File No: BIO/CT/23/000132
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: 13.05.2024

To,

M/s AstraZeneca Pharma India Limited,
Block N 1, 12th Floor, Manyata Embassy Business Park,
Rachenahalli Outer Ring Road, Bangalore – 560045,
Karnataka, India

Subject: Application for grant of permission to conduct Phase IV clinical trial titled – "A prospective, multi-center, Phase IV, single arm study to assess the safety of Trastuzumab Deruxtecan, an anti-HER2- antibody drug conjugate in Indian patients with unresectable or metastatic HER2-Positive Breast Cancer who have received a prior anti-HER2- Based Regimen (STRIDE)" vide protocol No. D9673L00012, version 1.0 dated 13 Sep 2023 - regarding

Ref.: Your Application No. BIO/CT04/FF/2023/40241 dated 30-Oct-2023

Sir,

With reference to your Application No.: BIO/CT04/FF/2023/40241 dated 30-Oct-2023, 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.

(XVII) Clinical Study Report (CSR) shall be submitted to this office after completion of the study.

Yours faithfully,

RAJEEV SINGH RAGHUVANSHI

Digitally signed by RAJEEV SINGH RAGHUVANSHI
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(Dr. Rajeev Singh Raghuvanshi)
Central Licensing Authority

File. No. BIO/CT/23/000132

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 AstraZeneca Pharma India Limited, Block N 1, 12th Floor, Manyata Embassy Business Park, Rachenahalli Outer Ring Road, Bangalore – 560045, Karnataka, India to conduct clinical trial of the new drug or investigational new drug as per Protocol No.:- D9673L00012, version 1.0 dated 13 Sep 2023 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.

RAJEEV SINGH RAGHUVANSHI

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Date: 2024.05.15 16:10:50 +05'30'

Place: New Delhi
Date: 13-May-2024

(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>Trastuzumab deruxtecan concentrate solution for infusion 100 milligram (mg) (r-DNA origin)</td></tr>
<tr><td>Therapeutic class:</td><td>Anti-cancer</td></tr>
<tr><td>Dosage form:</td><td>Single use sterile, lyophilized powder for concentrate for solution for infusion in vial</td></tr>
<tr><td>Composition:</td><td>Each vial contains –
<table>
<tr><th>Ingredients</th><th>Qty per vial[a]</th><th>Function</th></tr>
<tr><td>Trastuzumab deruxtecan IH</td><td>107 mg</td><td>Active ingredient</td></tr>
<tr><td>L-Histidine hydrochloride monohydrate JP/Ph. Eur</td><td>21.6 mg</td><td>Buffer</td></tr>
<tr><td>L-Histidine USP/JP/Ph. Eur</td><td>4.76 mg</td><td>Buffer</td></tr>
<tr><td>Sucrose NF/JP/Ph. Eur.</td><td>482 mg</td><td>Bulking agent</td></tr>
<tr><td>Polysorbate 80 Ph. Eur/NF/JP</td><td>1.61 mg</td><td>Surfactant</td></tr>
</table>
[a]The quantity per vial shows the composition of the lyophilized powder in vial. The composition contains the target excess fill volume of 5.35 ml (equivalent to 5.569mg) of compounded drug product solution to assure and extractable volume of 5ml.</td></tr>
<tr><td>Indications:</td><td>Trastuzumab deruxtecan is indicated for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received a prior anti- HER2-based regimen.</td></tr>
</table>

Details of clinical trial site:

S. No.	Name and Address of Clinical Trial Site	Ethics Committee Details	Name of Principal Investigator
1	Tata Memorial Hospital, Tata Memorial Centre, Dr. Ernest Borges Road, Parel (E), Mumbai, Maharashtra - 400012	TMH, Institutional Ethics Committee-I, Tata Memorial Hospital, Dr. E. Borges Road, Parel, Mumbai City, Maharashtra - 400012 ECR/170/Inst/MH/2013/RR-22	Dr Sudeep Gupta
2	All India Institute of Medical Sciences (AIIMS), Department of medical oncology, Dr. B.R..A I.R.C.H, Ansari Nagar, New Delhi, 110029	Institute Ethics Committee, All India Institute of Medical Sciences, Old OT Block, Room No. 102, Ansari Nagar, New Delhi, 110029 ECR/538/Inst/DL/2014/RR-20EC	Dr Ajay Gogia

3	VMMC And Safdurjung Hospital, Ring Road, Ansari Nagar, New Delhi - 110029	Institutional Ethics Committee, VMMC And Safdurjung Hospital, Ring Road Ansari Nagar New Delhi – 110029 ECR/593/Inst/DL/2014/RR-20	Dr Kaushal Kalra
4	Manipal Hospital, No. 98, HAL Airport Road, Bengaluru, Karnataka - 560017	Ethics Committee of Manipal Hospital, No 98, HAL Airport Road, Bangalore, Karnataka – 560017 ECR/34/Inst/KA/2013/RR-19	Dr Amit Rauthan
5	Amrita Institute of Medical Sciences, AIMS - Ponekkara Kochi Edappally Ernakulam Kerala - 682041	Institutional Ethics Committee, Amrita Institute of Medical Sciences, AIMS - Ponekkara Koch,i Edappally, Ernakulam Kerala – 682041 ECR/129/Inst/KL/2013/RR-19	Dr Pavithran K
6	Mahamana Pandit Madan Mohan Malaviya Cancer Centre, Sundar Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi, Uttar Pradesh - 221005	IEC, MPMMCC and HBCH Varanasi, Mahamana Pandit Madan Mohan Malaviya Cancer Centre, Sundar Bagiya, Near Nariya Gate Banaras Hindu University Campus, Varanasi Uttar Pradesh – 221005 ECR/1501/Inst/UP/2021	Dr Akhil Kapoor
7	Sir H N Reliance Foundation Hospital And Research Centre, Raja Ram Mohan Roy Road, Prarthana Samaj, Girgaum, Mumbai - 400004	IEC of Sir H N Reliance Foundation Hospital and Research Centre, Raja Ram Mohan Roy Road, Prarthana Samaj, Girgaum, Mumbai - 400004 ECR/1389/Inst/MH/2020	Dr Sewanti Limaye
8	Apollo Cancer Centre, No. 320, Padma Complex, Anna Salai, Chennai, 600035, Tamil Nadu	Institutional Ethics Committee - Clinical Studies, Apollo Hospitals Enterprises Limited, No-21, Greams Lane, off Greams road, Chennai, Tamil Nadu – 600006 ECR/37/Inst/TN/2013/RR-19	Dr Sankar Srinivasan