Admelog®
insulin lispro
injection 100 Units/mL

sanofi

Comparing the safety and efficacy of Admelog® vs. Humalog® in patients with Type 1 and 2 diabetes (SORELLA-1 & 2 studies)

Garg SK, *et al*. *Diabetes Technol Ther*. 2017;19(9):516–26.
Darwahl K, *et al*. *Diabetes Technol Ther*. 2018;20(1):1–10.

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

Admelog is indicated for the treatment of adults and children with diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis and for the initial stabilisation of diabetes mellitus.[1]

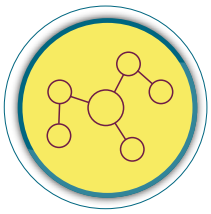
Key takeaway

Similar efficacy and safety results were observed for the biosimilar, Admelog and the reference drug, Humalog, in patients with T1DM and T2DM.[2,3]

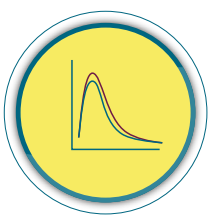
Why this matters

Biologics are often produced by cutting-edge technology and are able to help patients with chronic and often debilitating conditions. The development of biosimilars offers advantages to healthcare systems by improving patients' access to effective biological medicines with proven quality.[4]

Admelog is the first rapid-acting insulin biosimilar of Humalog approved in the UK and EU.[5] Since 1996, Humalog has been approved and marketed in the UK, EU, US and many other countries worldwide as a treatment to improve glycaemic control in adults and children with T1DM and T2DM.[2,3]



Admelog is a biosimilar of the reference product, Humalog. It has the same amino acid sequence and corresponding structure and was developed in accordance with the relevant UK, US and EU guidelines.[2,3]



Physicochemical analyses, *in vitro* and *in vivo* nonclinical studies have shown Admelog to be highly similar to Humalog, showing similar PK and PD activity.[2,3]

EU, European Union; HbA_{1c}, glycated haemoglobin; PD, pharmacodynamics; PK, pharmacokinetics; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; UK, United Kingdom; US, United States.

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SORELLA 1 & 2: Study aims

These studies aimed to show similar efficacy, safety profile, and immunogenicity of Admelog in comparison to Humalog in adult patients with T1DM (SORELLA-1) and T2DM (SORELLA-2). These patients were treated with multiple daily injections while using basal insulin glargine (Lantus®; insulin glargine 100 units/mL).[2,3]

SORELLA-1 & 2: Primary objective

To demonstrate noninferiority of Admelog vs. Humalog in terms of HbA_{1c} change from baseline to Week 26 at a noninferiority margin of 0.3% in adult patients with T1DM and T2DM, who were also using Lantus®.[2,3]

SORELLA-1 & 2: Safety outcomes

The percentage of participants reporting: at least one hypoglycaemic event; hypoglycaemic event rates; the occurrence of TEAEs (including hypersensitivity and injection site reactions); change in body weight and change in clinical laboratory and haematology parameters.[2,3]

HbA_{1c}, glycated haemoglobin; TEAEs, treatment-emergent adverse events; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

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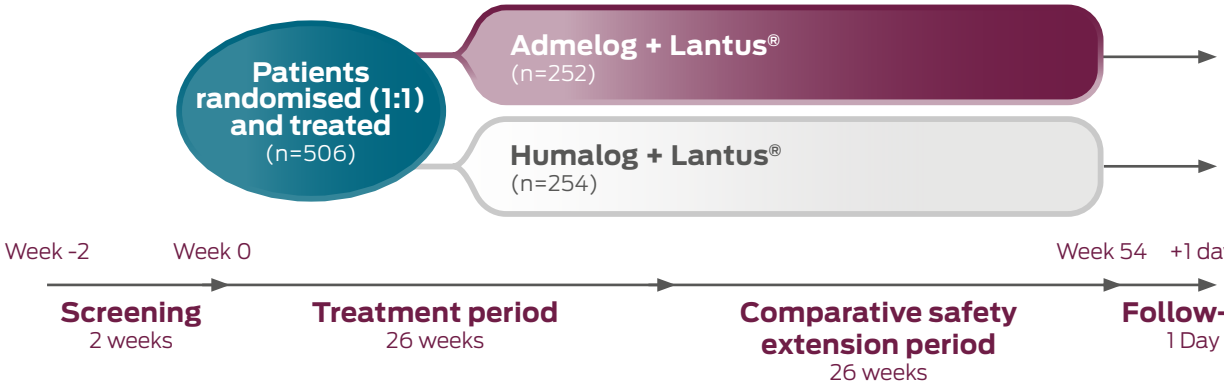
SORELLA-1 study:[2]

