

File No: BIO/CT/23/000119
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: 13.08.2023

To,

M/s. Sanofi Healthcare India Pvt. Ltd.
Sanofi House, CT Survey No. 117-B, L&T Business Park,
Saki Vihar Road, Powai, Mumbai 400072

Subject: Application for grant of permission to conduct Phase IV clinical trial titled – “Multicentre Phase IV single arm clinical trial to evaluate the safety and efficacy of a fixed ratio combination of Insulin Glargine and Lixisenatide in adult patients with Type 2 diabetes who are sub optimally controlled on oral anti-hyperglycemic drugs and/or basal Insulin/GLP-1 RA” vide protocol No. LPS18016, Amended Protocol 1.1, dated 18.06.2024- regarding
Ref.: Your Application No. BIO/CT04/FF/2023/39609 dated 15-Sept.-2023

Sir,

With reference to your Application No.:BIO/CT04/FF/2023/39609 dated 15-Sept.-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) You are required to submit the clinical study report after completion of the study.

RAJEEV SINGH
RAGHUVANSHI

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(Dr. Rajeev Singh Raghuvanshi)
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 Licensing Authority hereby permits M/s. Sanofi Healthcare India Pvt. Ltd., Sanofi House, CT Survey No. 117-B, L&T Business Park, Saki Vihar Road, Powai, Mumbai 400072 to conduct clinical trial of the new drug or investigational new drug trial titled as – “Multicentre Phase IV single arm clinical trial to evaluate the safety and efficacy of a fixed ratio combination of Insulin Glargine and Lixisenatide in adult patients with Type 2 diabetes who are sub optimally controlled on oral anti-hyperglycemic drugs and/or basal Insulin/GLP-1 RA” vide Protocol No.:- LPS18016, Amended Protocol 1.1, dated 18.06.2024 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:13-Aug-2024

RAJEEV SINGH
RAGHUVANSHI

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(Dr. Rajeev Singh Raghuvanshi)

