

Diary No: 29862
Date: 17.11.17

F. No 12-10/12-DC (Pt-9 Akums/Ademetionine)
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
FDA Bhawan, New Delhi - 110002 (India)
New Drugs Division

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

Dated: 08.01.18

To
M/s Akums Drugs & Pharmaceuticals Limited,
304, Mohan Place, L.S.C., Block C,
Saraswati Vihar, Delhi - 110 034.

Subject: Phase-IV, A Prospective, Multi-Center, Open-Label Trial to Evaluate the Efficacy and Safety of Heptral™ (Ademetionine Tablets) In Indian Patients with Alcoholic Liver Disease- regarding.

Reference: Your application no. ADPL/2017/SAMe/467 Dated-16/11/2017 on the subject mentioned above.

CT NOC No. CT/ND/117/2017

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: ADEM4005, Version 2, Revision 2, dated 16.10.2017** submitted to this Directorate.

Sr. No.	Investigator & Trial site	Ethics Committee Name/Registration Number
1.	Dr. Kishnadas D Government Medical College, Ulooroad, Thiruvananthapuram, Kerala 695011	Ethics Committee, Government Medical College, Ulooroad, Thiruvananthapuram, Kerala 695011. ECR/370/Inst/Ker/2013
2.	Dr. Meghraj Ingale, Dept. of Gastroenterology, Lokmanya Tilak Municipal Medical College, Dr. Baba Shaeb Ambedkar Medical Road, Sion (west), Mumbai-400022	Institutional Ethics Committee, Lokmanya Tilak Municipal Medical College staff and Research Society, LTM Medical college building, Dr. Baba Shaeb Ambedkar Medical Road, Sion (west), Mumbai-400022. ECR/266/Lokmanya/Inst/MH/2013
3	Dr. Gourdas Chaudhri Fortis memorial Research Institute, Sector-44, Gurugram, Haryana 122002	Institutional Ethics Committee, Fortis memorial Research Institute, Meeting Room, Lower Ground Floor, Fortis Memorial Research Institute, Sector-44, Gurugram, Haryana 122002. ECR/223/Inst/HR/2013
4	Dr. P Shravan Kumar, Gandhi Medical College and Hospital, Walker Town, MIGH Colony, Padmarao Nagar, Musheerabad, Secunderabad, Telangana 500003.	Institutional Ethics Committee, Principal Office, Gandhi Medical College, Secunderabad, Telangana 500003. ECR/180/Inst/AP/2013

5	Dr. Sangitanjan Dutta Marwari Hospital and Research Center, B-3, Sati Joymati Rd. Athgoan, Guwahati, Assam 781001	ECRC-HEC, MHRC Marwari Hospital and Research Center, B-3, Sati Joymati Rd. Athgoan, Guwahati, Assam 781001 ECR/487/Inst/AS/2013
6	Dr. Rakesh Kocchhar, Postgraduate Institute Medical Education and Research, Sector-12, Chandigarh-160012	Institutional Ethics Committee, Postgraduate Institute Medical Education and Research, Sector-12, Chandigarh-160012. ECR/25/Inst/CH/2013
7	Dr. Praveen Sharma, Sir Ganga Ram Hospital, Sir Ganga Ram Hospital Marg, Rajinder Nagar, New Delhi-110060.	Institutional Ethics Committee, Ethics Committee, Sir Ganga Ram Hospital, Sir, Rajinder Nagar, New Delhi-110060. ECR/20/Inst/DL/2013

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 Institutional Ethics Committee duly registered with CDSCO (under Rule 122DD of Drugs & Cosmetics Rules) should be obtained and submitted to this Directorate 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 fourteen 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 to be conducted by an Investigator 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, an audio-video recording of the informed consent process in case of vulnerable subjects in clinical trial of New Chemical Entity or New Molecular Entity including procedure of providing information to the subject and his understanding on such consent, shall be maintained by the investigator for record; provided that in case of clinical trial of anti-HIV and anti-leprosy drugs, only audio recording of the informed consent process of individual subject including the procedure of providing information to the subject and his understanding on such consent shall be maintained by the investigator for record, as per Government of India, Gazette Notification vide G. S. R. no. 611(E) dated 31.07.2015.
- m) The formulation intended to be used in the clinical trial shall be manufactured under GMP conditions using validated procedures and shall have ongoing stability programme.
- n) You are required to submit revised undertaking of the entire investigator, along with their GCP training, Undertaking by the Sponsors & Ethics Committee registration certificate before the initiation of this Phase IV Clinical trial.

Yours faithfully,



(Dr) G. N. Singh)
Drugs Controller General (India)

