Toujeo®
insulin glargine 300 units/mL

Real world evidence in UK adults with Type 1 diabetes switching to Toujeo®

A multicentre, UK, retrospective, observational study to assess the effectiveness of insulin glargine 300 units/mL in treating people with Type 1 diabetes mellitus in routine clinical practice (SPARTA)

sanofi

Pang T, *et al. Diabetic Medicine* October 2018

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

Evaluating real world outcomes of switching from basal insulin to Toujeo® in patients with T1DM

Study design and limitations

Objective

To evaluate real-world outcomes of switching from basal insulin to Toujeo® in patients with T1DM

Primary endpoint

Change in HbA_{1c} levels from baseline to Month 6 after Toujeo® initiation

Secondary endpoints included:

- Change in basal, prandial and total daily insulin doses from previous insulin therapy (baseline) to Month 6 and from Toujeo® initiation to Month 6
- Change in weight from baseline to Month 6
- Number of hypoglycaemic and ketoacidosis episodes (requiring A&E department visits or hospitalisation) during the 6 months before and after Toujeo® initiation
- Reasons for switching or discontinuation of previous diabetes therapy and Toujeo® post switch

Study design

- Retrospective, observational, single arm, descriptive study
- 8 participating NHS centres across the UK
- In total, 298 patients with T1DM were recruited
- Defined minimum (n=10) and maximum (n=100) patients enrolled in each centre
- Anonymised patient-level data collected from electronic medical notes and paper charts by members of the direct care team

Study limitations

- Data for HbA_{1c} are results from the "completer-finisher" subgroup population (n=175) who remained on treatment for at least 6 months post Toujeo® initiation and had paired HbA_{1c} data available
- Data are only listed for participants whose data were available in medical notes. Not all the data points are present for the overall cohort (n=298)
- Patient recall bias may lead to under-reporting of hypoglycaemic and DKA episodes in retrospective observational data
- Lack of a comparator group
- There are differences in the number of reports that could be gained for each endpoint

Additional post-hoc analyses included:

- Linear model comparing change in HbA_{1c} from baseline to 6 months versus baseline HbA_{1c}
- Change in HbA_{1c} from baseline to 6 months for the subgroups of participants previously on once-daily and twice-daily basal insulin

Inclusion criteria

- Patients with T1DM aged ≥18 to <75 years
- Prescribed Toujeo® ≥6 months before data collection
- HbA_{1c} levels recorded within 3 months before initiating Toujeo®

Map adapted from: Pang T, *et al. Diabetic Medicine* October 2018 Supplementary Data

NHS: National Health Service; **T1DM:** type 1 diabetes mellitus; **A&E:** accident and emergency

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GEOGRAPHICAL DISTRIBUTION OF THE EIGHT PARTICIPATING CENTRES

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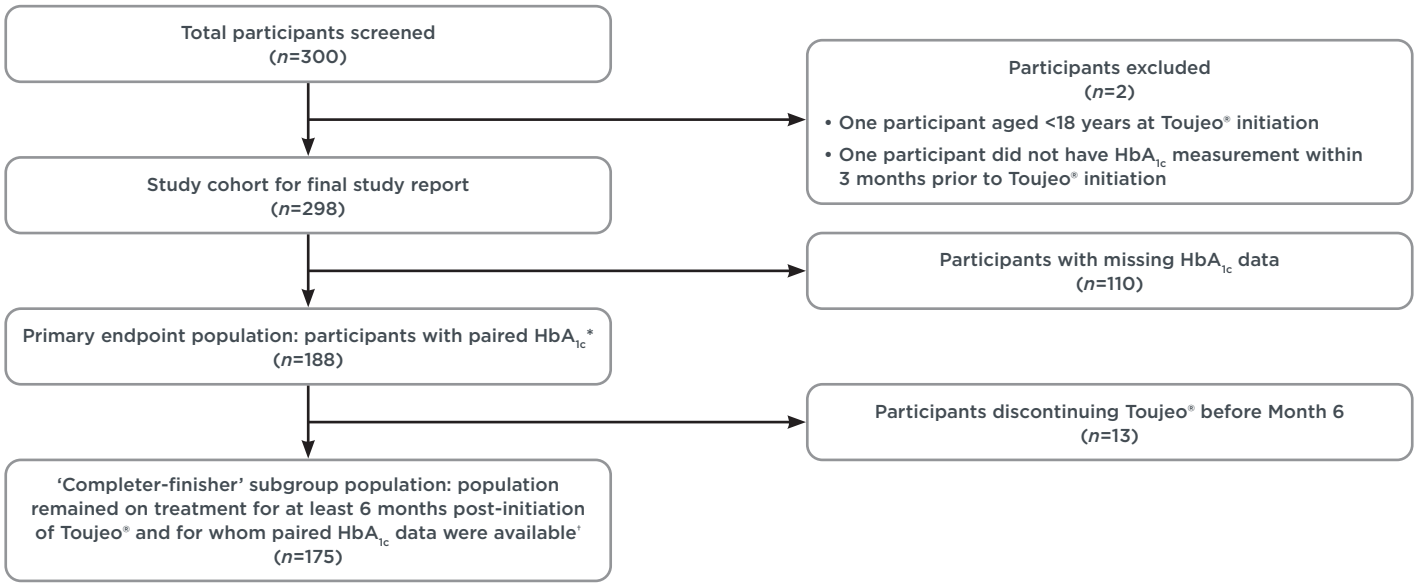
Evaluating real world outcomes of switching from basal insulin to Toujeo® in patients with T1DM

