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File No: CT/44/14 – DCG (I) Clinical Trial NOC No: - GCT/19/15

42052/01.10.14

GOVERNMENT OF INDIA
Directorate General of Health Services
Central Drugs Standard Control Organization
Office of Drugs Controller General (India)
(Global Clinical Trial Division)
FDA Bhawan, Kotla Road, New Delhi-110002
Tel No: 01123236965, Fax: 01123236971
E-mail: dci@nic.in

File No: CT/44/14 – DCG (I) Dated: 05/05/15

To,

M/s. Boehringer Ingelheim India Pvt. Ltd.,
1102, 11th Floor, Hallmark, Business Plaza,
Gurunanak Hospital Rd, Near Gurunanak Hospital,
Bandra (East), Mumbai - 400 051.

Subject: Permission for conducting a Phase IIIb clinical trial entitled "A prospective randomised, open label, blinded endpoint (PROBE) study to Evaluate DUAL antithrombotic therapy with dabigatran etexilate (110mg and 150mg b.i.d.) plus clopidogrel or ticagrelor vs. triple therapy strategy with warfarin (INR 2.0 – 3.0) plus clopidogrel or ticagrelor and aspirin in patients with non valvular atrial fibrillation (NVAF) that have undergone a percutaneous coronary intervention (PCI) with stenting (RE-DUAL PCI)"– regarding.

Clinical Trial NOC No.:- GCT/19/15

Reference: -Your letter No. BI/DCGI/CT/119/2014dated 26 Sept 2014 on the subject mentioned above.

Sir,

This Directorate has no objection to your conducting the subject mentioned clinical trial as per the provisions of Drugs & Cosmetics Rules under supervision of the following investigators and as per the **Protocol No: 1160.186 version 1.0 dated 26 Mar 2014** submitted to this Directorate.

1. Dr. Bhuwanesh Khandpal, Sir Ganga Ram Hospital, SGRH Marg, Old Rajinder Nagar, New Delhi-110 060.
2. Dr. Pravin Goel, Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGI), Raebareli Road, Lucknow-226 014, Uttar Pradesh.
3. Dr. Sharad Chandra, Dept. of Cardiology, King George's Medical University, Lucknow-226 003, Uttar Pradesh.
4. Dr. Upendra Kaul, Fortis Escorts Heart Institute, Okhla Road, New Delhi-110 025.
5. Dr. Gautam Sharma, All India Institute of Medical Sciences (AIIMS), Ansari Nagar, New Delhi-110 029.
6. Dr. Viveka Kumar, Max Super Speciality Hospital, 2, Press Enclave Road, New Delhi -110017.
7. Dr. K Jaishankar, Madras Medical Mission, 4-A, Dr. J.J. Ayalalithaa Nagar, Mogappair, Chennai-600 037, Tamil Nadu.
8. Dr. C.N. Manjunath, Sri Jayadeva Institute of Cardiovascular Sciences & Research, Jayanagar 9th Block, Bannerghatta Road, Bangalore-560 069.

9. Dr. K V Srikanth, Narayana Hrudayalaya Hospitals, 258/A, Bommansandra Industrial Area, Anekal Taluk, Bangalore-560 099.
10. Dr. Dhiman Kahali, B.M. Birla Heart Research Centre, 1/1 National Library Avenue Kolkat-700 027, West Bengal.
11. Dr. V.S. Prakash, M.S. Ramaiah Medical College and Hospitals, MSRIT post, New BEL Road, Bangalore-560 054, Karnataka.
12. Dr. Debashish Ghosh, Apollo Gleneagles Hospitals, Kolkata, 58 Canal Circular Road, Kolkata-700 054, West Bengal.
13. Dr. Charit Bhograj, Vikram Hospital, Bengaluru Pvt. Ltd., #71/1 Millers Road Opposite to ST. Annes's College Bengaluru-560 052.
14. Dr. Ajay Naik, Care Institute of Medical Sciences (CIMS) Hospital, Nr. Shukan Mall, CIMS Hosptal Road, Ahmedabad-380 060, Gujarat.
15. Dr. Bagirath R, Chinmaya Narayana Super Speciality Centre, Narayana Hrudayalaya Pvt. Ltd, CMH Road IndiraNagar, Bangalore-560 038.
16. Dr. Sunil Thanvi, Bhanubhai and Madhuben Patel Cardiac Centre, Shree Krishna Hospital and Medical Research Centre, Gokal Nagar, Karamsad-388 325, Gujarat.
17. Dr. M. Jyotsna, Nizam Institute of Medical Sciences, Dept. of Cardiology, Punjagutta, Hyderabad-500 082, Andhra Pradesh.
18. Dr. G Ravikumar, King George's Hospital, Maharanipeta, Vishakhapatnam-530 002, Andhra Pradesh.
19. Dr. Nitish Garg, Tagore Hospital & Heart Care Centre Pvt. Ltd., Banda Bahadur Nagar, Mahavir Marg, Jalandhar 144 008.
20. Dr. Rajneesh Kumar Calton, Christian Medical College & Hospital, Brown Road, Ludhiana-141 008, Punjab.
21. Dr. Santhosh Satheesh, Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Dept. of Cardiology, JIPMER, Puducherry-605 006.
22. Dr. N.G. Karandikar, B J Medical College and Sassoon General Hospitals, Dept. of Cardiology, B J Medical College & Sassoon Hospitals, Pune-411 001, Maharashtra.
23. Dr. Vinod Khandait, Dept. of Medicine, Government Medical College & Hospital, Medical College Square, Nagpur-440 003, Maharashtra.
24. Dr. Nagendra Singh Chouhan, Medanta- The Medicity, Sec-38, Gurgaon, Haryana-122 001.
25. Dr. Ajaykumar Mahajan, Dept. of Cardiology, 2nd Floor, Old OPD Building LTMGH Hospital, Sion Mumbai-400 022.
26. Dr. Pinto Nahata, Cardiology Research Cell, SP Medical College and associated group of hospitals, HRMC Cardiovascular Sciences & Research Centre, Bikaner-334 001, Rajasthan.
27. Dr. S.M. Sharma, SMS Medical College & Attached Hospital's, JLN Marg, Jaipur-302 004, Rajasthan.