Study design:

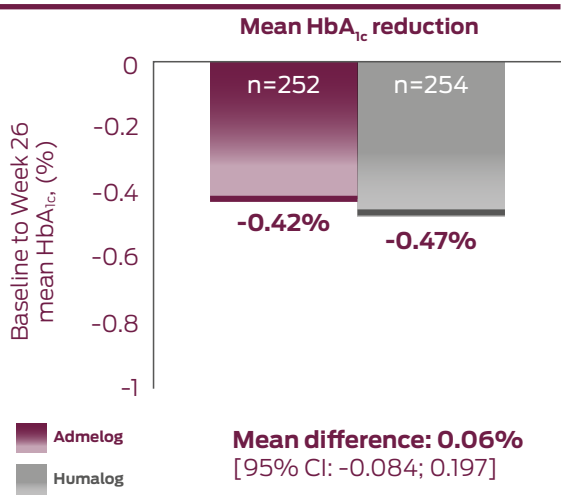
SORELLA-1 is a 52-week (26-week main study period including the evaluation of the primary efficacy endpoint and a 26-week safety extension period), multicentre two-arm parallel group randomised (1:1), controlled, open-label study of 507 people with T1DM on multiple daily injections of insulin lispro (Admelog) or insulin lispro (Humalog) in combination with insulin glargine (Lantus®) prior to screening.*



Adapted from Garg SK, *et al*. 2017.

Key findings:

- Similar mean HbA_{1c} reduction from baseline to Week 26 in Admelog and Humalog groups
- Noninferiority at prespecified 0.3% noninferiority margin and inverse noninferiority were demonstrated
- A small increase in HbA_{1c} occurred similarly in both treatment groups between Week 26 to Week 52
- The LS mean change in HbA_{1c} from baseline to Week 52 was similar in both treatment groups
  - LS mean (SEM): Admelog: -0.22 (0.057) vs. Humalog: -0.30 (0.056)
  - The LS mean difference between Admelog and Humalog was 0.07% (95% CI: -0.084–0.232)



Adapted from Garg SK, *et al*. 2017.

- Similar FPG decrease in both treatment groups and seven-point SMPG profile changes had improved similarly compared with baseline at all time points (except post-dinner for Humalog group and at bedtime for both groups)
- Immunogenicity: AIAs (incidence and prevalence) did not differ between groups

Safety findings:

- In both treatment groups, almost all patients had at least one hypoglycaemic episode, regardless of the category (Admelog [99.2%] and Humalog [100%])
- Severe hypoglycaemia was reported by a similar number of patients in the Admelog group (13.5%) and Humalog group (13.4%)
- 7.9% of patients in the Admelog group reported serious TEAEs vs. 7.5% in the Humalog group. The most common serious TEAE was hypoglycaemic unconsciousness (2.4% in both treatment groups)

AIA, anti-insulin antibody; CI, confidence interval; CSII, insulin pump therapy; FPG, fasting plasma glucose; HbA_{1c}, glycated haemoglobin; LS, least-square; PD, pharmacodynamics; PK, pharmacokinetics; SEM, standard error of the mean; SMPG, self-monitored plasma glucose; TEAEs, treatment-emergent adverse events; T1DM, type 1 diabetes mellitus.

*Eligible patients were ≥18 years old with T1DM diagnosed for at least 12 months at the time of the screening visit, with HbA_{1c} ranging between 7–10%. Excluded were patients with body-mass index ≥35 kg/m^2, noninsulin antidiabetic treatments or the use of CSII, history of severe hypoglycaemia requiring treatment by emergency room admission, and poor metabolic control requiring hospitalisation, all in the last 6 months before screening.