Central Licensing Authority

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

| Names of the new drug or investigational new drug: | Insulin Glargine and Lixisenatide Injection. (Fixed Ratio Combination of Insulin Glargine 100U/ml + Lixisenatide 33 mcg/ml and Insulin Glargine 100U/ml + Lixisenatide 50mcg/ml) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--|---|--|--|---------------------|--|--|---------------------------------|----------------|----------------|------------------------|------|-------|----------------------------------|------|------|---------------------------|-----|-----|---------------------------|-----|-----|---|--------|--------|---------------------------------|-------------|-------------|--------------------------------|-------------|-------------|------------------------------------|-----------|-----------|------------------------|----------------------------|--|
| Therapeutic class: | Antihyperglycemic | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dosage form: | Solution for Subcutaneous injection in prefilled pen. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Composition: | <p>Drug product is available as a sterile solution for injection in prefilled pen (contains 3 ml Cartridge) in two dosage strengths:</p> <ul style="list-style-type: none"> • 10-40 prefilled pen contains per mL 100 units insulin glargine and 50 mcg lixisenatide. • 30-60 prefilled pen contains per mL 100 units insulin glargine and 33 mcg lixisenatide. <table border="1" data-bbox="421 853 1461 1883"> <thead> <tr> <th>Name of Ingredients</th> <th>100 U/mL Insulin glargine with 50 µg/mL lixisenatide (Quantity in mg per ml)</th> <th>100 U/mL Insulin glargine with 33 µg/mL lixisenatide (Quantity in mg per ml)</th> </tr> </thead> <tbody> <tr> <td>Insulin glargine, Ph. Eur., USP</td> <td>3.6378 [100 U]</td> <td>3.6378 [100 U]</td> </tr> <tr> <td>Lixisenatide, In house</td> <td>0.05</td> <td>0.033</td> </tr> <tr> <td>Glycerol (85 per cent), Ph. Eur.</td> <td>20.0</td> <td>20.0</td> </tr> <tr> <td>Methionine, Ph. Eur., USP</td> <td>3.0</td> <td>3.0</td> </tr> <tr> <td>Metacresol, Ph. Eur., USP</td> <td>2.7</td> <td>2.7</td> </tr> <tr> <td>Zinc Chloride, Ph. Eur., USP^a</td> <td>0.0626</td> <td>0.0626</td> </tr> <tr> <td>Hydrochloric acid, Ph. Eur., NF</td> <td>q.s. pH 4.5</td> <td>q.s. pH 4.5</td> </tr> <tr> <td>Sodium hydroxide, Ph. Eur., NF</td> <td>q.s. pH 4.5</td> <td>q.s. pH 4.5</td> </tr> <tr> <td>Water for injection, Ph. Eur., USP</td> <td>q.s. 1 mL</td> <td>q.s. 1 mL</td> </tr> <tr> <td>Nitrogen, Ph. Eur., NF</td> <td colspan="2">Process aid for filtration</td> </tr> </tbody> </table> <p>^a Composition gives total zinc chloride amount from drug substance and from the manufacturing of the drug product.</p> | | | Name of Ingredients | 100 U/mL Insulin glargine with 50 µg/mL lixisenatide (Quantity in mg per ml) | 100 U/mL Insulin glargine with 33 µg/mL lixisenatide (Quantity in mg per ml) | Insulin glargine, Ph. Eur., USP | 3.6378 [100 U] | 3.6378 [100 U] | Lixisenatide, In house | 0.05 | 0.033 | Glycerol (85 per cent), Ph. Eur. | 20.0 | 20.0 | Methionine, Ph. Eur., USP | 3.0 | 3.0 | Metacresol, Ph. Eur., USP | 2.7 | 2.7 | Zinc Chloride, Ph. Eur., USP ^a | 0.0626 | 0.0626 | Hydrochloric acid, Ph. Eur., NF | q.s. pH 4.5 | q.s. pH 4.5 | Sodium hydroxide, Ph. Eur., NF | q.s. pH 4.5 | q.s. pH 4.5 | Water for injection, Ph. Eur., USP | q.s. 1 mL | q.s. 1 mL | Nitrogen, Ph. Eur., NF | Process aid for filtration | |
| Name of Ingredients | 100 U/mL Insulin glargine with 50 µg/mL lixisenatide (Quantity in mg per ml) | 100 U/mL Insulin glargine with 33 µg/mL lixisenatide (Quantity in mg per ml) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Insulin glargine, Ph. Eur., USP | 3.6378 [100 U] | 3.6378 [100 U] | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Lixisenatide, In house | 0.05 | 0.033 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Glycerol (85 per cent), Ph. Eur. | 20.0 | 20.0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Methionine, Ph. Eur., USP | 3.0 | 3.0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Metacresol, Ph. Eur., USP | 2.7 | 2.7 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Zinc Chloride, Ph. Eur., USP ^a | 0.0626 | 0.0626 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hydrochloric acid, Ph. Eur., NF | q.s. pH 4.5 | q.s. pH 4.5 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Sodium hydroxide, Ph. Eur., NF | q.s. pH 4.5 | q.s. pH 4.5 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Water for injection, Ph. Eur., USP | q.s. 1 mL | q.s. 1 mL | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Nitrogen, Ph. Eur., NF | Process aid for filtration | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Indications: | For treatment of adults patients with Obesity with insufficiently controlled type 2 diabetes mellitus to improve glycemic control as an adjunct to diet and exercise in addition to metformin with or without SGLT2 inhibitors, when this has not been provided by metformin alone or metformin combined with another oral glucose lowering medicinal product (sulfonylurea, glinide, DPP- | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

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| | 4 inhibitors or gliptins, and Sodium-glucose co-transporter 2 (SGLT2) inhibitors or gliflozins) or with basal insulin or with glucagon-like peptide-1 (GLP-1) receptor agonist. |
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Details of clinical trial site:

