ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 100 units/mL solution for injection in vial
Lyumjev 100 units/mL solution for injection in cartridge
Lyumjev 100 units/mL KwikPen solution for injection in pre-filled pen
Lyumjev 100 units/mL Junior KwikPen solution for injection in pre-filled pen
Lyumjev 100 units/mL Tempo Pen solution for injection in a pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL contains 100 units of insulin lispro* (equivalent to 3.5 mg).

Lyumjev 100 units/mL solution for injection in vial

Each vial contains 1000 units insulin lispro in 10 mL solution.

Lyumjev 100 units/mL solution for injection in cartridge

Each cartridge contains 300 units of insulin lispro in 3 mL solution.

Lyumjev 100 units/mL KwikPen solution for injection in pre-filled pen
Lyumjev 100 units/mL Tempo Pen solution for injection in pre-filled pen

Each pre-filled pen contains 300 units of insulin lispro in 3 mL solution.
Each pre-filled pen delivers 1 - 60 units in steps of 1 unit in a single injection.

Lyumjev 100 units/mL Junior KwikPen solution for injection in pre-filled pen

Each pre-filled pen contains 300 units of insulin lispro in 3 mL solution.
Each Junior KwikPen delivers 0.5 - 30 units in steps of 0.5 units in a single injection.

*produced in *E.coli* by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless, aqueous solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of diabetes mellitus in adults, adolescents and children aged 1 year and above.

4.2 Posology and method of administration

Posology

Lyumjev is a mealtime insulin for subcutaneous injection and should be administered zero to two minutes before the start of the meal, with the option to administer up to 20 minutes after starting the meal (see section 5.1).

Lyumjev 100 units/mL is suitable for continuous subcutaneous insulin infusion (CSII) and is used for both the bolus and basal insulin requirement.

The initial dose should take into account the type of diabetes, weight of the patient and their blood glucose levels.

The early onset of action must be considered when prescribing Lyumjev (see section 5.1). Continued adjustment of the dose of Lyumjev should be based on the patient's metabolic needs, blood glucose monitoring results, and glycaemic control goal. Dose adjustments may be needed, when switching from another insulin, with changes in physical activity, changes in concomitant medicinal products, changes in meal patterns (i.e., amount and type of food, timing of food intake), changes in renal or hepatic function or during acute illness to minimize the risk of hypoglycaemia or hyperglycaemia (see sections 4.4 and 4.5).

Switching from another mealtime insulin medicinal product

If converting from another mealtime insulin to Lyumjev, the change can be done on a unit-to-unit basis. The potency of insulin analogues, including Lyumjev, is expressed in units. One (1) unit of Lyumjev corresponds to 1 international unit (IU) of human insulin or 1 unit of other fast-acting insulin analogues.

Missed doses

Patients who forget a mealtime dose should monitor their blood glucose level to decide if an insulin dose is needed, and to resume their usual dosing schedule at the next meal.

Special populations

Elderly (≥ 65 years old)
The safety and efficacy of Lyumjev has been established in elderly patients aged 65 to 75 years. Close glucose monitoring is recommended and the insulin dose should be adjusted on an individual basis (see sections 4.8, 5.1 and 5.2). The therapeutic experience in patients ≥ 75 years of age is limited.

Renal impairment
Insulin requirements may be reduced in the presence of renal impairment. In patients with renal impairment, glucose monitoring should be intensified and the dose adjusted on an individual basis.

Hepatic impairment
Insulin requirements may be reduced in patients with hepatic impairment due to reduced capacity for gluconeogenesis and reduced insulin breakdown. In patients with hepatic impairment, glucose monitoring should be intensified and the dose adjusted on an individual basis.

Paediatric population
Lyumjev can be used in adolescents and children from the age of 1 year (see section 5.1). There is no clinical experience with the use of Lyumjev in children below the age of 3 years. Similar to adults, dosage should be adjusted individually. Lyumjev is recommended to be administered zero to two minutes before the start of the meal, with the option to administer up to 20 minutes after starting the meal when needed.

Method of administration

Patients should be trained on proper use and injection technique before initiating Lyumjev. Patients should be told to:

- Always check insulin labels before administration.
- Inspect Lyumjev visually before use and discard for particulate matter or discolouration.
- Injection or infusion sites should always be rotated within the same region in order to reduce the risk of lipodystrophy and cutaneous amyloidosis (see section 4.4 and 4.8).
- Carry a spare or alternative administration method in case their delivery system breaks.

Subcutaneous injection

Lyumjev should be injected subcutaneously into the abdomen, upper arm, thigh or buttocks (see section 5.2).

Lyumjev should generally be used in combination with an intermediate or long-acting insulin. A different injection site should be used if injecting at the same time as another insulin.

When injecting a blood vessel should not be entered.

Devices should be discarded if any part looks broken or damaged.

The needle should be discarded after each injection.

Lyumjev vials
If subcutaneous administration by syringe is necessary, a vial should be used.

The syringe must have 100 units/mL markings.

Patients using vials must never share needles or syringes.

Lyumjev cartridges
Lyumjev in cartridges is only suitable for subcutaneous injections from a Lilly reusable pen.

Lyumjev cartridges should not be used with any other reusable pen as the dosing accuracy has not been established with other pens.

The instructions with each individual pen must be followed for loading the cartridge, attaching the needle and administering the insulin injection.

To prevent the possible transmission of disease, each cartridge must be used by one patient only, even if the needle on the delivery device is changed.

Lyumjev KwikPens and Lyumjev Tempo Pen
The KwikPen , Junior KwikPen and Tempo Pen are only suitable for subcutaneous injections.

Lyumjev KwikPens are available in two concentrations: Lyumjev 100 units/mL KwikPen and Lyumjev 200 units/mL KwikPen. See the separate SmPC for Lyumjev 200 units/mL KwikPen. The KwikPen delivers 1 - 60 units in steps of 1 unit in a single injection. The Lyumjev 100 units/mL Junior KwikPen delivers 0.5 - 30 units in steps of 0.5 units in a single injection.

The Lyumjev 100 units/ml Tempo Pen delivers 1 – 60 units in steps of 1 unit in a single injection.

The number of insulin units is shown in the dose window of the pen regardless of concentration and no dose conversion should be done when transferring a patient to a new concentration or to a pen with a different dose step.

Lyumjev 100 units/mL Junior KwikPen is suitable for patients who may benefit from finer insulin dose adjustments.

The Tempo Pen can be used with the optional transfer module Tempo Smart Button (see section 6.6). As with any insulin injection, when using the Tempo Pen, Tempo Smart Button and the mobile application, the patient should be instructed to check their blood sugar levels when considering or making decisions about another injection if they are unsure how much they have injected.

For detailed user instructions, please refer to the instructions for use provided with the package leaflet.

To prevent the possible transmission of disease, each pen must be used by one patient only, even if the needle is changed.

CSII (insulin pump)
Use a pump suitable for insulin infusion. Fill the pump reservoir from a Lyumjev 100 units/mL vial.

Patients using a pump should follow the instructions provided with the pump and infusion set.
Use the correct reservoir and catheter for the pump.

When filling the pump reservoir avoid damaging it by using the correct needle length on the filling system. 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 (see section 4.4).

Intravenous use

Lyumjev 100 units/mL is available in vials if administration of intravenous injection is necessary. This medicinal product must not be mixed with any other insulin or any other medicinal product except those mentioned in section 6.6.

For instructions on dilution of the medicinal product before administration, see section 6.6.

Intravenous administration of Lyumjev 100 units/mL must be performed under medical supervision.

4.3 Contraindications

Hypoglycaemia.
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered medicinal product should be clearly recorded.

Hypoglycaemia

Hypoglycaemia is the most common adverse reaction of insulin therapy. The timing of hypoglycaemia usually reflects the time-action profile of the administered insulin formulations. Hypoglycaemia may occur earlier after an injection/infusion when compared to other mealtime insulins due to the earlier onset of action of Lyumjev (see section 5.1).

Hypoglycaemia can happen suddenly and symptoms may differ in each individual and change over time in the same individual. Severe hypoglycaemia can cause seizures, may lead to unconsciousness, may be life-threatening, or cause death. Symptomatic awareness of hypoglycaemia may be less pronounced in patients with longstanding diabetes.

Hyperglycaemia

The use of inadequate doses or discontinuation of treatment, may lead to hyperglycaemia and diabetic ketoacidosis; conditions which are potentially lethal.

Patients should be educated to recognize the signs and symptoms of ketoacidosis and to get immediate help when ketoacidosis is suspected.

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.

