East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG, Surrey Heath CCG, Crawley CCG, Horsham & Mid-Sussex CCG

Evidence review for Surrey Prescribing Clinical Network

Medicine and proposed indication	**Insulin glargine 300 units/mL (Toujeo Solostar®) pen for s.c. injection for type 2 diabetes**
Requested by	Local diabetologists

SUMMARY

Clinical Effectiveness

High-strength insulin products such as insulin glargine 300 units/ml (Toujeo) have been developed for people with type 1 or type 2 diabetes who have large daily insulin requirements to reduce the number and volume of injections. This evidence review will focus solely on its use in type 2 patients. In 3 randomised controlled trials (RCTs) in 2496 adults with type 2 diabetes, Toujeo had similar efficacy to insulin glargine 100 units/ml (Lantus) in terms of HbA1c reduction.

There was a statistically significant reduction in confirmed or severe nocturnal hypoglycaemia with Toujeo in 2 of the RCTs, but not in the third trial. Severe hypoglycaemic events were rare and not statistically significantly different between Toujeo and Lantus. NICE guideline for T2DM says that there is a risk of bias associated with reported hypoglycaemia and noted that self-reported hypoglycaemia may not be a reliable measure because a person's hypoglycaemia varies at different glucose levels.

Toujeo is not bioequivalent to Lantus and they are not interchangeable without dose adjustment. From NICE ESMN65: European Public Assessment Report (EPAR) states that the more gradual glucose lowering effect of Toujeo compared with Lantus did not translate into important advantages and the higher use of basal insulin may be a disadvantage. In order to obtain a similar effect on HbA1c, on average 12% higher doses of Toujeo than Lantus were used in people with type 2 diabetes.

NICE also report that metformin/insulin detemir had lower rates of hypoglycaemic events than metformin / insulin glargine in their evidence review and we don't know how rates of hypoglycaemia with Toujeo compared with insulin detemir.

Safety

The safety profile of Toujeo is largely similar to that of Lantus.

- From NICE ESMN65 a post-hoc meta-analysis (Ritzel et al 2015), showed the absolute reduction in nocturnal hypoglycaemia events was about 1 event per person per year (2.10 events per participant-year with Toujeo and 3.06 events per participant-year with Lantus: RR 0.69, 95% CI o.57 to 0.84, p=0.0002. Severe hypoglycaemia events at anytime of day were rare and not statistically significantly different between groups.
- The most frequent adverse events were nasopharyngitis (8.2% with Toujeo, 6.8% with Lantus)

and upper respiratory tract infection (6.5% with Toujeo, 5.8% with Lantus).

- In 3 RCTs (n=2496), similar numbers of participants reported injection site reactions with Toujeo (2.4%) and Lantus (3.1%), and similar numbers withdrew because of adverse events (1.4% with Toujeo and 1.3% with Lantus).

Patient factors

- Toujeo is a high-strength insulin. It is not simply interchangeable with other long-acting insulins and there is a potential risk of medication error. However, the dose window of the Toujeo pen shows the number of Toujeo units to be injected. Patients should read and understand the patient leaflet and education material and should have training on the correct use of Toujeo.
- Toujeo is given once daily, preferably at the same time each day but can be up to 3 hours before or after usual time.
- There was a reduction of approximately 1 confirmed or severe nocturnal event per person per year with Toujeo compared with Lantus. Severe hypoglycaemic events were rare and not statistically significantly different between Toujeo and Lantus (meta-analysis of 3 RCTs, n=2496)
- Body weight increased less with Toujeo than with Lantus (mean increase at 6 months 0.51 kg compared with 0.79 kg; p=0.039; meta-analysis of 3 RCTs, n=2496).
- The higher concentration of insulin in Toujeo means the volume to be injected is smaller, which may be less painful for people injecting large volumes.

