Dairy No.: 22583 dated 18.06.2018

Tele No.011-23236965
Fax.No.011-23236973

F. No. 12-07/16-DC(Pt-C)
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
New Drugs Division

FDA Bhawan, Kotla Road,
New Delhi-110002
Dated:
07 AUG 2020

To
M/s Ajanta Pharma Limited,
Ajanta House, 98,
Govt. Industrial Area,
Charkop, Kandiwali (W),
Mumbai – 400 067.

Subject: Grant of permission to undertake Phase III Clinical Trial titled "A Multicentric, Randomized, Double Blind, Parallel Group, Comparative, Phase-III Clinical Study to Evaluate the Efficacy, Safety and Tolerability of Azelnidipine 8mg plus Metoprolol Succinate ER 50mg Tablets and Azelnidipine 16mg plus Metoprolol Succinate ER 50mg Tablets Versus Azelnidipine Tablets 16mg and Metoprolol Succinate ER Tablets 50mg alone in Subjects with Stage 2 Hypertension" - regarding.

CT NOC No.: CT/ND/53/2020

Sir,

With reference to your application no. APL/DRA/DCGI/18/309 dated 13.06.2018, please find enclosed herewith the permission in Form CT-06, No. **CT/ND/53/2020** 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)
Drugs Controller General (India)
Central Licensing Authority

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 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 Licensing 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 Licensing 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 Licensing Authority electronically in the SUGAM portal;

(ix) In case of termination of any clinical trial the detailed reasons for such termination shall be communicated to the Central Licensing 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 Licensing 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 Licensing

Authority within thirty working days of the receipt of order issued by Central Licensing 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 Licensing Authority within thirty working days of receipt of the order issued by the Central Licensing 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 Licensing Authority who may be accompanied by officers of the State Licensing Authority or outside experts as authorized by the Central Licensing 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 Licensing 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 Licensing 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) Arm-D in proposed CT shall be deleted and sample size should be calculated accordingly.

(xx) The results of BE study shall be presented before the committee before initiation of Phase III CT.

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 Ajanta Pharma Limited, Ajanta House, 98, Govt. Industrial Area, Charkop, Kandiwali (W), Mumbai – 400 067** to conduct clinical trial of the new drug ~~or investigational new drug~~ as per protocol No. **APL/CT/18/02, Version 00 dated 09.02.2018** in the below mentioned clinical trial sites

2. Details of new drug or investigational new drug:

Names of the new drug or investigational new drug:	Azelnidipine 8 mg plus Metoprolol Succinate ER 50 mg Tablets and Azelnidipine 16 mg plus Metoprolol Succinate ER 50 mg Tablets
Therapeutic class:	Cardiovascular
Dosage form:	Tablet
Composition:	**1. Azelnidipine 16 mg + Metoprolol Succinate ER 50 mg Tablets** Each film-coated tablet contains Azelnidipine IP 16 mg Metoprolol succinate IP equivalent to 47.50 mg Metoprolol tartarate (as extended release) 50 mg **2. Azelnidipine 8 mg + Metoprolol Succinate ER 50 mg Tablets** Each film-coated tablet contains Azelnidipine IP 8 mg Metoprolol succinate IP equivalent to 47.50 mg Metoprolol tartarate (as extended release) 50 mg
Indications:	Azelnidipine and Metoprolol combination is indicated for the management of Stage-2 Hypertension

Details of clinical trial sites-

Sr. No.	Name of Principal Investigator & Trial sites	Ethics Committee Name/ Registration Number
1.	Dr. Mahmodullah Razi LPS Institute of Cardiology, GSVM Medical college, Rawatpur, Kanpur-208019, India	Ethics Committee GSVM Medical College, Principal office Swaroop Nagar, Kanpor-208002, UP, India ECR/680/Inst/UP/2014
2	Dr. K. Sunil Naik Rajiv Gandhi Institute of Medical Sciences and RIMS Govt. General Hospital, Srikakulam-532001,	Institutional Ethics Committee Rajiv Gandhi Institute of Medical Sciences & RIMS Government General Hospital, Srikakulam-532001, Andhra

	Andhra pradesh, India	Pradesh, India ECR/492/Inst/AP/2013/RR-16
3	Dr. RichaGiri Department of Medicine, Dr. Ram Manohar Lohiya Combined Hospital, VibhutiKhand, Gomti Nagar, Lucknow-226010	Dr. Ram Manohar Lohiya Institute of Medical Science, Lucknow ECR/913/Inst/UP/2017
4	Dr. Prajapati Vipulkumar Bachubhai Department of Medicine, GCS Medical College, Hospital and Research Centre, Opp. DRM Office, Nr. Chamunda Bridge, Naroda Road, Ahmedabad-380025, Gujarat, India	Institutional Ethics Committee, GCS Medical College, Hospital and Research Centre, Opp. DRM Office, Nr. Chamunda Bridge, Naroda Road, Ahmedabad-380025, Gujarat, India ECR/339/Inst/GJ/2013/RR-16
5	Dr. SantanuGuha Medical College and Hospital, 88, College Street, Kolkata-700073	Institutional Ethics Committee for Human Research, 88, College Street, Kolkata-700073 ECR/287/Inst/WB/2013/RR-16
6	Dr. PragatiBhole Department of Medicine, Government Medical College and Hospital, Near Hanuman Nagar, Medical College Square, Nagpur-440003	Institutional Ethics Committee, Department of Pharmacology, Government Medical College And Hospital, Nagpur- 440003 ECR/43/Inst/MH/2013/RR-16
7	Dr. Barama Srihari Department of Cardiology, Osmania Medical College and General Hospital, Afzalgunj, Hyderabad, T.S.-500012, India	Institutional Ethics Committee, Osmania Medical College, Koti, Hyderabad-500095, Telangana State, India ECR/300/Inst/AP/2013/RR-16
8	Dr. SubrataHalder Department of Medicine, 4th Floor, Ronald Ross Building, IPGME&R and SSKM Hospital, 244, AJC Bose Road, Kolkata-700020	IPGME&R and Oversight Committee, Institute of Post Graduate Medical Education and Research, Office of the Dean, 5th Floor, College Building, 244, AJC Bose Road, Kolkata-700020 ECR/35/Inst/WB/2013/RR-16
9	Dr. D. Anil Kumar Department of General Medicine, Gandhi Hospital, Musheerabad, Secunderabad-500019	Institutional Ethics Committee, Gandhi Medical College, Musheerabad, Secunderabad-500003 ECR/180/Inst/AP/2013/RR-16
10	Dr. Raju Badiger KLES Dr. Prabhakar Kore Hospital and MRC, Nehru Nagar, Belagavi, Karnataka-590010	Institutional Ethics Committee, KLE University, JN Medical College, Nehru Nagar, Belagavi, Karnataka-590010 ECR/211/Inst/KA/2013/RR-2016

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.

(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

New Delhi
Date: .....

07 AUG 2020