Toujeo®
insulin glargine 300U/mL

EDITION 1 (n=807)[1]

EDITION 2 (n=811)[1]

EDITION 3 (n=878)[1]

Post-hoc meta-analysis of clinical trials comparing Toujeo® vs insulin glargine 100 units/mL in people living with T2DM

A meta-analysis of three 6-month, Phase 3 clinical trials and their 6-month extension study[1,2]

Toujeo® is indicated for the treatment of diabetes mellitus in adults, adolescents, and children from the age of 6 years[3]

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Ritzel R, et al. Diabetes Obes Metab. 2015;17(9):859-67, & Ritzel R, et al. Diabetes Obes Metab. 2018;20(3):541-8.

This material is intended for healthcare professionals only.

Prescribing information and Adverse event reporting can be found at the back of this item.

Limitations of the design for these studies include the open-label nature of the treatment and the short study duration. The subgroup analyses by age group are *post-hoc* and should be interpreted with caution.[1] In addition, the meta-analysis was performed *post-hoc* and is exploratory in nature.[2]

T2DM, type 2 diabetes mellitus

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Reduce the risk of severe hypoglycaemia in T2DM patients[1,2]

Fear of severe hypoglycaemia is a common problem affecting T2DM patients[4]

Successful diabetes management, especially when using insulin, consists of a balance between achieving glycaemic control while reducing the risk of hypoglycaemia in patients[4]

+14%*

Early hypoglycaemia after insulin initiation in T2DM is associated with increased treatment discontinuation.[5] Significantly more patients with early hypoglycaemia (vs those without) discontinued their insulin treatment in a US retrospective cohort study (n=49,062) (P<0.0001)[5]

Key findings from a *post-hoc* meta-analysis of three 6-month, Phase 3 clinical trials** that compared Toujeo® vs insulin glargine 100 units/mL[1,2]

Better glycaemic control with Toujeo® vs insulin glargine 100 units/mL at 12 months

- HbA_{1c} levels over 12 months: LSM difference in change from baseline for Toujeo® vs insulin glargine 100 units/mL: −0.10% (95% CI −0.18 to −0.02) or −1.09 mmol/mol (95% CI −2.01 to −0.20; P=0.0174)
- **Less confirmed (≤3.9 mmol/L) or severe† nocturnal hypoglycaemia with Toujeo® vs insulin glargine 100 units/mL. Daytime rates were comparable.**
- Risk of confirmed (≤3.9 mmol/L) or severe† hypoglycaemia was 15% lower with Toujeo® vs insulin glargine 100 units/mL at night (RR 0.85 [95% CI 0.77–0.92]) and 6% lower at any time of day (RR 0.94 [95% CI 0.90–0.98])

* 68% of patients experiencing hypoglycaemia in the first 6 months discontinue basal insulin vs 54% of patients who have not experienced early hypoglycaemia[5]

**The following adult T2DM patient populations were pooled in this meta-analysis: EDITION 1 (n=807); EDITION 2 (n=811); EDITION 3 (n=878)

† Severe hypoglycaemia was defined as a hypoglycaemic event that required assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions

CI, confidence interval; **HbA_{1c},** glycated haemoglobin; **LSM,** least squares mean; **RR,** relative risk; **T2DM,** type 2 diabetes mellitus

Post-hoc meta-analysis of three 6-month, Phase 3 clinical trials* that compared Toujeo® vs insulin glargine 100 units/mL in a broad T2DM patient population[1,2]

EDITION 1[6]
(n=807)

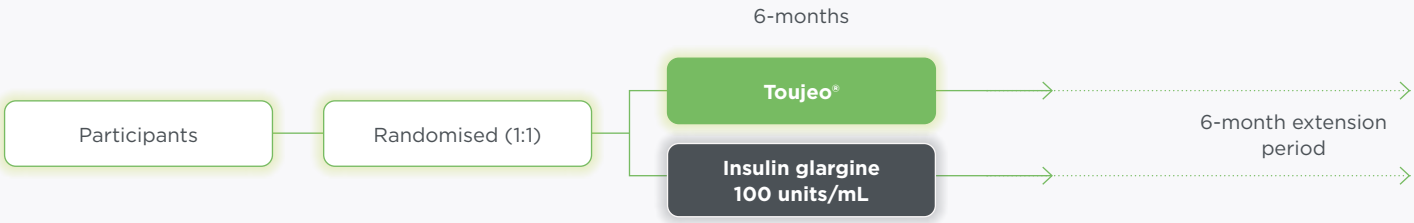
Basal switch in basal bolus regimen: Basal insulin (>42 units/day) plus mealtime bolus insulin (fast-acting analogue)

EDITION 2[7]
(n=811)

Basal switch in basal oral therapy: Basal insulin (>42 units/day) plus OAD (excluding SU)

EDITION 3[8]
(n=878)

Basal start in insulin naïve: OAD



6-month extension study design:

- Objective: To assess the clinical efficacy and safety of Toujeo® vs insulin glargine 100 units/mL
- Randomised (1:1), open-label, parallel-group, multicentre Phase 3 studies
- The EDITION programme was built with similar study design across trials
- The EDITION 1, 2, and 3 studies included a 6-month extension period, during which participants continued to receive their previously assigned basal insulin (Toujeo® or insulin glargine 100 units/mL)[1,2,6–8]
- Once-daily injections of Toujeo® or insulin glargine 100 units/mL in the evening were to be individually titrated once weekly throughout the 6-month extension period following the same dosing recommendations as the initial 6-month study, seeking a fasting SMPG of 4.4–5.6 mmol/L[1,2,6–8]

**Post-hoc,* patient-level meta-analysis of EDITION 1 (basal bolus switch), EDITION 2 (basal oral therapy switch), and EDITION 3 (basal oral therapy start) studies in adults with T2DM. Endpoints included change in HbA_{1c} reduction in the mITT population (all participants receiving ≥1 dose of study drug and with both baseline and ≥1 post-baseline assessment; n=2474) and hypoglycaemic events in the safety population (all participants receiving ≥1 dose of study drug; n=2496).

