#1 dispensed **basal insulin** as prescribed by **Endocrinologists**[1]*

TRESIBA®
insulin degludec injection

QUESTIONS AND ANSWERS

About once-daily Tresiba® (insulin degludec injection)

For your patients starting basal insulin

What is Tresiba® and what is it indicated for?

Tresiba® (insulin degludec injection) is an ultra-long-acting basal insulin analogue used to lower blood glucose.[2]*

Tresiba® is indicated for once-daily treatment of adults with diabetes mellitus to improve glycemic control.

Tresiba® is also indicated for the treatment of pediatric patients (>2 years old) with type 1 diabetes mellitus.

How did Tresiba® compare to Lantus®?

In an event-driven, non-inferiority clinical trial (of 2-year median duration) in patients with inadequately controlled type 2 diabetes (T2DM) at high risk of cardiovascular events.[2,3†]

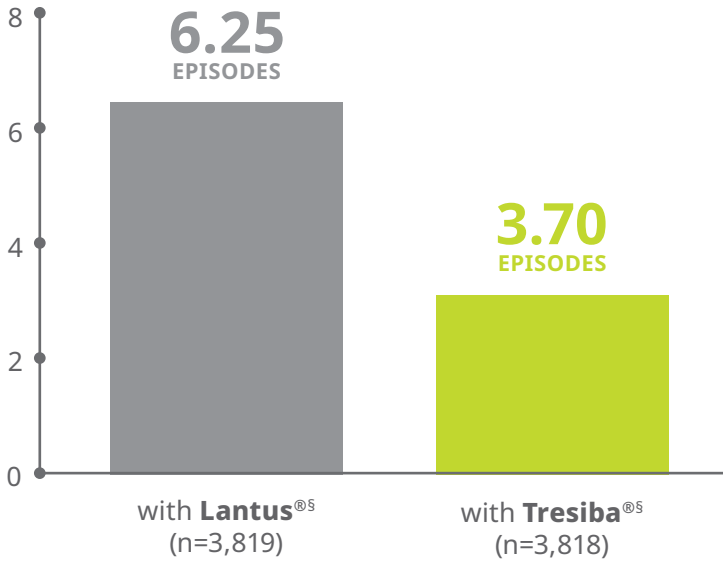
Tresiba® was non-inferior to Lantus® in time to occurrence of an Event Adjudication Committee-confirmed, 3-component major adverse cardiovascular event (**MACE**) (1° endpoint)

HAZARD RATE RATIO:‡ 0.91

(95% CI [0.78; 1.06] vs. Lantus®§)
3-component MACE occurred in 8.5% of the Tresiba® group (n=325) vs. 9.3% of the Lantus® group (n=356)

Tresiba® is not indicated for cardiovascular outcomes.

Low rate of severe hypoglycemia demonstrated (2° endpoint)¶



Rate of **severe hypoglycemia** per 100 patient-years of observation
Rate ratio**: 0.60 (0.48; 0.76)††

* Clinical significance has not been established.
† See back cover for full study design.
‡ Hazard rate ratio and 95% CI is based on a Cox proportional hazards regression.
§ In addition to standard of care for diabetes and cardiovascular disease.
¶ Severe hypoglycemia was defined as an episode requiring assistance of another person to actively administer carbohydrate, glucagon, or take other corrective actions.
** The rate ratio and 95% CI is based on a negative-binomial regression with log (PYO) as an offset.
†† Test for superiority evaluated at 5% level for significant (2-sided p<0.001). The Type I error was controlled by means of a pre-specified hierarchical testing strategy.
CI, confidence interval.

novo nordisk®

What is the duration of action and dosing for Tresiba®?

Duration of action: 42+ HOURS

Convenient once-daily dosing[2*†]

Example Tresiba® dosing case

Tresiba® should be dosed once daily, **preferably at the same time each day**. When administration at the same time of day is not possible, **Tresiba® allows for flexibility** in the timing of insulin administration, with a minimum of 8 hours between doses.

Fictitious case; may not be representative of all patients.