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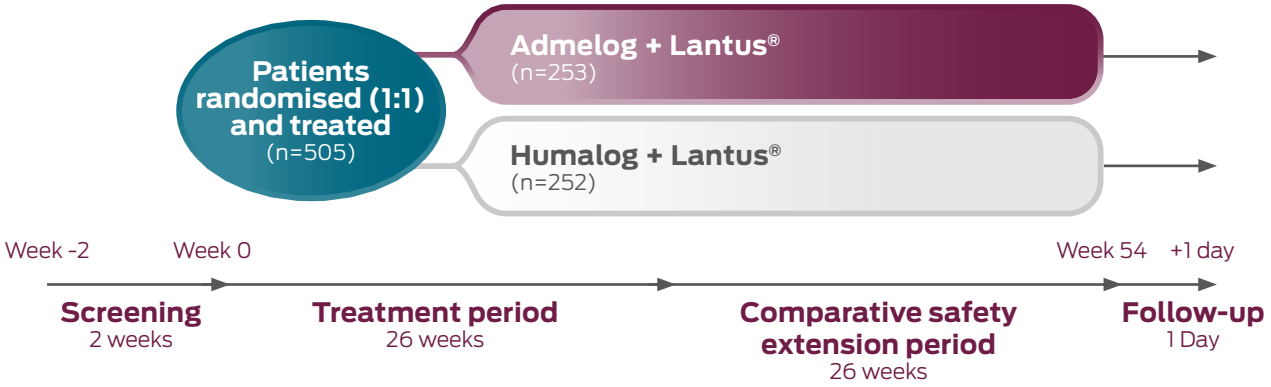
SORELLA-2 study:[3]

Study design:

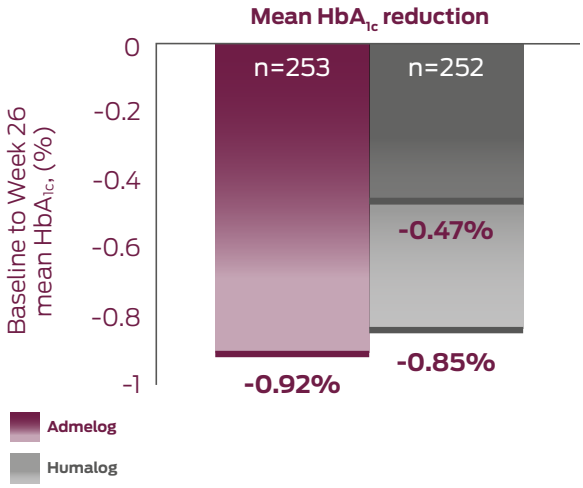
SORELLA-2 is a phase 3, 6-month, randomised (1:1), controlled, open-label study of 505 people with T2DM on insulin lispro or insulin aspart in combination with insulin glargine (Lantus®) prior to screening. The study compared the efficacy and safety of insulin lispro (Admelog) and insulin lispro (Humalog) in combination with Lantus® as a basal insulin. Anti-insulin antibody measurements were based on 245 Admelog subjects vs. 248 Humalog patients.*



Adapted from Derwahl KM, et al. 2018

Key findings:

- Similar mean HbA_{1c} reduction from baseline to Week 26 in Admelog and Humalog groups
- Noninferiority at prespecified 0.3% noninferiority margin and inverse noninferiority were demonstrated
- Similar mean FPG decrease in both treatment groups and seven-point SMPG profile changes had improved similarly compared with baseline at all time points
- Immunogenicity: AIAs (incidence and prevalence) did not differ between groups



Adapted from Derwahl KM, *et al*. 2018.

Safety findings:

- Similar rates of patients with at least one hypoglycaemic event, regardless of the category, reported at any time of the day (Admelog [68.4%] and Humalog [74.6%])
- Low occurrence of severe hypoglycaemia in both treatment groups (<0.1 per patient-year). 2.4% in the Admelog group vs. 1.6% in the Humalog group reported severe hypoglycaemia
- Lower percentage of serious TEAEs reported in Admelog group, 5.5% vs. Humalog group, 10.7%
- 46.6% in the Admelog group reported serious TEAEs vs. 42.9% in the Humalog group. The most common TEAE was nasopharyngitis (Admelog, 4.0% vs. Humalog, 2.0%)

AIA, anti-insulin antibody; CI, confidence interval; FPG, fasting plasma glucose; HbA_{1c}, glycated haemoglobin; SMPG, self-monitored plasma glucose; TEAEs, treatment-emergent adverse events; T2DM, type 2 diabetes mellitus.

