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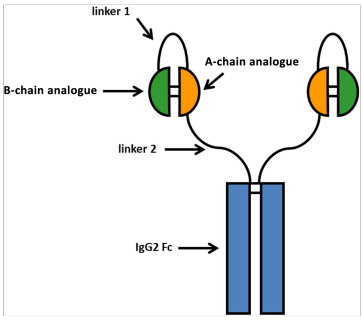


Insulin efsitora

Developer(s)

Eli Lilly

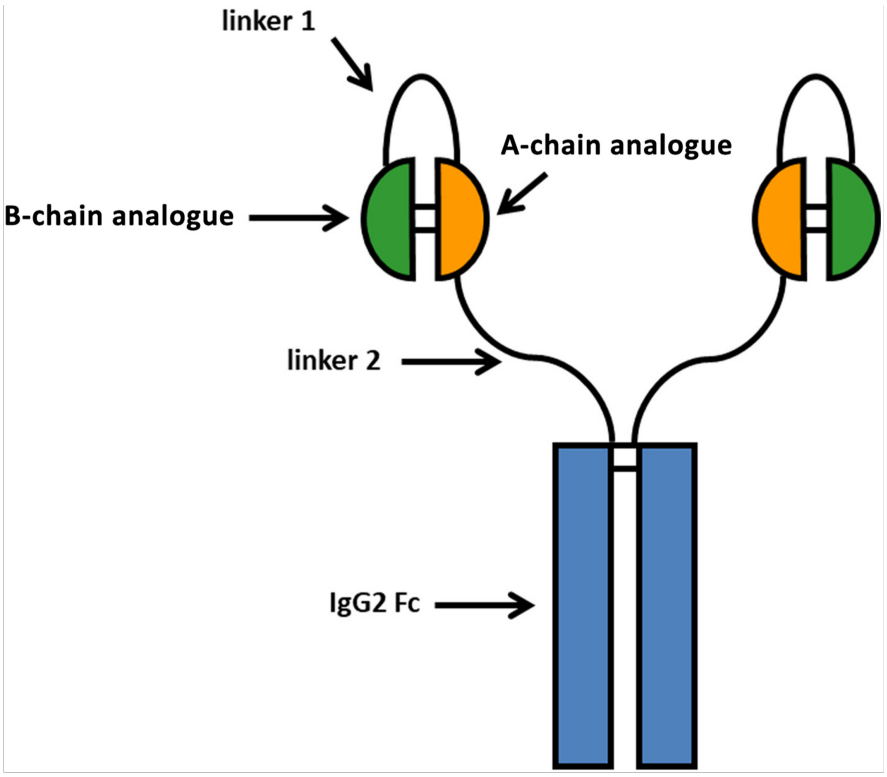
Originator

https://www.lilly.com/uk/

United States of America

Eli Lilly and Company, commonly known as Lilly, is an American multinational pharmaceutical company headquartered in Indianapolis, Indiana. Founded nearly 150 years ago, Lilly focuses on developing medicines that improve lives worldwide. The company is renowned for its contributions in biomedicine and pharmaceuticals, with a diverse portfolio including well-known products like Trulicity, Jardiance

Drug structure



Schematic of weekly basal insulin Fc (BIF) structure

Moyers, J. S., Hansen, R. J., Day, J. W., Dickinson, C. D., Zhang, C., Ruan, X., Ding, L., Brown, R. M., Baker, H. E., & Beals, J. M. (2022). Preclinical Characterization of LY3209590, a Novel Weekly

Drug information

Associated long-acting platforms

Solution

Administration route

Subcutaneous

Therapeutic area(s)

Diabetes

Use case(s)

Treatment

Use of drug

Ease of administration

Administered by a nurse
Self-administered
Administered by a community health worker
Administered by a specialty health worker

User acceptance

Not provided

Dosage

Available dose and strength

500 units/mL

Frequency of administration

Once weekly

Maximum dose

Not provided

Recommended dosing regimen

Dosage Regimen for Efsitora (500 units/mL): 1. Loading Dose (Week 1—First Injection Only): Administer a one-time loading dose calculated as usual daily basal insulin dose (units) × 7 (rounded to the nearest 10 units) × 3. This loading dose is intended to provide weekly basal coverage. 2. Maintenance Dose (Week 2 Onwards): Administer a weekly dose calculated as usual daily basal insulin dose (units) × 7 (rounded to the nearest 10 units) × 3. This dose should be given once weekly thereafter.