Cost implications

Alternative treatments	5×3 ml cartridge	5×3 ml pre-filled pen
Insulatard - NPH (isophane) insulin 100 units/ml solution	£22.90	£20.40
Humulin I - NPH (isophane) insulin 100 units/ml solution	£19.08	£21.70
Insuman Basal - NPH (isophane) insulin 100 units/ml solution	£17.50	£19.80
Lantus - insulin glargine 100 units/ml solution	£41.50	£41.50
Abasaglar - biosimilar insulin glargine 100 units/ml solution	£35.28	£35.28
Toujeo - high-strength insulin glargine 300 units/ml solution	-	3×1.5 ml pre-filled pen, £33.13[a]

Levemir - insulin detemir 100 units/ml solution	£42.00	£42.00 or £44.85
Tresiba - insulin degludec 100 units/ml solution	£72.00	£72.00
Tresiba - insulin degludec 200 units/ml solution		3×3 ml pre-filled pen, £86.40

Costs are excluding VAT; taken from MIMS (November 2015).

[a] The manufacturer has stated that Toujeo has been priced at a level to match the daily cost of Lantus on the basis of average insulin glargine usage in the EDITION trials (September 2015).

The cost of Toujeo assuming a 45 unit total daily dose (based on 12.74% increase dose compared with Lantus®) is £403 and the cost of Lantus assuming a 40 unit total daily dose is £404 per patient per year.

Insulin glargine biosimilars are expected imminently and anticipated to be 20-25% cheaper than Lantus.

Relevant guidance / reviews

NICE have published (December 2015), an evidence review on Type 2 diabetes mellitus in adults: high-strength insulin glargine 300 units/ml (Toujeo). The detail of this advice (ESNM65) can be found below:

https://www.nice.org.uk/advice/esnm65/chapter/key-points-from-the-evidence

Likely place in therapy relative to current treatments

Sanofi is losing its patent for insulin glargine 100 units/ml (Lantus), and therefore is very actively trying to promote the benefits of Toujeo.

Legal action is delaying the release of insulin glargine biosimilars (we are currently spending £1.8M across Surrey).

Insulin glargine biosimilar, Abasaglar, was launched in the UK in August 2015. This is around 15% lower than Lantus, with further reduction to 20-25% as more biosimilars enter the market. Furthermore incidents of type 2 diabetes are increasing which creates further cost pressures.

NICE suggests insulin determir is more cost-effective than insulin glargine, so potentially glargine is a third line insulin after NPH and detemir, because detemir has a better hypo profile in NICE analysis.

In September 2015; Sanofi announced it had reached a settlement agreement with Lilly, which addresses patents on Sanofi´s Lantus SoloSTAR® (insulin glargine). The agreement resolves a US patent infringement lawsuit regarding Lilly´s pursuit of regulatory approval for Basaglar that would compete with Lantus SoloSTAR. Sanofi and Lilly agreed to end that lawsuit and to discontinue similar disputes worldwide. Under the agreement, Lilly will pay royalties to Sanofi in exchange for a license to certain Sanofi patents. In the US, Lilly will not sell its insulin glargine product before Dec 15, 2016. The agreement does not include Lantus (vial), Toujeo® or combination products. The remaining settlement terms are confidential.

Recommendation to PCN for traffic light status of Insulin glargine 300 units/mL (Toujeo®) for type 2 diabetes
Options include: 1. Approve for all type 2 patients 2. Approve in line with SMC recommendation 3. Approve in line with NG28 – Management of Type 2 diabetes in adults possibly only as a third line after isophane and detemir in patients with symptomatic nocturnal hypoglycaemia 4. Decline PCN to consider two questions: 1. How can we be assured of the safety in implementing Toujeo alongside existing Lantus? 2. How can we risk assess?