Participant eligibility



Adapted from: Pang T, *et al. Diabetic Medicine* October 2018

Participant screening and eligibility. *The primary endpoint population included all participants with HbA_{1c} available both within 3 months pre-initiation and at Month 6 post-initiation, irrespective of whether they had discontinued Toujeo® by Month 6

†The primary endpoint subpopulation included participants with ongoing Toujeo® therapy at Month 6 with HbA_{1c} available both within 3 months pre-initiation and at Month 6 post-initiation if they remained on Toujeo® at Month 6

Baseline characteristics

Baseline patient demographic and clinical characteristics		Value	Number of patients (n)
Overall			298
Patient profile	Age: mean (SD), years	42.1 (14.0)	298
	Gender: Male, n (%)	152 (51)	298
	Ethnicity: White, n (%)	216 (72)	298
	Body weight: mean (SD), kg	81.2 (20.9)	225
	BMI: mean (SD), kg/m^2	28.3 (6.7)	161
Time since diagnosis	Mean time: mean (SD), years	20.3 (12.9)	272
	Median time: median (IQR), years	17.9 (10.4-29.7)	272
Clinical characteristics	HbA_{1c}: mean (SD), mmol/mol	79 (20.2)	298*
	HbA_{1c}: mean (SD), %	9.4 (1.8)	298*
	Number of patients with severe hypoglycaemic episodes in last 6 months, n (%)	6 (2)	298
	DKA in last 6 months, n (%)	4 (1)	298

Adapted from: Pang T, *et al. Diabetic Medicine* October 2018.

*Paired values recorded at baseline and 6 months

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Background therapy and reasons for discontinuation from previous BI

Background therapy		Value	Number of patients (n)
Overall			298
Insulin regimen, n (%)	Basal bolus	257 (86)	298
	Pre-mix	16 (5)	298
	Basal insulin only	20 (7)	298
	Bolus (prandial) only	5 (2)	298
Intermediate/long-acting insulins, n (%)	Basal bolus with once-daily basal insulin	170 (61)	277
	Basal bolus with twice-daily basal insulin	84 (30)	272
	Once-daily basal insulin only	9 (3)	272
	Twice-daily basal insulin only	11 (4)	272
	Not recorded	3 (1)	272
Insulin analogues, n (%)*	Insulin aspart	192 (64)	298
	Insulin glargine 100 units/mL	164 (55)	298
	Insulin detemir	103 (35)	298
	Insulin degludec	6 (2)	298
	Insulin lispro	59 (20)	298
	Insulin glulisine	16 (5)	298
	Novomix 30 (insulin aspart protamine-insulin aspart)	6 (2)	298
	Humalog Mix 25/75 (insulin lispro protamine-insulin lispro)	3(1)	298
	Humalog Mix 50/50 (insulin lispro protamine-insulin lispro)	2(1)	298
Reasons for discontinuation of previous basal insulin, n (%)	Lack of efficacy	157 (53)	298
	Difficulty with dosing	28 (9)	298
	Difficulty with device	3 (1)	298
	Due to adverse event	2 (1)	298
	Hypoglycaemia concerns	57 (19)	298
	Not known or recorded	51 (17)	298