*Eligible patients were ≥18 years old with HbA_{1c} ≥6.5% and ≤10% and T2DM diagnosed for at least 12 months. Excluded were patients with body-mass index ≥40 kg/m^2, the use of noninsulin injectable peptides, use of continuous subcutaneous insulin infusion, history of severe hypoglycaemia requiring treatment by emergency room admission, or poor metabolic control requiring hospitalisation, all within the last 6 months before screening.

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SORELLA-1 & 2 study limitations:

- The study population was predominately caucasian adults with a small number of other ethnic minorities included
- The open-label study design was chosen as the two injection devices could not be made indistinguishable

SORELLA-1 & 2 study conclusion:

The results from both controlled studies in patients with T1DM and T2DM supports **similar efficacy and safety profiles (including immunogenicity) of the biosimilar, Admelog** and the reference drug, Humalog.[2,3]

Prescribing Information: Admelog® (Insulin lispro 100 units/ml)

Please refer to Summary of Product Characteristics (SmPC) before prescribing. Presentations: Admelog 100 units/ml solution for injection in a vial, each containing 10ml of solution for injection, equivalent to 1000 units. Admelog 100 units/ml solution for injection in a cartridge or in a pre-filled pen each containing 3 ml of solution for injection, equivalent to 300 units insulin lispro.
Indication: For the treatment of adults and children with diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis and for the initial stabilisation of diabetes mellitus.
Dosage and Administrations: The dose should be determined by the physician, according to the requirement of the patient. Admelog may be given shortly before meals, when necessary can be given soon after meals. Insulin lispro takes effect rapidly and has a shorter duration of activity (2-5 hours) given subcutaneously as compared with regular insulin, regardless of injection site. The time course of action of any insulin may vary considerably in different individuals or at different times in the same individual and duration of action is dependent on dose, site of injection, blood supply, temperature, and physical activity. Admelog can be used in conjunction with longeracting insulin or oral sulphonylurea medicinal products, on the advice of a physician. Admelog in cartridges are only suitable for subcutaneous injections from a reusable pen. Admelog in pre-filled pen are only suitable for subcutaneous injections. Admelog solution for injection should be given by subcutaneous injection or by continuous subcutaneous infusion pump and may, although not recommended, also be given by intramuscular injection. If necessary, it may also be administered intravenously. If administration by syringe, intravenous injection or infusion pump is necessary, a vial should be used. *Subcutaneous administration:* Should be in the upper arms, thighs, buttocks, or abdomen. Injection sites should always be rotated within the same region in order to reduce the risk of lipodystrophy and cutaneous amyloidosis. Care should be taken when injecting to ensure that a blood vessel has not been entered. After injection, the site of injection should not be massaged. Patients must be educated to use the proper injection techniques. *Administration via an insulin infusion pump (Admelog vials only):* Admelog should not be mixed with any other insulin. Continuous subcutaneous insulin infusion (CSII) may be given in pump systems suitable for insulin infusion; only certain CE-marked insulin infusion pumps may be used. Before infusing, the manufacturer's instructions should be studied to ascertain the suitability or otherwise for the particular pump. Use the correct reservoir and catheter for the pump. The infusion set (tubing and cannula) should be changed in accordance with the instructions in the product information supplied with the infusion set. A pump malfunction or obstruction of the infusion set can result in a rapid rise in glucose levels. If an interruption to insulin flow is suspected, follow the instructions in the product literature. *Intravenous administration (Admelog vials only):* Should be carried out following normal clinical practice for intravenous injections; frequent monitoring of the blood glucose levels is required. **Special Populations:** *Renal/Hepatic impairment:* Insulin requirements may be reduced. Patients with chronic hepatic impairment may have diminished insulin sensitivity and therefore require an increased dose. *Paediatric population:* Admelog can be used in adolescents and children.
