File. No.: ND/CT21/FF/2023/38776
Date. 21-JUL-2023.

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

F. No. ND/MA/23/000130
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
New Drugs Division

FDA Bhawan, Kotla Road,
New Delhi-110002

To
M/s MSN Laboratories Private Limited,
MSN HOUSE - C24, INDUSTRIAL ESTATE,
SANATHNAGAR Hyderabad (India) - 500018

Subject: Grant of permission to conduct Phase III Clinical Trial title "A Randomized, Open Label, Multicentric, Parallel group, Active-Controlled Comparative Phase III Trial to Evaluate the Efficacy and Safety of Upadacitinib Extended Release Tablets in Comparison with Tofacitinib Tablets in Adults with moderately to severely active ulcerative colitis" vide protocol no. MSN/CT/Upada/2023-2024, Version 1.0 dated 26 Jun 2023-regarding.

Reference: Letter Ref. No. ND/CT21/FF/2023/38776 dated 21-JUL-2023.

Sir,

With reference to your application no. ND/CT21/FF/2023/38776 dated 21-JUL-2023, please find enclosed herewith the permission in Form CT-06, No. **CT/ND/47/2023** 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

Digitally signed by RAJEEV SINGH RAGHUVANSHI
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(Dr. Rajeev Singh Raghuvanshi)
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 utilised 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) Objective criteria for mild, moderate and Sever COVID patients should be clearly defined.

(xx) 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.

(xxi) It may kindly be noted that merely granting permission to conduct Clinical Trial study with the drug doesn't convey or imply that based Clinical Trial data generated with the drug, permission to market this drug will automatically be granted to you.

(xxii) **The firm should include QuantiFERON-TB Gold test for exclusion of latent Tb cases.**

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 MSN Laboratories Private Limited ,MSN HOUSE - C24, INDUSTRIAL ESTATE, SANATHNAGAR Hyderabad (India) - 500018 Telephone No.: 04030438712,8664,8302,8604 FAX: 04030438798 E-Mail : krreddy@msnlabs.com** to conduct clinical trial of the new drug as per protocol No. **Protocol no. MSN/CT/Upada/2023-2024, Version 1.0 dated 26 Jun 2023** 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:	Upadacitinib Extended Release Tablets 15mg, 30mg & 45mg.
Therapeutic class:	Janus kinase (JAK)1-selective inhibitor
Dosage form:	Tablet
Composition:	Each film coated tablet contains; Upadacitinib Extended Release 15mg Each Tablet contains Upadacitinib...15mg. Upadacitinib Extended Release 30mg Each Tablet contains Upadacitinib....30mg Upadacitinib Extended Release 45mg Each Tablet contains Upadacitinib.....45mg
Indications:	For the treatment of Adults with moderately to severely active ulcerative colitis who have had an inadequate response or intolerance to one or more TNF blockers.

Details of clinical trial sites-

Sr. No.	**Name of Principal Investigator & Trial sites**	**Ethics Committee Name/Registration Number**
1.	Dr Arka Banerjee, Department of Gastroenterology (SDLD) IPGME&R and SSKM Hospital,244, AJC Bose Road, Bhowanipore, Kolkata-700020	PGME & Research Oversight committee IPGME&R and SSKM Hospital **ECR/35/Inst/WB/2013/RR-13**
2.	Dr Tryambak Samanta, Medical College and Hospital, Kolkata, 88 College Street, Kolkata, West Bengal, India Pin Code: 700073	Institutional Ethics Committee for Human Research, Medical College and Hospital, 88 College Street, Kolkata-700073, West Bengal, India. **ECR/287/Inst/WB/2013/RR-19**

3.	Dr Mandar Doiphode, Sangvi MultispecialtyHospital,near Krushna Chowk, Krishna Nagar, New Sanghavi, Pimpri-Chinchwad, Maharashtra. IndiaPin Code:411027	IEC-SANGVI MULTISPECIALITY HOSPITAL. SANGVI MULTISPECIALITY HOSPITALS.NO .71/1/2/189, C.S .2387 KRUSHNA CHOWKKRISHNA NAGAR NEW SANGVI PUNE Pune Maharashtra -411027 I, India. **ECR/1865/Inst/MH/2023**
4.	Dr Dewesh Prakash Yadav, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh. India Pin Code: 221005	Institutional Ethics Committee IMS-BHU Varanasi Uttar Pradesh 221005. **ECR/526/Inst/UP/2014/RP-20**

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

Digitally signed by RAJEEV SINGH RAGHUVANSHI
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Date: 2024.01.15 11:42:29 +05'30'

(Dr. Rajeev Singh Raghuvanshi)
Central Licensing Authority

New Delhi