Toujeo®
insulin glargine 300 units/mL

EDITION 4 (N=549 adults [≥18 years])

Edition junior (N=463 children [6–17 years])

EDITION JP1 (N=243 adults [≥18 years])

Post-hoc meta-analysis of clinical trials comparing Toujeo® vs insulin glargine 100 units/mL in T1DM patients

A meta-analysis of three 6-month, Phase III clinical trials.[1]

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

sanofi

Danne T, *et al. Diabetes Obes Metab.* 2020;1–6. DOI: 10.1111/dom.14109. [Epub ahead of print]. This material is intended for healthcare professionals only.

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

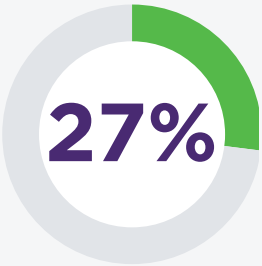
This study was funded by Sanofi UK. Limitations of the study were that the T1DM study pool consisted of heterogenous populations that may, however, represent a large multinational cohort of patients with T1DM eligible for Toujeo® and the analysis was performed *post-hoc* and is exploratory in nature.

November 2022 | MAT-GB-2103598 (v2.0)

Reduce the risk of severe hypoglycaemia in T1DM patients[1,3,4]

Severe hypoglycaemia is a common problem affecting T1DM patients.[3]

Despite the increased use of diabetes treatment technologies, many patients fail to achieve HbA_{1c} target levels and others frequently experience episodes of severe hypoglycaemia.[1,3,4]



of T1DM patients experience **≥1 episode of severe hypoglycaemia each year[3]**

The average T1DM patient spends **~9 hours out of glycaemic range each day[4]**

There remains a need in T1DM to identify insulin therapies that will enable patients to meet their glycaemic goals, whilst further reducing the risk of experiencing severe hypoglycaemia episodes.[3,4]

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

Comparable and effective HbA_{1c} reduction at 6 months with Toujeo® and insulin glargine 100 units/mL[1]

- HbA_{1c} LSM difference in the T1DM study pool from baseline to 6 months: Toujeo® (n=628), -0.38%; insulin glargine 100 units/mL (n=624), -0.44%. RR (95% CI): 0.05 (-0.04 to 0.15)

Lower risk of severe hypoglycaemia† with Toujeo® vs insulin glargine 100 units/mL in a broad population with T1DM in the full study period[1]

- Incidence of severe hypoglycaemia† from baseline to 6 months in the T1DM study pool: Toujeo® (n=629), 6.2%; insulin glargine 100 units/mL (n=624), 9.3%. OR (95% CI): 0.65 (0.42 to 0.98)

CI, confidence interval; **HbA_{1c}**, glycated haemoglobin; **LSM**, least squares mean; **OR**, odds ratio; **RR**, relative risk; **T1DM**, type 1 diabetes mellitus.

***The following T1DM patient populations were pooled in this meta-analysis: EDITION 4 (n=549): adult patients (age ≥18 years); EDITION JP 1 (n=243): adult patients (age ≥18 years); EDITION JUNIOR (n=463): children and adolescents (age 6–17 years).**

†Severe hypoglycaemia was defined as a) in *adults* as hypoglycaemic event that required assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions, or b) in *children and adolescents* as having altered mental status and inability to assist in their care, being semiconscious or unconscious, or in coma ± convulsions that may require parenteral therapy (glucagon and/or glucose).

Post-hoc meta-analysis of three 6-month, Phase III clinical trials* that compared Toujeo® vs insulin glargine 100 units/mL in a broad T1DM patient population[1]

Study design

Objective:[1]

- Assessing the risk of severe hypoglycaemia† with Toujeo® vs insulin glargine 100 units/mL

Study design:[1]

- *Post-hoc* meta-analysis of three 6-month, Phase III, randomised clinical trials*

EDITION 4 (N=549 adults [≥18 years])

Primary endpoint: Change in HbA_{1c} from baseline to Month 6[5]

Edition junior (N=463 children [6–17 years])

Primary endpoint: Non-inferiority in the efficacy of Toujeo® vs insulin glargine 100 units/mL in terms of change of HbA_{1c} from baseline to Month 6[6]

EDITION JP1 (N=243 adults [≥18 years])

Primary endpoint: Change in HbA_{1c} from baseline to Month 6[7]

Eligible patients:[1,5–7]