HbA_{1c}, glycated haemoglobin; **mITT,** modified intention-to-treat; **OAD,** oral antidiabetic drug; **SMPG,** self-monitored plasma glucose; **SU,** sulphonylureas; **T2DM,** type 2 diabetes mellitus

Endpoints of patient-level meta-analysis[1,2]*

Efficacy endpoint:

- Change in HbA_{1c} from baseline to 12 months

Main safety and tolerability endpoints included:

- Percentages of participants having at least one nocturnal (00:00–05:59 h) hypoglycaemic event and proportion of patients having at least one hypoglycaemic event at any time of day (24 h)

- Annualised rates (events per participant-year), of nocturnal and anytime hypoglycaemia by study period, and the cumulative mean number of hypoglycaemic events per participant

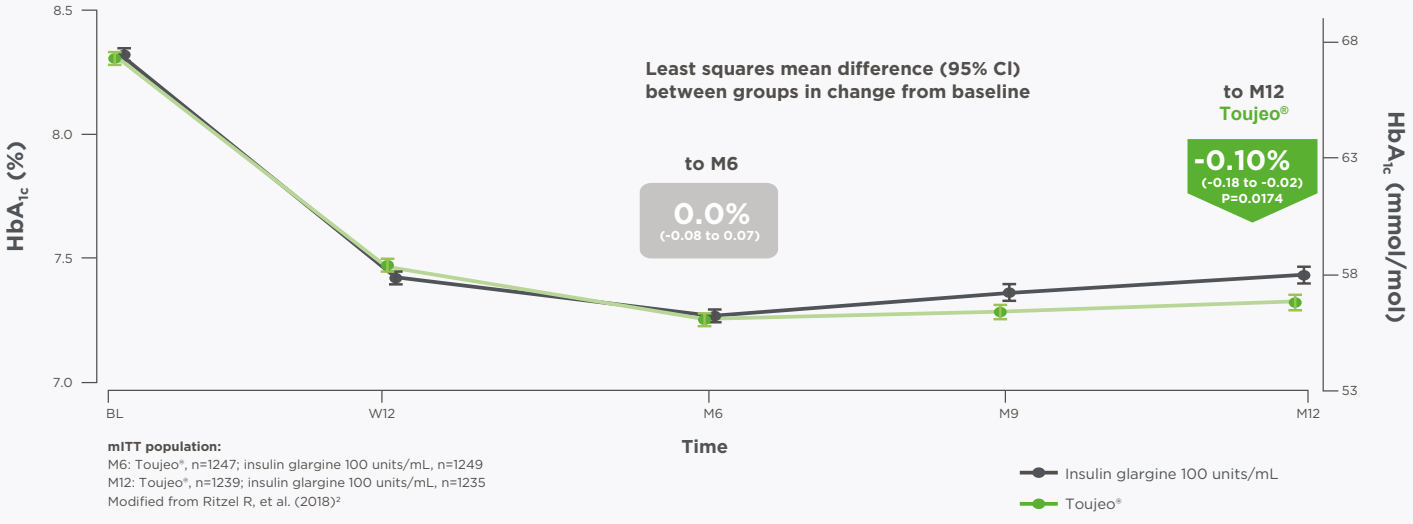
Limitations:

- The T2DM study pool consisted of a heterogenous population of patients, with variations in baseline characteristics between the populations reported; however, they represent a large multi-national cohort of patients with T2DM eligible for Toujeo®
- Although the results are supported by a prespecified pooled analysis of EDITION 2 and EDITION 3, the pooled analysis of all three EDITION studies was not prespecified and therefore should be considered *post-hoc* and exploratory in nature

Better glycaemic control with Toujeo® vs insulin glargine 100 units/mL at 12 months[2]

Patient-level meta-analysis of EDITION 1, 2, and 3 in a large population with T2DM

HbA_{1c} reduction over the 12-month treatment period



*Same study design across all trials

BL, baseline; **CI,** confidence interval; **HbA_{1c},** glycated haemoglobin; **M,** month; **T2DM,** type 2 diabetes mellitus; **W,** week

Less confirmed (≤3.9 mmol/L) or severe nocturnal hypoglycaemia with Toujeo® vs insulin glargine 100 units/mL[1,2]