Adapted from: Pang T, *et al. Diabetic Medicine* October 2018

*Of 298 patients, a total of n=19 also received a variety of human insulin products at baseline

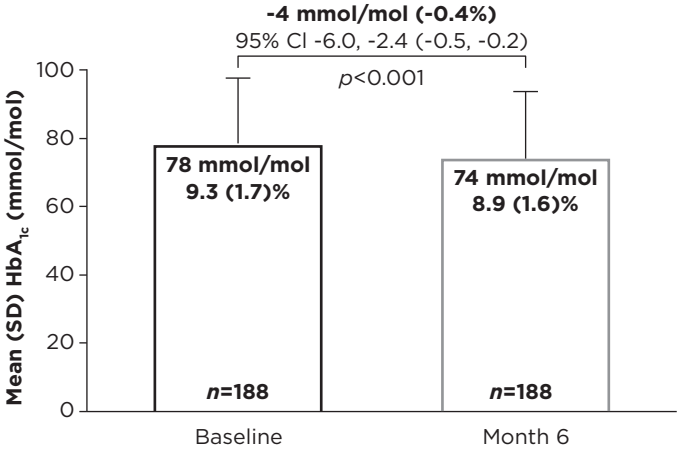
SD: standard deviation; **n:** participants with data available at baseline; **IQR:** interquartile range; **HbA_{1c}:** glycated haemoglobin; **BMI:** body mass index; **DKA:** diabetic ketoacidosis

Significant reduction in HbA_{1c} associated with Toujeo® and compared with previous basal insulin

Change in HbA_{1c} from baseline to Month 6 post-initiation with Toujeo®

Primary endpoint

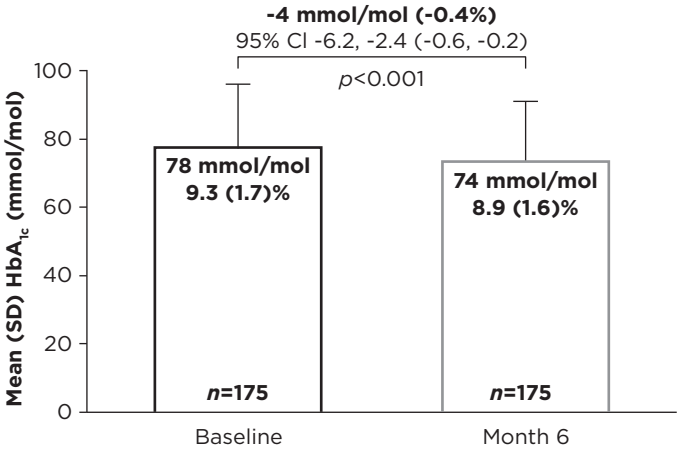
In the overall population



Adapted from: Pang T, *et al. Diabetic Medicine* October 2018

Primary endpoint

In the 'completer-finisher' sub-population*



Adapted from: Pang T, *et al. Diabetic Medicine* October 2018

Switching from previous basal insulin to Toujeo® in people with T1DM is associated with a 4 mmol/mol (0.4%) reduction in HbA_{1c} at 6 months

*Data for HbA_{1c} are results from the "completer-finisher" subgroup population (n=175) with the following characteristics: remaining on treatment for at least 6 months post Toujeo® initiation and paired HbA_{1c} data were available for those patients

