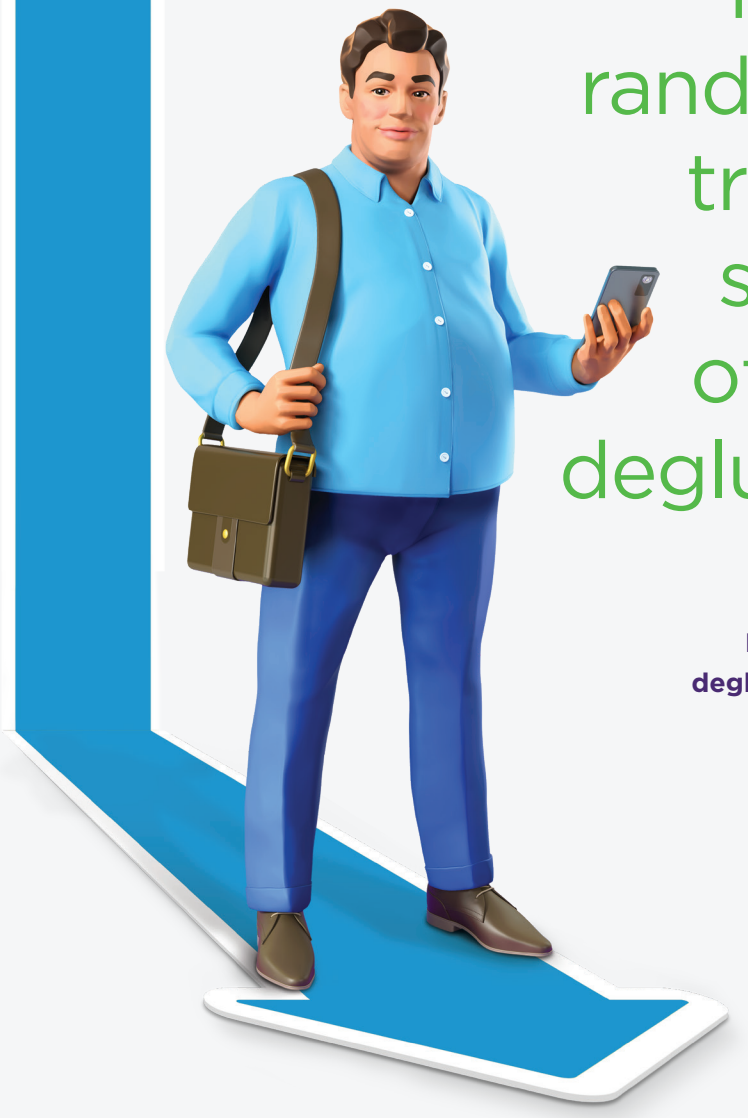
Toujeo®
insulin glargine 300 units/mL

BRIGHT



# First head-to-head randomised controlled trial to compare the safety and efficacy of Toujeo® vs insulin degludec 100 units/mL

**More similarities than differences testing Toujeo® vs degludec 100 units/mL in insulin-naïve type 2 diabetes: the randomised head-to-head BRIGHT trial.[1]**

Toujeo® is indicated for the treatment of diabetes mellitus in adults, adolescents and children from the age of 6 years.[2]

sanofi

Rosenstock J, *et al. Diabetes Care.* 2018;41:2147–2154.

This study was funded by Sanofi UK. Prescribing Information and Adverse event reporting can be found on the last page of this item.

MAT-GB-2103603 (v3.0) | November 2024

# Hypoglycaemia is a critical barrier to optimal glycaemic control and adherence[3–7]

**Successful diabetes management especially when using insulin, consists of a balance between achieving glycaemic control whilst reducing the risk of hypoglycaemia in patients[5]**

**The greatest insulin dose change and glycaemic lowering occurs during the active titration period[5]**

## Early hypoglycaemia

after insulin initiation in T2DM is associated with:

### Increased long-term hypoglycaemia risk

**~5.7x**

**more likely to have hypoglycaemia at 24 months***

(OR: 5.71, 95% CI: 4.67–6.99)[4]

### Increased treatment discontinuation

**+14%**

**Significantly more patients with early hypoglycaemia discontinued their insulin treatment ($p$<0.0001)**

(68% of patients experiencing hypoglycaemia in the first 6 months discontinue the basal insulin vs 54% of patients who have not experienced early hypoglycaemia)[6]

## Reducing hypoglycaemia during the titration period...


**Is critical for optimal glycaemic management[4,5,7]**

**May help patients to confidently optimise their dose. This could lead to better glycaemic control and less hypoglycaemia in the long-term[5]**

**CI**, confidence interval, **OR**, odds ratio; **T2DM**, type 2 diabetes mellitus.

*An observational, retrospective, longitudinal analysis of electronic medical records from 40,627 patients from 5 European countries and the USA. The study evaluated short and long-term glycaemic control and hypoglycaemia incidence in insulin-naïve T2DM patients.[4]