Insulin requirements and dose adjustments

Changes in insulin, insulin concentration, manufacturer, type, or method of administration may affect glycaemic control and predispose to hypoglycaemia or hyperglycaemia. These changes should be made cautiously under close medical supervision and the frequency of glucose monitoring should be increased. For patients with type 2 diabetes, dose adjustments in concomitant anti-diabetic treatment may be needed (see sections 4.2 and 4.5).

In patients with renal or hepatic impairment, glucose monitoring should be intensified and dose adjusted on an individual basis (see section 4.2).

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. Exercise taken immediately after a meal may increase the risk of hypoglycaemia.

Hyperglycaemia and ketoacidosis due to insulin pump device malfunction

Malfunction of the insulin pump or insulin infusion set can rapidly lead to hyperglycaemia and ketoacidosis. Prompt identification and correction of the cause of hyperglycaemia or ketosis is necessary. Interim subcutaneous injections with Lyumjev may be required.

Thiazolidinediones (TZDs) used in combination with insulin

TZDs can cause dose-related fluid retention, particularly when used in combination with insulin. Fluid retention may lead to or exacerbate heart failure. Patients treated with insulin and a TZD should be observed for signs and symptoms of heart failure. If heart failure develops, consider discontinuation of the TZD.

Hypersensitivity and allergic reactions

Severe, life-threatening, generalised allergy, including anaphylaxis, can occur with insulin medicinal products, including Lyumjev. If hypersensitivity reactions occur, discontinue Lyumjev.

Medication errors

Lyumjev should not be used by patients with visual impairment without help of a trained person.

To avoid medication errors between Lyumjev and other insulins, patients need to always check the insulin label before each injection.

Patients should always use a new needle for each injection to prevent infections and a blocked needle. In the event of a blocked needle it should be replaced with a new needle.

Tempo Pen

The Tempo Pen contains a magnet (see section 6.5) that may interfere with the functions of an implantable electronic medical device, such as a pacemaker. The magnetic field extends to approximately 1.5 cm.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e., essentially "sodium-free".

4.5 Interaction with other medicinal products and other forms of interaction

The following substances may reduce insulin requirement: Antidiabetic medicinal products (oral or injectable), salicylates, sulphonamides, certain antidepressants (monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors), angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor blocking agents, or somatostatin analogues.

The following substances may increase insulin requirement: oral contraceptives, corticosteroids, thyroid hormones, danazol, sympathomimetic agents, diuretics, or growth hormone.

Alcohol may increase or decrease the blood glucose lowering effect of Lyumjev. Consumption of large amounts of ethanol concomitantly with insulin use may lead to severe hypoglycaemia.

Beta-blockers may blunt the signs and symptoms of hypoglycaemia.

TZDs can cause dose-related fluid retention, particularly when used in combination with insulin, and exacerbate heart failure (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

A large amount of data on pregnant women (more than 1 000 pregnancy outcomes) indicate no malformative nor feto/neonatal toxicity of insulin lispro. Lyumjev can be used during pregnancy if clinically needed.

It is essential to maintain good control of an insulin-treated (insulin-dependent or gestational) diabetes patient throughout pregnancy. Insulin requirements usually fall during the first trimester and increase during the second and third trimesters. After delivery, insulin requirements normally return rapidly to pre-pregnancy values. Patients with diabetes should be advised to inform their doctor if they are pregnant or are contemplating pregnancy. Careful monitoring of glucose control is essential in pregnant patients with diabetes.

Breast-feeding

Lyumjev can be used during breast-feeding. Patients with diabetes who are breast-feeding may require adjustments in insulin dose, diet or both.

Fertility

Insulin lispro did not induce fertility impairment in animal studies.

4.7 Effects on ability to drive and use machines

The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or using machinery).

Patients should be advised to take precautions to avoid hypoglycaemia whilst driving, this is particularly important in those patients who have reduced or absent awareness of the warning signs of hypoglycaemia or have frequent episodes of hypoglycaemia. The advisability of driving should be considered in these circumstances.

4.8 Undesirable effects

Summary of safety profile

The most frequently reported adverse reaction during treatment is hypoglycaemia (very common) (see sections 4.2, 4.4 and 4.9).

The following related adverse reactions from clinical trials are listed below as MedDRA preferred term by system organ class and in order of decreasing incidence (very common: ≥ 1/10; common: ≥ 1/100 to < 1/10; uncommon: ≥ 1/1 000 to < 1/100; rare: ≥ 1/10 000 to < 1/1 000; very rare: < 1/10 000) and not known (cannot be estimated from the available data).

Table 1. Adverse reactions

MedDRA System Organ Class	Very common	Common	Uncommon	Not known
Metabolism and nutrition disorders	Hypoglycaemia			
Skin and subcutaneous tissue disorders			Lipodystrophy Rash Pruritus	Cutaneous amyloidosis
General disorders and administration site conditions	Infusion site reactions[a]	Injection site reactions[b] Allergic reactions[c]	Oedema	

[a]Reported in PRONTO-Pump-2
[b]Reported in PRONTO-T1D,PRONTO-T2D and PRONTO-Peds
[c]See section 4.8 Description of selected adverse events

Description of selected adverse reactions

Hypoglycaemia

Hypoglycaemia is the most commonly observed adverse reaction in patients using insulin. The incidence of severe hypoglycaemia in the 26 week Phase 3 adult clinical studies was 5.5 % in patients with type 1 diabetes mellitus and 0.9 % in patients with type 2 diabetes (see tables 2 and 3). In Study PRONTO-Peds, severe hypoglycaemia was reported in 0.7 % of paediatric patients treated with Lyumjev.

The symptoms of hypoglycaemia usually occur suddenly. They may include listlessness, confusion, palpitations, sweating, vomiting, and headache.

There were no clinically significant differences in the frequency of hypoglycaemia with administration of Lyumjev or the comparator (another medicinal product containing insulin lispro) across all studies. In studies where Lyumjev and the comparator were administered at different times relative to meals, there were no clinically relevant differences in the frequency of hypoglycaemia.

Hypoglycaemia may occur earlier after an injection/infusion of Lyumjev compared to other mealtime insulins due to the earlier onset of action.

Allergic reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, generalized skin reactions, angioedema, bronchospasm, hypotension, and shock may occur with any insulin, including Lyumjev.

Injection / Infusion site reactions

As with other insulin therapy, patients may experience rash, redness, inflammation, pain, bruising or itching at the site of Lyumjev injection or infusion.

In Studies PRONTO-T1D and PRONTO-T2D (multiple-dose injection [MDI] administration), injection site reactions occurred in 2.7 % of adult patients treated with Lyumjev. These reactions were usually mild and normally disappeared during continued treatment. Of the 1 116 patients who received Lyumjev, 1 discontinued treatment due to injection site reactions (< 0.1 %).

In Study PRONTO-Peds, injection site reactions occurred in 6.2 % of paediatric patients treated with Lyumjev. These events were mild or moderate. Of the 418 patients treated with Lyumjev, 2 discontinued treatment due to injection site reactions (< 0.5 %).

In Study PRONTO-Pump-2, infusion site reactions were reported in 38 % of patients treated with Lyumjev. The majority of these events were mild. Of the 215 patients treated with Lyumjev, 7 discontinued treatment due to infusion site reactions (3.3 %).

Immunogenicity

Administration of insulin can cause formation of insulin antibodies. The presence of anti-drug antibodies did not have a clinically meaningful effect on the pharmacokinetics, efficacy, or safety of Lyumjev.

Skin and subcutaneous tissue disorders

Lipodystrophy and cutaneous amyloidosis may occur at the injection site and delay local insulin absorption. Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions (see section 4.4).

Oedema

Cases of oedema have been reported with insulin therapy, particularly if previous poor metabolic control is improved by intensified insulin therapy.

Paediatric population

Safety and efficacy have been investigated in a therapeutic confirmatory trial in children with type 1 diabetes aged 3 to < 18 years. In the trial, 418 patients were treated with Lyumjev. The frequency, type and severity of adverse reactions observed in the paediatric population is consistent with the safety profile in adult patients.

Other special populations

Based on results from clinical trials with insulin lispro in general, the frequency, type and severity of adverse reactions observed in elderly patients and in patients with renal or hepatic impairment do not indicate any differences to the broader experience in the general population. The safety information in very elderly patients (≥ 75 years) or patients with moderate to severe renal impairment or hepatic impairment is limited (see section 5.1).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Overdose causes hypoglycaemia with accompanying symptoms that include listlessness, confusion, palpitations, sweating, vomiting, and headache.

Hypoglycaemia may occur as a result of an excess of insulin lispro relative to food intake, energy expenditure, or both. Mild episodes of hypoglycaemia usually can be treated with oral glucose. More severe episodes with coma, seizure, or neurologic impairment may be treated with glucagon or concentrated intravenous glucose. Sustained carbohydrate intake and observation may be necessary because hypoglycaemia may recur after apparent clinical recovery. Adjustments in drug dose, meal patterns, or exercise may be needed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in diabetes, insulins and analogues for injection, fast-acting, ATC code: A10AB04.