- Patients with T1DM for >1-year
- HbA_{1c} ≥7.0 and ≤10.0%

(EDITION 4 and JP1)

- HbA_{1c} ≥7.5 and ≤11.0%

(EDITION JUNIOR)

- Basal bolus insulin regimen

Primary objective:
Explore the risk for severe hypoglycaemia† with Toujeo® vs insulin glargine 100 units/mL in the pool of studied patients with T1DM

R 1:1

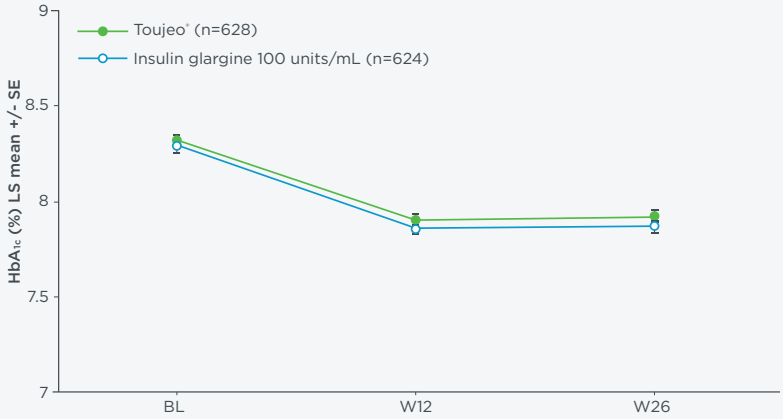
Toujeo®
Once daily (n=629)

Insulin glargine 100 units/mL
Once daily (n=626)

6-month treatment period

Comparable and effective HbA_{1c} reduction at 6 months with Toujeo® vs insulin glargine 100 units/mL[1]

HbA_{1c} reduction from baseline to Month 6‡



Adapted from Danne T, *et al. Diabetes Obes Metab.* 2020.

BL, baseline; **R**, randomisation; **SE**, standard error; **W**, Week

HbA_{1c} LSM difference in the T1DM study pool from baseline to 6 months:

- Toujeo®, -0.38%
- Insulin glargine 100 units/mL, -0.44%
- RR (95% CI): 0.05 (-0.04 to 0.15)

Non-inferiority confirmed at the 0.3% margin.

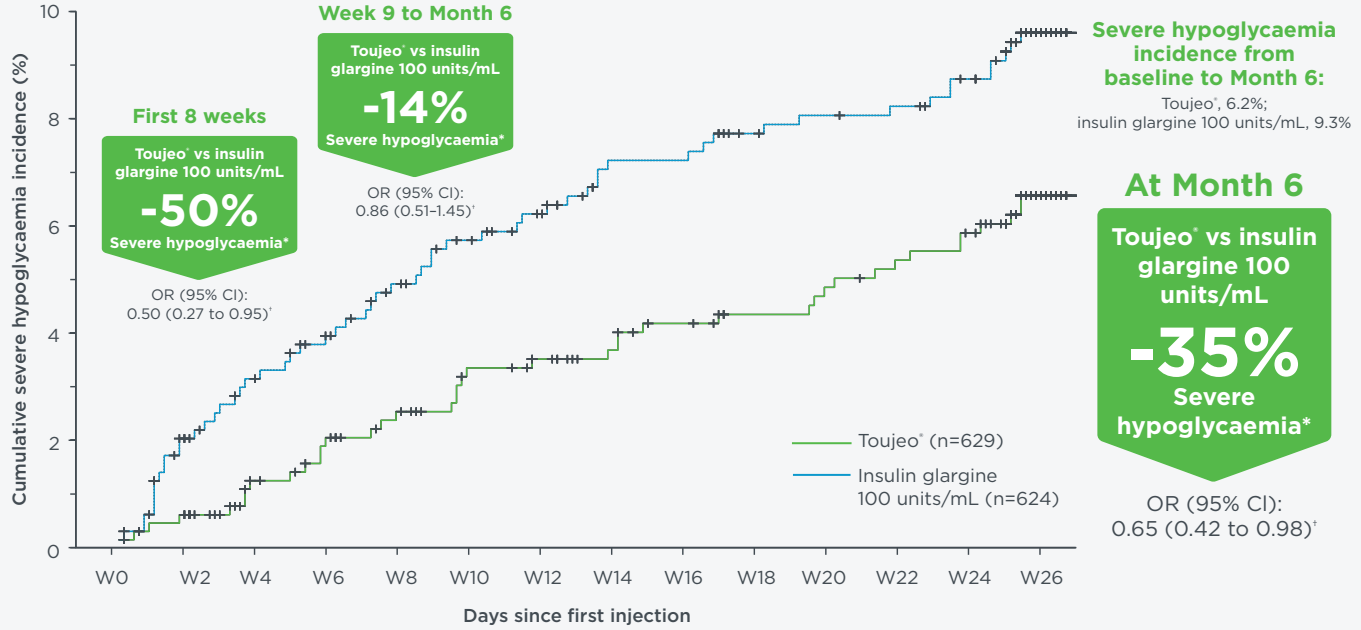
***The following T1DM patient populations that were pooled were EDITION 4 (n=549): adult patients (age ≥18 years), worldwide, EDITION JP 1 (n=243): adult patients (age ≥18 years), Japan and EDITION JUNIOR (n=463): children and adolescents (age 6–17 years), worldwide. The primary endpoint for each of the studies was non inferiority for HbA_{1c} reduction. All three trials had a similar design for regulatory purpose and achieved their primary endpoint of HbA_{1c} non inferiority of Toujeo® vs insulin glargine 100 units/mL.**

