, Thellakom PO Kottayam Kerala - 686630	**ECR/242/Inst/KL/2013/RR-19**
2	**Dr Hisham Ahamed** Amrita Institute of Medical Sciences and Research Centre, AIMS-Ponekkara.P.O, Kochi Kerala - 682041	Institutional Ethics Committee **ECR/129/Inst/KL/2013/RR-19**
3	**Dr Cecily Mary Majella** Tamil Nadu Government Mult-Super-Specialty Hospital, Omandurar Government Estate Chennai Tamil Nadu - 600002	Institutional Ethics Committee, TNGMSSH **ECR/1375/Inst/TN/2020**
4	**Dr Sanjay Porwal** KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Nehru Nagar, Belagavi Karnataka - 590010	Institutional Ethics Committee, KLE University **ECR/211/Inst/KA/2013/RR-24**
5	**Dr Ashwani Mehta** Sir Ganga Ram Hospital, Sir Ganga Ram Hospital Marg, Rajinder Nagar New Delhi Delhi - 110060	Sir Ganga Ram Hospital Ethics Committee **ECR/20/Inst/DL/2013/RR-19**
6	**Dr Devangkumar Maheshchandra Desai** Unicare Heart Institute and Research Centre, Acme Plaza, B-Wing, Near Sosyo Circle, Canal Road Surat Gujarat - 395002	UNITY HOSPITAL ETHICS COMMITTEE **ECR/1226/Inst/GJ/2019**
7	**Dr Dinesh Choudhary** Sardar Patel Medical College and Associate Group Hospitals, Department of Cardiology Bikaner Rajasthan - 334003	ETHICS COMMITTEE, S.P.MEDICAL COLLEGE **ECR/27/SP/Inst/RJ/2013/RR-19**
8	**Dr Mukund Kumbla** Omega Hospital, Mahaveer Circle, Kankanady, Mangalore Karnataka - 575002	Omega Ethical Committee **ECR/89/Inst/KA/2013/RR-20**
9	**Dr Sandeep Bansal** Vardhman Mahavir Medical College and Safdarjang Hospital, VMMC and Safdarjang Hospital, New Delhi Delhi - 110029	Institutional Ethics Committee VMMC and SJH **ECR/593/Inst/2014/RR-20**
10	**Dr Milind Gadkari** (KEM Hospital Research Centre, KEM Hospital, Diamond Jubilee Building, 5th Floor, Sardar Moodliar Road, Rasta peth, Pune - 411011, Maharashtra, India Pune	KEM Hospital Research Centre Ethics Committee,Pune **ECR/272/Inst/MH/2013/RR-22**

	Maharashtra - 411011	
11	**Dr Milan Chag** Marengo CIMS Hospital Pvt. Ltd., Plot No 67-1, Opp. Panchamrut Bungalows, Near Shukan Mall, Off. Science City Road, Sola Ahmedabad Gujarat - 380060	Ethics Committee of CIMS **ECR/206/Inst/GJ/2013/RR-24**
12	**Dr Ashish Deshpande** Oriion Citicare Super Speciality Hospital, 5-5-70, opposite Kalash Mangal Karyalaya, New Osmanpura, Aurangabad Maharashtra - 431005	Oriion Citicare Hospital Institutional EC **ECR/1548/Inst/MH/2021**
13	**Dr Anil Ramesh Jawahirani** Central India Cardiology Hospital and Research Institute, Plot No. 1, Pioneer Co-Op Housing Society, Gawande Lay out, Khamla Ring Road, Opp Sawarkar Garden, Khamla Nagpur Maharashtra - 440015	IEC Rughwani Child Care Centre and Hospital **ECR/1444/Inst/MH/2020**
14	**Dr Krishna Mala Konda Reddy** OSMANIA GENERAL HOSPITAL, Research Room, 2nd Floor ,Quliqutub Shah Building , Afzalgunj Hyderabad Telangana - 500012	Institutional Ethics Committee **ECR/300/Inst/AP/2013/RR-19**
15	**Dr Rakesh Kumar Aggarwal** Deep Heart Centre, Deep Hospital, 481, Model Town, Ludhiana Punjab - 141002	Institutional Ethics Committee Deep Hospital **ECR/525/Inst/PB/2014/RR-20**
16	**Dr Rama Chandra Barik** All India Institute of Medical Sciences, Bhubaneswar, Sijua Patrapada Bhubaneswar Orissa - 751019	Institutional Ethics Committee, AIIMS Bhubaneswar **ECR/534/Inst/OD/2014/RR-20**
17	**Dr Asit Das** IPGME and R and SSKM Hospital, IPGME and R-SSKM Hospital, 244, AJC Bose Road Kolkata West Bengal - 700020	IPGMEand R Research Oversight Committee **ECR/35/Inst/WB/2013/RR-24**
18	**Dr Dipak Ranjan Das** SCB Medical College and Hospital, SCB Medical College and Hospital, Behara Colony, Mangalabag Orissa - 753007	Institutional Ethics Committee **ECR/84/Inst/OR/2013/RR-20**
19	**Dr Prashant Manohar Jagtap** Viveka Super Specialty Hospitals and Research, Center Private Limited, Plot no 1A, Naik Layout, Subhash Nagar,	Viveka Hospital Ethics Committee **ECR/1639/Inst/MH/2021**

	Nagpur Maharashtra – 440022	
20	**Dr Sanjay Mittal** Medanta - The Medicity, Sector 38, Gurugram- 122001 Gurugram Haryana - 122001	Medanta Institutional Ethics Committee **ECR/282/Inst/H R/2013/RR -20**
21	**Dr Sandeep Seth** All India Institute of Medical Science, Room No- 2, Department of Cardiology, Sri Aurobindo Marg, Ansari Nagar, Ansari Nagar East, New Delhi Delhi - 110029	Institute Ethics Committee **ECR/538/Inst/DL/2014/RR-20**
22	**Dr Asif Hasan** Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Jawaharlal Nehru Medical College, Aligarh Muslim University, Civil Line, Aligarh Uttar Pradesh - 202002	Institutional Ethics Committee **ECR/1418/Inst/UP/2020**
23	**Dr MD Mahmodullah Razi** GSVM Medical College, LPS Cardiology, Swaroop Nagar, Kanpur Uttar Pradesh - 208002	Ethics Committee GSVM Medical College **ECR/680/Inst/UP/2014/RR-20**
24	**Dr Sagar Makode** All India Institute of Medical Science, Plot No. 2, Sector 20, Sumthana, Mihan, Nagpur Nagpur Maharashtra - 441108	Institutional Ethics Committee for Clinical Trial **ECR/1392/Inst/MH/2020**
25	**Dr Ajay Mahajan** Seth G S Medical College and K E M Hospital Mumbai, K.E.M.Hospital,4th Floor ,Cardiology Research Department ,CVTC Building ,Acharya Donde Marg, Parel Mumbai Maharashtra - 400012	Institutional Ethics Committee-I **ECR/229/Inst/MH/2013/RR-24**

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.

RAJEEV SINGH RAGHUVANSHI

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(Dr. Rajeev Singh Raghuvanshi)
Central Licensing Authority

New Delhi