Additional comments

Not provided

Dosage link(s)

Not provided

Drug information

Drug's link(s)

https://go.drugbank.com/drugs/DB19013

Generic name

Insulin efsitora (LY3209590) (basal insulin Fc)

Brand name

Not provided

Compound type

Biotherapeutic

Summary

Insulin efisitora alfa is a long-acting fusion protein administered once weekly for the management of type 2 diabetes mellitus. It exhibits a terminal half-life ($t_{1/2}$) of approximately 17 days, supporting a sustained and dose-dependent reduction in fasting blood glucose levels for five days or longer. The maximum observed plasma concentration (C_max) is approximately 30 nmol/L. Clinical trial data suggest that insulin efisitora alfa has a favorable safety profile, with no reports of severe hypoglycemia. However, at a 10 mg dose, 83% of patients experienced at least one adverse event.

Approval status

Not yet approved

Regulatory authorities

Not yet approved

Delivery device(s)

No delivery device

Scale-up and manufacturing prospects

Scale-up prospects

Not provided

Tentative equipment list for manufacturing

1. Bioreactor 2. Seed culture tanks 3. Homogenizer 4. Reaction vessel 5. Stirrer 6. Inert gas supply systems 7. Ultrafiltration units

Manufacturing

1. Recombinant Expression of Insulin in Saccharomyces cerevisiae 2. Purification of insulin analog 3. Site-specific conjugation 4. Purification of the conjugated insulin 5. Excipient addition and formulation preparation

Specific analytical instrument required for characterization of formulation

1. Ion-exchange chromatography/Reverse-phase chromatography/Size-exclusion chromatography 2. High-Performance Liquid Chromatography (HPLC)

Clinical trials

QWINT-1

Identifier

NCT05662332

Link

https://clinicaltrials.gov/study/NCT05662332

Phase

Phase III

Status

Completed

Sponsor

Eli Lilly and Company

More details

The main purpose of this study is to determine the efficacy and safety of insulin efsitora alfa (LY3209590) administered weekly using a fixed dose escalation compared to insulin glargine in adults with type 2 diabetes (T2D) who are starting basal insulin therapy for the first time.

Purpose

A Study of Insulin Efsitora Alfa (LY3209590) Compared to Glargine in Adult Participants With Type 2 Diabetes Who Are Starting Basal Insulin for the First Time (QWINT-1)

Interventions

Intervention 1

Insulin Efsitora Alfa

Intervention 2

Insulin Glargine

Countries

United States of America

Argentina

Mexico

Puerto Rico

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2023-01-14

Anticipated Date of Last Follow-up

2024-10-28

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2024-07-19

Actual Completion Date

2024-07-19

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Have a diagnosis of T2D according to the World Health Organization criteria. * Have an HbA1c of 7.0% to 10.0%, inclusive, at screening. * Are on a stable treatment of at least 1 antihyperglycemic medication, for at least 3 months prior to screening, and willing to continue the stable treatment for the duration of the study. * Are insulin naive Exceptions: * short-term insulin treatment for a maximum of 14 days, prior to screening, and * prior insulin treatment for gestational diabetes. Exclusion Criteria: * Have a diagnosis of type 1 diabetes (T1D), latent autoimmune diabetes, or specific type of diabetes other than T2D, for example, monogenic diabetes, diseases of the exocrine pancreas, or drug induced or chemical-induced diabetes. * Have a history of \>1 episod

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

795

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Weekly

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

Not provided

18237

Identifier

NCT05275400

Link

https://clinicaltrials.gov/study/NCT05275400

Phase

Phase III

Status

Completed

Sponsor

Eli Lilly and Company

More details

The reason for this study is to see if the study drug insulin efsitora alfa (LY3209590) is safe and effective in participants with Type 2 diabetes that have already been treated with basal insulin. The study consists of a 3-week screening/lead-in period, a 78-week treatment period and a 5-week safety follow-up period. The study will last up to 86 weeks.