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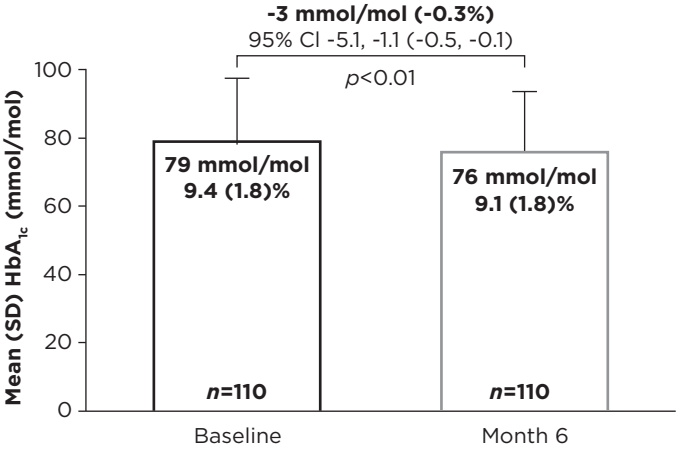
Post-hoc analyses of HbA_{1c} results for Toujeo® compared with previous basal insulin

Observations of HbA_{1c} reduction in subgroups

Observational retrospective studies can be limited by real-world-related biases with numerous confounders. It is worth noting that the observations outlined on this page relate to further post-hoc analyses of subgroups, and therefore that any related statistics were calculated post-hoc.

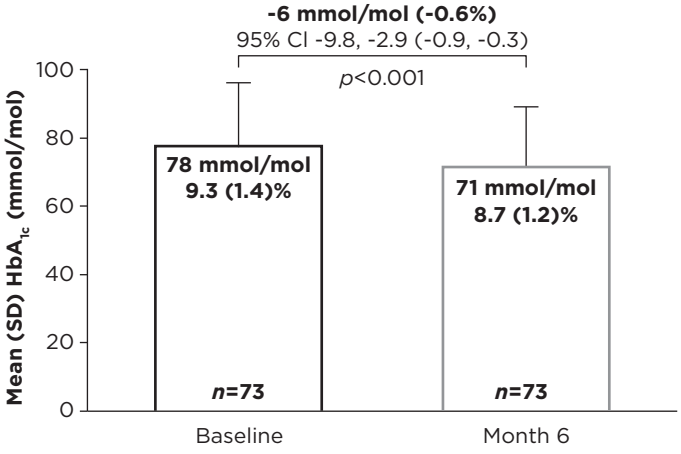
Post-hoc analysis

The subgroup of patients previously on once-daily basal insulin



Post-hoc analysis

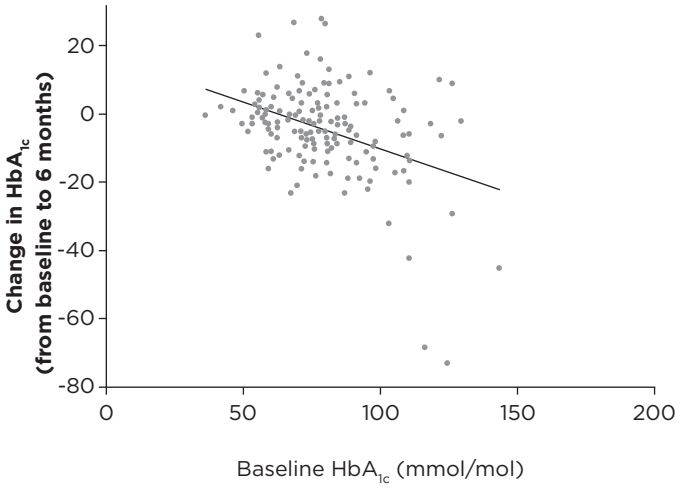
The subgroup of patients previously on twice-daily basal insulin



Post-hoc analysis

Change in HbA_{1c} (from baseline to Month 6 post-initiation of Toujeo) to baseline HbA_{1c}

- A post hoc analysis of the change in HbA_{1c} from baseline to 6 months vs baseline HbA_{1c} indicated that for every 1 mmol/mol that baseline HbA_{1c} was higher, the mean reduction in HbA_{1c} at 6 months would increase by 0.27 mmol/mol (linear model; p<0.001)
- This translates to an increased reduction of 0.27% for every 1% increment in baseline HbA_{1c}



