sanofi

Toujeo®
insulin glargine 300 units/mL

The observational ORION study[1]

Real-world safety and effectiveness of Toujeo® (insulin glargine 300 U/mL) in people with T2DM who fast during Ramadan

RWE data are subject to potential confounding bias usually associated with observational research.

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

*Safety and efficacy in patients of Toujeo® in children <6 years of age have not been established.

Before prescribing the product, always refer to the Summary of Product Characteristics.

Prescribing information can be found at the end of this document.

T2DM, type 2 diabetes mellitus.

References:
1. Hassanein M, *et al. Diabetes Res Clin Pract*. 2020;165:1−9.
2. Toujeo® (insulin glargine 300 U/mL) Summary of Product Characteristics

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ORION study: Study design

Aims

To evaluate the **safety and effectiveness of Toujeo®** in patients with T2DM during pre-Ramadan, Ramadan and post-Ramadan periods **in a real-world setting**[1]

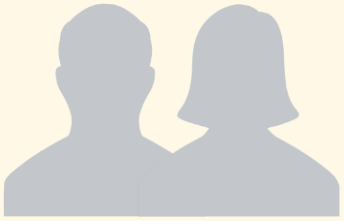
Method

Prospective, observational, international, multi-centre study conducted in 11 countries[1]

Primary endpoint

Percentage of participants experiencing ≥1 event of **severe and/or symptomatic documented hypoglycaemia** with SMPG ≤3.9 mmol/L (≤70 mg/dL) during Ramadan

Adults with T2DM who had been treated with Toujeo® for ≥8 weeks prior to study, prescribed as per routine clinical practice and planned to continue with Toujeo® through the Ramadan period and intended to fast for ≥15 days during Ramadan



493 patients eligible for assessment*

Pre-Ramadan	Ramadan Holy Month	Post-Ramadan
1–3 months	1 month	1 month†

Dose adjustments during Ramadan were made based on the advice of the treating physician, guided by IDF-DAR recommendations and individual patient characteristics

IDR-DAR, The International Diabetes Federation and the Diabetes and Ramadan International Alliance; **SMPG**, self-measured plasma glucose; **T2DM**, Type 2 diabetes mellitus.

*82.8% (n=404) of participants were considered to have a moderate/low risk of complications during fasting, determined by their physician according to IDF-DAR guideline criteria.[1]
†Hypoglycaemia and AEs occurring ≥1 month after the end of Ramadan were also recorded if the patient visit was made more than one month after Ramadan.[1]

References: 1. Hassanein M, *et al. Diabetes Res Clin Pract*. 2020;165:1−9.

ORION study: Secondary endpoints[1]

Hypoglycaemia

Incidence of ≥1 event of severe and/or symptomatic documented hypoglycaemia with SMPG <54 mg/dL, and event rates of severe and/or symptomatic documented hypoglycaemia with SMPG ≤3.9 mmol/L (≤70 mg/dL) and <3.0 mmol/L (<54 mg/dL) across the three time periods and by time of day

Effectiveness

Mean change in HbA_{1c}, FPG and SMPG, from pre- to post-Ramadan periods, and mean fasting SMPG in the evening (just before iftar) during the Ramadan period

Safety endpoints

AEs, including episodes of hyperglycaemia, and SAEs

AE, adverse event; **FPG**, fasting plasma glucose; **SAE**, serious adverse events; **SMPG**, self-measured plasma glucose.

References: 1. Hassanein M, *et al. Diabetes Res Clin Pract*. 2020;165:1−9.

Strengths and limitations

Strengths

- Adds to current body of evidence on the management of T2DM in Muslim individuals who fast during Ramadan
- Protocol enabled physicians to prescribe treatment as per routine practice, with reference to IDF-DAR recommendations suggested
- Study provides real-world data on effectiveness and safety profile of Toujeo® during Ramadan

Limitations

- Number of participants differed by region, as 11 countries were involved. Participants also varied in terms of geographical location and cultural differences (e.g. length of the fasting day and working hours) may have impacted the results
- Majority of participants were determined to be moderate/low risk, therefore data may not fully reflect safety profile of Toujeo® in high-risk populations

AE, adverse event; **Gla-300**, insulin glargine 300 U/mL; **IDF-DAR**, International Diabetes Federation Diabetes and Ramadan. **FPG**, fasting plasma glucose; **SAE**, serious adverse event; **SMPC**, self-measured plasma glucose

References: 1. Hassanein M, *et al. Diabetes Res Clin Pract*. 2020;165:1−9.