Purpose

A Study of Insulin Efsitora Alfa (LY3209590) Compared With Insulin Degludec in Participants With Type 2 Diabetes Currently Treated With Basal Insulin

Interventions

Intervention 1

Insulin Efsitora Alfa

Intervention 2

Insulin Degludec

Countries

United States of America
Argentina
Hungary
Japan
Korea, Republic of
Poland
Puerto Rico
Slovakia
Spain
Taiwan, Province of China

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2022-03-08

Anticipated Date of Last Follow-up

2024-05-24

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2024-05-15

Actual Completion Date

2024-05-15

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Have been diagnosed with Type 2 diabetes according to the World Health Organization (WHO) criteria treated with basal insulin * Are receiving ≥10 units of basal insulin per day and ≤110 units per day at screening * Have HbA1c value of 6.5% - 10% inclusive, at screening * Have a Body mass index (BMI) less than or equal to 45 kilogram/square meter (kg/m^2) * Have been treated with one of the following stable insulin regimens at least 90 days prior to screening: * once daily U100 or U200 of insulin degludec * once daily U100 or U300 of insulin glargine * once or twice daily U100 of insulin detemir, or * once or twice daily human insulin NPH * acceptable non

insulin glucose lowering therapies may include 0 to up to 3 of the following: * dipeptidyl peptidase (D

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

986

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Weekly

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

Not provided

QWINT-5

Identifier

NCT05463744

Link

https://clinicaltrials.gov/study/NCT05463744

Phase

Phase III

Status

Completed

Sponsor

Eli Lilly and Company

More details

The main purpose of this study is to measure the safety and efficacy of insulin efsitora alfa (LY3209590) compared with insulin degludec in participants with type 1 diabetes treated with multiple daily injection therapy.

Purpose

A Study of Insulin Efsitora Alfa (LY3209590) Compared With Insulin Degludec in Participants With Type 1 Diabetes Treated With Multiple Daily Injection Therapy

Interventions

Intervention 1

Insulin Efsitora Alfa

Intervention 2

Insulin Degludec

Countries

United States of America

Argentina

Japan

Poland

Puerto Rico

Slovakia

Taiwan, Province of China

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2022-08-12

Anticipated Date of Last Follow-up

2024-07-26

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2024-05-07

Actual Completion Date

2024-05-07

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Have a clinical diagnosis of type 1 diabetes for at least 1 year prior to screening * Have received treatment with basal-bolus insulin analog multiple daily injection therapy according to the local product label for at least 90 days prior to screening * Have an HbA1c value of 7.0% to 10.0%, inclusive, as determined by the central laboratory at screening. * Have a body mass index of ≤35 kilogram/square meter (kg/m^2) Exclusion Criteria: * Have a diagnosis of type 2 diabetes, latent autoimmune diabetes, or specific types of diabetes other than type 1 diabetes * Have a history of more than 1 episode of severe hypoglycemia, within the 6 months prior to screening. * Have a history of more than 1 episode of diabetic ketoacidosis or hyperosmolar state or coma requiring hos

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

692

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Weekly

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

Not provided

QWINT-2

Identifier

NCT05362058

Link

https://clinicaltrials.gov/study/NCT05362058

Phase

Phase III

Status

Completed

Sponsor

Eli Lilly and Company

More details

The purpose of this study is to determine the effect and safety of insulin efsitora alfa (LY3209590) compared to degludec in adult participants with type 2 diabetes who are starting basal insulin for the first time. The study consists of a 1-week screening period, a 2-week lead-in period, a 52-week treatment period, and a 5-week safety follow-up period. The study will last up to 60 weeks.