All graphs adapted from: Pang T, *et al. Diabetic Medicine* October 2018

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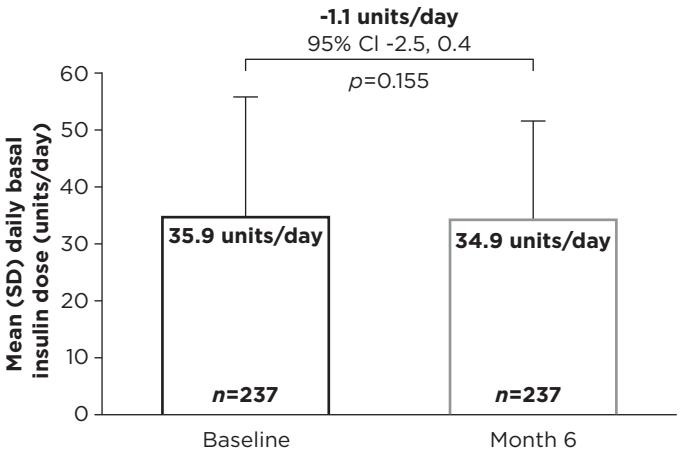
No significant differences in insulin dose or weight gain associated with Toujeo® and compared to previous basal insulin

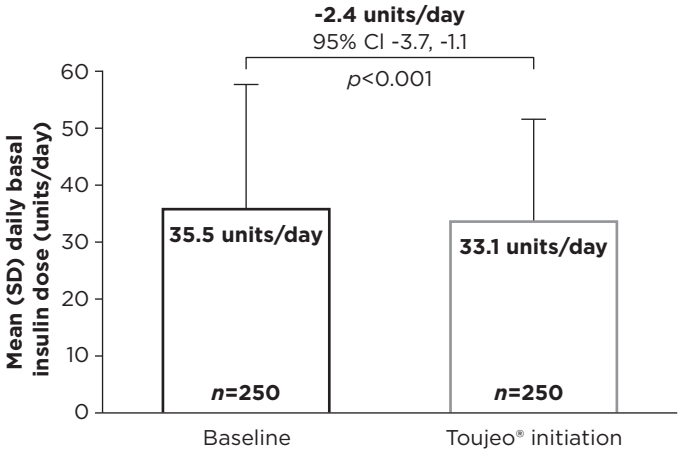
Changes in total daily insulin

- No significant difference in total daily insulin, basal insulin and prandial insulin dose from previous therapy dose at baseline to 6 months
- No significant difference in total insulin and prandial insulin dose from initiation with Toujeo® to Month 6

Total daily basal insulin dose from previous insulin therapy (baseline) to Month 6 post-initiation of Toujeo®

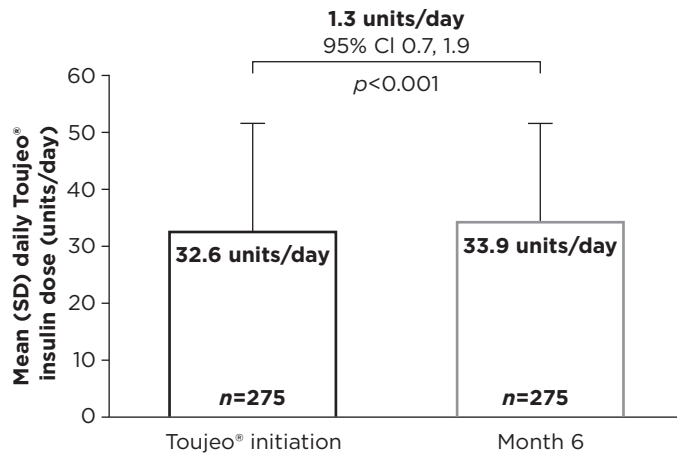


Total daily basal insulin dose from previous insulin therapy (baseline) to Toujeo® initiation



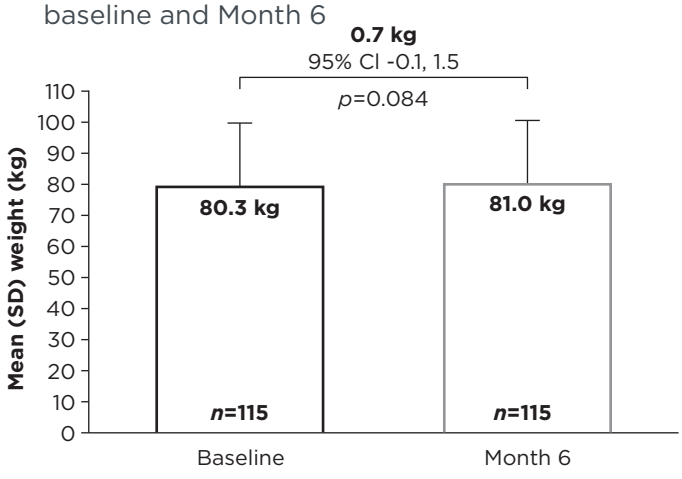
- A significant increase in the mean daily dose of Toujeo® from initiation to Month 6 of 1.3 units, which corresponded to an average of 0.8 dose adjustments per participant