Mechanism of action

The primary activity of Lyumjev is the regulation of glucose metabolism. Insulins, including insulin lispro, the active substance in Lyumjev, exert their specific action through binding to insulin receptors. Receptor-bound insulin lowers blood glucose by stimulating peripheral glucose uptake by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulins inhibit lipolysis and proteolysis, and enhance protein synthesis.

Lyumjev is a formulation of insulin lispro that contains citrate and treprostinil. Citrate increases local vascular permeability and treprostinil induces local vasodilation to achieve accelerated absorption of insulin lispro.

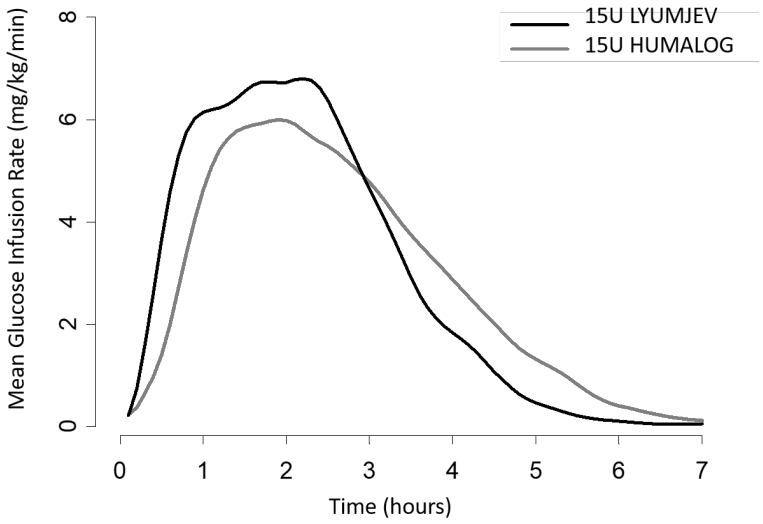
Pharmacodynamic effects

Early and late insulin action

A glucose clamp study was conducted in 40 type 1 diabetes patients given Lyumjev and Humalog subcutaneously as a single 15 unit dose. Results are provided in Figure 1. Lyumjev has been shown to be equipotent to Humalog on a unit for unit basis but its effect is more rapid with a shorter duration of action.

- Onset of action of Lyumjev was 20 minutes post dose, 11 minutes faster than Humalog.
- During the first 30 minutes post dose, Lyumjev had a 3-fold greater glucose lowering effect compared to Humalog.
- Maximum glucose-lowering effect of Lyumjev occurred between 1 and 3 hours after injection.
- The late insulin action, from 4 hours until the end of the glucose clamp, was 54 % lower with Lyumjev than observed with Humalog.
- The duration of action of Lyumjev was 5 hours, 44 minutes shorter than Humalog.
- The total glucose infused during the clamp was comparable between Lyumjev and Humalog.

Figure 1. Mean glucose infusion rate (GIR) in patients with type 1 diabetes after subcutaneous injection of Lyumjev or Humalog (15 unit dose)



Similarly, a faster early insulin action and a reduced late insulin action was observed with Lyumjev in type 2 diabetes patients.

Total and maximum glucose lowering effect of Lyumjev increased with dose within the therapeutic dose range. The early onset and total insulin action were similar when Lyumjev was administered in the abdomen, upper arm, or thigh.

Postprandial Glucose (PPG) Lowering

Lyumjev reduced the PPG during a standardized test meal over the complete 5 hour test meal period (change from premeal AUC(0 – 5 h)) compared to Humalog.

- In patients with type 1 diabetes, Lyumjev reduced the PPG during the 5 hour test meal period by 32 % when given at the start of the meal and 18 % when given 20 minutes after the start of the meal compared to Humalog.
- In patients with type 2 diabetes, Lyumjev reduced the PPG during the 5 hour test meal period by 26 % when given at the start of the meal and 24 % when given 20 minutes after the start of the meal compared to Humalog.

Comparison of Lyumjev 200 units/mL and Lyumjev 100 units/mL

The maximum and total glucose lowering were comparable for Lyumjev 200 units/mL or Lyumjev 100 units/mL. No dose conversion is required if transferring a patient between the strengths.

Clinical efficacy and safety

The efficacy of Lyumjev was evaluated in 4 randomised, active controlled trials in adults and 1 randomised, active controlled trial in paediatric patients with type 1 diabetes.

Type 1 Diabetes – Adults

PRONTO-T1D was a 26 week, treat-to-target, trial that evaluated the efficacy of Lyumjev in 1222 patients on multiple daily injection therapy. Patients were randomised to either blinded mealtime Lyumjev, blinded mealtime Humalog, or open-label postmeal Lyumjev, all in combination with either insulin glargine or insulin degludec. Mealtime Lyumjev or Humalog was injected 0 to 2 minutes before the meal and postmeal Lyumjev was injected 20 minutes after the start of the meal.

Efficacy results are provided in Table 2 and Figure 2.

37.4 % of patients treated with mealtime Lyumjev, 33.6 % of patients treated with mealtime Humalog and 25.6 % of patients treated with postmeal Lyumjev reached a target HbA1c of < 7 %.

Basal, bolus and total insulin doses were similar among study arms at 26 weeks.

Following the 26 week period, the two blinded treatment arms continued to 52 weeks. HbA1c was not statistically significantly different between treatments at the 52 week endpoint.

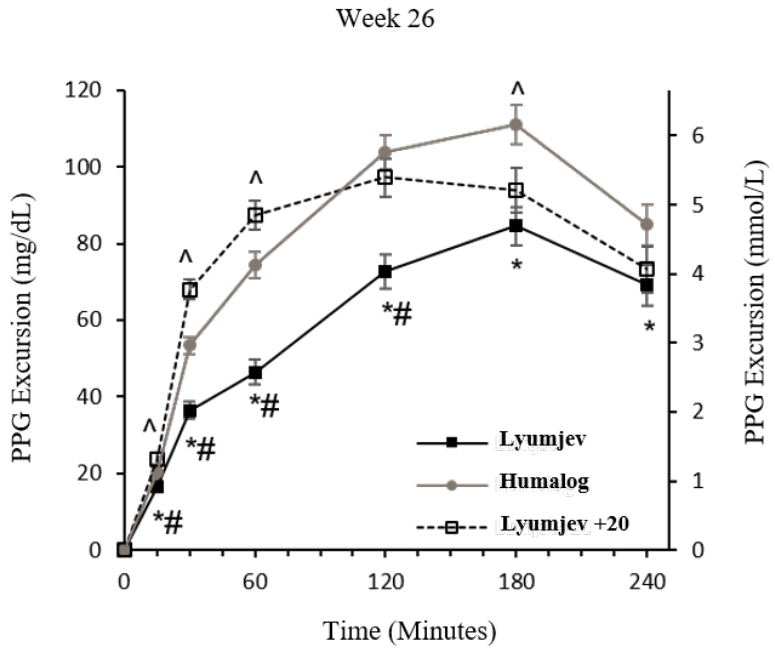
Table 2 Results from 26 week basal-bolus clinical trial in patients with type 1 diabetes

	Mealtime Lyumjev + basal insulin	**Mealtime Humalog + basal insulin**	**Postmeal Lyumjev + basal insulin**
Number of randomised subjects (N)	451	442	329
HbA_{1c} (%)			
Baseline → week 26	7.34 → 7.21	7.33→7.29	7.36→7.42
Change from baseline	-0.13	-0.05	0.08
Treatment difference	-0.08 [-0.16, -0.00][C]		0.13 [0.04, 0.22][D]
HbA_{1c} (mmol/mol)			
Baseline → week 26	56.7→55.3	56.7→56.1	56.9→57.6
Change from baseline	-1.4	-0.6	0.8
Treatment difference	-0.8 [-1.7, 0.00][C]		1.4 [0.5, 2.4][D]
1 hour postprandial glucose excursion (mg/dL) [A]			
Baseline → week 26	77.3 →46.4	71.5 →74.3	76.3→87.5
Change from baseline	-28.6	-0.7	12.5
Treatment difference	-27.9 [-35.3, -20.6][C,E]		13.2 [5.0, 21.4][D]
1 hour postprandial glucose excursion (mmol/L) [A]			
Baseline → week 26	4.29→2.57	3.97 →4.13	4.24→4.86
Change from baseline	-1.59	-0.04	0.70
Treatment difference	-1.55[-1.96, -1.14][C,E]		0.73 [0.28,1.19][D]
2 hour postprandial glucose excursion (mg/dL) [A]			
Baseline → week 26	112.7→72.7	101.6 →103.9	108.0 →97.2
Change from baseline	-34.7	-3.5	-10.2
Treatment difference	-31.2 [-41.1, -21.2][C,E]		-6.7 [-17.6, 4.3] [D].
2 hour postprandial glucose excursion (mmol/L) [A]			
Baseline → week 26	6.26→4.04	5.64→5.77	5.99→5.40
Change from baseline	-1.93	-0.20	-0.56
Treatment difference	-1.73 [-2.28, -1.18][C,E]		-0.37 [-0.98, -0.24][D]
Body weight (Kg)			
Baseline → week 26	77.3→77.9	77.3→78.2	77.6→78.1
Change from baseline	0.6	0.8	0.7
Treatment difference	-0.2 [-0.6, 0.1][A]		-0.1[-0.5, 0.3][D]
Severe hypoglycaemia [B] **(% of patients)**	5.5 %	5.7 %	4.6 %

Week 26 and change from baseline values are based on the least-squares means (adjusted means).
The 95 % confidence interval is stated in '*[ ]*'.
[A] Meal test
[B] Severe hypoglycaemia is defined as episode requiring assistance of another person due to patient's neurological impairment.