Kindly note that the clinical trial permission is subject to the following conditions:

a. Clinical trial shall be conducted in compliance with the approved protocols, requirements of Schedule Y, Good Clinical Practice Guidelines issued by this Directorate and other applicable regulations;

b. Approval of the Ethics Committee shall be obtained before initiation of the study;

c. Clinical trials shall be registered at Clinical trials Registry of India before enrolling the first patient for the study;

d. Annual status report of each clinical trial, as to whether it is ongoing, completed or terminated, shall be submitted to the Licensing Authority, and in case of termination of any clinical trial the detailed reasons for the same shall be communicated to the said Licensing Authority;

e. Any report of serious adverse event occurring during clinical trial study to the subject, after due analysis, shall be forwarded within ten days of its occurrence as per Appendix XI and in compliance with the procedures prescribed in Schedule Y;

f. In case of an injury or death during the study to the subjects, the applicant shall provide complete medical management and compensation in the case of trial related injury or death in accordance with rule 122 DAB and the procedures prescribed under Schedule Y, and the details of compensation provided in such cases shall be intimated to the Licensing Authority within thirty days of the receipt of the order of the said authority;

g. The premises of Sponsor including their employees, subsidiaries and branches, their agents, contractors and sub-contractors and clinical trial study sites shall be open to inspection by the officers authorized by the Central Drugs Standard Control Organization, who may be accompanied by an officer of the State Drug Control Authority concerned, to verify compliance to the requirements of Schedule Y, Good Clinical Practices guidelines for conduct of clinical trial in India and other applicable regulations;

h. The Sponsor including their employees, subsidiaries and branches, their agents, contractors and sub-contractors and clinical trial study sites and the Investigator shall allow officers authorized by the Central Drugs Standard Control Organization, who may be accompanied by an officer of the State Drug Control Authority concerned, to enter with or without prior notice, any premises of Sponsor including their employees, subsidiaries and branches, their agents, contractors and sub-contractors and clinical trial sites to inspect, search and seize any record, data, document, books, investigational drugs, etc. related to clinical trial and provide adequate replies to any queries raised by the inspecting authority in relation to the conduct of clinical trial.

i. Clinical trial shall be conducted only at those sites which are institutes/hospitals having adequate emergency facilities and duly registered Institutional Ethics committees.

j. The sponsor shall ensure that the number of clinical trials an investigator can undertake should be commensurate with the nature of the trial, facility available with the Investigator etc. However, under no circumstances the number of trials should be more than three at a time.

k. The details of payment/honorarium/financial support/fees paid by the Sponsor to the Investigator(s) for conducting the study shall be made available to this directorate before initiation of each of the trial sites.

l. In addition to the requirement of obtaining written informed consent, audio - visual recording of the informed consent process of each trial subject, including the procedure of providing information to the subject and his/her understanding on such consent is required to be done while adhering to the principles of confidentiality. Such audio-visual recording and related documentation shall be preserved. This is applicable to the new subjects to be

enrolled in all clinical trials including Global Clinical Trials. All the Sponsors /Investigators /Institutes/Organizations and other stake holders involved in conduct of clinical trials in the country are required to adhere to this requirement of audio-visual recording of informed consent process of trial subjects.

m. It may kindly be noted that merely granting permission to conduct clinical trials with the drug does not convey or imply that based on the clinical trial data generated with the drug, permission to market this drug in the country will automatically be granted to you.

Yours faithfully,

(Dr. V.G. Somani)
Joint Drugs Controller (India)