Total daily basal insulin dose from Toujeo® initiation to Month 6 post-initiation of Toujeo®



Changes in body weight

- No significant difference in weight between baseline and Month 6



All graphs adapted from: Pang T, *et al. Diabetic Medicine* October 2018 and Supplementary Data

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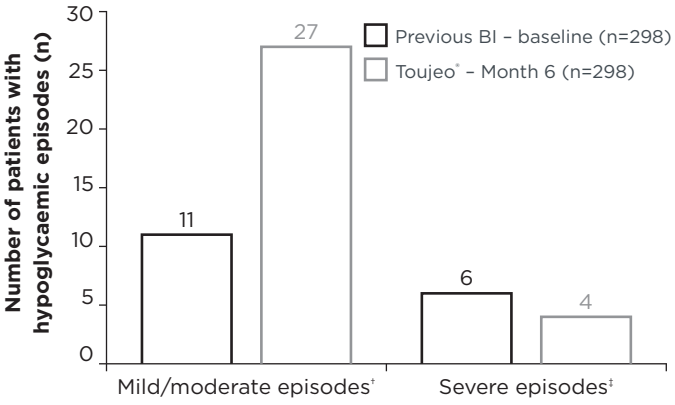
No significant differences in severe hypoglycaemia and DKA associated with Toujeo® and compared to previous basal insulin

Secondary safety endpoints – episodes of hypoglycaemia and DKA

Distribution of patients with documented hypoglycaemic* episodes

- No significant difference was observed in the number of patients reporting episodes of severe hypoglycaemia with Toujeo® compared to previous BI

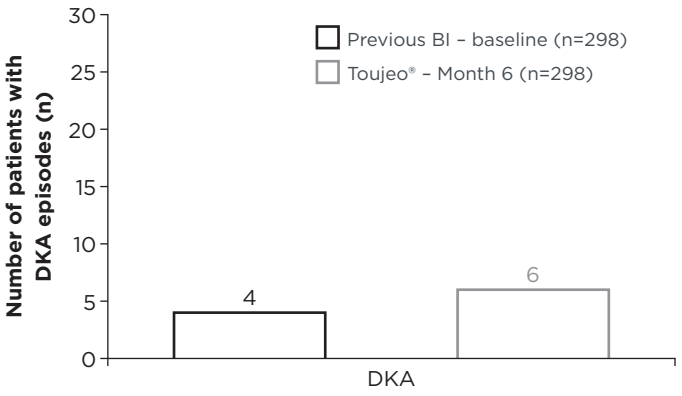


Adapted from: Pang T, *et al. Diabetic Medicine* October 2018

*Mild/moderate and severe categories not mutually exclusive. †Under-reporting of mild/moderate hypoglycaemic episodes occurs within the community; this means that the data here should be interpreted with caution. ‡Requiring third-party assistance.

Distribution of patients with DKA episodes

- No significant difference was observed in the number of patients reporting episodes of DKA requiring A&E visits or hospitalisation with Toujeo® compared to previous BI



Adapted from: Pang T, *et al. Diabetic Medicine* October 2018

BI: basal insulin; **DKA:** diabetic ketoacidosis; **A&E**: accident and emergency

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Additional secondary endpoints

Participants attending diabetes education programmes

	Prior to Toujeo® initiation n (%)	Following Toujeo® initiation n (%)
Structured diabetes education	**n=298**	**n=298**
Yes	17 (6)	19 (6)
No	268 (90)	265 (89)
Not known	13 (4)	14 (5)
Type of education	**n=17**	**n=19**
DAFNE	5 (29)	9 (47)
BERTIE/CHOICE*	4 (24)	4 (21)
WICKED	0	0
STEPH	4 (24)	2 (11)
DAFYDD	2 (12)	2 (11)
One-to-one with dietician	1 (6)	
3-h carbohydrate counting course		2 (11)
Not recorded	1 (6)	