# First head-to-head trial comparing Toujeo® vs degludec 100 units/mL meeting the primary endpoint[1,8,9]

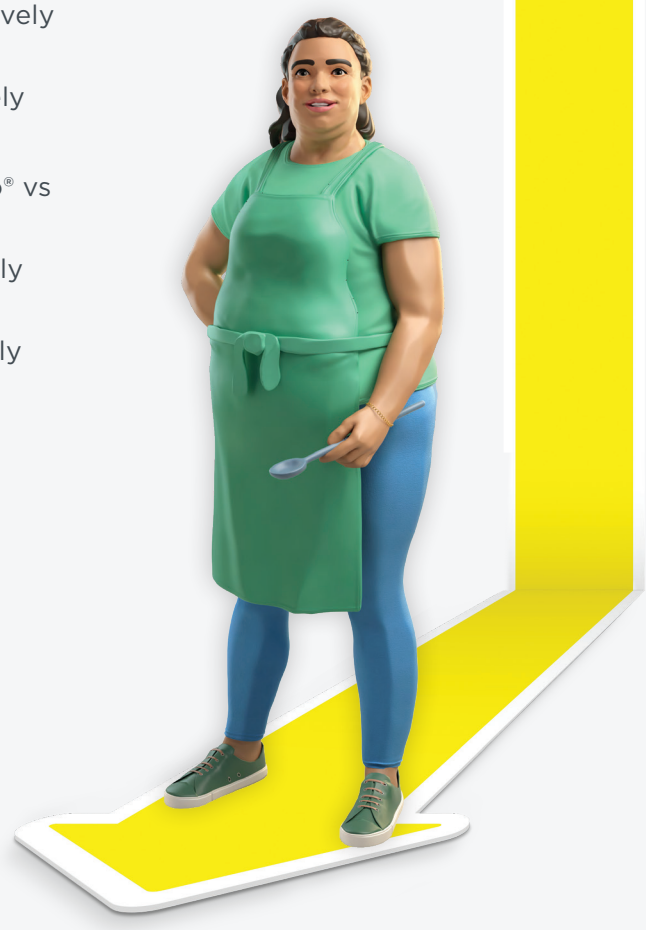
## Comparable and effective $HbA_{1c}$ reduction at 24 weeks[1,8,9]

- Non-inferiority of $HbA_{1c}$ reduction with Toujeo® vs degludec 100 units/mL (-1.64%; non-inferiority margin 0.3% [*p*<0.0001]). Change in $HbA_{1c}$ was similar between groups after 12 weeks (LS mean difference: 0.02% [95% CI:-0.08 to 0.12]: nominal *p*-value=0.667)

## Comparable incidence and event rates of hypoglycaemia during the maintenance phase* and in the full study period[1]

## Lower incidence and event rates of anytime† (24 h) confirmed hypoglycaemia with Toujeo® during the titration period‡[1]

- Incidence rates (%) with Toujeo® vs degludec 100 units/mL were:
  - ≤3.9 mmol/L: 47.4% vs 53.3%, respectively (RRR: -26%, ARR: -6.9%)
  - <3.0 mmol/L: 7.8% vs 11.7%, respectively (RRR: -37%, ARR: -3.9%)
- Event rates per patient-year with Toujeo® vs degludec 100 units/mL were:
  - ≤3.9 mmol/L: 8.08 vs 10.47, respectively (RRR: -23, ARR: -2.4%)
  - <3.0 mmol/L: 0.49 vs 0.86, respectively (RRR: -43, ARR: -0.4%



**ARR**, absolute risk reduction; **$HbA_{1c}$**, glycated haemoglobin; **LS**, least-square; **RRR**, relative risk reduction.

*Maintenance period: 13–24 weeks.

†Anytime (24 h) confirmed hypoglycaemia (≤3.9 mmol/L and <3.0 mmol/L).

‡Active titration period: 0–12 weeks

# First head-to-head randomised controlled trial of Toujeo® vs degludec 100 units/mL[1,10]

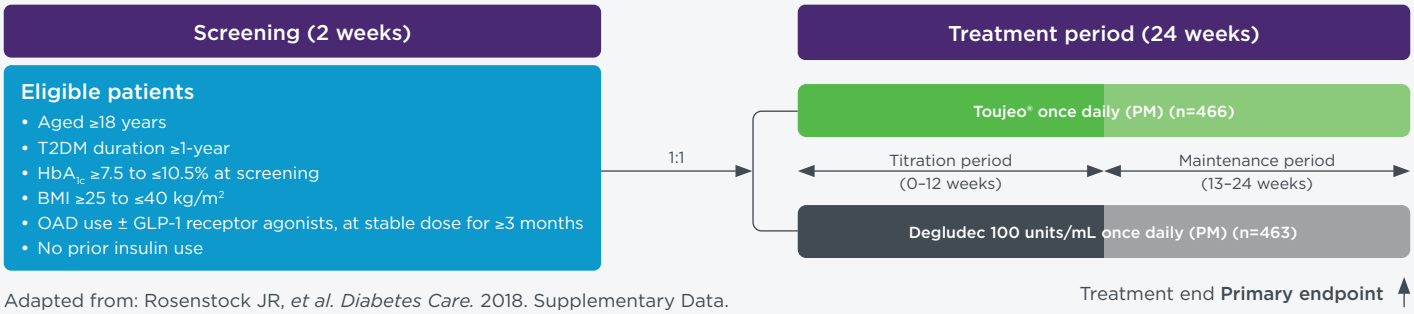
## Study design and limitations

### Objective:[1]

To compare Toujeo® vs degludec 100 units/mL in this first head-to-head randomised controlled trial.