| S. No. | Name and Address of Clinical Trial Site | Ethics Committee Details | Name of Principal Investigator |
|--------|---|---|--------------------------------|
| 1 | Post Graduate Institute of Medical Education and Research, Chandigarh - 160012, India | Institutional Ethics Committee, Post Graduate Institute of Medical Education and Research, Room 6006, IEC Office, 6th Floor, P N Chuttani Block, Chandigarh- 160012, India EC Reg. No.: ECR/25/Inst/CH/2 013/RR-20 | Dr. Sanjay Kumar Bhadada |
| 2 | IPGMER and SSKM Hospital, 244 A.J.C. Bose Road, Kolkata 700020 India | IPGMEandR Research Oversight Committee IPGMEandR, 244 Acharya JC Bose Road, Kolkata 700020, India EC Reg. No.: ECR/35/Inst/WB/2013/RR-19 | Dr. Sujoy Ghosh |
| 3 | Room No. 137, 1st Floor, Department of Endocrinology, G.S.V.S. PGI., G.S.V.M. Medical College, Swaroop Nagar, Kanpur- 208002, U.P., India | Ethics Committee, G.S.V.M medical College, Kanpur, Swaroop Nagar, Kanpur- 208005, U.P., India EC Reg. No.: ECR/680/Inst/UP/2014/RR-20 | Dr. Shivendra Verma |
| 4 | Max Super Specialty Hospital, Saket (A Unit of Devki Devi Foundation) 2, Press Enclave Road, Saket, New Delhi 110017 | Institutional Ethics Committee, Service Floor, Office of Ethics Committee, East Block, Near to Conference Room, Max Super Specialty Hospital, Saket. (A unit of Devki devi foundation), 2, Press Enclave Road, Saket, New Delhi- 110017 EC Reg. No.: ECR/110/Inst/DL/2013/RR-19 | Dr. Ambrish Mithal |
| 5 | Eternal Hospital, 3A Jagatpura Road, Near Jawahar Circle, Jaipur-302017, Rajasthan, India | Eternal Heart Care Center and Research Institute IEC, Eternal Hospital, 3A Jagatpura Road, Near Jawahar Circle, Jaipur 302017, Rajasthan, India. EC Reg. No.: ECR/615/Inst/RJ/2014/RR-20 | Dr. Sailesh Lodha |
| 6 | M S Ramaiah Medical College and Hospitals, M S Ramaiah Nagar, MSRIT Post, Bangalore – 560054, India | Ethics Committee, M S Ramaiah Medical College and Hospitals, M S Ramaiah Nagar, MSRIT Post, Bangalore – 560054, India EC Reg. No.: ECR/215/Inst/KA/2013/RR-22 | Dr. Pramila Kalra |
| 7 | TOTALL Diabetes Hormone Institute Pvt. Ltd. A unit of Diabetes Thyroid Hormone | Ethics committee of Diabetes Thyroid Hormone Research Institute Private Limited Indore-452010, MP | Dr. Sunil Jain |

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|----|---|--|---------------------------|
| | Research Institute Pvt. Ltd., BCM Health Island PU-4, Scheme No. 54, Near Bombay Hospital, Behind Prestige Institute of Management, Indore- 452010, MP | EC Reg. No.: ECR/409/Inst/MP/2013/RR-19 | |
| 8 | Care Outpatient Center, H No 8-2620/ A-E, Ground Floor C Block, Road No 10, Banjara Hills, Hyderabad- 500034, Telangana | Institutional Ethics Committee, Care Hospital, In Patient Building, 4th Floor, 6- 3248/2, Road No 1, Banjara Hills, Hyderabad-500034, TS EC Reg. No.: ECR/94/Inst/AP/2013/RR-21 | Dr. Bipin Kumar Sethi |
| 9 | Fortis Hospital, A Block, Shalimar Bagh, New Delhi New Delhi-110088, India | Institutional Ethics Committee, Fortis Hospital, Shalimar Bagh, New Delhi- 110088, India EC Reg. No.: ECR/513/Inst/DL/2014/RR-20 | Dr. Danendra Sahu |
| 10 | Sahyadri Super Specialty Hospital, 30-C Erandawane, Karve Road, Pune 411004, Maharashtra, India | Sahyadri Hospitals Ltd. Ethics committee Sahyadri Clinical Research & Development Center (A Unit of Sahyadri Hospitals Ltd.), 33/34B, Makarand Bhawe Path, Karve Road, Pune- 411004 Maharashtra, India EC Reg. No: ECR/493/Inst/MH/2013/RR-19 | Dr. Uday Keshav Phadke |