

## Insulin efsitora

## Developer(s)

Eli Lilly

Originator

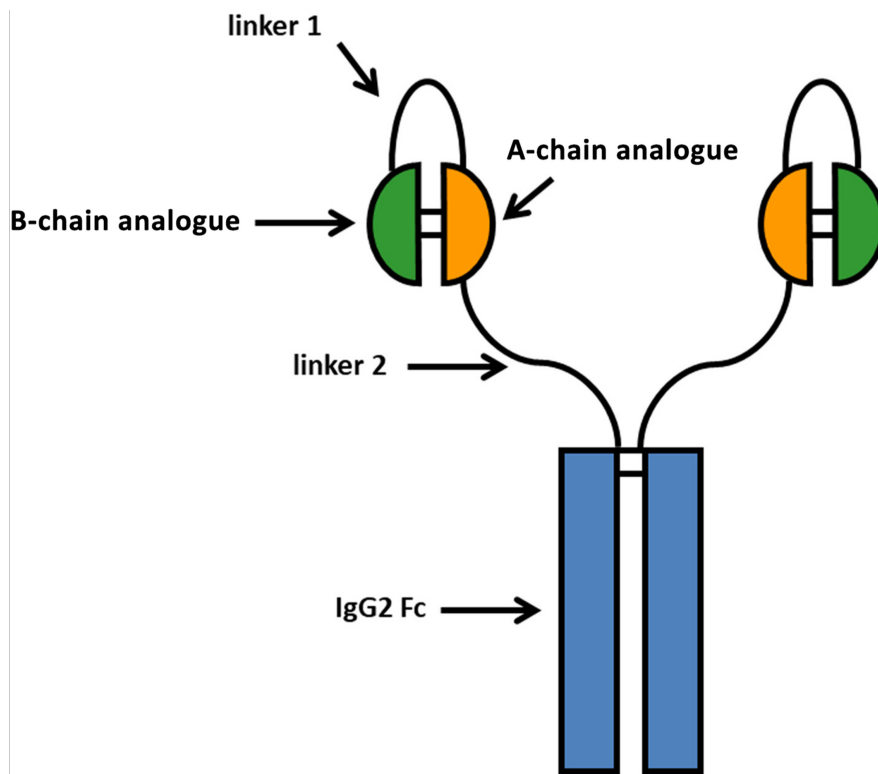
<https://www.lilly.com/uk/>

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)  $\times$  7 (rounded to the nearest 10 units)  $\times$  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)  $\times$  7 (rounded to the nearest 10 units)  $\times$  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)**

Not provided

# **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 resources**

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**

2025-05-15

### **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  $\geq 10$  units of basal insulin per day and  $\leq 110$  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 ( $\text{kg/m}^2$ ) \* 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 resources**

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**

2025-06-19

### **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  $\leq 35$  kilogram/square meter ( $\text{kg/m}^2$ ) 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 resources**

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 treatment

## **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 resources**

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  $\geq 10$  units of total basal insulin per day at screening. \* Are receiving  $\leq 2$  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 resources**

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>

**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](#).).

Bergental, 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