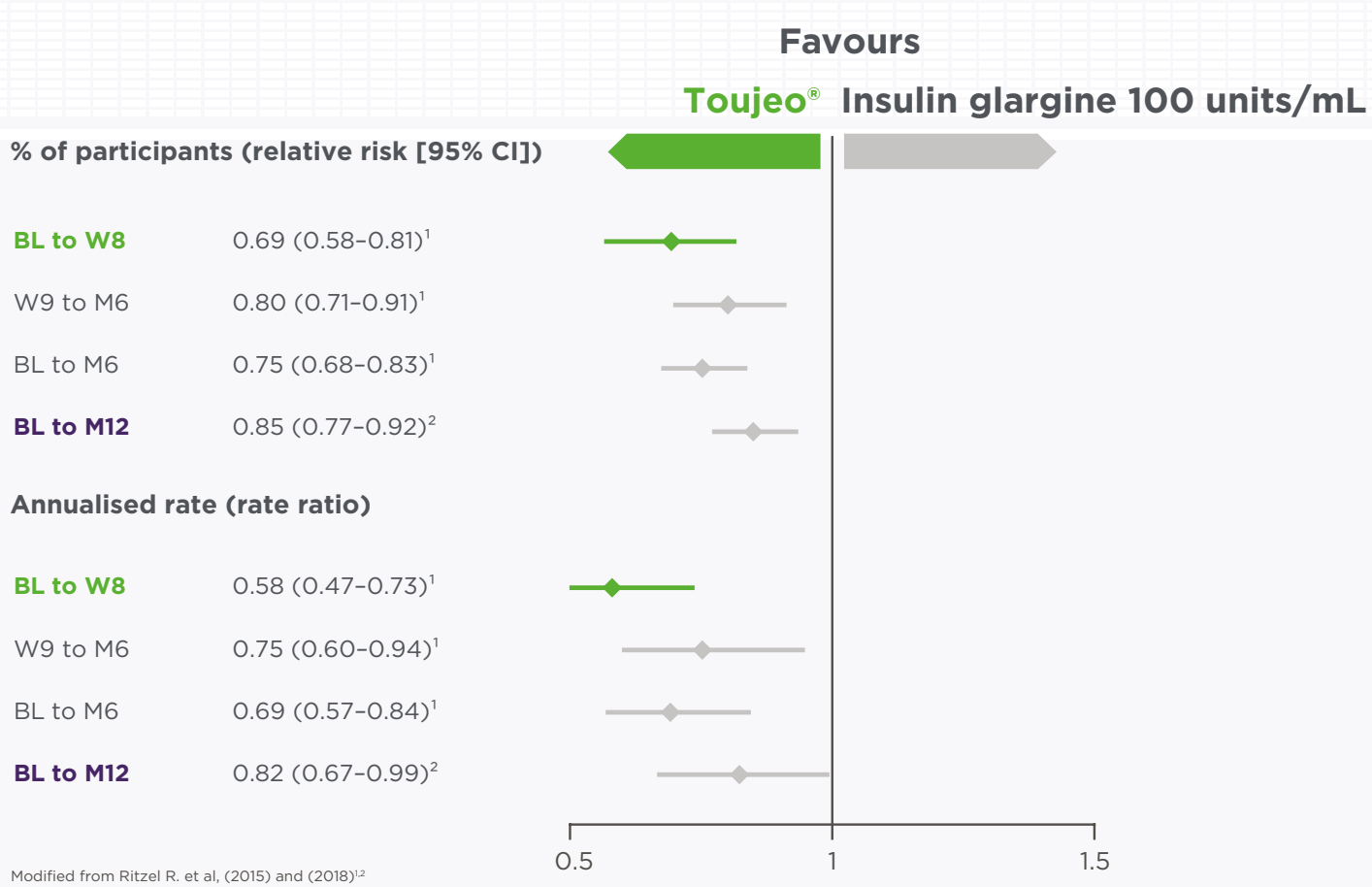
Patient-level meta-analysis of EDITION 1, 2, and 3 in a large population with T2DM

NOCTURNAL (confirmed [≤3.9 mmol/L] or severe hypoglycaemia)[1,2]

	Titration period (BL to W8)	Maintenance period (W9 to M6)	6 months (BL to M6)	12 months (BL to M12)
% of participants (relative risk)	Toujeo® -31%	Toujeo® -20%	Toujeo® -25%	Toujeo® -15%
	0.69 (95% CI 0.58–0.81)[1]	0.80 (95% CI 0.71–0.91)[1]	0.75 (95% CI 0.68–0.83)[1]	0.85 (95% CI 0.77–0.92)[2]
Annualised rate (rate ratio)	Toujeo® -42%	Toujeo® -25%	Toujeo® -31%	Toujeo® -18%
	0.58 (95% CI 0.47–0.73)[1]	0.75 (95% CI 0.60–0.94)[1]	0.69 (95% CI 0.57–0.84)[1]	0.82 (95% CI 0.67–0.99)[2]

Modified from Ritzel R. et al, (2015) and (2018)[1,2]
Safety population: Toujeo®, n=1242; insulin glargine 100 units/mL, n=1246

NOCTURNAL (confirmed [≤3.9 mmol/L] or severe hypoglycaemia)[1,2]



Modified from Ritzel R. et al, (2015) and (2018)[1,2]
Safety population: Toujeo®, n=1242; insulin glargine 100 units/mL, n=1246

BL, baseline; **CI,** confidence interval; **M,** month; **T2DM,** type 2 diabetes mellitus; **W,** week

Less confirmed (≤3.9 mmol/L) or severe anytime hypoglycaemia with Toujeo® vs insulin glargine 100 units/mL[1,2]