[C] The difference is for mealtime Lyumjev – mealtime Humalog.
[D] The difference is for postmeal Lyumjev – mealtime Humalog.
[E] Statistically significant in favour of mealtime Lyumjev.

Figure 2. Time course of blood glucose excursion during mixed-meal tolerance test at week 26 in patients with type 1 diabetes



PPG = Postprandial glucose
Lyumjev and Humalog administered at mealtime
Lyumjev + 20 = Lyumjev was injected 20 minutes after the start of the meal.
*p < 0.05 for pairwise comparison on Lyumjev versus Humalog
^p < 0.05 for pairwise comparison on Lyumjev +20 versus Humalog
#p < 0.05 for pairwise comparison on Lyumjev +20 versus Lyumjev

Continuous glucose monitoring (CGM) in Type 1 Diabetes – Adults

A subset of patients (N = 269) participated in an evaluation of the 24 hour ambulatory glucose profiles captured with blinded CGM. At the 26 week assessment, patients treated with mealtime Lyumjev demonstrated statistically significant improvement in PPG control during CGM assessment of glucose excursions or incremental area under the curve (AUC) 0 - 2 hours, 0 - 3 hours, and 0 - 4 hours after meals compared to patients treated with Humalog. Patients treated with mealtime Lyumjev reported statistically significantly longer time in range (6 am to midnight) with 603 minutes in range, (3.9 to 10 mmol/L, 71 – 180 mg/dL), and 396 minutes in range (3.9 to 7.8 mmol/L, 71 to 140 mg/dL), 44 and 41 minutes longer than Humalog patients respectively.

Type 2 Diabetes – Adults

PRONTO-T2D was a 26 week, treat-to-target trial that evaluated the efficacy of Lyumjev in 673 patients were randomised to either blinded mealtime Lyumjev or to blinded mealtime Humalog, both in combination with a basal insulin (insulin glargine or insulin degludec) in a basal-bolus regimen. Mealtime Lyumjev or mealtime Humalog was injected 0 - 2 minutes before the meal. Efficacy results are provided in Table 3 and Figure 3.

58.2 % of patients treated with mealtime Lyumjev and 52.5 % of patients treated with mealtime Humalog reached a target HbA1c of < 7 %.

Basal, bolus and total insulin doses were similar among study arms at the end of the trial.

Table 3 Results from 26 week basal-bolus clinical trial in patients with type 2 diabetes

	Mealtime Lyumjev + basal insulin	**Mealtime Humalog + basal insulin**
Number of randomised subjects (N)	336	337
HbA_{1c} (%)		
Baseline → week 26	7.28→6.92	7.31→6.86
Change from baseline	-0.38	-0.43
Treatment difference	0.06 [-0.05, 0.16]	
HbA_{1c} (mmol/mol)		
Baseline → week 26	56.0→52.1	56.4→51.5
Change from baseline	-4.1	-4.7
Treatment difference	0.6 [-0.6, 1.8]	
1 hour postprandial glucose excursion (mg/dL)[A]		
Baseline → week 26	76.6→63.1	77.1→74.9
Change from baseline	-13.8	-2.0
Treatment difference	-11.8 [-18.1, -5.5][C]	
1 hour postprandial glucose excursion (mmol/L)[A]		
Baseline → week 26	4.25→3.50	4.28→4.16
Change from baseline	-0.77	-0.11
Treatment difference	-0.66 [-1.01, -0.30][C]	
2 hour postprandial glucose excursion (mg/dL)[A]		
Baseline → week 26	99.3→80.4	99.6→97.8
Change from baseline	-19.0	-1.6
Treatment difference	-17.4 [-25.3, -9.5][C]	
2 hour postprandial glucose excursion (mmol/L)[A]		
Baseline → week 26	5.51→4.47	5.53→5.43
Change from baseline	-1.06	-0.09
Treatment difference	-0.96 [-1.41, -0.52][C]	
Body weight (Kg)		
Baseline → week 26	89.8→91.3	90.0 →91.6
Change from baseline	1.4	1.7
Treatment difference	-0.2 [-0.7, 0.3]	
Severe hypoglycaemia (% of patients)[B]	0.9 %	1.8 %

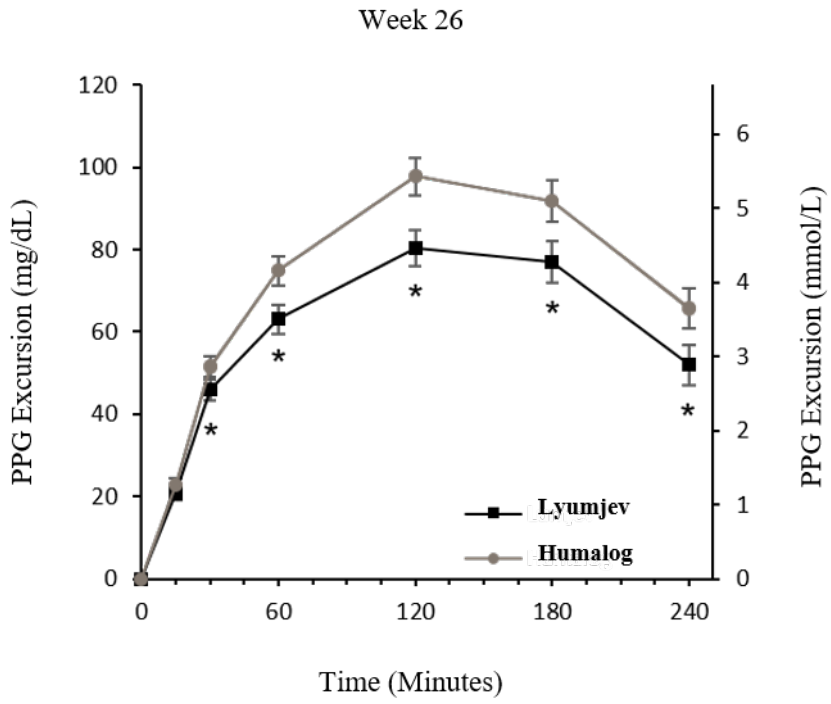
Week 26 and change from baseline values are based on the least-squares means (adjusted means).
The 95 % confidence interval is stated in '*[ ]*'. The difference is for mealtime Lyumjev – mealtime Humalog.

[A] Meal test

[B] Severe hypoglycaemia is defined as episode requiring assistance of another person due to patient's neurological impairment.

[C] Statistically significant in favour of mealtime Lyumjev.

Figure 3. Time course of blood glucose excursion during mixed-meal tolerance test at week 26 in patients with type 2 diabetes



PPG = Postprandial glucose
Lyumjev and Humalog administered at mealtime
Data are LSM (SE), *p < 0.05

Type 1 Diabetes – Adults. CSII

PRONTO-Pump was a 12 week cross over design (2 periods of 6 weeks), double-blind, trial that evaluated the compatibility and safety of Lyumjev and Humalog with an external CSII System in patients who wore a continuous glucose monitor throughout the study. There were no statistically significant treatment difference in the rate or incidence of infusion set failures (n = 49).

In period 1 of the cross over study, Lyumjev had a numerically greater reduction in mean HbA1c than Humalog. Lyumjev reduction was -0.39 % [- 4.23 mmol/mol] from a baseline of 6.97 % [52.68 mmol/mol] and Humalog reduction was - 0.25 % [- 2.78 mmol/mol] from a baseline of 7.17 % [54.89 mmol/mol]. Lyumjev had a statistically significantly longer mean duration of time with glucose in target ranges 71 – 140 mg/dL (3.9 to 7.8 mmol/L) within 1 and 2 hours after the start of breakfast compared to Humalog.