Initiating Tresiba® for your patients[2†‡]

Insulin-naïve

Adults with T2DM
- Start with **10 Units** followed by individual dosage adjustments

T1DM
- Calculate total daily insulin dose as **0.2–0.4** Units/kg/day
  - **Initiate Tresiba® as ⅓–½** of total daily insulin requirement
  - Administer remainder as mealtime insulin

Switching from another basal insulin

Adults with T2DM
- **1:1** from once-daily basal insulin
- **Reduce dose by 20%** from twice-daily basal insulin or Toujeo®

T1DM
- Reduce dose by 20%

- Close glucose monitoring is recommended during the transfer and in the following weeks
- If needed, adjust doses and timing of concurrent mealtime insulin or antidiabetic treatments

How could you get this patient started with Tresiba®?

Patient Profile

Margot
- 62 years of age
- Type 2 diabetes
- Insulin-naïve

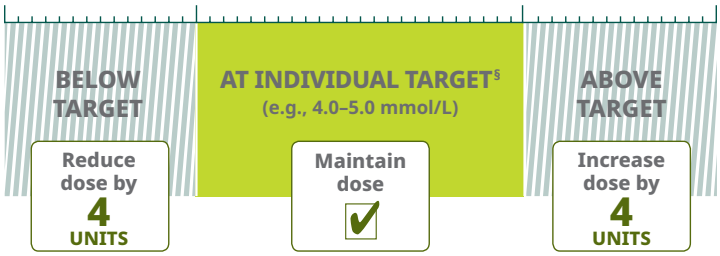
Starting Tresiba®
- Start with **10 Units** dosed once daily followed by individual dosage adjustments

For more dosage and administration instructions, please refer to the Product Monograph.

How can Tresiba® be titrated in patients with type 2 diabetes?

Example dosing and titration schedule[4]

Once-daily Tresiba® can be **titrated once a week** based on **that morning's** fasting (pre-breakfast) glucose measurement:



Adapted from Philis-Tsimikas, et al., 2013.

Margot has been titrating her dose up by 4 Units every week because she has not reached her pre-breakfast glucose target. At 4 weeks, she will be taking 22 Units of Tresiba® daily.

What if Margot missed a dose of Tresiba®?

Example Tresiba® dosing case

- Margot takes her Tresiba® consistently, every day at 7 am
- Margot was up early taking care of her grandson and forgot to take her dose. She should:
  - Take her dose **as soon as she remembers**
- Margot remembers her forgotten dose at lunch time, 12 pm, so she takes her dose immediately
  - Since there are **more than 8 hours** between 12 pm and 7 am, she can **return to her usual dosing time** the next morning and remain consistent with her usual dosing schedule

No dose recalculations are needed to determine the dose of Tresiba®. The dose counter shows the dose dialed in Units.

How is Tresiba® stored?

Before first use:
Store Tresiba® in a refrigerator (2°C–8°C).
In use:
After first opening or if carried as a spare, Tresiba® can be stored at room temperature (not above 30°C) or in a refrigerator (2°C–8°C) for 56 days (8 weeks).[2]

How is Tresiba® supplied?

Tresiba® is administered as a subcutaneous injection and is available in the FlexTouch® prefilled pen.[2]

Dosage Form	FlexTouch® 200 Units/mL	FlexTouch® 100 Units/mL
Maximum Units per Injection	160 Units	80 Units
Units per Pen	600 Units	300 Units
Dose Increment	2 Units	1 Unit
Pens per Box	3 Pens	5 Pens
Units per Box	1,800 Units	1,500 Units

What are the features of the FlexTouch® pen?

- Easy to use—the only prefilled pen with a light-touch button and no push-button extension[5]*
- End-of-dose click to confirm dose delivery[6]*
- Rated significantly easier to use by patients and HCPs (all $p<0.0001$)[5,7]
  - **83%** of patients and HCPs preferred to use FlexTouch® versus SoloSTAR® (n=120) and **85%** preferred to use FlexTouch® versus KwikPen™ (n=160)*
    - 9% for SoloStar®, 6% had no preference (n=120)
    - 4% for KwikPen™, 9% had no preference (n=160)

* Clinical significance has not been established.
† The dosage of Tresiba® should be individualized and titrated under the supervision of a healthcare provider in accordance with the metabolic needs of the patient and the glycemic control target and with appropriate glucose monitoring.
‡ Please refer to the Product Monograph for complete dosing information.
§ From Diabetes Canada Guideline: Glycemic targets should be individualized. Diabetes Canada targets may differ. Please see guideline for more information.[8]
Fictitious case; may not be representative of all patients.
T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus.