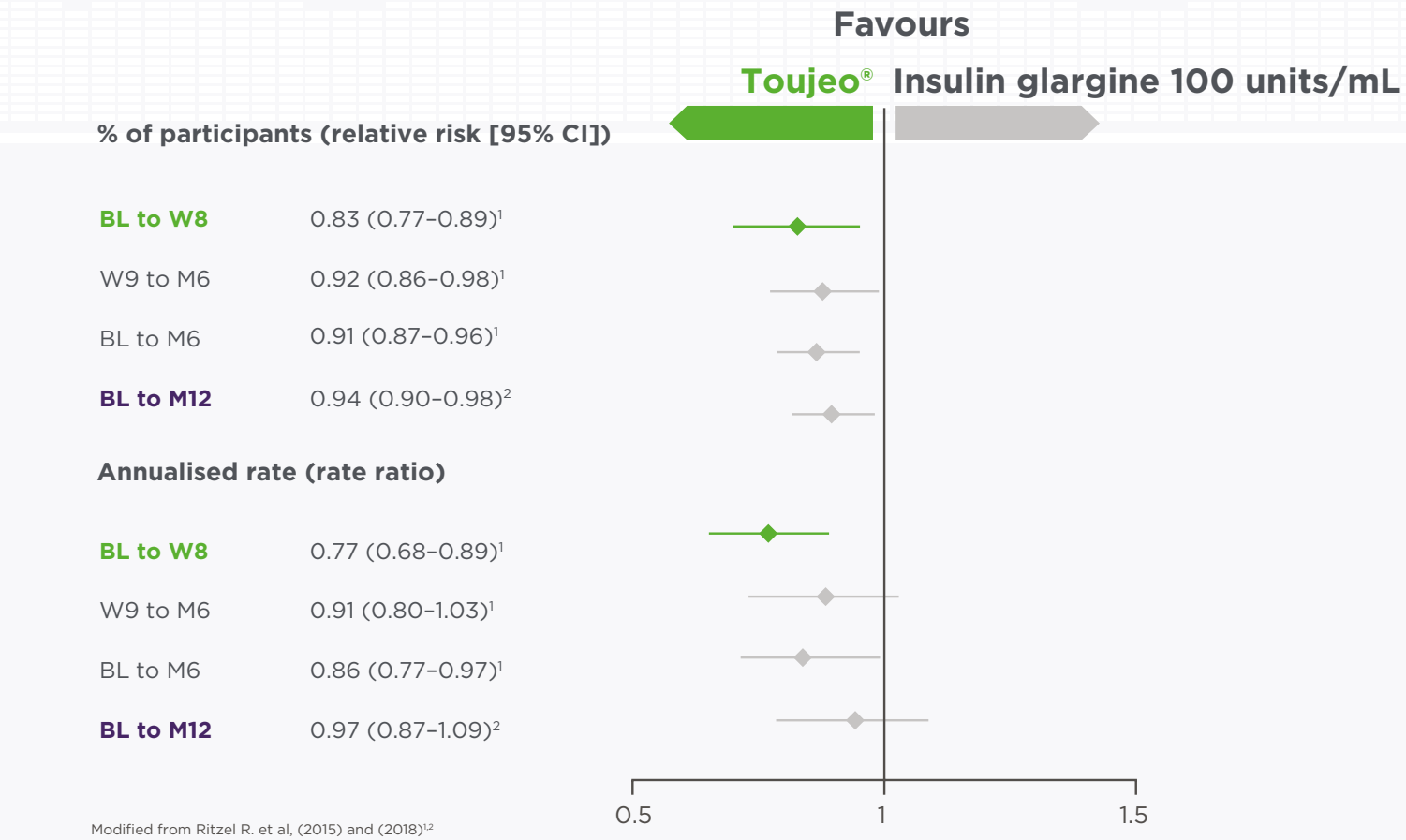
Patient-level meta-analysis of EDITION 1, 2, and 3 in a large population with T2DM

ANYTIME (confirmed [≤3.9 mmol/L] or severe hypoglycaemia)

	Titration period (BL to W8)	Maintenance period (W9 to M6)	6 months (BL to M6)	12 months (BL to M12)
% of participants (relative risk)	Toujeo® -17%	Toujeo® -8%	Toujeo® -9%	Toujeo® -6%
	0.83 (95% CI 0.77–0.89)[1]	0.92 (95% CI 0.86–0.98)[1]	0.91 (95% CI 0.87–0.96)[1]	0.94 (95% CI 0.90–0.98)[2]
Annualised rate (rate ratio)	Toujeo® -23%	Toujeo® -9%	Toujeo® -14%	Toujeo® -3%
	0.77 (95% CI 0.68–0.89)[1]	0.91 (95% CI 0.80–1.03)[1]	0.86 (95% CI 0.77–0.97)[1]	0.97 (95% CI 0.87–1.09)[2]

Modified from Ritzel R. et al, (2015) and (2018)[1,2]
Safety population: Toujeo®, n=1242; insulin glargine 100 units/mL, n=1246

ANYTIME (confirmed (≤3.9 mmol/L) or severe hypoglycaemia)[1,2]



Modified from Ritzel R. et al, (2015) and (2018)[1,2]
Safety population: Toujeo®, n=1242; insulin glargine 100 units/mL, n=1246

BL, baseline; **CI,** confidence interval; **M,** Month; **T2DM,** type 2 diabetes mellitus; **W,** Week