PRONTO-Pump-2 was a 16 week randomised (1:1), double-blind, trial that evaluated the efficacy of Lyumjev in 432 patients with type 1 diabetes currently using continuous subcutaneous insulin infusion. Patients were randomised to either blinded Lyumjev (N = 215) or blinded Humalog (N = 217). Mealtime Lyumjev or Humalog boluses were initiated 0 to 2 minutes before the meal.

At week 16, Lyumjev was non-inferior to Humalog in reducing HbA1c. Lyumjev reduction was -0.06 % [- 0.7 mmol/mol] from a baseline of 7.56 % [59.1 mmol/mol] and Humalog reduction was -0.09 % [- 1.0 mmol/mol] from a baseline of 7.54 % [58.9 mmol/mol]. The treatment difference was 0.02 % [95 % CI: - 0.06, 0.11] and 0.3 mmol/mol [95 % CI: - 0.6, 1.2], respectively compared to Humalog.

Following a standardized test meal, treatment with Lyumjev demonstrated statistically significantly lower 1 hour and 2 hour postprandial glucose. The treatment difference was - 1.34 mmol/L [95 % CI: - 2.00, - 0.68] and -1.54 mmol/L [95 % CI:- 2.37, - 0.72], respectively compared to Humalog.

Special populations

Elderly
In the two 26 week clinical studies (PRONTO-T1D and PRONTO-T2D), 187 of 1 116 (17 %) Lyumjev treated patients with type 1 diabetes or type 2 diabetes were ≥ 65 years of age and 18 of 1 116 (2 %) were ≥ 75 years of age. No overall differences in safety or effectiveness were observed between elderly patients and younger patients.

Paediatric population

PRONTO-Peds was a 26-week, randomised (2:2:1), treat-to-target, trial that evaluated the efficacy of Lyumjev in 716 patients with type 1 diabetes, aged 3 to < 18 years. Patients were randomised to either blinded mealtime Lyumjev (N = 280), blinded mealtime Humalog (N = 298), or open-label postmeal Lyumjev (N = 138), all in combination with basal insulin (insulin glargine, insulin degludec or insulin detemir). Mealtime Lyumjev or Humalog was injected 0 to 2 minutes before the meal and postmeal Lyumjev was injected within 20 minutes after the start of the meal.

Insulin doses were similar in all treatment groups at baseline and at 26 weeks.

Table 4. Results from 26 week PRONTO-Peds trial in paediatric patients with type 1 diabetes

	Mealtime Lyumjev + basal insulin	**Mealtime Humalog + basal insulin**	**Postmeal Lyumjev + basal insulin**
Number of randomised subjects (N)	280	298	138
HbA_{1c} (%) (mean)			
Baseline → week 26	7.78 → 7.85	7.81 → 7.88	7.77 → 7.86
Change from baseline	0.06	0.09	0.07
Treatment difference	-0.02 [-0.17, 0.13][A]		-0.02 [-0.20, 0.17][B]
HbA_{1c} (mmol/mol)			
Baseline → week 26	61.6 → 62.4	61.8 → 62.6	61.4 → 62.4
Change from baseline	0.71	0.94	0.77
Treatment difference	-0.23 [-1.84, 1.39][A]		-0.17 [-2.15, 1.81][B]

Week 26 and change from baseline values are based on the least-squares means (adjusted means).
The 95 % confidence interval is stated in '*[ ]*'.
[A]The difference is for mealtime Lyumjev – mealtime Humalog.
[B] The difference is for postmeal Lyumjev – mealtime Humalog.

5.2 Pharmacokinetic properties

Absorption

Absorption of insulin lispro was accelerated and the duration of exposure was shorter in healthy subjects and patients with diabetes following injection of Lyumjev compared to Humalog. In patients with type 1 diabetes:

- Insulin lispro appeared in circulation approximately 1 minute after injection of Lyumjev, which was five minutes faster than Humalog .
- Time to 50 % maximum concentration was 14 minutes shorter with Lyumjev compared to Humalog.

- Following injection of Lyumjev, there was seven times more insulin lispro in circulation during the first 15 minutes compared to Humalog and three times more insulin lispro during the first 30 minutes compared to Humalog.
- After administration of Lyumjev the time to maximum insulin lispro concentration was achieved at 57 minutes.
- Following injection of Lyumjev there was 41 % less insulin lispro in circulation after 3 hours following injection compared to Humalog.
- The duration of insulin lispro exposure for Lyumjev was 60 minutes shorter compared to Humalog.
- The total insulin lispro exposure (ratio and 95 % CI of 1.03 (0.973, 1.09) and maximum concentration (ratio and 95 % CI of 1.06 (0.97, 1.16) were comparable between Lyumjev and Humalog.

In type 1 patients, the day-to-day variability [CV %] of Lyumjev was 13 % for total insulin lispro exposure (AUC, 0 - 10h) and 23 % for maximum insulin lispro concentration ($C_{max)}$.The absolute bioavailability of insulin lispro after subcutaneous administration of Lyumjev in the abdomen, upper arm and thigh was approximately 65 %. The accelerated absorption of insulin lispro is maintained regardless of injection site (abdomen, upper arm and thigh). No exposure data are available following injection in the buttocks.

Maximum concentration and time to maximum concentration were comparable for the abdomen and upper arm regions; time to maximum concentration was longer and maximum concentration lower for the thigh.

Total insulin lispro exposure and maximum insulin lispro concentration increased proportionally with increasing subcutaneous doses of Lyumjev within the dose range from 7U to 30U.

CSII

The absorption of insulin lispro was accelerated when Lyumjev was administered by CSII in patients with type 1 diabetes.
- Time to reach 50 % maximum concentration was 14 minutes, 9 minutes shorter than for Humalog.
- Following administration of Lyumjev, 1.5 times more insulin lispro was available during the first 30 minutes compared to Humalog.

Comparison of Lyumjev 200 units/mL and Lyumjev 100 units/mL

The results of a study in healthy subjects demonstrated that Lyumjev 200 units/mL is bioequivalent to Lyumjev 100 units/mL following administration of a single 15 unit dose for the area under serum insulin lispro concentration-time curve from time zero to infinity and maximum insulin lispro concentration. The accelerated insulin lispro absorption after administration of 200 units/mL was similar to that observed with Lyumjev 100 units/mL. No dose conversion is required if transferring a patient between the strengths.

Distribution

The geometric mean (% coefficient of variation [CV %]) volume of distribution of insulin lispro (Vd) was 34 L (30 %) after intravenous administration of Lyumjev as a bolus injection of a 15 unit dose in healthy subjects.

Elimination

The geometric mean (CV %) clearance of insulin lispro was 32 L/hour (22 %) and the median half-life of insulin lispro was 44 minutes after intravenous administration of Lyumjev as a bolus injection of a 15 unit dose in healthy subjects.

Special populations

Age, gender, and race did not affect the pharmacokinetics and pharmacodynamics of Lyumjev.

Paediatric population

Children (8 - 11 years) and adolescents (12 - 17 years) with type 1 diabetes on multiple daily injection (MDI) and CSII therapy were studied in a cross-over design to assess the insulin lispro pharmacokinetics and pharmacodynamics following a 0.2 U/kg dose of Lyumjev and Humalog.

The pharmacokinetic differences between Lyumjev and Humalog were, overall, similar in children and adolescents as observed in adults. Following a subcutaneous injection, Lyumjev showed an accelerated absorption with a higher early insulin lispro exposure in children (8 – 11 years) and adolescents (12 – 17 years) whilst maintaining a similar total exposure, maximum concentration and time to maximum concentration compared to Humalog. Following a subcutaneous bolus infusion with CSII therapy, there was a trend towards an accelerated absorption in children and adolescents whilst total exposure, maximum concentration and time to maximum concentration were similar compared to Humalog.

Patients with renal and hepatic impairment

Renal and hepatic impairment is not known to impact the pharmacokinetics of insulin lispro.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development after exposure to insulin lispro.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol
Magnesium chloride hexahydrate
Metacresol
Sodium citrate dihydrate
Treprostinil sodium
Zinc oxide
Water for injections
Hydrochloric acid and sodium hydroxide (for pH adjustment)

6.2 Incompatibilities

This medicinal product must not be mixed with any other insulin or any other medicinal product except those mentioned in section 6.6.