### Study design:[1,10]

A 24-week randomised, multicentre, open label, non-inferiority study in insulin-naïve patients with T2DM.




Adapted from: Rosenstock JR, *et al. Diabetes Care.* 2018. Supplementary Data.

### Primary endpoint:[1]

- Change in $HbA_{1c}$ levels from baseline to Week 24

### Secondary endpoints included:[1]

- Change in fasting SMPG and variability of 24-hour SMPG from baseline to Week 24
- Incidence and event rates of confirmed hypoglycaemia during the 24-week on-treatment period, the active titration period (Weeks 0–12), and the maintenance period (Weeks 13–24)
- Other safety outcomes included body weight and AEs

### Dose adjustment algorithm[1,10]

| Median* fasting SMPG, mg/dL (mmol/L) | Toujeo® and degludec 100 units/mL dose change |
|---|---|
| >140 (>7.8) | +6 units |
| >120–≤140 (>6.7–≤7.8) | +4 units |
| >100–≤120 (>5.6–≤6.7) | +2 units |
| ≥80–≤100 (≥4.4–≤5.6) | 0 |
| <80 (<4.4) or 1 symptomatic confirmed hypoglycaemia episode in preceding week | -2 units or at investigator's discretion |

Adapted from: Rosenstock JR, *et al. Diabetes Care.* 2018. Supplementary Data.

### Study limitations:[1]

- Open-label design. Blinding patients to the identity of the two pens was not possible
- Relatively short duration of intervention (24 weeks)

**AEs**, adverse events; **BMI**, body mass index; **GLP-1**, glucagon-like peptide-1 receptor agonist; **OAD**, oral antihyperglycaemic drugs; **SMPG**, self-monitored plasma glucose.

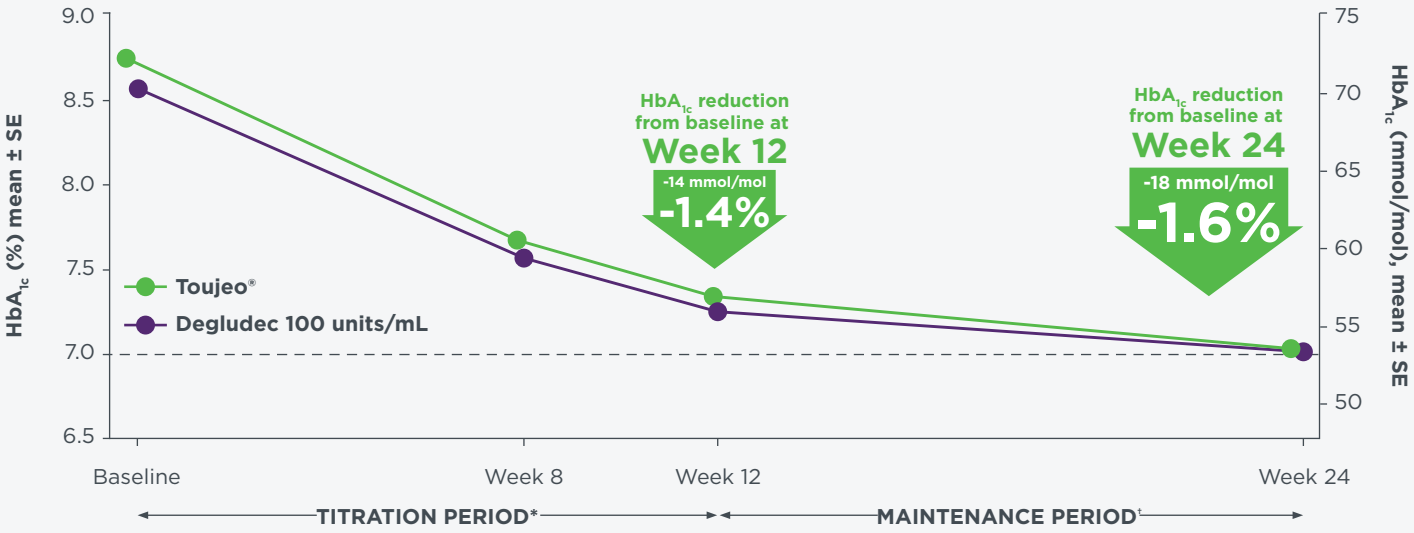
*From last three measurements. Once daily subcutaneous self-injection, between 18:00 h and 20:00 h. Titrated to fasting self-measured plasma glucose of 4.4–5.6 mmol/L (80–100 mg/dL). Background therapies were not changed unless safety concerns necessitated dose reduction or discontinuation.

# Comparable and effective $HbA_{1c}$ reduction with Toujeo® and degludec 100 units/mL at 24 weeks[1,8,9]

## Primary endpoint: Change in $HbA_{1c}$ levels over the 24-week treatment period

- Change in $HbA_{1c}$ was similar between Toujeo® vs degludec 100 units/mL, meeting the primary endpoint
- LSM change in $HbA_{1c}$ from baseline to Week 12 with Toujeo® was -1.37% vs -1.39% with degludec 100 units/mL. LSM difference: -0.02% (95% CI: -0.08 to 0.12), nominal *p*-value=0.677
- LSM change in $HbA_{1c}$ from baseline to Week 24 with Toujeo® was -1.64% vs -1.59% with degludec 100 units/mL, ($p<0.0001$)
  - LSM change from baseline to Week 24 ± SE was -18.0 ± 0.4 mmol/mol (-1.64 ± 0.04%) for Toujeo® vs -17.4 ± 0.4 mmol/mol (-1.59 ± 0.04%) for degludec 100 units/mL. LSM difference for Toujeo® vs degludec 100 units/mL of -0.05% (95% CI: -0.15 to 0.05)

### Change in $HbA_{1c}$ from baseline to study end at Week 24[1,9]




Adapted from: Rosenstock JR, *et al. Diabetes Care.* 2018; NIH US National Library of Medicine. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT02738151. [Accessed: November 2024].