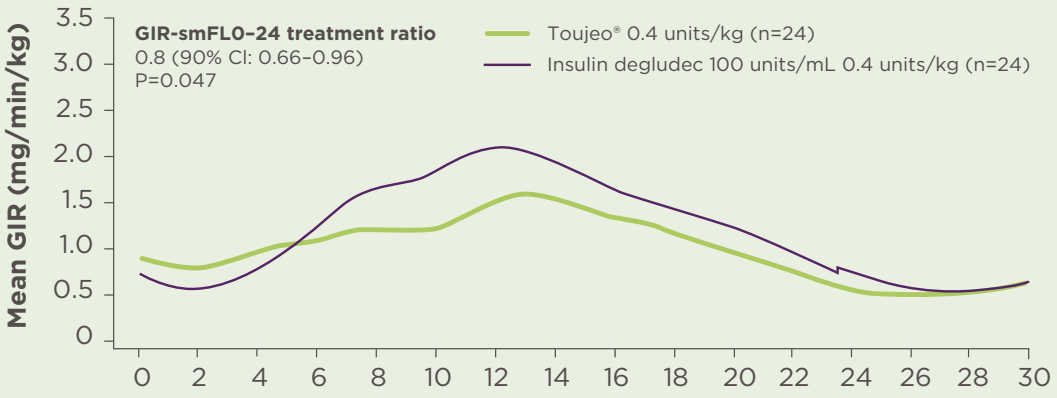
Toujeo® is associated with a flatter PK/PD profile vs insulin degludec[9]

Compared with insulin degludec, Toujeo® at a clinically relevant dose (0.4 units/kg/day) provides a more stable and evenly distributed PK/PD profile with less within-day fluctuation in adults with T1DM.[9]

Toujeo® also had a 20% lower (P=0.047) within-day variability of the smoothed GIR curve vs insulin degludec.[9]

The within-day variability of the smoothed GIR curve was similar between Toujeo® 0.6 units/kg/day and insulin degludec 0.6 units/kg/day. Both insulins provided exposure and activity until 30 hours (end of clamp).[9]

GIR profiles at the 0.4 units/kg/day dose level in steady state



Lower within-day fluctuation

Toujeo® -20%

vs insulin degludec 100 units/mL
Treatment ratio (90% CI):
0.80 (0.66–0.96); P=0.047

Modified from Bailey TS, et al. (2018)[9]

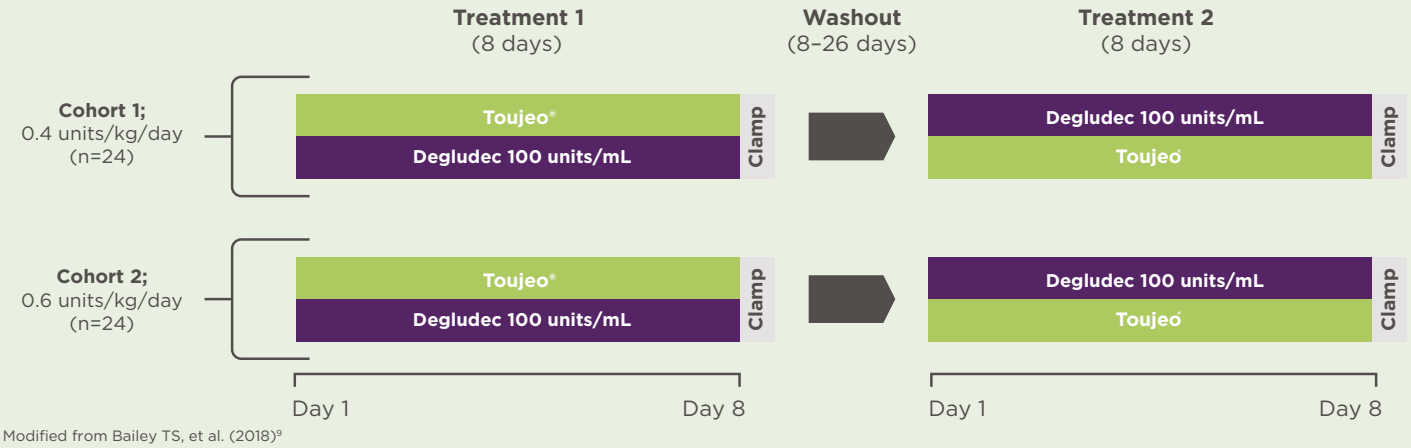
Study design[9]

This study was a single-centre, randomised, double-blind, two-treatment, two-period, two-sequence, cross-over, euglycaemic clamp study in two parallel cohorts of adult patients with T1DM (n=48) to compare the PK/PD properties of 0.4 and 0.6 units/kg/day Toujeo® with the same dose levels of insulin degludec 100 units/mL.[9]

Main study endpoint:
Fluctuations of the smoothed GIR curve over 24 hours

Treatment during the washout period was unchanged from that received prior to the study.

For GIR and BG data a smoothing factor (LOESS factor 0.15) was applied.



Modified from Bailey TS, et al. (2018)[9]

BG, blood glucose; **GIR-smFL0-24,** fluctuation of the smoothed GIR over 24 hours; **GIR,** glucose infusion rate; **LOESS,** Locally Weighted Scatter-plot Smoother; **CI,** confidence interval; **PD,** pharmacodynamics; **PK,** pharmacokinetics; **T1DM,** type 1 diabetes mellitus

References

1. Ritzel R, et al. Diabetes Obes Metab. 2015;17:859–867;
2. Ritzel R, et al. Diabetes Obes Metab. 2018;20:541–548;
3. Toujeo® Summary of Product Characteristics;
4. Colin IM, et al. Diabetes Ther. 2020;11:1835–1847;
5. Dalal M, et al. Curr Med Res Opin. 2017;33:209–214;
6. Riddle MC, et al. Diabetes Care. 2014;37:2755–2762;
7. Yki-Järvinen H, et al. Diabetes Care. 2014;37:3235–3243;
8. Bolli GB, et al. Diabetes Obes Metab. 2015;17:386–394;
9. Bailey TS, et al. Diabetes Metab. 2018;44:15–21.