6.3 Shelf life

Lyumjev 100 units/mL solution for injection in cartridge
Lyumjev 100 units/mL KwikPen solution for injection in pre-filled pen
Lyumjev 100 units/mL Junior KwikPen solution for injection in pre-filled pen
Lyumjev 100 units/mL Tempo Pen solution for injection in pre-filled pen

Before use
3 years

After first use
28 days

Lyumjev 100 units/mL solution for injection in vial

Before use
2 years

After first use
28 days

When the vial is diluted for intravenous use
Chemical, physical in-use stability has been demonstrated for 14 days at 2–8 °C and 20 hours at 20-25 °C when protected from light. From a microbiological point of view, the medicinal product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would not normally be longer than 24 hours at 2-8 °C, unless dilution has taken place in controlled and validated aseptic conditions (see section 6.6).

6.4 Special precautions for storage

Before use

Store in the refrigerator (2 °C - 8 °C).
Do not freeze.
Store in the original package in order to protect from light

After first use

Do not store above 30 °C.
Do not freeze.

Lyumjev 100 units/mL solution for injection in vial

Store in the original package in order to protect from light.

Lyumjev 100 units/mL solution for injection in cartridge

Do not refrigerate.
Keep the cap on the pen once cartridge inserted, in order to protect from light.

Lyumjev 100 units/mL KwikPen solution for injection in pre-filled pen
Lyumjev 100 units/mL Junior KwikPen solution for injection in pre-filled pen
Lyumjev 100 units/mL Tempo Pen solution for injection in pre-filled pen

Do not refrigerate.
Keep the cap on the pen in order to protect from light.

6.5 Nature and contents of container

Lyumjev 100 units/mL solution for injection in vial

Type I clear glass vials, sealed with halobutyl stoppers and secured with aluminium seals.

10 mL vial: Packs of 1 or 2 vials or 5 (5 packs of 1) vials.

Lyumjev 100 units/mL solution for injection in cartridge

Type I clear glass cartridges, sealed with disc seals secured with aluminium seals and halobutyl plungers.

3 mL cartridge: Packs of 2, 5 or 10 cartridges.

Lyumjev 100 units/mL KwikPen solution for injection in pre-filled pen

Type I clear glass cartridges, sealed with disc seals secured with aluminium seals and halobutyl plungers.

The 3 mL cartridges are sealed in a disposable pen injector KwikPen .

The medicinal product is packed in a white carton with dark blue bands and an image of the pen. The KwikPen is taupe, the dose knob is blue with raised ridges on side.

3 mL KwikPen: Packs of 2 pre-filled pens, 5 pre-filled pens or a multipack of 10 (2 packs of 5) pre-filled pens.

Lyumjev 100 units/mL Junior KwikPen solution for injection in pre-filled pen

Type I clear glass cartridges, sealed with disc seals secured with aluminium seals and halobutyl plungers.

The 3 mL cartridges are sealed in a disposable pen injector Junior KwikPen.

The medicinal product is packed in a white carton with stripes of peach, light blue and dark blue bands and an image of the pen. The Junior KwikPen is taupe, the dose knob is peach with raised ridges on end and side.

3 mL Junior KwikPen: Packs of 2 pre-filled pens, 5 pre-filled pens or a multipack of 10 (2 packs of 5) pre-filled pens.

Lyumjev 100 units/mL Tempo Pen solution for injection in pre-filled pen

Type I clear glass cartridges, sealed with disc seals secured with aluminium seals and halobutyl plungers.

The 3 mL cartridges are sealed in a disposable pen injector Tempo Pen. The Tempo Pen contains a magnet (see section 4.4).

The medicinal product is packed in a white carton with stripes of dark blue and green bands. The Tempo Pen is taupe, the dose knob is blue with raised ridges around the entire side.

3 mL Tempo Pen: Packs of 5 pre-filled pens or a multipack of 10 (2 packs of 5) pre-filled pens.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Lyumjev should look clear and colourless. It should not be used if it is cloudy, coloured, or has particles or clumps in it.

Lyumjev should not be used if it has been frozen.

A new needle must always be attached before each use. Needles must not be re-used. Needles are not included.

Lyumjev 100 units/mL solution for injection in vial

Intravenous use

Lyumjev 100 units/mL vial can be diluted to concentrations of 0.1 to 1.0 unit/mL in 5 % glucose solution for injection or sodium chloride 9 mg/mL (0.9 %) solution for injection for intravenous use. Compatibility has been demonstrated in ethylene-propylene copolymer and polyolefin with polyvinyl chloride bags.

It is recommended that the system is primed before starting the infusion to the patient.

CSII

Lyumjev 100 units/mL vial can be used to fill a continuous insulin infusion pump for a maximum of 9 days. Tubings in which the inner surface materials are made of polyethylene or polyolefin have been evaluated and found compatible with pump use.

Lyumjev 100 units/mL Tempo Pen solution for injection in pre-filled pen

The Tempo Pen is designed to work with the Tempo Smart Button. The Tempo Smart Button is an optional product that can be attached to the Tempo Pen dose knob and aids in transmitting Lyumjev dose information from the Tempo Pen to a compatible mobile application. The Tempo Pen injects insulin with or without the Tempo Smart Button attached. To transmit data to the mobile application, follow the instructions provided with the Tempo Smart Button and the instructions with the mobile application.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V., Papendorpseweg 83, 3528 BJ Utrecht, The Netherlands.

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1422/001
EU/1/20/1422/002
EU/1/20/1422/003
EU/1/20/1422/004
EU/1/20/1422/005
EU/1/20/1422/006
EU/1/20/1422/007
EU/1/20/1422/008
EU/1/20/1422/009
EU/1/20/1422/010
EU/1/20/1422/011
EU/1/20/1422/012
EU/1/20/1422/016
EU/1/20/1422/017

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24 March 2020

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 200 units/mL KwikPen solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL contains 200 units insulin lispro*(equivalent to 6.9 mg).

Each pre-filled pen contains 600 units of insulin lispro in 3 mL solution.

Each KwikPen delivers 1 - 60 units in steps of 1 unit in a single injection.

* produced in *E.coli* by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless, aqueous solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of diabetes mellitus in adults.

4.2 Posology and method of administration

Posology

Lyumjev is a mealtime insulin for subcutaneous injection and should be administered zero to two minutes before the start of the meal, with the option to administer up to 20 minutes after starting the meal (see section 5.1).

The initial dose should take into account the type of diabetes, weight of the patient and their blood glucose levels.

The early onset of action must be considered when prescribing Lyumjev (see section 5.1). Continued adjustment of the dose of Lyumjev should be based on the patient's metabolic needs, blood glucose monitoring results, and glycaemic control goal. Dose adjustments may be needed, when switching from another insulin, with changes in physical activity, changes in concomitant medicinal products, changes in meal patterns (i.e., amount and type of food, timing of food intake), changes in renal or hepatic function or during acute illness to minimize the risk of hypoglycaemia or hyperglycaemia (see sections 4.4 and 4.5).

Switching from another mealtime insulin medicinal product

If converting from another mealtime insulin to Lyumjev, the change can be done on a unit-to-unit basis. The potency of insulin analogues, including Lyumjev, is expressed in units. One (1) unit of Lyumjev corresponds to 1 international unit (IU) of human insulin or 1 unit of other fast-acting insulin analogues.

Missed doses

Patients who forget a mealtime dose should monitor their blood glucose level to decide if an insulin dose is needed, and to resume their usual dosing schedule at the next meal.

Special populations

Elderly (≥ 65 years old)
The safety and efficacy of Lyumjev has been established in elderly patients aged 65 to 75 years. Close glucose monitoring is recommended and the insulin dose should be adjusted on an individual basis (see sections 4.8, 5.1 and 5.2). The therapeutic experience in patients ≥ 75 years of age is limited.

Renal impairment
Insulin requirements may be reduced in the presence of renal impairment. In patients with renal impairment, glucose monitoring should be intensified and the dose adjusted on an individual basis.

Hepatic impairment
Insulin requirements may be reduced in patients with hepatic impairment due to reduced capacity for gluconeogenesis and reduced insulin breakdown. In patients with hepatic impairment, glucose monitoring should be intensified and the dose adjusted on an individual basis.

Paediatric population
The safety and efficacy of Lyumjev 200 units/mL in children and adolescents below 18 years of age have not been established

Method of administration

Patients should be trained on proper use and injection technique before initiating Lyumjev. Patients should be told to:

- Always check insulin labels before administration.
- Inspect Lyumjev visually before use and discard for particulate matter or discolouration.
- Injection sites should always be rotated within the same region in order to reduce the risk of lipodystrophy and cutaneous amyloidosis (see section 4.4 and 4.8).
- Ensure when injecting that a blood vessel has not been entered.
- Discard the needle after each injection
- Discard devices if any part looks broken or damaged.
- Carry a spare or alternative administration method in case their delivery system breaks.

Lyumjev should be injected subcutaneously into the abdomen, upper arm, thigh or buttocks (see section 5.2).