ORION study: Baseline demographics[1]

Demographics/characteristics

Age, years, mean ± SD*	54.4 ± 11.0
Gender, male, n (%)	255 (51.7)
female, n (%)	238 (48.3)
BMI, kg/m^2, mean ± SD	29.7 ± 5.3
Duration of T2DM	
(median [Q1:Q3])	9.1 (5:15)
<10 years, n(%)	263 (53.3)
≥10 years, n(%)	230 (46.7)
HbA$_{1c}$, mmol/mol, mean ± SD	52 ± 4
Risk level associated with fasting n(%)†	
Moderate/low	404 (82.8)
High	70 (14.3)
Very high	14 (2.9)

Time since first insulin treatment, years (median [Q1:Q3])	1.0 (0.3:3.0)
Duration of Toujeo® treatment, months (median [Q1:Q3])	4.1 (3.0:9.0)
Toujeo® dose, mean ± SD	
U	24.9 ± 12.2
U/kg	0.3 ± 0.14
Comorbidity (%)	
Diabetic neuropathy	128 (26.0)
Diabetic retinopathy	65 (13.2)
Impaired renal function	71 (14.4)
Coronary heart disease	40 (8.1)

Eligible population, n=493

*83.2% of participants were <65 years and only 16 patients were 75 or over. †n=488. Risk was assessed by investigator.

Data are mean ± SD, n (%) or median (IQR, for diabetes duration only) of eligible population

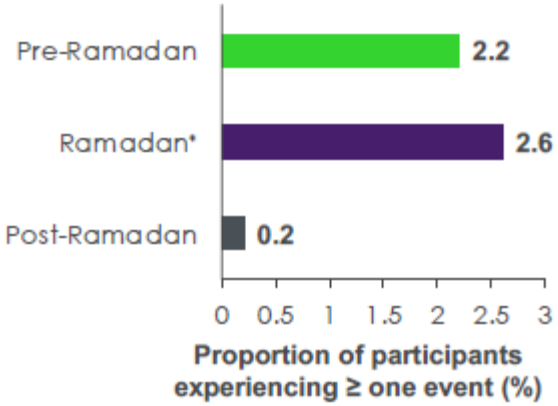
BMI, body mass index;; **IQR**, interquartile range; **SD**, standard deviation; **T2DM**, type 2 diabetes

References: 1. Hassanein M, *et al. Diabetes Res Clin Pract*. 2020;165:1−9.

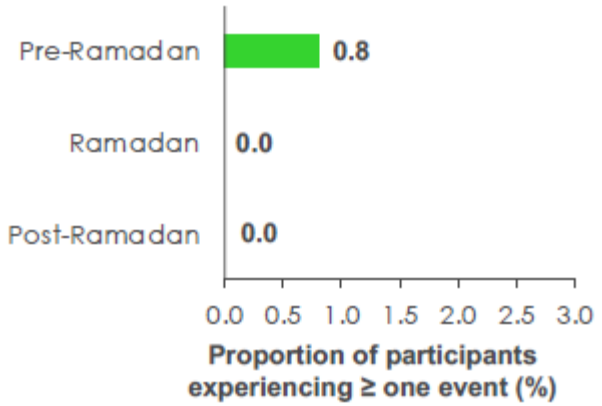
ORION study: Incidence of hypoglycaemia[1]

Similar incidence of hypoglycaemia in the pre-Ramadan and Ramadan periods

Severe and/or symptomatic documented hypoglycaemia with blood glucose **≤3.9 mmol/L (≤70 mg/dL)**[1]



Severe and/or symptomatic documented hypoglycaemia with blood glucose **≤3.0 mmol/L (≤54 mg/dL)**[1]