Prescribing Information: Toujeo® (insulin glargine 300 units/mL) (GB)

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

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.*

GB List Price: SoloStar 3 x 1.5ml pens: £32.14; DoubleStar 3 x 3ml pens: £64.27

Legal Category: POM **Marketing Authorisation Number**: SoloStar 3 Pen pack: PLGB 04425/0817; DoubleStar 3 Pen pack: PLGB 04425/0818. **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: September 2022

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

Prescribing Information: Toujeo® (insulin glargine 300 units/mL) (NI)

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

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.

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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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Prescribing Information: Toujeo® (insulin glargine 300 units/ml) Please refer to Summary of Product Characteristics (SmPC) before prescribing. Presentation: Toujeo SoloStar and DoubleStar 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. 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. The dose regimen (dose and timing) should be adjusted according to individual response. 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:** 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. The safety and efficacy of Toujeo in children and adolescents below 6 years of age have not been established.

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 prefilled pen, A new sterile needle must be attached before each injection. Needles must not be re-used. *Pregnancy and lactation:* There are 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. Prescribers should consult the SmPC in relation to other adverse reactions. **Legal Category:** POM. **Marketing Authorisation Number:** SoloStar 5 pen pack: EU/1/00/133/035; DoubleStar 5 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, 18 Riverwalk, Citywest Business Campus, Dublin 24 or contact IEmedinfo@sanofi.com.

Date of preparation: July 2022.

Adverse events should be reported. Reporting forms and information can be found at www.hpra.ie; email: medsafety@hpra.ie Adverse events should also be reported to Sanofi Ireland Ltd. Tel: 01 403 5600. Alternatively, send via email to IEPharmacovigilance@sanofi.com

Prescribing Information: Lantus® (insulin glargine) 100 units/ml solution for injection (GB)

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

Presentations: Lantus 100 units/ml solution for injection in a vial or in a cartridge. Lantus SoloStar 100 units/ml solution for injection in a pre-filled pen. Lantus cartridges and Solostar pre- filled pens each contain 3 ml of solution for injection, equivalent to 300 units insulin glargine. Each vial contains 10 ml of solution for injection, equivalent to 1000 units.

Indications: Treatment of diabetes mellitus in adults, adolescents and children of 2 years or above.

Dosage and administration: Lantus is administered subcutaneously once daily, at any time but at the same time each day. 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. Lantus dosage should be individually adjusted. In type 2 diabetes mellitus, Lantus can also be used in combination with orally active antidiabetic medicinal products. Lantus must not be mixed with other insulins or diluted. Switch from twice daily NPH insulin to Lantus: To reduce the risk of nocturnal and early morning hypoglycaemia, patients who are changing their basal insulin regimen from a twice daily NPH insulin to a once daily regimen with Lantus should reduce their daily dose of basal insulin by 20 – 30% during the first weeks of treatment. Switch from Toujeo (insulin glargine) 300 units/ml to Lantus: Lantus and Toujeo are not bioequivalent and are not directly interchangeable. To reduce the risk of hypoglycemia, patients who are changing their basal insulin regimen from an insulin regimen with once daily Toujeo to a once daily regimen with Lantus should reduce their dose by approximately 20%. Switching from other insulins to Lantus: When switching from a treatment regimen with an intermediate or long-acting insulin to a regimen with Lantus, a change of the dose of the basal insulin may be required and the concomitant antidiabetic treatment may need to be adjusted (dose and timing of additional regular insulins or fast-acting insulin analogues or the dose of oral antidiabetic medicinal products). Close metabolic monitoring is recommended during, and for a period after, transition from other insulins to Lantus. 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.

Special populations: Elderly, renal or hepatic impairment: Insulin requirements may be diminished. Paediatric population (<2 years of age): No data are available.

Contraindications: Hypersensitivity to insulin glargine or any excipients.

Precautions and warnings: Lantus is not the insulin of choice for treatment of diabetic ketoacidosis. In case of insufficient glucose control or a tendency to hypo/hyperglycaemic episodes all relevant factors must be reviewed before dose adjustment is considered. Transferring a patient to another type or brand of insulin should be done under strict medical supervision. 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. Injection technique: 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. Intercurrent illness also requires intensified metabolic monitoring. Hypoglycaemia: Particular caution should be exercised, and intensified blood 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. The prolonged effect of subcutaneous Lantus may delay recovery from hypoglycaemia. Due to more sustained basal insulin supply with Lantus, less nocturnal but earlier morning hypoglycaemia can be expected. Insulin antibodies: administration may cause insulin antibodies to form. Rarely, this may necessitate dose adjustment. Pioglitazone: Cases of cardiac failure have been reported, especially in patients with risk factors for development of cardiac heart failure. Patients on this combination should be observed and 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 Lantus and other insulins. Lantus Solostar is only suitable for subcutaneous injections from its pre-filled pen. Lantus cartridges are only suitable for subcutaneous injections from specific reusable pens (please refer to SmPC for further details). If administration by syringe is necessary, a vial should be used. ***Interactions:*** A number of substances affect glucose metabolism and may require dose adjustment of Lantus. ***Pregnancy and lactation:*** No clinical data on exposed pregnancies from controlled clinical trials are available. A large amount of post-marketing data indicates no specific adverse effects of Lantus in pregnancy. Use of Lantus in pregnancy can be considered if clinically needed. Insulin requirements may decrease during the first trimester and generally increase during the second and third trimesters. Immediately after delivery, insulin requirements decline rapidly (increased risk of hypoglycaemia). Careful monitoring of glucose control is essential. It is unknown if Lantus is excreted in breast milk.