Medicine details	
Name and brand name	Insulin glargine 300 units/mL (Toujeo Solostar®)
Licensed indication, formulation and usual dosage	Toujeo is a basal insulin for once-daily sub-cut administration at any time of the day, preferably at the same time every day. When needed, people can administer Toujeo up to 3 hours before or after their usual time of administration. The dose regimen (dose and timing) should be adjusted according to individual response. In patients with type 2 diabetes mellitus, Toujeo® can also be given together with other anti-hyperglycaemic medicinal products. Initiation in patients with type 2 diabetes mellitus: the recommended daily starting dose is 0.2 units/kg followed by individual dose adjustments.
Summary of mechanism of action, and relevant pharmacokinetics	Toujeo is a new formulation based on the insulin glargine molecule but has flatter and more prolonged pharmacokinetic/dynamic profile than Lantus and offers the benefit of a smaller volume of subcutaneous injection versus Lantus.
Important drug interactions	A number of substances affect glucose metabolism and may require dose adjustment of insulin glargine. Substances that may enhance the blood-glucose-lowering effect and increase susceptibility to hypoglycaemia include anti-hyperglycaemic medicinal products, angiotensin converting enzyme (ACE) inhibitors, disopyramide, fibrates, fluoxetine, monoamine oxidase (MAO) inhibitors, pentoxifylline, propoxyphene, salicylates and sulfonamide antibiotics. Substances that may reduce the blood-glucose-lowering effect include corticosteroids, danazol, diazoxide, diuretics, glucagon, isoniazid, oestrogens and progestogens, phenothiazine derivatives, somatropin, sympathomimetic medicinal products (e.g. adrenaline, salbutamol, terbutaline), thyroid hormones, atypical antipsychotic medicinal products (e.g. clozapine and olanzapine) and protease inhibitors. Beta-blockers, clonidine, lithium salts or alcohol may either potentiate or weaken the blood-glucose-lowering effect of insulin. Pentamidine may cause hypoglycaemia, which may sometimes be followed by hyperglycaemia. In addition, under the influence of sympatholytic medicinal products such as

	beta-blockers, clonidine, guanethidine and reserpine, the signs of adrenergic counter-regulation may be reduced or absent.
Monitoring requirements	Metabolic monitoring requirements are similar to that required for other insulin preparations.
Prescribing considerations	Switch from insulin glargine 100 units/ml to Toujeo 1. Switching from insulin glargine 100 units/ml to once-daily Toujeo can be done unit-to-unit based on previous dose. 2. A higher Toujeo dose (approximately 10–18%) may be needed to achieve target ranges for plasma glucose levels. Switch from other basal insulins to Toujeo • Switching from once-daily basal insulins to once-daily Toujeo can be done unit-to-unit based on previous dose. • Switching from twice-daily basal insulins to once-daily Toujeo, the recommended initial Toujeo dose is 80% of the total daily dose of basal insulin that is being discontinued. When switching from a treatment regimen with an intermediate or long-acting insulin product to a regimen with Toujeo, a change of the dose of the basal insulin may be required and the concomitant anti-hyperglycaemic treatment may need to be adjusted. Switch from Toujeo to insulin glargine 100 units/ml or other basal insulin products • People who are changing their basal insulin regimen from once-daily Toujeo to a once-daily regimen with insulin glargine 100 units/ml should reduce their dose by 20%. • Switching from Toujeo to insulin glargine 100 units/ml results in an increased risk of hypoglycaemic events, mainly in the first week after the switch – the dose of insulin glargine 100 units/ml should therefore be reduced.
Other considerations	The Medicines and Healthcare Products Regulatory Agency (MHRA) recommends that it is good practice to prescribe insulin glargine products by brand name to ensure that substitution of a biosimilar product does not occur when the medicine is dispensed by the pharmacist. The use of brand names in all stages of the medicines supply chain for insulin glargine will be essential to allow differentiation between the various forms, which is vital for post-launch pharmacovigilance and to ensure patient safety (avoidance of inadvertent switching).

	Pharmacists should challenge any prescriptions for insulin by its generic rather than trade name, to ensure that the product dispensed is the correct one intended for the patient. Interestingly Sanofi informed its shareholders in 2013 that they were developing Toujeo to be launched at the same time as Lantus lost its patent.

