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D. No. 1085, P-1205154
Dated – 28.01.2019

F. No. 12-61/2018-DC (Pt-Synokem-SND)
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organisation
(Subsequent New Drugs Division)

Dated 01 MAR 2019

To,

M/s Synokem Pharmaceuticals Ltd.,
Plot No. 35-36, Sector 6A, Integrated
Industrial state (SIDCUL), Ranipur (BHEL),
Haridwar-249403.

Subject: A Phase III, Multi-center, Prospective, Randomized, Double Blind, Single Dummy, Active Controllerd, Comparative Clinical Study to evaluate the efficacy, safety and Tolerability of Norethisterone CR Tablets 15mg Versus Norethisterone Tablets 5mg to arrest bleeding in women with Heavy Menstrual Bleeding (HMB) / Abnormal Uterine bleeding (AUB) due to Hormonal Imbalance - regarding.

CT NOC No. CT/SND/15/2019

Reference: Your application dated 25.01.2019 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 investigator and as per the **Protocol No: CR/CT/18/006, Phase III, and Version 02, dated 04-12-2018** submitted to this Directorate.

S.No	Investigator and Trial site	Ethics Committee Name and Registration Number
1	Dr. Tapasi Pati, Dept. of Obstetrics and Gynaecology, Institute of Medical Science (IMS) and SUM Hospital, S'O'A University, K8, Kalinga Nagar, Bhubaneswar Odisha-7510003	Ethics Committee, Institute of Medical Sciences (IMS) and SUM Hospital, S'O'A University, K8, Kalinga Nagar, Bhubaneswar Odisha-7510003 ECR/627/Inst/OR/2014/RR-17
2	Dr. S. Anitha, In-Patient Block, Dept. of Obstetrics and Gynaecology, Gandhi Hospital, Musheerabad, Secunderabad, Telanagana-500003	Institutional Ethics Committee, Gandhi Medical College/Gandhi Hospital Musheerabad, Secunderabad, Telanagana-500003

3	Dr. Moushmi Parpillewar, Department of OBGY, Government and Hospital, Medical College Square, Near Hanuman Nagar, Nagpur-440003	Institutional of Ethics Committee, Department of Pharmacology, Government and Hospital, Medical College Square, Near Hanuman Nagar, Nagpur-440003 ECR/43/Inst/MH/2013/RR-16
4	Dr. Madhavender Jain, Bansal Hospital & Research Centre, 04, Janakpuri-1st, Imli Phatak, Jaipur-302005	Institutional Ethics Committee, Bansal Hospital & Research Centre, 04, Janakpuri-1st, Imli Phatak, Jaipur-302005 ECR/826/Inst/RJ/2016
5	Dr. Tulugu Sasikala, Department of Gynaecology, Rajiv Gandhi Institute of Medical Sciences & RIMS Government General Hospital, Srikakulam-532001, Andhra Pradesh	Institutional Ethics Committee, Rajiv Gandhi Institute of Medical Sciences & RIMS Government General Hospital, Srikakulam-Andhra Pradesh-532001 ECR/492/Inst/AP/2013/RR-16
6	Dr. Sonali Girish Varsat, Janam Multi-Specialty Hospital, Madhav Complex, Near Sanand Police Station, Sanand, Ahmedabad	Medilink Ehtics Committee, Basement, Medilink Hospital, Nr, Shyamal Cross Road, 132 ft Ring, Road, Satellite, Ahmedabad-380015 ECR/344/Inst/GJ/2013/RR-16
7	Dr. Seema Upadhyay, Department of Obstetrics & Gynaecology, GSVM Medical College, Swaroop Nagar, Kanpur-208002	Ethica Committee, GSVM Medical College, Principal Office, GSVM Medical College, Swaroop Nagar, Kanpur-208002 ECR/680/Inst/UP/2014/RR-17
8	Dr. Arcana Sinha, Department of Obstetrics and Gynaecology, Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna, Bihar-800014	Institutional Ethics Committee, Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna, Bihar-800014 ECR/640/Inst/BR/2014/RR-17
9	Dr. Sujata Deo, Department of Gynaecology King Geroge's Medical University Chowk Lucknow	Institutional Ethics Committee, Research cell Administrative Block KGMU Lucknow - 226003 ECR/262/Inst/2013/RR-16

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 (CTRI) 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.

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 bulk drug to be used in manufacturing of finished formulation intended to be used in the clinical trial and clinical trial batches of finished formulation shall be manufactured under GMP conditions using validated procedures and shall have ongoing stability programme.**

n) If the clinical trial batches are different from that of the primary batches for which data have been submitted, stability reports for clinical trial batches are to be submitted as per Appendix IX of schedule Y of drugs and Cosmetics Rules for Drug substances and formulation along with Clinical Study Report.

o) 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.

p) Informed consent documents (ICD) viz. Patient Information Sheet (PIS) and Informed Consent Form (ICF) complete in all respect as per the requirements specified in Appendix V of Schedule Y of the Drugs and Cosmetics Rules, 1945 must be got approved from respective Ethics Committee and submitted to CDSCO before enrolling first subject at the respective site.

Yours faithfully,

(Dr. S. Eswara Reddy)
Drugs Controller General (India)
& Licensing Authority