Adverse reactions: Very common: Hypoglycaemia. Prolonged or severe hypoglycaemia may be life-threatening. Overdose may lead to severe and sometimes long-term and life-threatening hypoglycaemia. Common: Lipohypertrophy, injection site reactions. Uncommon: Lipoatrophy. Rare: Allergic reactions, visual impairment, retinopathy and oedema. Very rare: Dysgeusia, myalgia. Frequency not known: Cutaneous amyloidosis. *Prescribers should consult the SmPC in relation to other adverse reactions.*

Legal category: POM.

GB list price and Marketing Authorisation Number(s): 1 x 10ml Lantus vial (PLGB 04425/0814): £25.69; 5 x 3ml Lantus cartridge (PLGB 04425/0815): £34.75; 5 x 3ml Lantus SoloStar (PLGB 04425/0816): £34.75.

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

For more information please contact: Medical Information, Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. uk-medicalinformation@sanofi.com.

Date of preparation: October 2022

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

Prescribing Information: Lantus® (insulin glargine) 100 units/ml solution for injection (NI)

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

Presentations: Lantus 100 units/ml solution for injection in a vial or in a cartridge. Lantus SoloStar 100 units/ml solution for injection in a pre-filled pen. Lantus cartridges and Solostar pre- filled pens each contain 3 ml of solution for injection, equivalent to 300 units insulin glargine. Each vial contains 10 ml of solution for injection, equivalent to 1000 units.

Indications: Treatment of diabetes mellitus in adults, adolescents and children of 2 years or above.

Dosage and administration: Lantus is administered subcutaneously once daily, at any time but at the same time each day. 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. Lantus dosage should be individually adjusted. In type 2 diabetes mellitus, Lantus can also be used in combination with orally active antidiabetic medicinal products. Lantus must not be mixed with other insulins or diluted. Switch from twice daily NPH insulin to Lantus: To reduce the risk of nocturnal and early morning hypoglycaemia, patients who are changing their basal insulin regimen from a twice daily NPH insulin to a once daily regimen with Lantus should reduce their daily dose of basal insulin by 20 – 30% during the first weeks of treatment. Switch from Toujeo (insulin glargine) 300 units/ml to Lantus: Lantus and Toujeo are not bioequivalent and are not directly interchangeable. To reduce the risk of hypoglycemia, patients who are changing their basal insulin regimen from an insulin regimen with once daily Toujeo to a once daily regimen with Lantus should reduce their dose by approximately 20%. Switching from other insulins to Lantus: When switching from a treatment regimen with an intermediate or long-acting insulin to a regimen with Lantus, a change of the dose of the basal insulin may be required and the concomitant antidiabetic treatment may need to be adjusted (dose and timing of additional regular insulins or fast-acting insulin analogues or the dose of oral antidiabetic medicinal products). Close metabolic monitoring is recommended during, and for a period after, transition from other insulins to Lantus. 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.

Special populations: Elderly, renal or hepatic impairment: Insulin requirements may be diminished. Paediatric population (<2 years of age): No data are available.

Contraindications: Hypersensitivity to insulin glargine or any excipients.

Precautions and warnings: Lantus is not the insulin of choice for treatment of diabetic ketoacidosis. In case of insufficient glucose control or a tendency to hypo/hyperglycaemic episodes all relevant factors must be reviewed before dose adjustment is considered. Transferring a patient to another type or brand of insulin should be done under strict medical supervision. 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. Injection technique: 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. Intercurrent illness also requires intensified metabolic monitoring. Hypoglycaemia: Particular caution should be exercised, and intensified blood 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. The prolonged effect of subcutaneous Lantus may delay recovery from hypoglycaemia. Due to more sustained basal insulin supply with Lantus, less nocturnal but earlier morning hypoglycaemia can be expected. Insulin antibodies: administration may cause insulin antibodies to form. Rarely, this may necessitate dose adjustment. Pioglitazone: Cases of cardiac failure have been reported, especially in patients with risk factors for development of cardiac heart failure. Patients on this combination should be observed and 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 Lantus and other insulins. Lantus Solostar is only suitable for subcutaneous injections from its pre-filled pen. Lantus cartridges are only suitable for subcutaneous injections from specific reusable pens (please refer to SmPC for further details). If administration by syringe is necessary, a vial should be used. ***Interactions:*** A number of substances affect glucose metabolism and may require dose adjustment of Lantus. ***Pregnancy and lactation:*** No clinical data on exposed pregnancies from controlled clinical trials are available. A large amount of post-marketing data indicates no specific adverse effects of Lantus in pregnancy. Use of Lantus in pregnancy can be considered if clinically needed. Insulin requirements may decrease during the first trimester and generally increase during the second and third trimesters. Immediately after delivery, insulin requirements decline rapidly (increased risk of hypoglycaemia). Careful monitoring of glucose control is essential. It is unknown if Lantus is excreted in breast milk.

Adverse reactions: Very common: Hypoglycaemia. Prolonged or severe hypoglycaemia may be life-threatening. Overdose may lead to severe and sometimes long-term and life-threatening hypoglycaemia. Common: Lipohypertrophy, injection site reactions. Uncommon: Lipoatrophy. Rare: Allergic reactions, visual impairment, retinopathy and oedema. Very rare: Dysgeusia, myalgia. Frequency not known: Cutaneous amyloidosis. *Prescribers should consult the SmPC in relation to other adverse reactions.*

Legal category: POM.