**LSM**, least squares mean; **SE**, standard error.

Study population were insulin-naive. No specific safety concerns were reported. Overall, 202 (43.7%) and 221 (47.8%) of participants in the Toujeo® and degludec 100 units/mL treatment groups, respectively, reported adverse events during the 24-week study period.

Week 12 intention to treat population: Toujeo®, n=448; insulin degludec 100 units/mL, n=445.[9] Week 24 intention to treat population: Toujeo®, n=462; degludec 100 units/mL, n=462.[1]

*Active titration period: 0–12 weeks.

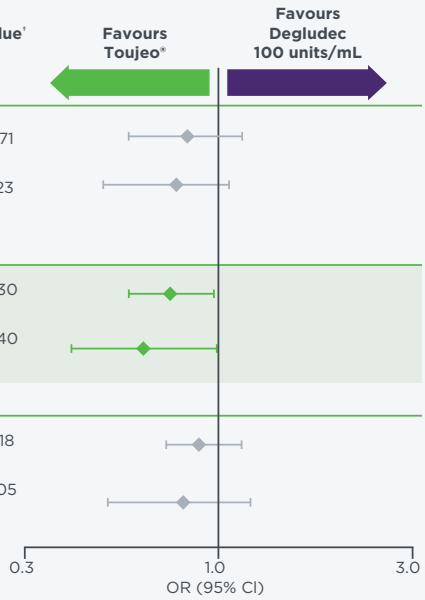
†Maintenance period: 13–24 weeks.

# Anytime hypoglycaemia incidence and events rates with Toujeo® vs degludec 100 units/mL*[1]

## Anytime hypoglycaemia incidence

Incidence %

| | Toujeo* | Degludec 100 units/mL | OR (95% CI) | *p*-value† |
|---|---|---|---|---|
| **Full study period (0–24 weeks)** | | | | |
| Confirmed (≤3.9 mmol/L) | 66.5 | 69.0 | 0.88 (0.66 to 1.17) | 0.371 |
| Confirmed (<3.0 mmol/L) | 14.7 | 18.4 | 0.76 (0.53 to 1.08) | 0.123 |
| **Titration period (0–12 weeks)** | | | | |
| Confirmed (≤3.9 mmol/L) | 47.4 | 54.3 | 0.74 (0.57 to 0.97) | 0.030 |
| Confirmed (<3.0 mmol/L) | 7.8 | 11.7 | 0.63 (0.40 to 0.99) | 0.040 |
| **Maintenance period (13–24 weeks)** | | | | |
| Confirmed (≤3.9 mmol/L) | 54.1 | 55.8 | 0.93 (0.72 to 1.22) | 0.618 |
| Confirmed (<3.0 mmol/L) | 9.8 | 11.2 | 0.86 (0.56 to 1.33) | 0.505 |




Incidence

-26% ARR -6.9%

-37% ARR -3.9%

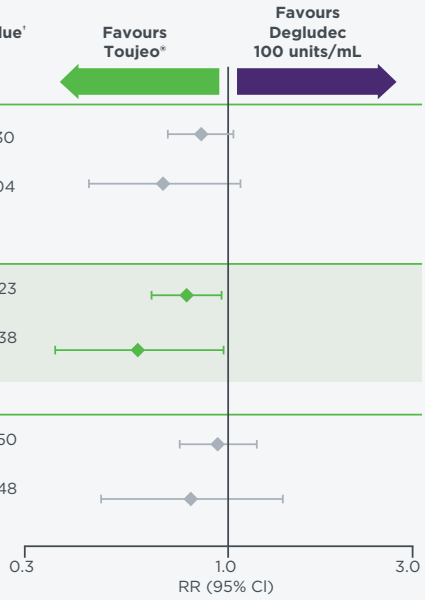
Adapted from: Rosenstock JR, *et al. Diabetes Care.* 2018.

The incidence rates of anytime hypoglycaemia (≤3.9 mmol/L and <3.0 mmol/L) were lower in the titration period with Toujeo® vs degludec 100 units/mL and comparable in both treatment groups during the maintenance period and during the full study period (66.5% vs 69.0%, respectively). The direction of effect was in favour of Toujeo® for confirmed hypoglycaemia incidence vs degludec 100 units/mL.

