File No: BIO/CT/22/000115
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(Biological Division)

From:

The Drugs Controller General, India
Directorate General of Health Services,

FDA Bhawan, Kotla Road,
New Delhi-110002
Dated:19.05.2023

To,

M/s Johnson and Johnson Private Limited,
L. B. S. Marg, Mulund (West), Mumbai,
Maharashtra (India) – 400080

Subject: Application for grant of permission to conduct Phase IV clinical trial titled – "An Open Label, Multicentre, Phase IV Study of Ustekinumab to Evaluate Its Safety in Indian Subjects with Crohn's Disease (CD)" vide Protocol No.: CNTO1275CRD4045, Version Nil; dated 03 October 2022 – regarding

Ref.: Your Application No. BIO/CT04/FF/2022/34404 dated 19-Oct-2022

Sir,

With reference to your Application No.: BIO/CT04/FF/2022/34404 dated 19-Oct-2022, please find enclosed herewith the permission in Form CT-06 for conduct of subject clinical trial under the provisions of New Drugs and Clinical Trial Rules, 2019.

The permission granted by the Central Licensing Authority to conduct clinical trial under this Chapter shall be subject to following conditions, namely:

(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;

(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 Chapter VI 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 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) 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;

(XV) 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;

(XVI) The sponsor and the investigator shall maintain the data integrity of the data generated during clinical trial.

Yours faithfully,

RAJEEV SINGH RAGHUVANSHI

Digitally signed by RAJEEV SINGH RAGHUVANSHI
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Date: 2023.05.19 17:38:12 +05'30'

(Dr. Rajeev Singh Raghuvanshi)
Central Licensing Authority

File. No. BIO/CT/22/000115

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 Johnson and Johnson Private Limited, L. B. S. Marg, Mulund (West), Mumbai, Maharashtra (India) – 400080 to conduct Phase IV clinical trial of the new drug or investigational new drug as per Protocol No.:- CNTO1275CRD4045, Version Nil dated 03 October 2022 in the below mentioned clinical trial sites.

2. Details of new drug and clinical trial site [as per Annexure].

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.

Place: New Delhi
Date: 19-May-2023

RAJEEV SINGH RAGHUVANSHI

Digitally signed by RAJEEV SINGH RAGHUVANSHI
Date: 2023.05.19 17:38:25 +05'30'

(Dr Rajeev Singh Raghuvanshi)
Central Licensing Authority

Annexure:

Details of new drug or investigational new drug:

<table>
<tr><td>Names of the new drug or investigational new drug:</td><td>Ustekinumab (r-DNA origin)</td></tr>
<tr><td>Therapeutic class:</td><td>Immunosuppressive</td></tr>
<tr><td>Dosage form:</td><td>1. Concentrate solution for IV infusion in single use vial 130 mg/ 26 ml,
2. Solution for injection (Sub cutaneous) in pre-filled syringe 45 mg/0.5 ml & 90 mg/ml.</td></tr>
<tr><td>Composition:</td><td>Composition of the Ustekinumab 130 mg in single use vial:
<table>
<tr><th>Ingredient</th><th>Quantity per vial</th><th>Function</th></tr>
<tr><td>Ustekinumab, In-House</td><td>135 mg</td><td>Active</td></tr>
<tr><td>L-Histidine, USP/Ph. Eur./JP</td><td>21[a] mg</td><td>Buffer</td></tr>
<tr><td>L-Histidine Hydrochloride Monohydrate, Ph. Eur./JP</td><td>28[a] mg</td><td>Buffer</td></tr>
<tr><td>Sucrose, NF/Ph. Eur./JP</td><td>2295 mg</td><td>Stabilizer/Tonicifier</td></tr>
<tr><td>Polysorbate 80, NF/Ph. Eur./JP</td><td>10.8 mg</td><td>Surfactant</td></tr>
<tr><td>L-Methionine, USP/Ph. Eur./JP</td><td>10.8 mg</td><td>Anti-oxidant</td></tr>
<tr><td>EDTA disodium salt dihydrate[b] USP/Ph. Eur./JP</td><td>0.54 mg</td><td>Metal chelator</td></tr>
<tr><td>Water for Injection, USP/Ph. Eur./JP</td><td>q.s. ad 27.0 mL[c]</td><td>Diluent</td></tr>
</table>
[a]Calculated values based on total concentration of histidine (10 mM at pH 6.0) in formulation buffer due to the large dilution of drug substance (DS) (1:18) with formulation buffer.

[b]Denoted as: Edetate disodium in USP, Disodium edetate in Ph. Eur., and Disodium edetate hydrate in JP.

[c]Drug product contains a target 1.0 mL overfill to assure that a 26.0 mL nominal volume is delivered.