†Severe hypoglycaemia was defined as a) in *adults* as hypoglycaemic event that required assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions, or b) in *children and adolescents* as having altered mental status and inability to assist in their care, being semiconscious or unconscious, or in coma ± convulsions that may require parenteral therapy (glucagon and/or glucose).

‡Results are in the efficacy population (Toujeo®, n=628; insulin glargine 100 units/mL, n=624).

Lower risk of severe hypoglycaemia* with Toujeo® in a broad population with T1DM vs insulin glargine 100 units/mL[1]

Incidence of severe hypoglycaemia from baseline to Month 6*†

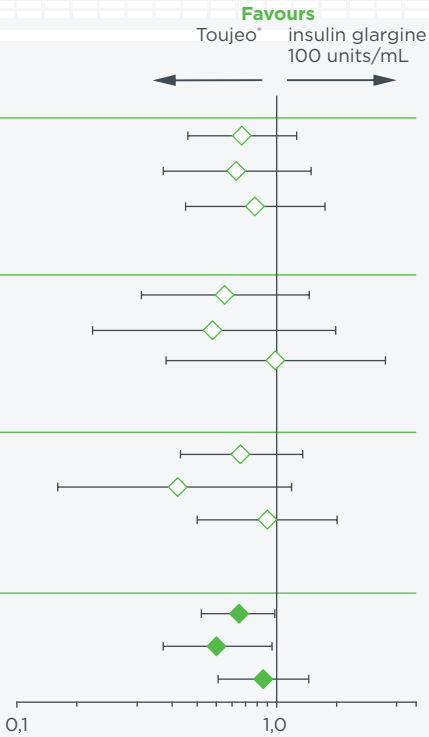


Adapted from Danne T, *et al. Diabetes Obes Metab.* 2020.

Toujeo® was associated with lower risk of severe hypoglycaemia compared to insulin glargine 100 units/mL in the full study period, and even more so during the titration period.[1]

Severe hypoglycaemia incidence*†

	Incidence (%) Toujeo® n=629	Incidence (%) insulin glargine 100 units/mL n=624	OR† (95% CI) Toujeo® vs insulin glargine 100 units/mL
EDITION 4 n=549			
BL to Month 6	6.6	9.5	0.67 (0.36; 1.26)
BL to Week 8	3.3	5.1	0.63 (0.27; 1.49)
Week 9 to Month 6	4.0	5.1	0.78 (0.35; 1.75)
EDITION JP 1 n=243			
BL to Month 6	5.7	9.9	0.55 (0.21; 1.46)
BL to Week 8	2.5	5.0	0.48 (0.12; 1.98)
Week 9 to Month 6	4.1	4.1	0.99 (0.28; 3.52)
EDITION JUNIOR n=463			
BL to Month 6	6.0	8.8	0.66 (0.33; 1.35)
BL to Week 8	1.3	3.9	0.32 (0.08; 1.19)
Week 9 to Month 6	5.2	5.7	0.90 (0.40; 2.01)
T1DM STUDY POOL n=1,255			
BL to Month 6	6.2	9.3	0.65 (0.42; 0.98)
BL to Week 8	2.4	4.6	0.50 (0.27; 0.95)
Week 9 to Month 6	4.5	5.1	0.86 (0.51; 1.45)t