## Anytime hypoglycaemic events

Event rates per patient-year

| | Toujeo* | Degludec 100 units/mL | RR (95% CI) | *p*-value† |
|---|---|---|---|---|
| **Full study period (0–24 weeks)** | | | | |
| Confirmed (≤3.9 mmol/L) | 9.34 | 10.83 | 0.86 (0.71 to 1.04) | 0.130 |
| Confirmed (<3.0 mmol/L) | 0.61 | 0.88 | 0.69 (0.45 to 1.08) | 0.104 |
| **Titration period (0–12 weeks)** | | | | |
| Confirmed (≤3.9 mmol/L) | 8.08 | 10.47 | 0.77 (0.62 to 0.96) | 0.023 |
| Confirmed (<3.0 mmol/L) | 0.49 | 0.86 | 0.57 (0.34 to 0.97) | 0.038 |
| **Maintenance period (13–24 weeks)** | | | | |
| Confirmed (≤3.9 mmol/L) | 10.64 | 11.21 | 0.95 (0.76 to 1.19) | 0.650 |
| Confirmed (<3.0 mmol/L) | 0.73 | 0.91 | 0.81 (0.48 to 1.39) | 0.448 |




Event rates

-23% ARR -2.4%

-43% ARR -0.4%

Adapted from: Rosenstock JR, *et al. Diabetes Care.* 2018.

The event rates per patient-year of anytime hypoglycaemia (≤3.9 mmol/L and <3.0 mmol/L) were lower in the titration period with Toujeo® vs degludec 100 units/mL and comparable in both treatment groups during the maintenance period and during the full study period (9.3 and 10.8, respectively). The direction of effect was in favour of Toujeo® for confirmed hypoglycaemia event rate vs degludec 100 units/mL.

**RR**, rate ratio.

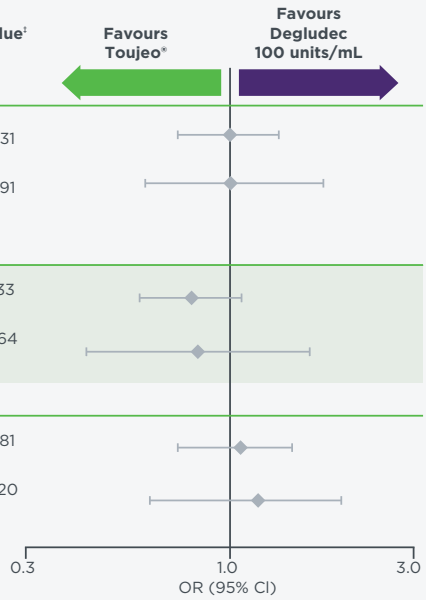
*Safety population (Toujeo®, n=462; degludec 100 units/mL, n=462). †**All *p*-values for secondary endpoints are analysed as nominal.**

# Nocturnal hypoglycaemia incidence and event rates with Toujeo® vs degludec 100 units/mL*†[1]

## Nocturnal hypoglycaemia incidence

Incidence %

| | Toujeo* | Degludec 100 units/mL | OR (95% CI) | *p*-value‡ |
|---|---|---|---|---|
| **Full study period (0–24 weeks)** | | | | |
| Confirmed (≤3.9 mmol/L) | 28.6 | 28.8 | 0.99 (0.74 to 1.32) | 0.931 |
| Confirmed (<3.0 mmol/L) | 6.1 | 6.1 | 1.00 (0.58 to 1.72) | 0.991 |
| **Titration period (0–12 weeks)** | | | | |
| Confirmed (≤3.9 mmol/L) | 15.2 | 18.8 | 0.77 (0.54 to 1.08) | 0.133 |
| Confirmed (<3.0 mmol/L) | 2.8 | 3.5 | 0.80 (0.38 to 1.69) | 0.564 |
| **Maintenance period (13–24 weeks)** | | | | |
| Confirmed (≤3.9 mmol/L) | 21.4 | 21.0 | 1.03 (0.74 to 1.42) | 0.881 |
| Confirmed (<3.0 mmol/L) | 4.5 | 3.8 | 1.18 (0.61 to 2.29) | 0.620 |



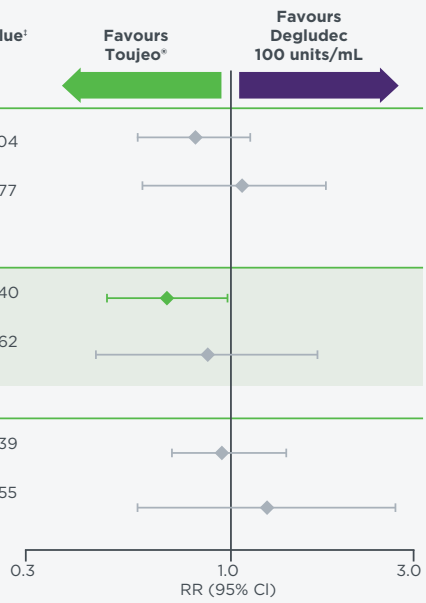

Adapted from: Rosenstock JR, *et al. Diabetes Care.* 2018.