<u>Composition of the Ustekinumab 45 mg (0.5 mL) & 90 mg (1.0 mL) in PFS:</u>
<table>
<tr><th>Ingredient</th><th>Quantity per 90 mg PFS</th><th>Quantity per 45 mg PFS</th><th>Function</th></tr>
</table></td></tr>
</table>

	Ustekinumab, In-House	90 mg	45 mg	Active
	Sucrose, NF/EP	76 mg	38 mg	Tonicifier
	L-histidine[a], USP/EP	1.0 mg	0.5 mg	Buffer
	Polysorbate 80, NF/EP	0.04 mg	0.02 mg	Surfactant
	Water for injection, USP/EP	q.s. to 1 mL	q.s. to 0.5 mL	Solvent
	[a]L-histidine was quantified as total histidine			
Indications:	Ustekinumab is indicated for: • Inducing and maintaining clinical response, • Inducing and maintaining clinical remission, • Eliminating corticosteroid use, • Inducing endoscopic healing, • Improving health-related quality of life in adults with moderately to severely active Crohn's disease who: • have failed or were intolerant to immunomodulators or corticosteroids or • were corticosteroid dependent or • have failed or were intolerant to one or more anti-TNF treatment			

Details of clinical trial site:

S. No.	Name and Address of Clinical Trial Site	Ethics Committee Details	Name of Principal Investigator
1	All India Institute of Medical Sciences,Gastroenterogy and Human Nutrition Unit, All India Institute of Medical Sciences, Ansari Nagar, New Delhi-110029, India	Institute Ethics Committee; All India Institute of Medical Sciences, Room No. 102, First Floor, Old O.T. Block, Ansari Nagar, New Delhi-110029, India EC Reg. No.: ECR/538/Inst/DL/2014/RR-20	Dr. Saurabh Kedia
2	B. J .Government Medical College and Sassoon General Hospitals, Sassoon Road, Somwar Peth, Pune -411001 Maharashtra, India.	IEC B.J.G.M.C and Sassoon General Hospital; B.J.G.M.C and Sassoon General Hospital, Sassoon Road, Station Road, Pune, Maharashtra 411001 India EC Reg. No.: ECR/280/Inst/Maha/2013/RR-19	Dr. Jadhav Kirankumar Puna
3	Fortis Hospital L,udhiana Chandigarh Road, near Radha Soami Satsang Bhawan, Village-Mundian Kalan, Ludhiana, Punjab-141015, India	Institutional Ethics Committee;Fortis Hospital, Mundian Khurd, Ludhiana, Punjab-141015, India EC Reg. No.: ECR/746/Inst/PB/2015/RR-18	Dr. Nitin Shankar Behl

4	Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna, Bihar-800014	Institutional Ethics Committee;Indira Gandhi Institute of Medical Sciences, Sheikhpura, Pafira, Bihar-800014 EC Reg. No.: ECR/640/Inst/BR/2014/RR-20	Dr. Vishwa Mohan Dayal
5	Government Medical College, Trivandrum. Department of Medical Gastroenterology, Superspeciality Block, Govt Medical College, Thiruvananthapuram Kerala 695 011 India	Human Ethics Committee; Department of Pharmacology, Academic Block Govt Medical College Trivandrum EC Reg. No.: ECR/370/Inst/Ker/2013/RR-20	Dr. Krishnadas Devadas
6	M S Ramaiah Medical College and Hospitals, M S Ramaiah Nagar, MSRIT Post, Bangalore 560-054	ETHICS COMMITTEE; M S Ramaiah Medical College and Hospitals, MS Ramaiah Nagar, MSRIT Post, Bangalore 560-054 EC Reg. No.: ECR/215/Inst/KA/2013/RR-22	Dr. Avinash Balekuduru
7	SRM Institutes for Medical Sciences (SIMS); No. 1 Jawaharlal Nehru Salai, 100 feet road, Vadapalani, Chennai, Tamilnadu-600026	Institutional Ethics Committee- SRM Institutes for Medical; No. 1 Jawaharlal Nehru Salai, 100 feet road, Vadapalani, Chennai, Tamilnadu-600026 EC Reg. No.: ECR/805/Inst/TN/2016/RR-22	Dr. Siddhartha Ramakrishna
8	Shree Giriraj Multispeciality Hospital, A Unit of Shree Giriraj Lifecare Private Limited, 27 - Navjyot Park Comer, 150 Feet Ring Road, Rajkot- 360005.	Sanjeevani Metropolis Healthcare Private Ltd; Shree Giriraj MultiSpeciality Hospital, 27, Navjot Park Comer, 150 Feet Ring Road, Rajkot-360005, India EC Reg. No.: ECR/74/INST/GJ/2013/RR-19	Dr. Mehta Chetan Nalin
9	Surat Institute of digestive sciences (SIDS), SIDS Hospital and research centre, A unit of SIDS healthcare Pvt. Ltd., J J Empire Building & Tapi Villa Building, Vijay Nagar Gate No-3, Beside Nirman Bhavan, Opposite Gandhi College, Near Dayalji ashram, Majura Gate, ring road, Surat-395002, Gujarat, India.	Surat Institute of Digestive Sciences Ethics Committee; Surat Institute of Digestive Sciences, Vijay Nagar Gate No-3, besides Nirman Bhavan, opposite Gandhi College,Majura Gate, Ring Road, Surat-395002, Gujarat, India. EC Reg. No.: ECR/813/Inst/GJ/2016/RR-19	Dr. Rajiv Manhar Mehta