Incidence of severe hypoglycaemia* from baseline to Month 6 in the T1DM study pool:

- Toujeo® (n=629), 6.2%
- Insulin glargine 100 units/mL (n=624), 9.3%
- OR (95% CI): 0.65 (0.42 to 0.98)

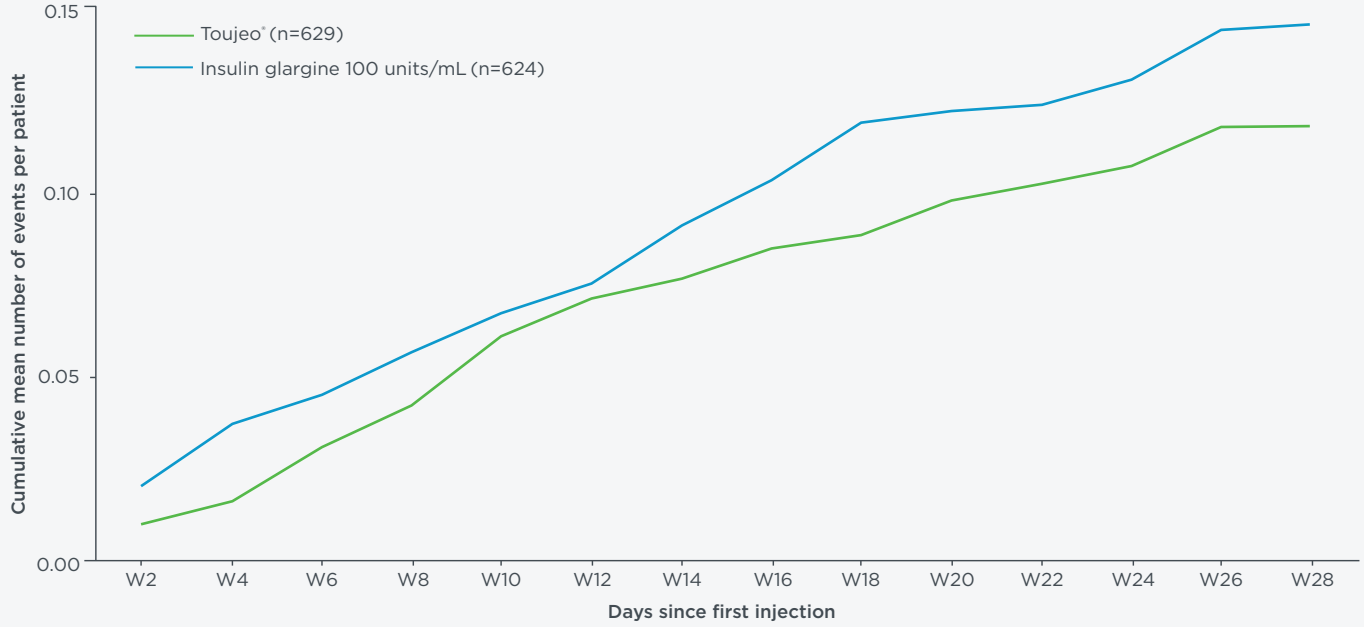
Adapted from Danne T, *et al. Diabetes Obes Metab.* 2020.

*Severe hypoglycaemia was defined as a) in *adults* as hypoglycaemic event that required assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions, or b) in *children and adolescents* as having altered mental status and inability to assist in their care, being semiconscious or unconscious, or in coma ± convulsions that may require parenteral therapy (glucagon and/or glucose).

†OR based on logistic model with treatment as fixed effects, and by adding study as fixed effect for the T1DM study pool; cumulative incidences curves were calculated using Kaplan-Meier estimates.

Numerically lower event rates of severe hypoglycaemia* with Toujeo® in a broad population with T1DM vs insulin glargine 100 units/mL[1]

Severe hypoglycaemia event rate in T1DM study pool†

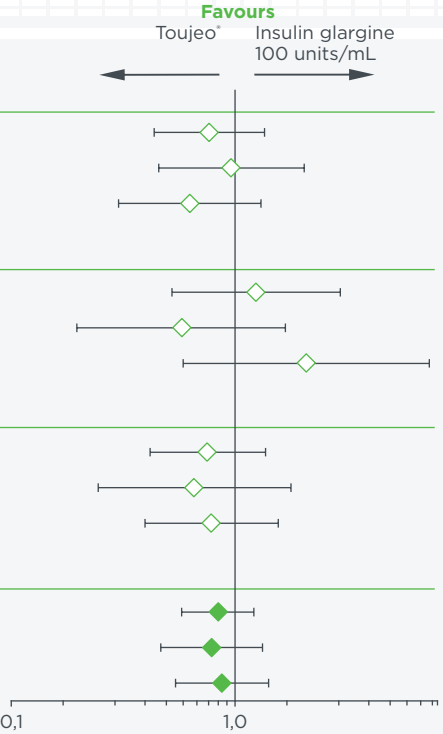


Adapted from Danne T, *et al. Diabetes Obes Metab.* 2020.