**During the titration period, incidence rates of nocturnal hypoglycaemia† (≤3.9 mmol/L and <3.0 mmol/L) were comparable across both treatment groups. Incidence (≤3.9 mmol/L) during the full study period was comparable for both treatments; 28.6% with Toujeo® and 28.8% with degludec 100 units/mL. No difference between treatments over 24 weeks was seen in the incidence of confirmed hypoglycemia at the <3.0 mmol/L threshold.**

## Nocturnal hypoglycaemic events

Event rates per patient-year

| | Toujeo* | Degludec 100 units/mL | RR (95% CI) | *p*-value‡ |
|---|---|---|---|---|
| **Full study period (0–24 weeks)** | | | | |
| Confirmed (≤3.9 mmol/L) | 1.83 | 2.26 | 0.81 (0.58 to 1.12) | 0.204 |
| Confirmed (<3.0 mmol/L) | 0.24 | 0.22 | 1.09 (0.60 to 2.00) | 0.777 |
| **Titration period (0–12 weeks)** | | | | |
| Confirmed (≤3.9 mmol/L) | 1.42 | 2.20 | 0.65 (0.43 to 0.98) | 0.040 |
| Confirmed (<3.0 mmol/L) | 0.16 | 0.19 | 0.85 (0.40 to 1.79) | 0.662 |
| **Maintenance period (13–24 weeks)** | | | | |
| Confirmed (≤3.9 mmol/L) | 2.24 | 2.33 | 0.96 (0.66 to 1.40) | 0.839 |
| Confirmed (<3.0 mmol/L) | 0.33 | 0.26 | 1.27 (0.57 to 2.83) | 0.555 |





Adapted from: Rosenstock JR, *et al. Diabetes Care.* 2018.

**During the titration period, event rates of nocturnal hypoglycaemia (≤3.9 mmol/L) were lower with Toujeo® vs degludec 100 units/mL (1.4 vs 2.2 events per patient-year, respectively). Whilst the rate of nocturnal hypoglycaemia (<3.0 mmol/L) was comparable with both groups. Event rates (≤3.9 mmol/L) during the full study period were comparable with Toujeo® and degludec 100 units/mL (1.8 and 2.3 events per patient-year, respectively) and the event rates (<3.0 mmol/L) were also comparable during the full study period.**

*Safety population (Toujeo®, n=462; degludec 100 units/mL, n=462). Only 1 participant experienced severe hypoglycaemia (1 event) in the Toujeo® group due to a skipped evening meal and not reducing her insulin dose after a previous non-severe event. †Nocturnal (00:00–05:59 h) confirmed hypoglycaemia (≤3.9 mmol/L and <3.0 mmol/L). ‡**All *p*-values for secondary endpoints are analysed as nominal.**

# First head-to-head randomised controlled trial to compare the safety and efficacy of Toujeo® vs degludec 100 units/mL[1,4,5,7–9]

## Conclusions

In adult insulin naïve T2DM patients, the BRIGHT study showed:[1]

- Comparable and effective $HbA_{1c}$ reduction at 24 weeks, meeting its primary endpoint*[1,8,9]
- Comparable incidence and event rates of anytime confirmed hypoglycaemia in the maintenance† and full study period[1]
- Toujeo® provided lower incidence and event rates of anytime‡ (24 h) hypoglycaemia during the titration period§[1]

## Reducing hypoglycaemia during the titration period...


**Is critical for optimal glycaemic management[4,5,7]**

**May help patients to confidently optimise their dose. This could lead to better glycaemic control and less hypoglycaemia long-term[5]**

*Primary endpoint $p<0.0001$ for non-inferiority; The LSM change from baseline to Week 24 ± SE was -18.0 ± 0.4 mmol/mol (-1.64 ± 0.04%) for Toujeo® vs -17.4 ± 0.4 mmol/mol (-1.59 ± 0.04%) for degludec 100 units/mL. LSM difference for Toujeo® vs degludec 100 units/mL of -0.05%; 95% CI: -0.15 to 0.05.

†Maintenance period: 13–24 weeks.

‡Anytime (24 h) confirmed hypoglycaemia (≤3.9 mmol/L and <3.0 mmol/L);

§Active titration period: 0–12 weeks.

**Nocturnal (00:00–05:59 h) confirmed hypoglycaemia (≤3.9 mmol/L and <3.0 mmol/L).

# Prescribing Information: Toujeo® (insulin glargine 300 units/ml)

Please refer to Summary of Product Characteristics (SmPC) before prescribing.

**Presentation:** Toujeo pre-filled pens each ml contains 300 units of insulin glargine. SoloStar pen contains 1.5ml (450 units) of solution for injection. DoubleStar pen contains 3ml (900 units) of solution for injection.

**Indication:** Treatment of diabetes mellitus in adults, adolescents and children from the age of 6 years**.**

**Dosage and Administration:** Toujeo is administered subcutaneously, by injection into the abdominal wall, the deltoid or the thigh, once daily, at any time of the day, preferably at the same time every day. The dose regimen (dose and timing) should be adjusted according to individual response. Injection sites must be rotated within a given injection area from one injection to the next in order to reduce the risk of lipodystrophy and cutaneous amyloidosis. Do not administer intravenously. In type 1 diabetes mellitus, Toujeo must be combined with short-/rapid-acting insulin to cover mealtime insulin requirements. In patients with type 2 diabetes mellitus, recommended daily starting dose is 0.2 units/kg followed by individual dose adjustments. Toujeo can also be given together with other anti-hyperglycaemic medicinal products. Switch between insulin glargine 100 units/ml and Toujeo: Insulin glargine 100 units/ml and Toujeo are not bioequivalent and are not directly interchangeable. When switching from insulin glargine 100 units/ml to Toujeo, this can be done on a unit-to-unit basis, but a higher Toujeo dose (approximately 10-18%) may be needed to achieve target ranges for plasma glucose levels. When switching from Toujeo to insulin glargine 100 units/ml, the dose should be reduced (approximately by 20%). Switching from other basal insulins to Toujeo: A change of dose and/or timing of the basal insulin and concomitant anti-hyperglycaemic treatment may be required. Dose adjustments may also be required if the patient's weight or lifestyle changes, the timing of insulin dose is changed or other circumstances arise that increase susceptibility to hypo- or hyperglycaemia. Toujeo must not be mixed or diluted with any other insulin or other medicinal products. Close metabolic monitoring is recommended during a switch and in the initial weeks thereafter. SoloStar 1-80 units per single injection in steps of 1 unit and DoubleStar 2-160 units in steps of 2 units. When changing from Toujeo SoloStar to Toujeo DoubleStar, if the patient's previous dose was an odd number then the dose must be increased or decreased by 1 unit. Toujeo DoubleStar prefilled pen is recommended for patients requiring at least 20 units per day.

