Amber with Guidance (Amber-G) = *To be recommended or initiated by a specialist* with follow up prescribing and monitoring by primary care clinicians.*
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Barnsley Hospital NHS Foundation Trust | South West Yorkshire Partnership NHS Foundation Trust | South Yorkshire Integrated Care Board

Toujeo® (High strength Insulin glargine 300 units/ml) Amber G Guideline for use in adults and children over 6years.

Prescribe by brand name

The details of side-effects, cautions, contraindications and interactions are not a complete list and the current BNF (https://www.medicinescomplete.com/#/) and the SmPC (https://www.medicines.org.uk/emc/) remain authoritative.

Background Information[1,2]	In the UK there are currently three different insulin glargine products. The first to be launched was Lantus® and has been used widely since launch. Two further products are Abasaglar® (insulin glargine biosimilar) and Toujeo® (high strength insulin glargine 300 units/ml). Toujeo® (300 units/mL) has a different formulation to Lantus®. It has been designed as a longer-acting product. Bioequivalence and inter-changeability between the two products does not, therefore, exist and direct substitution between Lantus® and Toujeo® is not expected. When switching from intermediate or long-acting insulin treatment regimens (including Lantus®) to Toujeo®, blood glucose monitoring and dose adjustment will be required.[1] Guidance relating to switching to Toujeo® from other insulins can be found in the Summary of Product Characteristics. The potency of Toujeo® is stated in units. These units are exclusive to Toujeo® and are not the same as IU or the units used to express the potency of other insulin analogues. **Toujeo® is available as two pre-filled pens – SoloStar® and DoubleStar®:** Each SoloStar® pen contains 1.5 ml of solution for injection, equivalent to 450 units. Each DoubleStar® pen contains 3 ml of solution for injection, equivalent to 900 units.
BNF therapeutic class	6.01.01.02
Indication[1,2]	In adults Toujeo® will be recommended or initiated by a specialist with follow up prescribing and monitoring by primary care clinicians in line with the amber-G classification. In children over 6yrs Toujeo® will be recommended or initiated by the specialist paediatric diabetes team with prescribing in primary care and 3monthly monitoring and follow up in paediatric diabetes clinic. In children under 6yrs Toujeo® use would remain as a red classification and as such would be initiated, monitored and prescribed by the paediatric diabetes teams.
Dosage and administration[1,2,3]	Toujeo® is a basal insulin for once-daily administration at any time of the day, preferably at the same time every day. If necessary, patients may administer Toujeo® up to three hours before or after their usual administration time. The dose regimen (dose and timing) should be adjusted according to individual response.

	Toujeo® is administered subcutaneously by injection in the abdominal wall, the deltoid or the thigh. Injection sites must be rotated within a given injection area from one injection to the next to reduce the risk of lipodystrophy and cutaneous amyloidosis. 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 may be required. Toujeo® is only available as a pre-filled pen formulation (SoloStar® pen or DoubleStar® pen) and must be administered in this form, or severe overdose could result. If patients miss a dose they should be advised to check their blood sugar before resuming their once-daily dosing schedule. Patients should be instructed not to inject a double dose to make up for a forgotten dose. 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, Toujeo® can also be given together with other anti-hyperglycaemic medicinal products. The dose window of Toujeo® SoloStar and Toujeo® DoubleStar pre-filled pens shows the number of units of Toujeo® to be injected. The Toujeo® SoloStar and Toujeo® DoubleStar pre-filled pens have been specifically designed for Toujeo® and no dose re-calculation is required for either pen. With Toujeo® SoloStar pre-filled pen, a dose of 1-80 units per single injection, in steps of 1 unit, can be injected. With Toujeo® DoubleStar pre-filled pen a dose of 2-160 units per single injection, in steps of 2 units, can be injected. When changing from Toujeo® SoloStar to Toujeo® DoubleStar, if the patient's previous dose was an odd number (e.g. 23 units) then the dose must be increased or decreased by 1 unit (e.g. 24 or 22 units). Toujeo® DoubleStar prefilled pen is recommended for patients requiring at least 20 units per day. Toujeo® should be stored in the fridge at 2-8ºC until first use. Before first use, the pen must be stored at room temperature for at least 1 hour.Toujeo® may then be stored at room temperature below 30 ºC for 6 weeks. Once opened do not refrigerate. The pen cap must be replaced on the pen after each injection in order to protect from light. <u>Initiation:</u> For patients with type 2 diabetes mellitus, the recommended daily starting dose is 0.2 units/kg followed by individual dose adjustments. For patients with type 1 diabetes mellitus, Toujeo® is to be used once-daily with meal-time insulin and requires individual dose adjustments. <u>Elderly population (≥65 years old):</u> In the elderly, progressive deterioration of renal function may lead to a steady decrease in insulin requirements. <u>Renal impairment:</u> In patients with renal impairment, insulin requirements may be diminished due to reduced insulin metabolism. <u>Hepatic impairment:</u> In patients with hepatic impairment, insulin requirements may be diminished due to reduced capacity for gluconeogenesis and reduced insulin metabolism.