Potential patient group (if appropriate to include)	
Brief description of disease	Type 2 diabetes is a chronic metabolic condition characterised by insulin resistance and insufficient pancreatic insulin production, resulting in high blood glucose levels. Type 2 diabetes is commonly associated with obesity, physical inactivity, raised blood pressure and disturbed blood lipid levels, and therefore is recognised to have an increased cardiovascular risk. It is associated with long-term microvascular and macrovascular complications, together with reduced quality of life and life expectancy
Potential patient numbers per 100,000	In 2011 the UK prevalence of diabetes was 4.45%. About 90% of patients with diabetes have type 2 disease.
Outcomes required	Achieving good glycaemic control is important in minimising the risk of long-term diabetes related complications. In the UK, between 2007 and 2012, there has been an increase in complications.

Summary of current treatment pathway

The updated NICE guideline NG28 - Type 2 diabetes in adults: management; published December 2015, recommends that when insulin therapy is necessary, it should be started from a choice of a number of insulin types and regimens. NPH insulin injected once or twice daily according to need is the preferred option. Insulin detemir or insulin glargine can be considered as an alternative in certain circumstances. There are several insulin glargine products available including Lantus, the biosimilar Abasaglar or high-strength Toujeo, see below:

NG 28 Type 2 diabetes in adults: management

Second intensification of drug treatment

1.6.27 In adults with type 2 diabetes, if dual therapy with metformin and another oral drug (see recommendation 1.6.25) has not continued to control HbA1c to below the person's individually agreed threshold for intensification, consider either:

- triple therapy with:
    - metformin, a DPP-4 inhibitor and a sulfonylurea **or**
    - metformin, pioglitazone and a sulfonylurea **or**
- starting insulin-based treatment (see recommendations 1.6.32–1.6.34). **[new 2015]**

1.6.34 Start insulin therapy for adults with type 2 diabetes from a choice of a number of insulin types and regimens:

- Offer NPH insulin injected once or twice daily according to need.
- Consider starting both NPH and short-acting insulin (particularly if the person's HbA1c is 75 mmol/mol [9.0%] or higher), administered either:
    - separately **or**
    - as a pre-mixed (biphasic) human insulin preparation.
- Consider, as an alternative to NPH insulin, using insulin detemir or insulin glargine if:
    - the person needs assistance from a carer or healthcare professional to inject insulin, and use of insulin detemir or insulin glargine would reduce the frequency of injections from twice to once daily **or**
    - the person's lifestyle is restricted by recurrent symptomatic hypoglycaemic episodes **or**
    - the person would otherwise need twice-daily NPH insulin injections in combination with oral glucose-lowering drugs.
- Consider pre-mixed (biphasic) preparations that include short-acting insulin analogues, rather than pre-mixed (biphasic) preparations that include short-acting human insulin preparations, if:
    - a person prefers injecting insulin immediately before a meal **or**
    - hypoglycaemia is a problem **or**
    - blood glucose levels rise markedly after meals. **[2015]**

1.6.35 Consider switching to insulin detemir or insulin glargine from NPH insulin in adults with type 2 diabetes:

- who do not reach their target HbA1c because of significant hypoglycaemia **or**
- who experience significant hypoglycaemia on NPH insulin irrespective of the level of HbA1c reached **or**
- who cannot use the device needed to inject NPH insulin but who could administer their own insulin safely and accurately if a switch to one of the long-acting insulin analogues was made **or**
- who need help from a carer or healthcare professional to administer insulin injections and for whom switching to one of the long-acting insulin analogues would reduce the number of daily injections. **[2015]**

Scottish Medicines Consortium (SMC) Insulin glargine (Toujeo®) has been accepted for restricted use within NHS Scotland for the treatment of type 1 or type 2 diabetes mellitus in adults aged 18 years and above. In patients with type 2 diabetes it should be restricted to those who suffer from recurrent episodes of hypoglycemia or require assistance with their insulin injections.It should be used in patients in whom treatment with an insulin analogue is appropriate. Insulin glargine 300 units/mL (Toujeo®) has similar efficacy but is not bioequivalent to insulin glargine 100 units/mL (Lantus®) and therefore not interchangeable without dose adjustment. At doses that provide comparable glycaemic control, Toujeo® is available at a similar cost to Lantus®.

