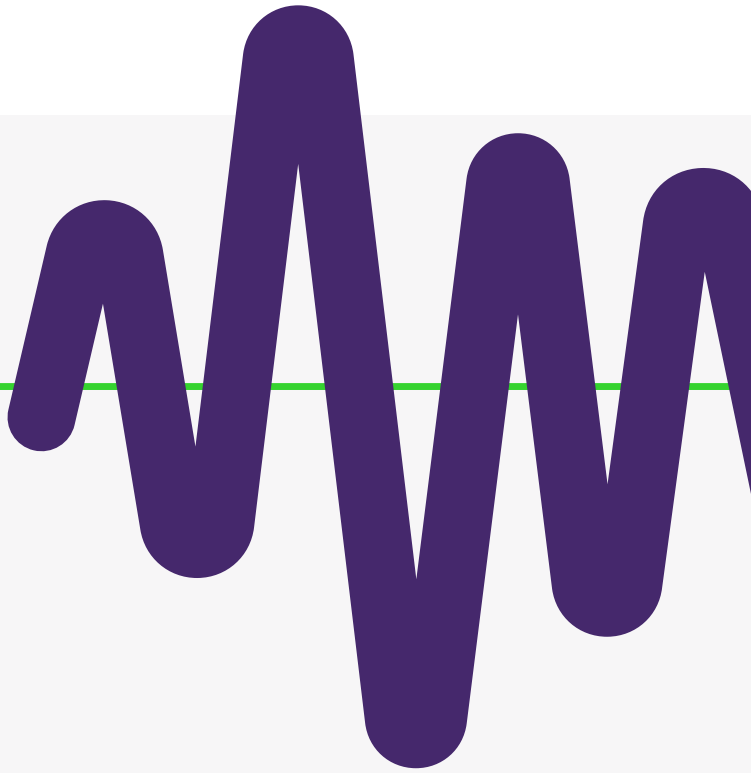
sanofi



Beyond HbA_{1c}, it is time to think **Time-in-Range**

Understanding Time-in-Range, its assessment, impact, and the targets to aim for

Prescribing information and Adverse event reporting can be found on the last page of this item.