Purpose

A Study of Insulin Efsitora Alfa (LY3209590) Compared to Degludec in Adults With Type 2 Diabetes Who Are Starting Basal Insulin for the First Time

Interventions

Intervention 1

Insulin Efsitora Alfa

Intervention 2

Insulin Degludec

Countries

United States of America
Brazil
Canada
China
Czechia
Germany
Greece
Japan
Korea, Republic of
Mexico
Puerto Rico

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2022-06-03

Anticipated Date of Last Follow-up

2025-05-05

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2024-04-10

Actual Completion Date

2024-04-10

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Have diagnosis of Type 2 diabetes (T2D) according to the World Health Organization Criteria * Have an Hemoglobin A1c (HbA1c) of 7.0 percent (%) - 10.5% inclusive, at screening * Are on a stable treatment with 1 to 3 antihyperglycemic medication for at least 3 months prior to screening and willing to continue the stable treatment for the duration of the study * These antihyperglycemic medications are accepted in the study * dipeptidyl peptidase-4 (DPP-4) inhibitors * sodium-glucose cotransporter 2 (SGLT2) inhibitors * biguanides, such as metformin * alpha-glucosidase inhibitors * glucagon-like peptide-1 (GLP-1) receptor agonists, oral

or injectable * Sulfonylureas, or * Thiazolidinediones. * Are insulin naïve. Exceptions: * short-term insulin treatmen

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

928

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Weekly

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

Not provided

QWINT-4

Identifier

NCT05462756

Link

https://clinicaltrials.gov/study/NCT05462756

Phase

Phase III

Status

Completed

Sponsor

Eli Lilly and Company

More details

The reason for this study is to evaluate if the once-weekly study drug insulin efsitora alfa (LY3209590) is safe and effective compared with daily insulin glargine in participants with Type 2 diabetes (T2D) that have already been treated with basal insulin and at least 2 injections per day of prandial insulin. The study consists of a 3-week screening/lead-in period, a 26-week treatment period and a 5-week safety follow-up period. The study will last up to 34 weeks.

Purpose

A Study of Insulin Efsitora Alfa (LY3209590) as a Weekly Basal Insulin Compared to Insulin Glargine in Adult Participants With Type 2 Diabetes on Multiple Daily Injections

Interventions

Intervention 1

Insulin Efsitora Alfa

Intervention 2

Insulin Lispro (U100)

Intervention 3

Insulin Glargine (U100)

Countries

United States of America

Argentina

Germany

India

Italy

Mexico

Puerto Rico

Spain

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2022-08-11

Anticipated Date of Last Follow-up

2025-04-10

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2024-02-27

Actual Completion Date

2024-02-27

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Have a diagnosis of T2D according to the world health organization (WHO) criteria, currently treated with basal insulin and at least 2 injections of prandial insulin per day. * Are receiving ≥10 units of total basal insulin per day at screening. * Are receiving ≤2 units/kilogram/day of total daily insulin at screening * Have an HbA1c value of 7.0% to 10%, inclusive, as determined by the central laboratory at screening * Have been treated with a stable regimen of one of the following basal insulins used according to local product label with or without noninsulin diabetes therapy for at least

90 days prior to screening * once daily U-100 or U-200 insulin degludec * once daily U-100 or U-300 insulin glargine * once or twice daily U-100 insulin detemir or * once

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

730

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Weekly

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

Not provided

Excipients

Proprietary excipients used

No proprietary excipient used

Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration

No novel excipient or existing excipient used

Residual solvents used

No residual solvent used

Patent info

Description

Methods of treating diabetes

Brief description

Described herein are fixed doses and dosing regimens for long-acting insulin receptor agonists suitable for once-weekly dosing, such as weekly basal insulin-Fc (BIF).

Representative patent

US20240082363A1

Category

Not provided

Patent holder

Eli Lilly and Co

Exclusivity

Not provided

Expiration date

Not provided

Status

Pending

Supporting material

Publications

Wysham, C., Bajaj, H. S., Del Prato, S., Franco, D. R., Kiyosue, A., Dahl, D., Zhou, C., Carr, M. C., Case, M., Firmino Gonçalves, L., & QWINT-2 Investigators (2024). Insulin Efsitora versus Degludec in Type 2 Diabetes without Previous Insulin Treatment. *The New England journal of medicine*, *391*(23), 2201–2211. https://doi.org/10.1056/NEJMoa2403953

Abstract

Background: Insulin efsitora alfa (efsitora) is a new basal insulin designed for once-weekly administration. Data on safety and efficacy have been limited to small, phase 1 or phase 2 trials.