Contraindications: Hypoglycaemia, hypersensitivity to insulin lispro or to any of the 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. *Transferring to another type/ brand of insulin:* Should be done under strict medical supervision and may result in the need for change in dose. For fast-acting insulins, any patient also on basal insulin must optimise dose of both insulins to obtain glucose control across the whole day, particularly nocturnal/fasting glucose control. *Injection technique:* 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 or hyperglycaemia:* Conditions which may make the early warning symptoms of hypoglycaemia different or less pronounced include long duration of diabetes, intensified insulin therapy, diabetic nerve disease or medications such as beta-blockers. Uncorrected hypoglycaemic or hyperglycaemic reactions can cause loss of consciousness, coma, or death. Inadequate dose or discontinuation of treatment, especially in insulin dependent diabetics, may lead to hyperglycaemia and diabetic ketoacidosis; conditions which are potentially lethal. *Dose adjustment:* Insulin requirements may be increased during illness or emotional disturbances. Adjustment of dose may also be necessary if patients undertake increased physical activity or change their usual diet. *In combination with pioglitazone:* Cases of cardiac failure have been reported, especially in patients with risk factors for development of heart failure. Patients using this combination 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:* Patients must be instructed to always check the insulin label before each injection to avoid mix-ups between Admelog and other insulin products. Patients must visually verify the dialled units on the dose counter of the pen. Patients who are blind or have poor vision must be instructed to always get help/assistance from another person who has good vision and is trained in using the insulin device. *Excipients:* This medicine is essentially "sodium-free". *Pregnancy:* It is essential to maintain good control of the insulin-treated (insulin-dependent or gestational diabetes) patient throughout pregnancy. Patients with diabetes should be advised to inform their doctor if they are pregnant or are contemplating pregnancy. Careful monitoring of glucose control, as well as general health, is essential in pregnant patients with diabetes. *Breastfeeding:* Patient may require adjustments in insulin dose, diet or both.
Interactions: The physician should be consulted when using other medicinal products in addition to Admelog. Insulin requirements may be increased by medicinal products with hyperglycaemic activity and reduced in the presence of medicinal products with hypoglycaemic activity.
Adverse Reactions: Hypoglycaemia is the most frequent adverse reaction. Oedema has been reported, particularly if previous poor metabolic control is improved by intensified insulin therapy. *Common (≥1/100 to <1/10):* Local allergy. *Uncommon (≥1/1,000 to <1/100):* Lipodystrophy. *Rare (≥1/10,000 to <1/1,000):* Systemic allergy. *Not known (cannot be estimated from the available data):* Cutaneous amyloidosis. *Prescribers should consult the SmPC in relation to other adverse reactions.*
Legal Category: POM.
Marketing Authorisation (MA) Holder: Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK
UK List price and MA Numbers: *Admelog 100 units/ml solution for injection in vial 1 x 10ml:* £14.12 – PLGB 04425/0822. *Admelog 100 units/ml solution for injection in cartridge 5x 3ml:* £21.23 – PLGB 04425/0823. *Admelog 100 units/ml solution for injection in pre-filled pen 5 x 3ml:* £22.10 – PLGB 04425/0824.
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: August 2022 (MAT-GB- 2200442 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