Lyumjev should generally be used in combination with an intermediate or long-acting insulin. A different injection site should be used if injecting at the same time as another insulin.

The Lyumjev 200 units/mL KwikPen is only suitable for subcutaneous injections.

Lyumjev 200 units/mL should not be administered using a continuous subcutaneous insulin infusion (CSII) pump.

Lyumjev 200 units/mL should not be administered intravenously.

Lyumjev is available in two concentrations: Lyumjev 200 units/mL KwikPen and Lyumjev 100 units/mL KwikPen. See the separate SmPC for Lyumjev 100 units/mL KwikPen. The KwikPen delivers 1 - 60 units in steps of 1 unit in a single injection. The number of insulin units is shown in the dose window of the pen regardless of concentration and no dose conversion should be done when transferring a patient to a new concentration or to a pen with a different dose step.

For detailed user instructions, please refer to the instructions for use provided with the package leaflet.

To prevent the possible transmission of disease, each pen must be used by one patient only, even if the needle is changed.

4.3 Contraindications

Hypoglycaemia.
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered medicinal product should be clearly recorded.

Hypoglycaemia

Hypoglycaemia is the most common adverse reaction of insulin therapy. The timing of hypoglycaemia usually reflects the time-action profile of the administered insulin formulations. Hypoglycaemia may occur earlier after an injection when compared to other mealtime insulins due to the earlier onset of action of Lyumjev (see section 5.1).

Hypoglycaemia can happen suddenly and symptoms may differ in each individual and change over time in the same individual. Severe hypoglycaemia can cause seizures, may lead to unconsciousness, may be life-threatening, or cause death. Symptomatic awareness of hypoglycaemia may be less pronounced in patients with longstanding diabetes.

Hyperglycaemia

The use of inadequate doses or discontinuation of treatment, may lead to hyperglycaemia and diabetic ketoacidosis; conditions which are potentially lethal.

Patients should be educated to recognize the signs and symptoms of ketoacidosis and to get immediate help when ketoacidosis is suspected.

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.

Insulin requirements and dose adjustments

Changes in insulin, insulin concentration, manufacturer, type, or method of administration may affect glycaemic control and predispose to hypoglycaemia or hyperglycaemia. These changes should be made cautiously under close medical supervision and the frequency of glucose monitoring should be increased. For patients with type 2 diabetes, dose adjustments in concomitant anti-diabetic treatment may be needed (see sections 4.2 and 4.5).

In patients with renal or hepatic impairment, glucose monitoring should be intensified and dose adjusted on an individual basis (see section 4.2).

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. Exercise taken immediately after a meal may increase the risk of hypoglycaemia.

Thiazolidinediones (TZDs) used in combination with insulin

TZDs can cause dose-related fluid retention, particularly when used in combination with insulin. Fluid retention may lead to or exacerbate heart failure. Patients treated with insulin and a TZD should be observed for signs and symptoms of heart failure. If heart failure develops, consider discontinuation of the TZD.

Hypersensitivity and allergic reactions

Severe, life-threatening, generalised allergy, including anaphylaxis, can occur with insulin medicinal products, including Lyumjev. If hypersensitivity reactions occur, discontinue Lyumjev.

Medication errors

Lyumjev should not be used by patients with visual impairment without help of a trained person.

To avoid medication errors between Lyumjev and other insulins, patients need to always check the insulin label before each injection.

Do not transfer insulin from the Lyumjev Pen 200 units/mL to a syringe. The markings on the insulin syringe will not measure the dose correctly and can result in overdose and severe hypoglycaemia.

Patients should always use a new needle for each injection to prevent infections and a blocked needle. In the event of a blocked needle it should be replaced with a new needle.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e., essentially "sodium-free".

4.5 Interaction with other medicinal products and other forms of interaction

The following substances may reduce insulin requirement: Antidiabetic medicinal products (oral or injectable), salicylates, sulphonamides, certain antidepressants (monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors), angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor blocking agents, or somatostatin analogues.

The following substances may increase insulin requirement: oral contraceptives, corticosteroids, thyroid hormones, danazol, sympathomimetic agents, diuretics, or growth hormone.

Alcohol may increase or decrease the blood glucose lowering effect of Lyumjev. Consumption of large amounts of ethanol concomitantly with insulin use may lead to severe hypoglycaemia.

Beta-blockers may blunt the signs and symptoms of hypoglycaemia.

TZDs can cause dose-related fluid retention, particularly when used in combination with insulin, and exacerbate heart failure (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

A large amount of data on pregnant women (more than 1 000 pregnancy outcomes) indicate no malformative nor feto/neonatal toxicity of insulin lispro. Lyumjev can be used during pregnancy if clinically needed.

It is essential to maintain good control of an insulin-treated (insulin-dependent or gestational) diabetes patient throughout pregnancy. Insulin requirements usually fall during the first trimester and increase during the second and third trimesters. After delivery, insulin requirements normally return rapidly to pre-pregnancy values. Patients with diabetes should be advised to inform their doctor if they are pregnant or are contemplating pregnancy. Careful monitoring of glucose control is essential in pregnant patients with diabetes.

Breast-feeding

Lyumjev can be used during breast-feeding. Patients with diabetes who are breast-feeding may require adjustments in insulin dose, diet or both.

Fertility

Insulin lispro did not induce fertility impairment in animal studies.

4.7 Effects on ability to drive and use machines

The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or using machinery).

Patients should be advised to take precautions to avoid hypoglycaemia whilst driving, this is particularly important in those patients who have reduced or absent awareness of the warning signs of hypoglycaemia or have frequent episodes of hypoglycaemia. The advisability of driving should be considered in these circumstances.

4.8 Undesirable effects

Summary of safety profile

The most frequently reported adverse reaction during treatment is hypoglycaemia (very common) (see sections 4.2, 4.4 and 4.9).

The following related adverse reactions from clinical trials are listed below as MedDRA preferred term by system organ class and in order of decreasing incidence (very common: ≥ 1/10; common: ≥ 1/100 to < 1/10; uncommon: ≥ 1/1 000 to < 1/100; rare: ≥ 1/10 000 to < 1/1 000; very rare: < 1/10 000) and not known (cannot be estimated from the available data).

Table 1. Adverse reactions

MedDRA System Organ Class	Very common	Common	Uncommon	Not known
Metabolism and nutrition disorders	Hypoglycaemia			
Skin and subcutaneous tissue disorders			Lipodystrophy Rash Pruritus	Cutaneous amyloidosis
General disorders and administration site conditions		Injection site reactions Allergic reactions*	Oedema	

*See section 4.8 Description of selected adverse events

Description of selected adverse reactions

Hypoglycaemia

Hypoglycaemia is the most commonly observed adverse reaction in patients using insulin The incidence of severe hypoglycaemia in the 26 week Phase 3 clinical studies was 5.5 % in patients with type 1 diabetes mellitus and 0.9 % in patients with type 2 diabetes (see tables 2 and 3).
The symptoms of hypoglycaemia usually occur suddenly. They may include listlessness, confusion, palpitations, sweating, vomiting, and headache.

There were no clinically significant differences in the frequency of hypoglycaemia with administration of Lyumjev or the comparator (another medicinal product containing insulin lispro) across all studies. In studies where Lyumjev and the comparator were administered at different times relative to meals, there were no clinically relevant differences in the frequency of hypoglycaemia.

Hypoglycaemia may occur earlier after an injection of Lyumjev compared to other mealtime insulins due to the earlier onset of action.

Allergic reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, generalized skin reactions, angioedema, bronchospasm, hypotension, and shock may occur with any insulin, including Lyumjev.

Injection site reactions

As with other insulin therapy, patients may experience rash, redness, inflammation, pain, bruising or itching at the site of Lyumjev injection. These reactions are usually mild and usually disappear during continued treatment.

Immunogenicity

Administration of insulin can cause formation of insulin antibodies. The presence of anti-drug antibodies did not have a clinically meaningful effect on the pharmacokinetics, efficacy, or safety of Lyumjev.

Skin and subcutaneous tissue disorders

Lipodystrophy and cutaneous amyloidosis may occur at the injection site and delay local insulin absorption. Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions (see section 4.4).

Oedema

Cases of oedema have been reported with insulin therapy, particularly if previous poor metabolic control is improved by intensified insulin therapy.

Special populations

Based on results from clinical trials with insulin lispro in general, the frequency, type and severity of adverse reactions observed in elderly patients and in patients with renal or hepatic impairment do not indicate any differences to the broader experience in the general population. The safety information in very elderly patients (≥ 75 years) or patients with moderate to severe renal impairment or hepatic impairment is limited (see section 5.1).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Overdose causes hypoglycaemia with accompanying symptoms that include listlessness, confusion, palpitations, sweating, vomiting, and headache.