**Special Populations:** Elderly, renal and hepatic impairment: Insulin requirements may be diminished in the elderly or patients with renal or hepatic impairment. Paediatric population: When switching basal insulin to Toujeo, dose reduction of basal and bolus insulin needs to be considered on an individual basis, in order to minimise the risk of hypoglycaemia.

**Contraindications**: Hypersensitivity to insulin glargine or any excipients.

**Precautions and Warnings:** Traceability: In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. Toujeo is not the insulin of choice for treatment of diabetic ketoacidosis. Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. There is a potential risk of delayed insulin absorption and worsened glycaemic control following insulin injections at sites with these reactions. A sudden change in the injection site to an unaffected area has been reported to result in hypoglycaemia. Blood glucose monitoring is recommended after the change in the injection site, and dose adjustment of antidiabetic medications may be considered. Hypoglycaemia: In case of insufficient glucose control or a tendency to hyper/hypoglycaemic episodes, the patient's adherence to the prescribed treatment regimen, injection sites and proper injection technique and all other relevant factors must be reviewed before dose adjustment is considered. Particular caution should be exercised, and intensified blood glucose monitoring is advisable for patients in whom hypoglycaemic episodes might be of clinical relevance and in those where dose adjustments may be required. Warning signs of hypoglycaemia may be changed, less pronounced or absent in certain risk groups, potentially resulting in severe hypoglycaemia and loss of consciousness. Risk groups include patients in whom glycaemic control is markedly improved, hypoglycaemia develops gradually, an autonomic neuropathy is present, or who are elderly. The prolonged effect of subcutaneous insulin glargine may delay recovery from hypoglycaemia. Intercurrent illness: Requires intensified metabolic monitoring and often it is necessary to adjust the insulin dose. Insulin antibodies: administration may cause insulin antibodies to form. Use with pioglitazone: Cases of cardiac failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for development of cardiac heart failure. If the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Pioglitazone should be discontinued if any deterioration in cardiac symptoms occurs. Medication errors: Insulin labels must always be checked before each injection to avoid errors between Toujeo and other insulins. Patients must be instructed to never use a syringe to remove Toujeo from the SoloStar or DoubleStar pre-filled pen, A new sterile needle must be attached before each injection. Needles must not be re-used. ***Pregnancy and breast-feeding:*** There is no data from exposed pregnancies in controlled clinical trials. However, there is a large amount of data on use of insulin glargine 100 units/ml in pregnant women indicating no specific adverse effects on pregnancy and no specific malformative nor feto/neonatal toxicity. The use of Toujeo may be considered during pregnancy, if clinically needed. Careful monitoring of glucose control is essential. It is unknown if insulin glargine is excreted in breast milk. ***Interactions:*** Substances that affect glucose metabolism may require adjustment of insulin glargine.

**Adverse Reactions**: Very common: Hypoglycaemia. Prolonged or severe hypoglycaemia may be life-threatening. Common: Lipohypertrophy, injection site reactions, including redness, pain, itching, hives, swelling, or inflammation. Frequency not known: Cutaneous amyloidosis. *Prescribers should consult the SmPC in relation to other adverse reactions.*

**Legal Category:** POM

**List Price and Marketing Authorisation Number(s):** SoloStar 3 x 1.5ml pens (PLGB 04425/0817): £32.14
DoubleStar 3 x 3ml pens (PLGB 04425/0818): £64.27

**Marketing Authorisation Holder:** Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK

**Further information is available from:** Medical Information, Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. uk-medicalinformation@sanofi.com.

**Date of preparation:** October 2024.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
Adverse events should also be reported to Sanofi Tel: 0800 090 2314. Alternatively, send via email to UK-drugsafety@sanofi.com

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**Presentation:** Toujeo SoloStar pre-filled pens each ml contains 300 units of insulin glargine. SoloStar pen contains 1.5ml (450 units) of solution for injection. DoubleStar pen contains 3ml (900 units) of solution for injection.