Evidence review

This evidence summary is based on the 3 main phase 3 studies of Toujeo in adults with type 2 diabetes (EDITION 1, EDITION 2 and EDITION 3). EDITION 1 was in adults with type 2 diabetes who were using basal and mealtime insulin. In EDITION 2, adults with type 2 diabetes were using oral blood glucose lowering drugs and basal insulin; and in EDITION 3, adults with type 2 diabetes were insulin-naive. The objective of these RCTs was to demonstrate that insulin glargine 300 units/ml (Toujeo) is non-inferior to insulin glargine 100 units/ml (Lantus) in terms of HbA1c reduction and, based on its pharmacodynamic and pharmacokinetic profiles, is associated with a lower risk of hypoglycaemia.

- In EDITION 1 (n=807), EDITION 2 (n=811) and EDITION 3 (n=878), once-daily insulin glargine 300 units/ml (Toujeo) was non-inferior to once-daily insulin glargine 100 units/ml (Lantus) in adults with type 2 diabetes. A similar reduction in HbA1c from baseline to month 6 was seen in both treatment groups in each study. In EDITION 1 the difference between groups was 0.00% [0.00 mmol/mol], 95% confidence interval [CI] −0.11 to 0.11% [−1.2 to 1.2 mmol/mol] in people who were already using basal and mealtime insulin at baseline. In EDITION 2 the difference was −0.01% [0.1 mmol/mol], 95% CI −0.14 to 0.12% [−1.5 to 1.3 mmol/mol] in people who were using oral blood glucose lowering drugs and basal insulin at baseline. In EDITION 3, in people who were insulin-naive at baseline, the difference was 0.04% [0.4 mmol/mol], 95% CI −0.09 to 0.17% [−1.0 to 1.9 mmol/mol]. These differences were all below the pre-specified non-inferiority margin of 0.4%.
- A similar proportion of participants in both treatment groups in each trial also achieved HbA1c below 7.0% (53 mmol/mol) at month 6.
- The percentage of participants experiencing at least 1 confirmed or severe nocturnal hypoglycaemic event between week 9 and month 6 was statistically significantly lower with Toujeo compared with Lantus in EDITION 1 and EDITION 2, but not in EDITION 3:
    - 36% with Toujeo and 46% with Lantus in EDITION 1 (relative risk [RR] 0.79; 95% CI 0.67 to 0.93, p=0.0045)
    - 22% with Toujeo and 28% with Lantus in EDITION 2 (RR 0.77; 95% CI 0.61 to 0.99,

p=0.038)

- 16% with Toujeo and 17% with Lantus in EDITION 3 (RR 0.89; 95% CI 0.66 to 1.20)
- severe nocturnal hypoglycaemic events were rare in all 3 RCTs and too few for meaningful analysis in each trial.

- In a post-hoc meta-analysis of the 3 RCTs (Ritzel et al 2015), the annualised rate of confirmed or severe nocturnal events over the 6-month study period was 31% lower with Toujeo compared with Lantus (2.10 events per participant-year with Toujeo and 3.06 events per participant-year with Lantus; RR 0.69, 95% CI 0.57 to 0.84, p=0.0002). This is a reduction of approximately 1 confirmed or severe nocturnal event per person per year, which is of debatable clinical significance. Severe hypoglycaemic events at any time of day were rare and not statistically significantly different between groups; the percentage of participants experiencing at least 1 severe event at any time of day was 2.3% in the Toujeo group and 2.6% in the Lantus group (RR 0.85, 95% CI 0.52 to 1.39).
- At 6 months the basal insulin dose was approximately 12% higher with Toujeo than with Lantus in a meta-analysis of the 3 RCTs in adults with type 2 diabetes (Ritzel et al 2015). The mean basal insulin dose at month 6 was 0.85 units/kg/day with Toujeo and 0.76 units/kg/day with Lantus. The dose of Toujeo was 10% higher in EDITION 1 and EDITION 2, and 17% higher in EDITION 3.
- In the 3 RCTs in adults with type 2 diabetes, the number of participants with any adverse event or any serious adverse event was similar in the Toujeo and Lantus groups. Body weight increased with both Toujeo and Lantus, but at month 6 the mean increase was smaller with Toujeo (0.51 kg) than with Lantus (0.79 kg; p=0.039).
- The EPAR states that the safety profile of Toujeo is largely similar to that of Lantus and no additional safety signals were detected. The most frequent adverse events were nasopharyngitis (8.2% with Toujeo, 6.8% with Lantus) and upper respiratory tract infection (6.5% with Toujeo, 5.8% with Lantus). Most of the adverse events were mild to moderate in intensity. Events of severe intensity were reported in 5.1% of the Toujeo group and 4.1% of the Lantus group, with the most frequent in both groups being hypoglycaemia (0.5% with Toujeo and 0.8% with Lantus).
- An important risk with high-strength insulin glargine 300 units/ml (Toujeo) is possible medication errors with other insulins of lower strengths. Toujeo is not bioequivalent to insulin glargine 100 units/ml (Lantus) and dose adjustment is needed. However, the dose window of the Toujeo pen shows the number of Toujeo units to be injected.
- The primary end point of the EDITION 1, 2 and 3 (total n=2496) was an HbA1c end point at