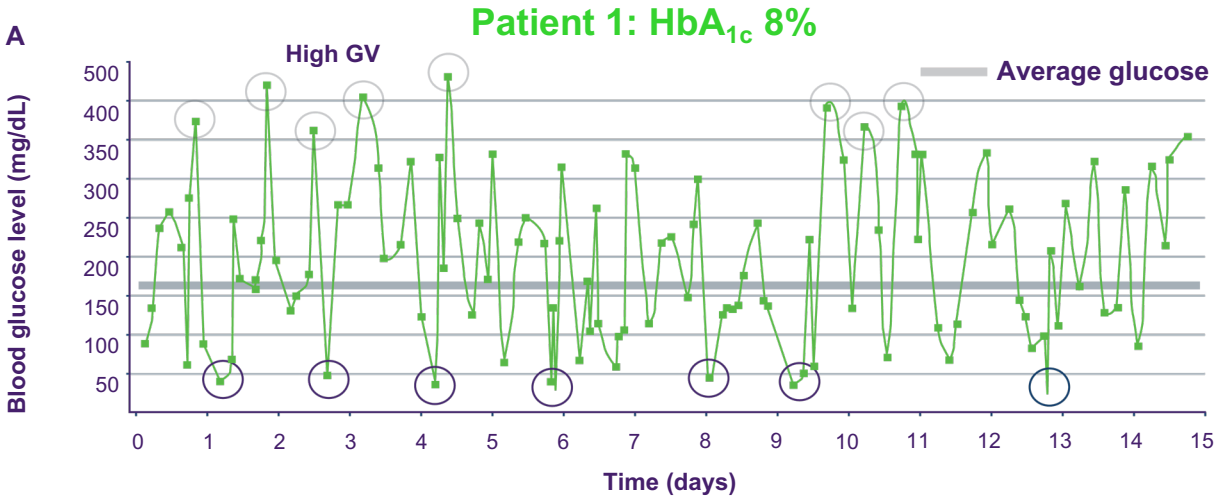
MAT-XU-2404615 v1.0 | November 2024

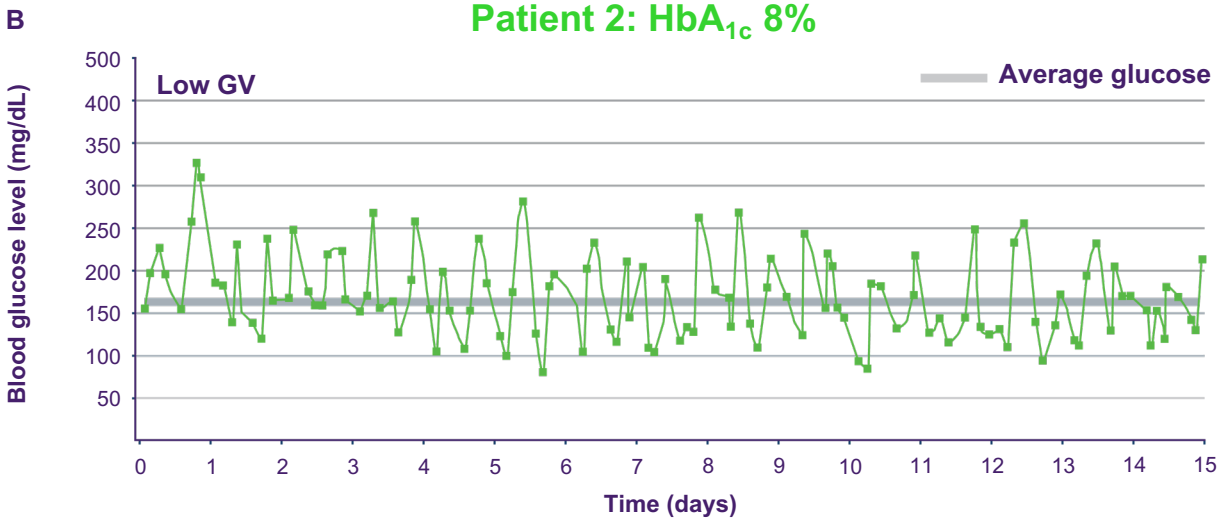
Glycaemic variability

Glycaemic variability (GV) is a common challenge for people with diabetes and has been associated with a higher risk for serious consequences.[1,2]

Managing glycaemia based on HbA_{1c} tells us little about the variability of blood glucose individuals in diabetes. For instance, it is known today that two people with an identical HbA_{1c} level can have markedly different degrees of GV.[3]

In the figures below, patient 1 has high GV, reflected by numerous episodes of both hypo- and hyperglycaemia, whereas low GV in patient 2 resulted in no such episodes.[3]