T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

Prescribing Information: Lantus® (insulin glargine) 100 units/ml solution for injection

Please refer to Summary of Product Characteristics (SmPC) before prescribing.
Presentations: Lantus 100 units/ml solution for injection in a vial or in a cartridge. Lantus SoloStar 100 units/ml solution for injection in a pre-filled pen. Lantus cartridges and Solostar prefilled pens each contain 3 ml of solution for injection, equivalent to 300 units insulin glargine. Each vial contains 10 ml of solution for injection, equivalent to 1000 units.
Indications: Treatment of diabetes mellitus in adults, adolescents and children of 2 years or above.
Dosage and administration: Lantus is administered subcutaneously once daily, at any time but at the same time each day. 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. Lantus dosage should be individually adjusted. In type 2 diabetes mellitus, Lantus can also be used in combination with orally active antidiabetic medicinal products. Lantus must not be mixed with other insulins or diluted. *Switch from twice daily NPH insulin to Lantus:* To reduce the risk of nocturnal and early morning hypoglycaemia, patients who are changing their basal insulin regimen from a twice daily NPH insulin to a once daily regimen with Lantus should reduce their daily dose of basal insulin by 20 – 30% during the first weeks of treatment. *Switch from Toujeo (insulin glargine) 300 units/ml to Lantus:* Lantus and Toujeo are not bioequivalent and are not directly interchangeable. To reduce the risk of hypoglycemia, patients who are changing their basal insulin regimen from an insulin regimen with once daily Toujeo to a once daily regimen with Lantus should reduce their dose by approximately 20%. *Switching from other insulins to Lantus:* When switching from a treatment regimen with an intermediate or long-acting insulin to a regimen with Lantus, a change of the dose of the basal insulin may be required and the concomitant antidiabetic treatment may need to be adjusted (dose and timing of additional regular insulins or fast-acting insulin analogues or the dose of oral antidiabetic medicinal products). Close metabolic monitoring is recommended during, and for a period after, transition from other insulins to Lantus. 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.
Special populations: *Elderly, renal or hepatic impairment:* Insulin requirements may be diminished. *Paediatric population (<2 years of age):* No data are available.
Contraindications: Hypersensitivity to insulin glargine or any excipients.
Precautions and warnings: Lantus is not the insulin of choice for treatment of diabetic ketoacidosis. In case of insufficient glucose control or a tendency to hypo/hyperglycaemic episodes all relevant factors must be reviewed before dose adjustment is considered. Transferring a patient to another type or brand of insulin should be done under strict medical supervision. *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. *Injection technique:* 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. Intercurrent illness also requires intensified metabolic monitoring. *Hypoglycaemia:* Particular caution should be exercised, and intensified blood 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. The prolonged effect of subcutaneous Lantus may delay recovery from hypoglycaemia. Due to more sustained basal insulin supply with Lantus, less nocturnal but earlier morning hypoglycaemia can be expected. *Insulin antibodies:* administration may cause insulin antibodies to form. Rarely, this may necessitate dose adjustment. *Pioglitazone:* Cases of cardiac failure have been reported, especially in patients with risk factors for development of cardiac heart failure. Patients on this combination should be observed and 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 Lantus and other insulins. Lantus Solostar is only suitable for subcutaneous injections from its pre-filled pen. Lantus cartridges are only suitable for subcutaneous injections from specific reusable pens (please refer to SmPC for further details). If administration by syringe is necessary, a vial should be used. ***Interactions:*** A number of substances affect glucose metabolism and may require dose adjustment of Lantus. ***Pregnancy and lactation:*** No clinical data on exposed pregnancies from controlled clinical trials are available. A large amount of post-marketing data indicates no specific adverse effects of Lantus in pregnancy. Use of Lantus in pregnancy can be considered if clinically needed. 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. It is unknown if Lantus is excreted in breast milk.
Adverse reactions: *Very common:* Hypoglycaemia. Prolonged or severe hypoglycaemia may be life-threatening. Overdose may lead to severe and sometimes long-term and life-threatening hypoglycaemia. *Common:* Lipohypertrophy, injection site reactions. *Uncommon:* Lipoatrophy. *Rare:* Allergic reactions, visual impairment, retinopathy and oedema. *Very rare:* Dysgeusia, myalgia. *Frequency not known:* Cutaneous amyloidosis. *Prescribers should consult the SmPC in relation to other adverse reactions.*
Legal category: POM.
GB list price and Marketing Authorisation Number(s): 1 x 10ml Lantus vial (PLGB 04425/0814): £25.69; 5 x 3ml Lantus cartridge (PLGB 04425/0815): £34.75; 5 x 3ml Lantus SoloStar (PLGB 04425/0816): £34.75.
Marketing Authorisation Holder: Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK.
For more information please contact: Medical Information, Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. uk-medicalinformation@sanofi.com.
Date of preparation: October 2022.
MAT-XU-2204110 (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.
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References:
1. Admelog Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/13083/smpc. Date accessed: May 2023.
2. Garg SK, *et al. Diabetes Technol Ther.* 2017;19(9):516–26.
3. Darwahl K, *et al. Diabetes Technol Ther.* 2018; 20(1):1–10.
4. European Commission. Community register of medicinal products for human use. Admelog. Available at: https://ec.europa.eu/health/documents/community-register/html/h1203.htm. Date accessed: May 2023.
5. EMA. Biosimilar Medicines. Available at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/general/general_content_001832.jsp. Date accessed: May 2023.

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