6 months. Extension studies to 12 months have been completed, and published for 2 of the RCTs. There are very limited patient-oriented outcome data for the effects of Toujeo on macrovascular or microvascular outcomes, and very limited long-term safety data for the 300 units/ml insulin glargine strength specifically.

Safety and tolerability

In a post-hoc patient-level meta-analysis of EDITION 1, EDITION 2 and EDITION 3 (n=2496; Ritzel et al 2015), no differences in the safety profile of Toujeo and Lantus were seen. Treatment-emergent adverse events were reported by 712 (57.3%) people in the Toujeo group and 669 (53.7%) people in the Lantus group, with 65 (5.2%) and 62 (5.0%) people reporting serious events respectively. Similar numbers of participants reported injection site reactions (2.4% with Toujeo and 3.1% with Lantus), and similar numbers withdrew because of adverse events (1.4% with Toujeo and 1.3% with Lantus). Deaths occurred in 4 people in the Toujeo group and 3 people in the Lantus group, but none of these were considered to be related to study treatment.

Body weight increased with both Toujeo and Lantus, but at month 6 the mean increase was smaller with Toujeo (0.51 kg) than with Lantus (0.79 kg; p=0.039). In EDITION 1, body weight increased by 0.9 kg in both groups at month 6. In EDITION 2, the weight gain at 6 months was 0.08 kg with Toujeo and 0.66 kg with Lantus (p=0.015), and in EDITION 3 it was 0.49 kg with Toujeo and 0.71 kg with Lantus (no statistically significant difference).

In the European public assessment report (EPAR) for Toujeo, all people from phase 1, 2 or 3 studies who were randomised and received at least 1 dose of Toujeo were evaluated for safety. This includes people with type 1 and type 2 diabetes, and some people who were treated for at least 1 year. Across all studies (n=1546 for Toujeo and n=1550 for Lantus) the number and overall pattern of adverse events were comparable between treatment groups. The most frequent adverse events were nasopharyngitis (8.2% with Toujeo, 6.8% with Lantus) and upper respiratory tract infection (6.5% with Toujeo, 5.8% with Lantus). Most of the adverse events were mild to moderate in intensity. Events of severe intensity were reported in 5.1% of the Toujeo group and 4.1% of the Lantus group, with the most frequent in both groups being hypoglycaemia (0.5% with Toujeo and 0.8% with Lantus).

The EPAR reports that the safety profile of Toujeo is largely similar to that of Lantus and no additional safety signals were detected for Toujeo with regard to injection site reactions, hypersensitivity reactions, malignancy, hepatic safety or cardiovascular safety. However, the Toujeo clinical development programme was not designed specifically to address cardiovascular risk because this has been established for Lantus. The percentage of people with any major cardiovascular event was low and comparable with Toujeo and Lantus.

An important risk with high-strength insulin glargine 300 units/ml (Toujeo) is possible medication errors with other insulins of lower strengths. The European Medicines Agency has recently consulted on guidance to minimise the potential risk of medication errors associated with the availability of high-strength insulins and fixed combinations of insulin with another non-insulin injectable blood glucose lowering agent (MHRA Drug Safety Update April 2015).