NI list price and Marketing Authorisation Number(s): 1 x 10ml Lantus vial (EU/1/00/134/012): £25.69; 5 x 3ml Lantus cartridge (EU/1/00/134/006): £34.75; 5 x 3ml Lantus SoloStar (EU/1/00/134/033): £34.75. **Marketing Authorisation Holder**: Sanofi Aventis Deutschland GmbH, D-65926 Frankfurt am Main, Germany.

For more information please contact: Medical Information, Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. uk-medicalinformation@sanofi.com.

Date of preparation: October 2022

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Adverse events should also be reported to Sanofi Tel: 0800 090 2314. Alternatively, send via email to UK-drugsafety@sanofi.com

Prescribing Information: Lantus® (insulin glargine) 100 units/ml solution for injection (IE)

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

Presentations: Lantus 100 units/ml solution for injection in a vial or in a cartridge. Lantus SoloStar 100 units/ml solution for injection in a pre-filled pen. Lantus cartridges and Solostar pre- filled pens each contain 3 ml of solution for injection, equivalent to 300 units insulin glargine. Each vial contains 10 ml of solution for injection, equivalent to 1000 units.

Indications: Treatment of diabetes mellitus in adults, adolescents and children of 2 years or above.

Dosage and administration: Lantus is administered subcutaneously once daily, at any time but at the same time each day. 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. Lantus dosage should be individually adjusted. In type 2 diabetes mellitus, Lantus can also be used in combination with orally active antidiabetic medicinal products. Lantus must not be mixed with other insulins or diluted. Switch from twice daily NPH insulin to Lantus: To reduce the risk of nocturnal and early morning hypoglycaemia, patients who are changing their basal insulin regimen from a twice daily NPH insulin to a once daily regimen with Lantus should reduce their daily dose of basal insulin by 20-30% during the first weeks of treatment. Switch from Toujeo (insulin glargine) 300 units/ml to Lantus: Lantus and Toujeo are not bioequivalent and are not directly interchangeable. To reduce the risk of hypoglycemia, patients who are changing their basal insulin regimen from an insulin regimen with once daily Toujeo to a once daily regimen with Lantus should reduce their dose by approximately 20%. Switching from other insulins to Lantus: When switching from a treatment regimen with an intermediate or long-acting insulin to a regimen with Lantus, a change of the dose of the basal insulin may be required and the concomitant antidiabetic treatment may need to be adjusted (dose and timing of additional regular insulins or fast-acting insulin analogues or the dose of oral antidiabetic medicinal products). Close metabolic monitoring is recommended during, and for a period after, transition from other insulins to Lantus. 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.

Special populations: Elderly, renal or hepatic impairment: Insulin requirements may be diminished. Paediatric population (<2 years of age): No data are available.

Contraindications: Hypersensitivity to insulin glargine or any excipients.

Precautions and warnings: Lantus is not the insulin of choice for treatment of diabetic ketoacidosis. In case of insufficient glucose control or a tendency to hypo/hyperglycaemic episodes all relevant factors must be reviewed before dose adjustment is considered. Transferring a patient to another type or brand of insulin should be done under strict medical supervision. 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. Injection technique: 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. Intercurrent illness also requires intensified metabolic monitoring. Hypoglycaemia: Particular caution should be exercised, and intensified blood 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. The prolonged effect of subcutaneous Lantus may delay recovery from hypoglycaemia. Due to more sustained basal insulin supply with Lantus, less nocturnal but earlier morning hypoglycaemia can be expected. Insulin antibodies: administration may cause insulin antibodies to form. Rarely, this may necessitate dose adjustment. Pioglitazone: Cases of cardiac failure have been reported, especially in patients with risk factors for development of cardiac heart failure. Patients on this combination should be observed and 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 Lantus and other insulins. Lantus Solostar is only suitable for subcutaneous injections from its pre-filled pen. Lantus cartridges are only suitable for subcutaneous injections from specific reusable pens (please refer to SmPC for further details). If administration by syringe is necessary, a vial should be used. ***Interactions:*** A number of substances affect glucose metabolism and may require dose adjustment of Lantus. ***Pregnancy and lactation:*** No clinical data on exposed pregnancies from controlled clinical trials are available. A large amount of post-marketing data indicates no specific adverse effects of Lantus in pregnancy. Use of Lantus in pregnancy can be considered if clinically needed. Insulin requirements may decrease during the first trimester and generally increase during the second and third trimesters. Immediately after delivery, insulin requirements decline rapidly (increased risk of hypoglycaemia). Careful monitoring of glucose control is essential. It is unknown if Lantus is excreted in breast milk.

Adverse reactions: Very common: Hypoglycaemia. Prolonged or severe hypoglycaemia may be life-threatening. Overdose may lead to severe and sometimes long-term and life-threatening hypoglycaemia. Common: Lipohypertrophy, injection site reactions. Uncommon: Lipoatrophy. Rare: Allergic reactions, visual impairment, retinopathy and oedema. Very rare: Dysgeusia, myalgia. Frequency not known: Cutaneous amyloidosis. *Prescribers should consult the SmPC in relation to other adverse reactions.*

Legal category: POM.

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

Marketing Authorisation Number(s): Vial : EU/1/00/134/012; Cartridge: EU/1/00/134/006; SoloStar: EU/1/00/134/033.

For more information please contact: Sanofi, 18 Riverwalk, Citywest Business Campus, Dublin 24. IEmedinfo@sanofi.com.

Date of preparation: October 2022

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