

File No: BIO/CT/20/000058
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

To,

M/s Bristol-myers Squibb India Pvt. Ltd.,
6th Floor, Tower 1, The India Bulls Finance Centre,
Senapati Bapat Marg, Elphinstone (West), Mumbai (India) – 400013

Subject: Application for grant of permission to conduct clinical trial entitled – “A Phase 4 Study of Nivolumab in Combination with Ipilimumab in Patients with Previously Untreated Advanced Renal Cell Carcinoma and Intermediate- or Poor-risk Factors conducted in India” as per Protocol No.: CA209-7C9, Version No. 1.0, dated 06-Feb-2020 - regarding

Ref.: Your Application No. BIO/CT04/FF/2020/19570 dated 11-May-2020

Sir,

With reference to your Application No.: BIO/CT04/FF/2020/19570 dated 11-May-2020, please find enclosed herewith the permission in FORM CT-06 for conduct of subject Phase IV 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,

**VENUGOPAL
GIRDHARILAL
SOMANI**

Digitally signed by VENUGOPAL
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(Dr. V. G. Somani)
Central Licensing Authority

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 Licencing Authority hereby permits M/s Bristol-myers Squibb India Pvt. Ltd., 6th Floor, Tower 1, The India Bulls Finance Centre Senapati Bapat Marg, Elphinstone (West), Mumbai (India) – 400013 to conduct clinical trial of the new drug or investigational new drug as per Protocol No.: CA209-7C9, Version No. 1.0, dated 06-Feb-2020 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:

VENUGOPAL
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(Dr. V. G. Somani)

Central Licencing Authority

Annexure:**Details of new drug or investigational new drug:**

Names of the new drug	Ipilimumab (r-DNA origin) Injection, 50 mg/10 mL (5 mg/mL)	
Therapeutic class:	Anticancer	
Dosage form:	Concentrate solution for infusion	
Composition:	Name of Ingredients	Quantity per 50 mg Vial (mg)
	Ipilimumab (in-house specification)	53.5
	Tris Hydrochloride (in-house specification)	33.7
	Sodium Chloride (USP/Ph.Eur)	62.6
	Mannitol (USP and Ph.Eur.)	107.0
	Pentetic Acid (USP)	0.42
	Polysorbate 80 (NF/Ph.Eur.)	1.18
	Sodium Hydroxide (USP/Ph.Eur./JP or IH)	q.s. to pH 7.0
	Hydrochloric Acid (NF or in-house specification)	q.s. to pH 7.0
	Water for Injection (USP/Ph.Eur.)	q.s. to 10.7 mL
	Nitrogen (NF/Ph.Eur.)	-
Indications:	Ipilimumab is indicated for treatment of patients with intermediate or poor risk, previously untreated advanced Renal Cell Carcinoma, in combination with Nivolumab.	

Details of clinical trial sites:

S. No.	Name and Address of Clinical Trial Site	Ethics Committee Details	Name of Principal Investigator
1	Tata Memorial Hospital, Tata Memorial Hospital, Dr. E Borges Road, Parel, Mumbai Maharashtra - 400012	TMH, Institutional Ethics Committee-I & II Tata Memorial Hospital Dr. Ernest Borges Road, Parel, Mumbai City Maharashtra - 400012 India EC Reg. No.: ECR/170/Inst/MH/2013/RR-19 & ECR/414/Inst/MH/2013/RR-19	Dr Kumar Prabhash
2	HealthCare Global Enterprises Limited, P. kalingarao Road, Sampangiram nagar Bangalore Karnataka - 560027	HCG Central Ethics Committee HCG-Bangalore institute of Oncology HCG Towers, Tower-I P. Kalinga Rao Road, Sampangiram Nagar, Bengaluru Urban Karnataka - 560027 India EC Reg. No.: ECR/386/Inst/KA/2013/RR-19	Dr Shekar Gowda Patil
3	Manipal Hospital, 98, HAL Airport Road, Bangalore, Karnataka - 560017	Ethics Committee of Manipal Hospitals No 98, HAL Airport Road, Bangalore Urban Karnataka - 560017 India EC Reg. No.: ECR/34/Inst/KA/2013/RR-19	Dr Amit Rauthan
4	All India Institute of Medical Sciences, Dr. B.R.A. Institute Rotary Cancer Hospital, Ansari Nagar, Department of Medical Oncology, New Delhi - 110029	Ethics Committee, All India Institute of Medical Sciences Room 102, 1st floor, Old O.T. block, Ansari Nagar, New Delhi - 110029 EC Reg. No.: ECR/547/Inst/DL/2014/RR-17	Dr Ranjit Sahoo

S. No.	Name and Address of Clinical Trial Site	Ethics Committee Details	Name of Principal Investigator
5	Regional Cancer Centre, Medical College P.O, Thiruvanthapuram, Kerala - 695011	Human Ethics Committee RCC Regional Cancer Centre Medical College Campus Thiruvananthapuram, Kerala - 695011 India EC Reg. No.: ECR/21/Inst/Ker/2013/RR-2019	Dr Lakshmi Haridas K
6	Ruby hall Clinic, Grant Medical Foundation Ruby Hall clinic, 40 Sassoon Road, Pune Maharashtra - 411001	Poona Medical Research Foundation Ruby Hall Clinic, 40, Sassoon Road, Pune, Maharashtra - 411001, India EC Reg. No.: ECR/24/Inst/MH/2013/RR-19	Dr Minish Jain
7	Mumbai Oncocare Centre, Cellcure cancer Center Pvt Ltd, Majithia Apartment, God Gift Premises, S V Road, Ville Parle, Mumbai Maharashtra - 400056	Mumbai Oncocare Central IEC Cellcure cancer Center Pvt Ltd, Majithia Apartment, God Gift Premises, S V Road, Ville Parle, Mumbai Suburban, Maharashtra - 400056, India EC Reg. No.: ECR/1277/Inst/MH/2019	Dr Vashishth Maniar
8	Kokilaben Dhirubhai Ambani Hospital, Rao Saheb, Achutrao Patwardhan Marg, Four Bungalows, Andheri West, Mumbai Maharashtra - 400053	Institutional Ethics Committee Kokilaben Dhirubhai Ambani Hospital & Medical Research Institute Rao saheb Achutrao Patwardhan Marg, Four Bungalows Andheri West Mumbai Mumbai City Maharashtra - 400053 India EC Reg. No.: ECR/141/Inst/MH/2013/RR-19	Dr Sewanti Limaye
9	Rajiv Gandhi Cancer Institute and Research Centre, Rajiv Gandhi Cancer Institute and Research Centre, Sir Chotu Ram Marg, Rohini Institutional Area, Sector 5, Rohini, New Delhi - 110085	Institutional Review Board Rajiv Gandhi Cancer Institute and Research Centre Rohini Sector V Rohini west Metro station Delhi South West Delhi, Delhi - 110085 India EC Reg. No.: ECR/10/Inst/DL/2013/RR-19	Dr Vineet Talwar
10	Narayana Superspeciality Hospital, 120-1, Andul Road, Howrah, West Bengal -71103	NSH Ethics Committee Narayana Superspeciality Hospital 120/1 Andul road Howrah, West Bengal - 71103 India EC Reg. No.: ECR/1006/Inst/WB/2018	Dr M V Chandrakanth