	Paediatric population: Toujeo® can be used in adolescents and children from the age of 6 years based on the same principles as for adult patients. The safety and efficacy of Toujeo® in children below 6 years of age has not been established. No data are available.
Cautions and Contraindications[1,2,4]	**Cautions** The same cautions as those with the use of any insulin/insulin glargine also apply to Toujeo®. See SmPC section 4.4 special warnings and precautions for use. Changing from insulin glargine 100 units/ml to Toujeo®: Since insulin glargine 100 units/ml and Toujeo® are not bioequivalent and are not interchangeable, switching may result in the need for a change in dose and should only be done under strict medical supervision. 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. Conversely, if switching patients from Toujeo® to insulin glargine 100units/ml, the dose should be reduced by approximately 20% to prevent hypoglycaemia. Close monitoring will be required in both instances. Changing from other insulins to Toujeo®: Changing a patient between another type or brand of insulin and Toujeo® should be done under strict medical supervision. Changes in strength, brand (manufacturer), type (regular, NPH, lente, long-acting, etc.), origin (animal, human, human insulin analogue) and/or method of manufacture may result in the need for a change in dose. For further information consult the SmPC[3] or the Educational risk measures Toujeo® 300units/ml solution for injection in a pre-filled pen- Guide for healthcare professionals[4]. Combination of Toujeo® 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. This should be kept in mind if treatment with the combination of pioglitazone and Toujeo® is considered. 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 prevention: Insulin label must always be checked before each injection to avoid medication errors between Toujeo® and other insulins. A new sterile needle must be attached before each injection. Patients must also be instructed to not re-use needles. Re-use of needles increases the risk of blocked needles which may cause underdosing or overdosing. Patients must visually verify the number of selected units on the dose counter of the pen. Patients who are blind or have poor vision should be instructed to get help/assistance from another person who has good vision and is trained in using the insulin device. **Contraindications** Hypersensitivity to the active substance or to any of the excipients.
Pregnancy and breast feeding[1,2]	**Pregnancy** There is no clinical experience with use of Toujeo® in pregnant women. For insulin glargine no clinical data on exposed pregnancies from controlled clinical studies are available. A large amount of data on pregnant women (more than 1,000 pregnancy outcomes with a medicinal product containing insulin glargine 100 units/ml) indicate no specific adverse effects on pregnancy and no specific malformative nor feto/neonatal toxicity of insulin glargine. Animal data do not indicate reproductive toxicity. The use of Toujeo® may be considered during pregnancy, if clinically needed. It is essential for patients with pre-existing or gestational diabetes to maintain good metabolic control throughout pregnancy to prevent adverse outcomes associated with hyperglycaemia. 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. **Breast feeding** It is unknown whether insulin glargine is excreted in human milk. No metabolic effects of ingested insulin glargine on the breast-fed new born/infant are anticipated since insulin glargine as a peptide is digested into amino acids in the human gastrointestinal tract. Breast-feeding women may require adjustments in insulin dose and diet.
Adverse Drug Reactions[1,2]	The safety profile of Toujeo® is similar to insulins in general. Extra care should be taken with respect to the use of Toujeo® due to the high concentration of insulin. Prescribers are reminded to ensure they check they have selected the appropriate presentation on the practice system before prescribing. See SMPC for full side effect profile. Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme: www.mhra.gov.uk/yellowcard
Monitoring	There are no specific monitoring requirements for Toujeo® other than the routine monitoring undertaken for all insulins.
Interactions[1,2]	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 therefore increase susceptibility to hypoglycaemia: • oral antidiabetic medicines, angiotensin converting enzyme (ACE) inhibitors, disopyramide, fibrates, fluoxetine, monoamine oxidase (MAO) inhibitors, pentoxifylline, propoxyphene, salicylates, somatostatin analogues and sulphonamide antibiotics. Substances that may reduce the blood-glucose-lowering effect: • corticosteroids, danazol, diazoxide, diuretics, glucagon, isoniazid, oestrogens, progestogens, phenothiazine derivatives, somatropin, sympathomimetic medicinal products (e.g. epinephrine, 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.
Additional information[4,5,6]	The MHRA[4] published an alert on 29/4/2015 entitled 'High Strength, fixed combination and biosimilar insulin products: minimising the risk of medication error.' This can be accessed online at https://www.gov.uk/drug-safety-update/high-strength-fixed-combination-and-biosimilar-insulin-products-minimising-the-risk-of-medication-error Before Toujeo® is prescribed, the MHRA advises prescribers to: 1) Consult the SmPC and educational material (see below). 2) Ensure that patients read the patient information leaflet and education material.