Is Tresiba® covered by provincial formularies?

Tresiba® is covered by most provincial formularies across Canada*—including in Quebec as a general benefit†

Clinical use:
- Not recommended for treatment of diabetic ketoacidosis

Contraindication:
- During episodes of hypoglycemia

Most serious warnings and precautions:

Hypoglycemia is the most common adverse effect of insulin
- Glucose monitoring is required
- Uncorrected hypo- or hyperglycemic reactions can cause loss of consciousness, coma and even death
- Use caution and medical supervision when converting insulin products

Administration
- Inspect visually prior to administration and only use if solution appears clear and colourless
- Do not mix with any other insulin, administer intravenously or use in insulin infusion pumps

Other relevant warnings and precautions:
- Refer to respective product monographs for concomitant oral antidiabetic agents for their warnings and precautions
- Stress or concomitant illness, especially infections and febrile conditions, may change insulin requirements
- Tresiba® should not be diluted
- Combination with thiazolidinediones (TZD) not indicated in type 2 diabetes; can cause heart failure and edema
- Risks associated with sharing insulin delivery devices
- Hyperglycemia
- Risk of hypokalemia
- Dosing may need to be adjusted in patients with renal and/or hepatic impairment
- Risk of immune responses (e.g., systemic allergic reactions or antibody production)
- Pregnant and nursing women
- Pediatrics
- Geriatrics

For more information:

Please consult the Product Monograph at www.Tresibapm-e.ca for more information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece.

The Product Monograph is also available by calling us at 1-800-465-4334.

* Public formulary coverage is available in all provinces with the exception of British Columbia.
† Tresiba® was previously listed as an exceptional medication for treatment of diabetes where a prior trial with an intermediate-acting insulin has not allowed for adequate control of the glycemic profile without causing an episode of serious hypoglycemia or frequent episodes of hypoglycemia.

References:

1. Data on file: IQVIA data. Novo Nordisk Canada Inc. November 2020.
2. Tresiba® Product Monograph. Novo Nordisk Canada Inc., 2019.
3. Marso SP, et al. Efficacy and safety of degludec versus glargine in type 2 diabetes. *N Eng J Med*. 2017;377(8):723-732. 7,637 patients with inadequately controlled type 2 diabetes and atherosclerotic cardiovascular disease were randomized to either Tresiba® or Lantus® in a randomized, double-blind, treat-to-target, event-driven clinical trial. Each was administered once-daily between dinner and bedtime in addition to standard of care for diabetes and cardiovascular disease for a median duration of 2 years. Event Adjudication Committee (EAC)-confirmed 3-component major adverse cardiovascular event (MACE) was defined as cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke. Non-inferiority of Tresiba® to Lantus® was considered confirmed if the upper limit of the two-sided 95% confidence interval for the hazard ratio of MACE was below 1.3.
4. Philis-Tsimikas A, et al. Insulin degludec once-daily in type 2 diabetes: Simple or step-wise titration (BEGIN: once simple use). *Adv Ther*. 2013;30(6):607-622.
5. Bailey T, et al. Usability and preference evaluation of a prefilled insulin pen with a novel injection mechanism by people with diabetes and healthcare professionals. *Curr Med Res Opin*. 2011;27(10):2043-2052.
6. Pfützner A, et al. Accuracy and preference assessment of prefilled insulin pen versus vial and syringe with diabetes patients, caregivers, and healthcare professionals. *Curr Med Res Opin.* 2013;29(5):475-481.
7. Oyer D, et al. Ease of use and preference of a new versus widely available prefilled insulin pen assessed by people with diabetes, physicians and nurses. *Expert Opin Drug Deliv.* 2011;8(10):1259-1269.
8. Diabetes Canada Clinical Practice Guidelines Expert Committee. Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. *Can J Diabetes*. 2018;42:S1-S325.

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