Methods: We conducted a 52-week, phase 3, parallel-design, open-label, treat-to-target trial involving adults with type 2 diabetes who had not previously received insulin. Participants were randomly assigned in a 1:1 ratio to receive efsitora or degludec. The primary end point was the change in the glycated hemoglobin level from baseline to week 52; we hypothesized that efsitora would be noninferior to degludec (noninferiority margin, 0.4 percentage points). Secondary and safety end points included the change in the glycated hemoglobin level in subgroups of participants using and not using glucagon-like peptide-1 (GLP-1) receptor agonists, the percentage of time that the glucose level was in the target range of 70 to 180 mg per deciliter in weeks 48 through 52, and hypoglycemic episodes.

Results: A total of 928 participants underwent randomization (466 to the efsitora group and 462 to the degludec group). The mean glycated hemoglobin level decreased from 8.21% at baseline to 6.97% at week 52 with efsitora (least-squares mean change, -1.26 percentage points) and from 8.24% to 7.05% with degludec (least-squares mean change, -1.17 percentage points) (estimated treatment difference, -0.09 percentage points; 95% confidence interval [CI], -0.22 to 0.04), findings that showed noninferiority. Efsitora was noninferior to degludec with respect to the change in the glycated

hemoglobin level in participants using and not using GLP-1 receptor agonists. The percentage of time that the glucose level was within the target range was 64.3% with efsitora and 61.2% with degludec (estimated treatment difference, 3.1 percentage points; 95% CI, 0.1 to 6.1). The rate of combined clinically significant or severe hypoglycemia was 0.58 events per participant-year of exposure with efsitora and 0.45 events per participant-year of exposure with degludec (estimated rate ratio, 1.30; 95% CI, 0.94 to 1.78). No severe hypoglycemia was reported with efsitora; six episodes were reported with degludec. The incidence of adverse events was similar in the two groups.

Conclusions: In adults with type 2 diabetes who had not previously received insulin, once-weekly efsitora was noninferior to once-daily degludec in reducing glycated hemoglobin levels. (Funded by Eli Lilly; QWINT-2 ClinicalTrials.gov number, NCT05362058.).

Bergenstal, R. M., Philis-Tsimikas, A., Wysham, C., Carr, M. C., Bue-Valleskey, J. M., Botros, F. T., Blevins, T., & Rosenstock, J. (2024). Once-weekly insulin efsitora alfa: Design and rationale for the QWINT phase 3 clinical development programme. *Diabetes, obesity & metabolism*, *26*(8), 3020–3030. https://doi.org/10.1111/dom.15604

Aims: Insulin efsitora alfa (efsitora) is a once-weekly basal insulin. This review describes the study design and rationale of the efsitora phase 3 Once Weekly (QW) Insulin Therapy (QWINT) clinical development programme, including the five trials, QWINT-1 through QWINT-5.

Materials and methods: The five trials included insulin-naïve adults (QWINT-1 and -2) with type 2 diabetes (T2D), adults with T2D previously treated with basal insulin (QWINT-3 and -4), and QWINT-5 in adults with type 1 diabetes. All five trials were designed as multicentre, randomized, controlled, open-label, treat-to-target studies to investigate the efficacy and safety of efsitora versus active once-daily basal insulin comparators (insulin glargine U100 or insulin degludec U100). The primary objective of each trial is to compare the change in HbA1c from baseline to week 26 or 52 between efsitora and the active comparator. The key secondary objectives include change in

fasting glucose, insulin dose and continuous glucose monitoring variables, and patient-reported outcome questionnaires.

Conclusions: The QWINT development programme includes a racially and geographically diverse population to provide important information regarding the efficacy and safety of efsitora and its clinical management of people with diabetes.

Additional documents

No documents were uploaded

Useful links

There are no additional links

Access principles

Collaborate for development

Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Not provided

Share technical information for match-making assessment

Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Not provided

Work with MPP to expand access in LMICs

In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Not provided

Comment & Information

Not provided