**Indication:** Treatment of diabetes mellitus in adults, adolescents and children from the age of 6 years**.**

**Dosage and Administration:** Toujeo is administered subcutaneously, by injection into the abdominal wall, the deltoid or the thigh, once daily, at any time of the day, preferably at the same time every day. The dose regimen (dose and timing) should be adjusted according to individual response. Injection sites must be rotated within a given injection area from one injection to the next in order to reduce the risk of lipodystrophy and cutaneous amyloidosis. Do not administer intravenously. In type 1 diabetes mellitus, Toujeo must be combined with short-/rapid-acting insulin to cover mealtime insulin requirements. In patients with type 2 diabetes mellitus, recommended daily starting dose is 0.2 units/kg followed by individual dose adjustments. Toujeo can also be given together with other anti-hyperglycaemic medicinal products. *Switch between insulin glargine 100 units/ml and Toujeo:* Insulin glargine 100 units/ml and Toujeo are not bioequivalent and are not directly interchangeable. When switching from insulin glargine 100 units/ml to Toujeo, this can be done on a unit-to-unit basis, but a higher Toujeo dose (approximately 10-18%) may be needed to achieve target ranges for plasma glucose levels. When switching from Toujeo to insulin glargine 100 units/ml, the dose should be reduced (approximately by 20%). *Switching from other basal insulins to Toujeo:* A change of dose and/or timing of the basal insulin and concomitant anti-hyperglycaemic treatment may be required. Dose adjustments may also be required if the patient's weight or lifestyle changes, the timing of insulin dose is changed or other circumstances arise that increase susceptibility to hypo- or hyperglycaemia. Toujeo must not be mixed or diluted with any other insulin or other medicinal products. Close metabolic monitoring is recommended during a switch and in the initial weeks thereafter. SoloStar 1-80 units per single injection in steps of 1 unit and DoubleStar 2-160 units in steps of 2 units. When changing from Toujeo SoloStar to Toujeo DoubleStar, if the patient's previous dose was an odd number then the dose must be increased or decreased by 1 unit. Toujeo DoubleStar prefilled pen is recommended for patients requiring at least 20 units per day.

**Special Populations:** *Elderly, renal and hepatic impairment:* Insulin requirements may be diminished in the elderly or patients with renal or hepatic impairment. *Paediatric:* When switching basal insulin to Toujeo, dose reduction of basal and bolus insulin needs to be considered on an individual basis, in order to minimise the risk of hypoglycaemia.

**Contraindications**: Hypersensitivity to insulin glargine or any excipients.

**Precautions and Warnings:** *Traceability:* In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. Toujeo is not the insulin of choice for treatment of diabetic ketoacidosis. Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. There is a potential risk of delayed insulin absorption and worsened glycaemic control following insulin injections at sites with these reactions. A sudden change in the injection site to an unaffected area has been reported to result in hypoglycaemia. Blood glucose monitoring is recommended after the change in the injection site, and dose adjustment of antidiabetic medications may be considered. *Hypoglycaemia:* In case of insufficient glucose control or a tendency to hyper/hypoglycaemic episodes, the patient's adherence to the prescribed treatment regimen, injection sites and proper injection technique and all other relevant factors must be reviewed before dose adjustment is considered. Particular caution should be exercised, and intensified blood glucose monitoring is advisable for patients in whom hypoglycaemic episodes might be of clinical relevance and in those where dose adjustments may be required. Warning signs of hypoglycaemia may be changed, less pronounced or absent in certain risk groups, potentially resulting in severe hypoglycaemia and loss of consciousness. Risk groups include patients in whom glycaemic control is markedly improved, hypoglycaemia develops gradually, an autonomic neuropathy is present, or who are elderly. The prolonged effect of subcutaneous insulin glargine may delay recovery from hypoglycaemia. *Intercurrent illness:* Requires intensified metabolic monitoring and often it is necessary to adjust the insulin dose. *Insulin antibodies:* administration may cause insulin antibodies to form. *Use with pioglitazone:* Cases of cardiac failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for development of cardiac heart failure. If the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Pioglitazone should be discontinued if any deterioration in cardiac symptoms occurs. *Medication errors:* Insulin labels must always be checked before each injection to avoid errors between Toujeo and other insulins. Patients must be instructed to never use a syringe to remove Toujeo from the SoloStar or DoubleStar pre-filled pen, A new sterile needle must be attached before each injection. Needles must not be re-used. ***Pregnancy and breast-feeding:*** There is no data from exposed pregnancies in controlled clinical trials. However, there is a large amount of data on use of insulin glargine 100 units/ml in pregnant women indicating no specific adverse effects on pregnancy and no specific malformative nor feto/neonatal toxicity. The use of Toujeo may be considered during pregnancy, if clinically needed. Careful monitoring of glucose control is essential. It is unknown if insulin glargine is excreted in breast milk. ***Interactions:*** Substances that affect glucose metabolism may require adjustment of insulin glargine.

**Adverse Reactions**: *Very common:* Hypoglycaemia. Prolonged or severe hypoglycaemia may be life-threatening. *Common:* Lipohypertrophy, injection site reactions, including redness, pain, itching, hives, swelling, or inflammation. *Not known:* Cutaneous amyloidosis. *Prescribers should consult the SmPC in relation to other adverse reactions.*

**NI List Price:** SoloStar 5 x 1.5ml pens: £53.57; DoubleStar 3 x 3ml pens: £64.27.

**Legal Category:** POM

**Marketing Authorisation Number**: SoloStar 5 Pen pack: EU/1/00/133/035; DoubleStar 3 Pen pack: EU/1/00/133/038.

**Marketing Authorisation Holder:** Sanofi Aventis Deutschland GmbH, D-65926 Frankfurt am Main, Germany.

**Further information is available from:** Medical Information, Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. uk-medicalinformation@sanofi.com.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Sanofi Tel: 0800 090 2314. Alternatively, send via email to UK-drugsafety@sanofi.com

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