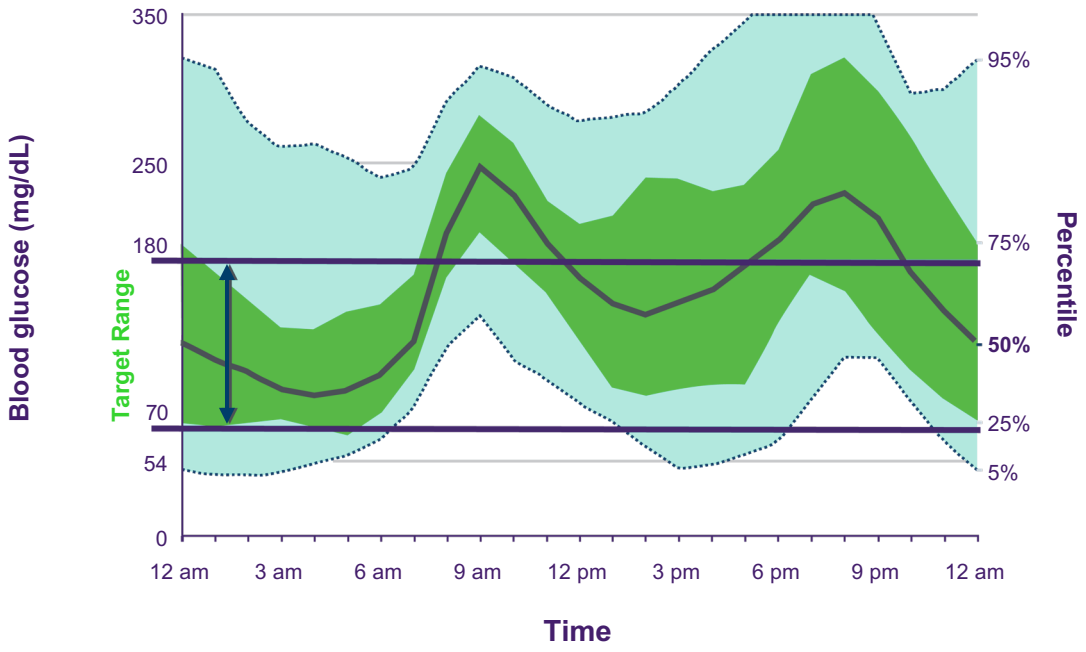


GV: glycaemic variability
Adapted from Kovatchev B & Cobelli C. 2016[3]

What is Time-in-Range?

Time-in-Range (TIR) represents a new key metric for glycaemic control. It is defined as the percentage of time over a 24-hour period in which blood glucose levels fall within a target range.[4]

Ambulatory glucose profile



Target range (70–180 mg/dL)

Adapted from Battelino T et al., 2019[4]

Evaluating TIR can aid understanding of whether hypoglycaemia (represented by time-below-range) or hyperglycaemia (time-above-range) are improving with treatment over time.[5]

Consequently, as per the 2019 International Consensus on Time-in-Range, TIR has been identified as a metric of glycaemic control that provides more actionable information than HbA_{1c} alone.[4]

The impact of Time-in-Range

Optimising TIR may be useful in effective diabetes management and could help to reduce the risk of negative consequences for patients.[6-7]

Studies have shown the following risks associated with reductions in TIR:

Beck, 2019:[6]

- A post hoc analysis of 1440 people with **type 1 diabetes mellitus (T1DM)** in the Diabetes Control and Complications Trial (DCCT). Measurements were collected via fingerstick samples rather than continuous glucose monitoring.[6]
- A **10% drop in TIR increased the risk of retinopathy by 64%** (95% CI 51,78) and **increased the risk of microalbuminuria by 40%** (95% CI 25, 56).[6]

Mayeda, 2020:[7]

- A prospective cohort study of 105 people with **type 2 diabetes mellitus (T2DM)** treated with insulin or sulfonylurea and measured via continuous glucose monitoring.[7]
- A **10% drop in TIR increased the risk of distal peripheral neuropathy by 25%** (95% CI 1.02, 1.52) in people with T2DM and chronic kidney disease.[7]

TIR is an important physical and emotional measure of success for people with diabetes.

In an online survey of **1026 people with T1DM** and **1154 people with T2DM taking insulin:**