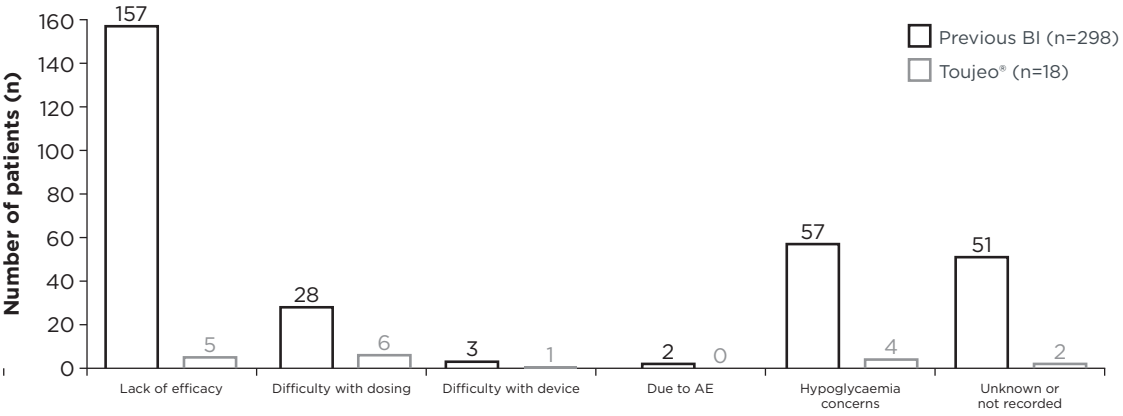
*BERTIE and CHOICE are combined participant numbers

DAFNE: Dose Adjustment for Normal Eating; **BERTIE:** Beta Cell Education Resources for Training in Insulin and Eating; **CHOICE:** CHO and Insulin Calculation Education; **WICKED:** Working with Insulin, Carbs, Ketones and Exercise to manage Diabetes; **STEPH:** Structured Education for People with Type 1 Diabetes; **DAFYDD:** Dose Adjustment for your Daily Diet

Adapted from: Pang T, *et al. Diabetic Medicine* October 2018 Supplementary Data

Reasons for discontinuation of Toujeo® therapy

Reasons for discontinuation of Toujeo®, n (%)	Lack of efficacy	5 (28)
	Difficulty with dosing	6 (33)
	Difficulty with device	1 (6)
	Due to adverse event	0 (0)
	Hypoglycaemia concerns	4 (22)
	Not known or recorded	2 (11)



Adapted from: Pang T, *et al. Diabetic Medicine* October 2018

Evaluating real world outcomes of switching from basal insulin to Toujeo® in patients with T1DM

Conclusions

This descriptive, retrospective study represents the real-world experience of using Toujeo® in patients with T1DM in the UK

Switching from previous basal insulin to Toujeo® in people with T1DM is associated with:

- 4 mmol/mol (0.4%) reduction in HbA_{1c} at 6 months*
- No clinically relevant changes in BI dose**
- No significant difference in the number of patients reporting episodes of severe hypoglycaemia or DKA**
- No significant change in body weight†

In a post-hoc analysis, a 6 mmol/mol (0.6%) reduction in HbA_{1c} was observed in those switching from twice-daily basal insulin

*Results from the "completer-finisher" subgroup population (n=175)

**Results observed for reported patients

† No significant change in body weight for patients for whom data were available (n=115, Δ 0.7kg, p=0.084)

T1DM: Type 1 diabetes mellitus; **HbA_{1c}:** glycated haemoglobin; **BI:** basal insulin; **DKA:** diabetic ketoacidosis

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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 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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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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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

Reference: Pang T, *et al.* A multicentre, UK, retrospective, observational study to assess the effectiveness of insulin glargine 300 units/ml in treating people with Type 1 diabetes mellitus in routine clinical practice (SPARTA) plus supplementary data. *Diabetic Medicine* 25 October 2018 https://doi.org/10.1111/dme.13847 [epub ahead of print]

Toujeo®
insulin glargine 300units/mL