The MHRA advice in Drug Safety Update April 2015 is that before starting treatment with a high strength, fixed combination or biosimilar insulin product, healthcare professionals should:

- consult the summary of product characteristics and any educational material
- ensure that patients read and understand the patient leaflet and any patient education material
- ensure that patients receive appropriate training on the correct use of the product

- give patients a patient booklet and Insulin Passport (or safety card)
- warn patients only to use insulin as they have been trained because using it any other way may result in a dangerous overdose or underdose.

The Toujeo guidance for healthcare professionals recommends that the trade name and concentration (Toujeo SoloStar 300 units/ml) must be written on each prescription for Toujeo, along with the recommended dose in units. The dose window of the Toujeo SoloStar pen shows the number of units of Toujeo to be injected. The guidance advises patients that Toujeo is not bioequivalent and not interchangeable with any other basal insulin including insulin glargine 100 units/ml, without individualised dose adjustment. Blood glucose monitoring is needed during the switch and the initial weeks thereafter.

A further "real world" study of more than 4500 patients will compare Toujeo with other basal insulins. Initial results are expected in 2017.

Equity / Stakeholder views (if relevant)	
Decisions of local Trusts DTCs and neighbouring APCs	Local trusts are awaiting outcome from the PCN. Toujeo has not been accepted in the following: • Crawley Horsham & Mid Sussex CCG • Tayside Formulary • Leeds
Recommendations from national / regional decision making groups	

Health economic considerations	
Cost per year per patient	The cost of Toujeo assuming a 45 unit total daily dose (based on 12.74% increase dose compared with Lantus®) is £403 and the cost of Lantus assuming a 40 unit total daily dose is £404 per patient per year. Percentage increase in average weighted dose of Toujeo® versus Lantus from all trials in the EDITION program. Data supplied by the manufacturer.
Alternative treatments cost per patient per year	Basal insulin supply for adults with type 2 diabetes can be provided by: • NPH (isophane) insulin (for example, Insulatard, Humulin I or Insuman Basal) **or** • long-acting insulin analogues: insulin glargine (Lantus, the biosimilar Abasaglar or high-strength Toujeo), insulin detemir (Levemir) or insulin degludec (Tresiba). Toujeo (insulin glargine 300 units/ml) is the third insulin to be approved in Europe at a higher strength than the European Union-wide standard of 100 units/ml. Insulin degludec (Tresiba) and insulin lispro (Humalog) are already available at a 200 units/ml strength.

The cost of Toujeo and other basal insulins will depend on the preparation chosen and the insulin dosage used. The manufacturer has stated that Toujeo has been priced at a level to match the daily cost of Lantus on the basis of average insulin glargine usage in the EDITION trials.

Alternative treatments	5×3 ml cartridge	5×3 ml pre-filled pen
Insulatard - NPH (isophane) insulin 100 units/ml solution	£22.90	£20.40
Humulin I - NPH (isophane) insulin 100 units/ml solution	£19.08	£21.70
Insuman Basal - NPH (isophane) insulin 100 units/ml solution	£17.50	£19.80
Lantus - insulin glargine 100 units/ml solution	£41.50	£41.50
Abasaglar - biosimilar insulin glargine 100 units/ml solution	£35.28	£35.28
Toujeo - high-strength insulin glargine 300 units/ml solution	-	3×1.5 ml pre-filled pen, £33.13[a]
Levemir - insulin detemir 100 units/ml solution	£42.00	£42.00 or £44.85
Tresiba - insulin degludec 100 units/ml solution	£72.00	£72.00
Tresiba - insulin degludec 200 units/ml solution		3×3 ml pre-filled pen, £86.40

Costs are excluding VAT; taken from MIMS (November 2015).

[a] The manufacturer has stated that Toujeo has been priced at a level to match the daily cost of Lantus on the basis of average insulin glargine usage in the EDITION trials (September 2015).

Other financial considerations (if

relevant)	
Health economic data (if available)	

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