No participants experienced severe hypoglycaemia during Ramadan or post-Ramadan; one participant experienced one severe hypoglycaemia event during the pre-Ramadan period

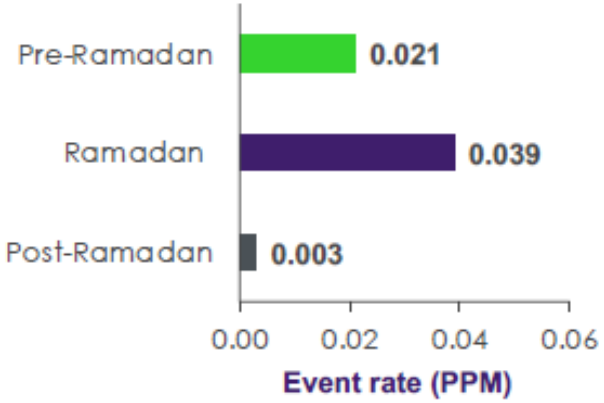
*Primary endpoint.

n=493 for evaluable population

References: 1. Hassanein M, *et al. Diabetes Res Clin Pract*. 2020;165:1−9.

ORION study: Rate of hypoglycaemia[1]

Severe and/or symptomatic documented hypoglycaemia with blood glucose **≤3.9 mmol/L (≤70 mg/dL)**[2]



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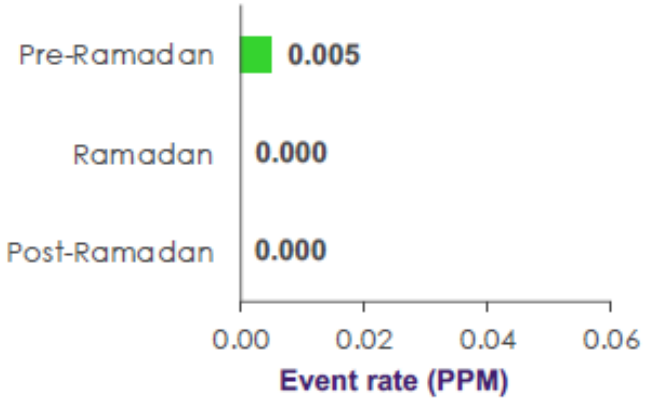


Most events of severe and/or symptomatic documented hypoglycaemia ≤3.9 mmol/L (≤70mg/dL) that were recorded during Ramadan occurred during fasting (11/13 events)[2]