	3) Ensure that patients receive appropriate training on the correct use of the product and that they are aware that using insulin in any other way may result in dangerous overdose or under-dose. 4) Closely monitor blood glucose levels over the first few weeks of treatment and adjust doses of other anti-diabetic products accordingly. Please note that the educational material contained in the MHRA alert link only applies to Toujeo® SoloStar. Toujeo® DoubleStar was not available at the time of the MHRA alert. Information on Toujeo® 300 SoloStar solution for injection in a pre-filled pen and Toujeo® 300 DoubleStar solution for injection in a pre-filled pen specifically for healthcare professionals can be found at the following link: Toujeo® 300 SoloStar® and Toujeo® 300 Doublestar® guide for healthcare professionals (November 2019). Patient specific information on Toujeo® 300 SoloStar solution for injection in a pre-filled pen and Toujeo® 300 DoubleStar solution for injection in a pre-filled pen can be found at the following link: Toujeo® 300 units/ml, solution for injection in a pre-filled pen - Guide for patients and/or carers (May 2019). A patient held card is also available from the manufacturers. For patients within primary care, these cards can be obtained from the Medicines Management Team or downloaded via the following links: Toujeo® DoubleStar - Insulin passport (Digital).pdf (mysanofiinsulin.co.uk). Toujeo® Solostar insulin passport link
Ordering information	Sanofi products are only available to order direct via AAH and Phoenix wholesalers. Pharmacies who hold accounts with both AAH and Alliance or Phoenix and Alliance may order via Alliance using the Third Party Ordering System (TPOS).

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https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf

Development Process

This guidance has been produced by Joy Power (Medicines Management Pharmacist) following an AMBER-G classification status of Toujeo® by the Barnsley Area Prescribing Committee. This guideline has been subject to consultation and endorsement by Endocrinology and Diabetology and was ratified by the Area Prescribing Committee on 12th July 2023.

Appendix A – Toujeo® prescribing initiation checklist

Current insulin (if applicable)		Date current insulin course completed:	Current insulin dose:	Current dosing time:
Toujeo® Preparation	Tick Box	Toujeo® Dose (units):	Date Toujeo® to start:	Toujeo® dosing time:
Toujeo® Solostar	☐			
Toujeo® Doublestar	☐			
Counselling of patient to include: 1. Toujeo® delivery: • Loading • Priming • Dialing up correct dose • Timing of dose (same time each day but 3hr window either side if needed) 2. Toujeo® storage: • 2-8ºC prior to use • Expires 6 weeks after removal from fridge. (Make diary entry when removed from fridge) 3. Hypoglycaemia: • Signs/symptoms • Causes/prevention • Treatment • Diabetes identification 4. Glucose checks: • Recommend monitoring schedule 5. Sharps disposal 6. Driving	☐	Comments		
Monitoring: 1. Ensure patient knows who to call to arrange blood tests 2. Ensure patient knows where the blood tests will take place (GP, Phlebotomy etc.)	☐ ☐	Comments		

Please note monitoring of paediatric patients (6 – 18yrs) would be undertaken in routine 3 monthly paediatric outpatient clinic appointments.