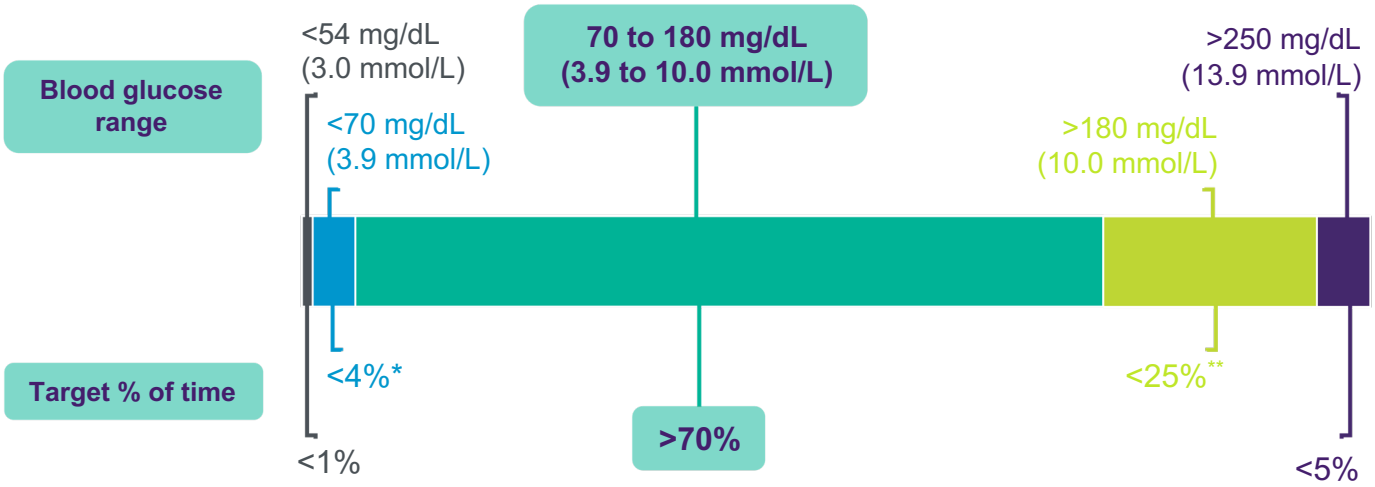
57% people with T1DM and **45%** of people with T2DM taking insulin ranked TIR as the measurable therapy outcome that had the biggest impact on daily life with diabetes.[8]

54% of people with T1DM and **36%** T2DM taking insulin ranked TIR as the highest driver of a positive mindset.[8]

MAT-XU-2404615 v1.0 | November 2024

Which Time-in-Range target should you aim for?

International guidelines recommend a target of >70% TIR (70–180 mg/dL) for most adult patients with T1DM or T2DM:[4]



Hypoglycaemia

<1 hour per day
with blood glucose <70 mg/dL (<3.9 mmol/L)

<15 minutes per day
with blood glucose <54 mg/dL (<3.0 mmol/L)

TIR

>16 hours, 48 mins per day

Hyperglycaemia

<1 hour, 12 mins per day
with blood glucose >250 mg/dL (>13.9 mmol/L)

<6 hours per day
with blood glucose >180 mg/dL (>10.0 mmol/L)

*Includes percentage of values <54 mg/dL (3.0 mmol/L). **Includes percentage of values >250 mg/dL (13.9 mmol/L)
TIR: Time-in-Range
Adapted from Battelino T et al., 2019[4]

Each incremental 5% increase in TIR is associated with clinically significant benefits for adults with T1DM or T2DM.[4]

References

1. Monnier L, Colette C, Wojtusciszyn A, et al. Toward defining the threshold between low and high glucose variability in diabetes. Diabetes Care. 2017;40(7):832–838.

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4. Battelino T, Danne T, Bergenstal RM, et al. Clinical targets for continuous glucose monitoring data interpretation: recommendations from the International Consensus on Time in Range. Diabetes Care. 2019;42(8):1593–1603.

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7. Mayeda L, Katz R, Ahmad I, et al. Glucose time in range and peripheral neuropathy in type 2 diabetes mellitus and chronic kidney disease. BMJ Open Diabetes Research & Care. 2020;8:e000991.

8. Runge AS, Kennedy L, Brown AS, et al. Does Time-in-Range matter? Perspectives from people with diabetes on the success of current therapies and the drivers of improved outcomes. Clinical Diabetes. 2018;36(2):112–119.

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

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

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

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

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

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

Contraindications: Hypersensitivity to insulin glargine or any excipients.

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

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

Legal Category: POM

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

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

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

Date of preparation: October 2024.

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

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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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