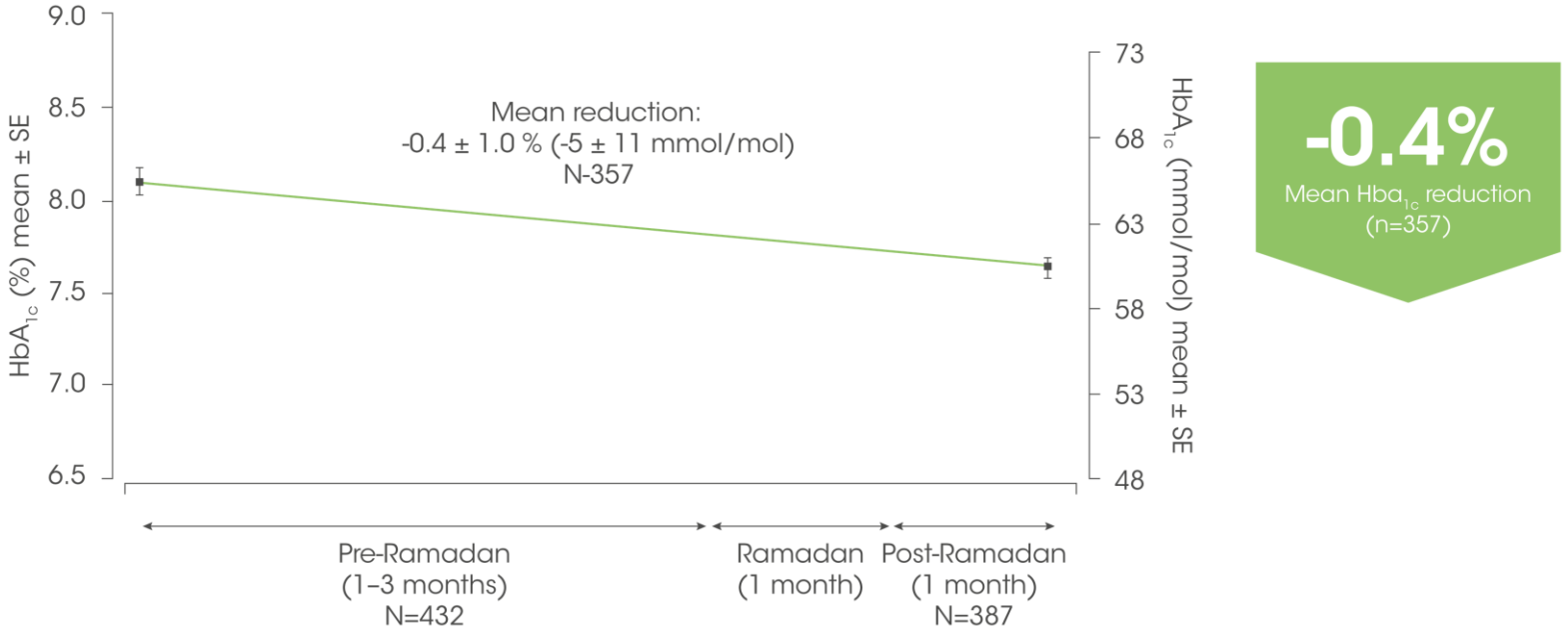
N=493 for evaluable population.

PPM, per patient-month

References: 1. Hassanein M, *et al. Diabetes Res Clin Pract*. 2020;165:1−9.

ORION study:
A reduction in HbA_{1c} occurred from Pre- to Post-Ramadan[1]

Mean HbA_{1c} Pre- to Post-Ramadan



Fasting may have contributed to the reduction in HbA_{1c} levels from the pre-Ramadan to post-Ramadan period.

HbA1c, glycated haemoglobin

References: 1. Hassanein M, *et al. Diabetes Res Clin Pract*. 2020;165:1–9.

ORION study: Adverse events[1]

94.5% completed the study

	Toujeo® (N=493)	
	Throughout study, n (%)	During Ramadan, n (%)
Any AE	27 (5.5)	15 (3.0)
Any SAE	5 (1.0)	2 (0.4)
Any AE considered related to Toujeo®	1 (0.2)	0
Any AE leading to discontinuation of Toujeo®	1 (0.2)	1 (0.2)
Hyperglycaemia	3 (0.6)	2 (0.4)
Death	0	0

No hyperglycaemia events were considered serious, related to Toujeo® or resulted in discontinuation of Toujeo®

One non-serious AE, accidental dose, was considered related to Toujeo® (this did not occur during Ramadan).

AE, adverse event; **SAE**, serious adverse event.

References: 1. Hassanein M, *et al. Diabetes Res Clin Pract*. 2020;165:1–9.

ORION study: Key takeaways

In a real-world clinical setting, the use of Toujeo® in people with T2DM who fasted during Ramadan was associated with:

Similar incidence of severe and/or symptomatic documented hypoglycaemia in the pre-Ramadan and Ramadan periods[1]

No participants reported severe hypoglycaemia during Ramadan or post-Ramadan; one participant reported severe hypoglycaemia in pre-Ramadan[1]

HbA_{1c} reduction pre- to post-Ramadan[1]

The second generation basal insulin - Toujeo® in combination with oral agents was used during the Ramadan period without an added risk of hypoglycaemia being observed versus the pre Ramadan period [1]

2021 IDF-DAR Practical Guidance refers to ORION[2]

References: 1. Hassanein M, *et al. Diabetes Res Clin Pract.* 2020;165:1−9. **2**. Hassanein M et al. Diabetes Research and Clinical Practice. 2022; 185: 109185

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.

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