Treatment with Toujeo® was associated with a numerically lower event rate of severe hypoglycaemia* compared to insulin glargine 100 units/mL from baseline to 6 months.[1]

Severe hypoglycaemia event rates*‡

	Events per patient/year Toujeo® n=629	Insulin glargine 100 units/mL n=624	OR† (95% CI) Toujeo® vs insulin glargine 100 units/mL
EDITION 4 n=549			
BL to Month 6	0.24	0.34	0.71 (0.34; 1.48)
BL to Week 8	0.41	0.43	0.95 (0.36; 2.53)
Week 9 to Month 6	0.16	0.29	0.55 (0.21; 1.42)
EDITION JP 1 n=243			
BL to Month 6	0.32	0.22	1.33 (0.43; 4.09)
BL to Week 8	0.16	0.32	0.49 (0.12; 1.96)§
Week 9 to Month 6	0.39	0.15	2.60 (0.50; 13.50)
EDITION JUNIOR n=463			
BL to Month 6	0.18	0.27	0.69 (0.32; 1.50)
BL to Week 8	0.17	0.28	0.58 (0.16; 2.11)
Week 9 to Month 6	0.19	0.26	0.73 (0.30; 1.78)
T1DM STUDY POOL n=1,255			
BL to Month 6	0.23	0.29	0.80 (0.49; 1.29)
BL to Week 8	0.27	0.36	0.73 (0.37; 1.44)
Week 9 to Month 6	0.22	0.25	0.84 (0.45; 1.57)



Event rate of severe hypoglycaemia* from baseline to Month 6 in the T1DM study pool:

- Toujeo® (n=629), 0.23
- Insulin glargine 100 units/mL (n=624), 0.29
- RR (95% CI): 0.80 (0.49 to 1.29)

Adapted from Danne T, *et al. Diabetes Obes Metab.* 2020.

*Severe hypoglycaemia was defined as a) in *adults* as hypoglycaemic event that required assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions, or b) in *children and adolescents* as having altered mental status and inability to assist in their care, being semiconscious or unconscious, or in coma ± convulsions that may require parenteral therapy (glucagon and/or glucose).

†Results are in the safety population (Toujeo®, n=629; insulin glargine 100 units/mL, n=624).

‡RR based on negative binominal model with treatment as fixed effect and logarithm of the treatment-emergent period as offset and by adding study fixed effect for the T1DM study pool. Model calculated with low event numbers (3 vs 6 events).

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

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 hypoor 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 prefilled pen, A new sterile needle must be attached before each injection. Needles must not be re-used. ***Pregnancy and breastfeeding:*** 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.
MAT-XU-2203098 (V1.0)

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)

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 hypoor 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 prefilled pen, A new sterile needle must be attached before each injection. Needles must not be re-used. ***Pregnancy and breastfeeding:*** 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.
Date of preparation: September 2022.
MAT-XI-2200061 (V1.0)

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

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 prefilled 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.
MAT-XU-2204110 (V1.0)

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

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 prefilled 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
MAT-XI-2200071 (V1.0)

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

References: 1. Danne T, *et al. Diabetes Obes Metab.* 2020;1–6. DOI: 10.1111/dom.14109. [Epub ahead of print]. **2.** Toujeo® Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/6938/smpc. [Accessed: November 2022]. **3.** Leiter LA, *et al. Diabetes.* 2005;29:186–192. **4.** Agiostratidou G, *et al. Diabetes Care.* 2017;40:1622–1630. **5.** Home PD, *et al. Diabetes Care.* 2015;38:2217–2225. **6.** Danne T, *et al. Diabetes Care.* 2020. DOI:10.2337/dc19-1926. [Epub ahead of print]. **7.** Matsuhisa M, *et al. Diab Obes Met.* 2016;18:375–383.