Hypoglycaemia may occur as a result of an excess of insulin lispro relative to food intake, energy expenditure, or both. Mild episodes of hypoglycaemia usually can be treated with oral glucose. More severe episodes with coma, seizure, or neurologic impairment may be treated with glucagon or concentrated intravenous glucose. Sustained carbohydrate intake and observation may be necessary because hypoglycaemia may recur after apparent clinical recovery. Adjustments in drug dose, meal patterns, or exercise may be needed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in diabetes, insulins and analogues for injection, fast-acting, ATC code: A10AB04.

Mechanism of action

The primary activity of Lyumjev is the regulation of glucose metabolism. Insulins, including insulin lispro, the active substance in Lyumjev, exert their specific action through binding to insulin receptors. Receptor-bound insulin lowers blood glucose by stimulating peripheral glucose uptake by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulins inhibit lipolysis and proteolysis, and enhance protein synthesis.

Lyumjev is a formulation of insulin lispro that contains citrate and treprostinil. Citrate increases local vascular permeability and treprostinil induces local vasodilation to achieve accelerated absorption of insulin lispro.

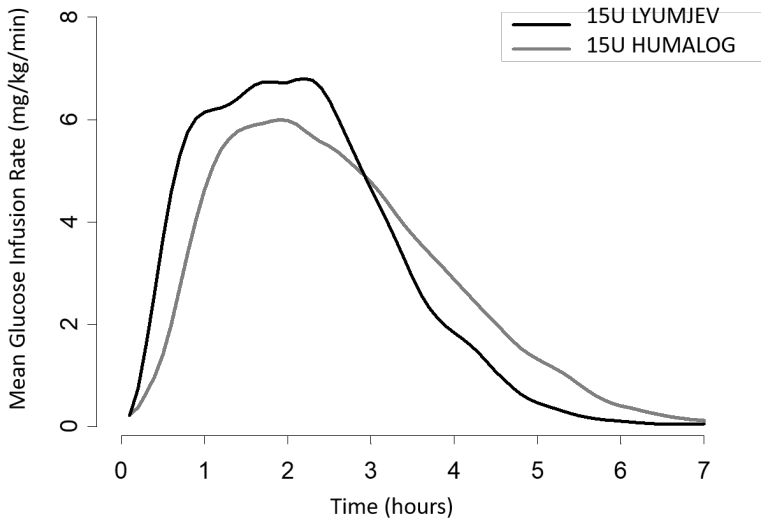
Pharmacodynamic effects

Early and late insulin action

A glucose clamp study was conducted in 40 type 1 diabetes patients given Lyumjev and Humalog subcutaneously as a single 15 unit dose. Results are provided in Figure 1. Lyumjev has been shown to be equipotent to Humalog on a unit for unit basis but its effect is more rapid with a shorter duration of action.

- Onset of action of Lyumjev was 20 minutes post dose, 11 minutes faster than Humalog.
- During the first 30 minutes post dose, Lyumjev had a 3-fold greater glucose lowering effect compared to Humalog.
- Maximum glucose-lowering effect of Lyumjev occurred between 1 and 3 hours after injection.
- The late insulin action, from 4 hours until the end of the glucose clamp, was 54 % lower with Lyumjev than observed with Humalog.
- The duration of action of Lyumjev was 5 hours, 44 minutes shorter than Humalog.
- The total glucose infused during the clamp was comparable between Lyumjev and Humalog.

Figure 1. Mean glucose infusion rate (GIR) in patients with type 1 diabetes after subcutaneous injection of Lyumjev or Humalog (15 unit dose)



Similarly, a faster early insulin action and a reduced late insulin action was observed with Lyumjev in type 2 diabetes patients.

Total and maximum glucose lowering effect of Lyumjev increased with dose within the therapeutic dose range. The early onset and total insulin action were similar when Lyumjev was administered in the abdomen, upper arm, or thigh.

Postprandial Glucose (PPG) Lowering

Lyumjev reduced the PPG during a standardized test meal over the complete 5 hour test meal period (change from premeal AUC(0-5h)) compared to Humalog.

- In patients with type 1 diabetes, Lyumjev reduced the PPG during the 5 hour test meal period by 32 % when given at the start of the meal and 18 % when given 20 minutes after the start of the meal compared to Humalog.

- In patients with type 2 diabetes, Lyumjev reduced the PPG during the 5 hour test meal period by 26 % when given at the start of the meal and 24 % when given 20 minutes after the start of the meal compared to Humalog.

Comparison of Lyumjev 200 units/mL and Lyumjev 100 units/mL

The maximum and total glucose lowering were comparable for Lyumjev 200 units/mL or Lyumjev 100 units/mL No dose conversion is required if transferring a patient between the strengths.

Clinical efficacy and safety

The efficacy of Lyumjev was evaluated in 2 randomised, active controlled trials in adults.

Type 1 Diabetes – Adults

PRONTO-T1D was a 26 week, treat-to-target, trial that evaluated the efficacy of Lyumjev in 1222 patients on multiple daily injection therapy. Patients were randomised to either blinded mealtime Lyumjev, blinded mealtime Humalog , or open-label postmeal Lyumjev , all in combination with either insulin glargine or insulin degludec. Mealtime Lyumjev or Humalog was injected 0 to 2 minutes before the meal and postmeal Lyumjev was injected 20 minutes after the start of the meal. Efficacy results are provided in Table 2 and Figure 2.

37.4 % of patients treated with mealtime Lyumjev, 33.6 % of patients treated with mealtime Humalog and 25.6 % of patients treated with postmeal Lyumjev reached a target HbA1c of < 7 %.

Basal, bolus and total insulin doses were similar among study arms at 26 weeks.

Following the 26 week period, the two blinded treatment arms continued to 52 weeks. HbA1c was not statistically significantly different between treatments at the 52 week endpoint.

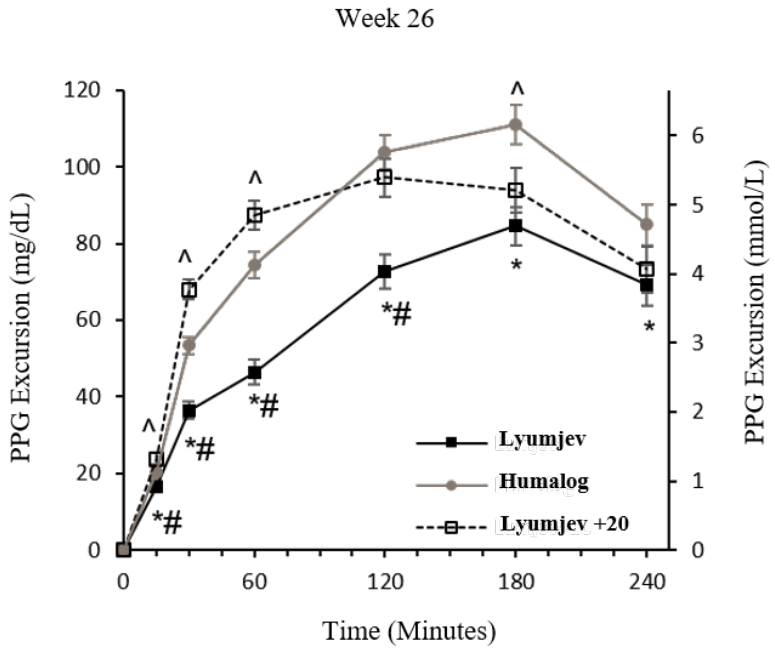
Table 2 Results from 26 week basal-bolus clinical trial in patients with type 1 diabetes

	Mealtime Lyumjev + basal insulin	Mealtime Humalog + basal insulin	Postmeal Lyumjev + basal insulin
Number of randomised subjects (N)	451	442	329
HbA_{1c} (%)			
Baseline → week 26	7.34 → 7.21	7.33→7.29	7.36→7.42
Change from baseline	-0.13	-0.05	0.08
Treatment difference	-0.08 [-0.16, -0.00][C]		0.13 [0.04, 0.22][D]
HbA_{1c} (mmol/mol)			
Baseline → week 26	56.7→55.3	56.7→56.1	56.9→57.6
Change from baseline	-1.4	-0.6	0.8
Treatment difference	-0.8 [-1.7, 0.00][C]		1.4 [0.5, 2.4][D]
1 hour postprandial glucose excursion (mg/dL) [A]			
Baseline → week 26	77.3 →46.4	71.5 →74.3	76.3→87.5
Change from baseline	-28.6	-0.7	12.5
Treatment difference	-27.9 [-35.3, -20.6][C,E]		13.2 [5.0, 21.4][D]
1 hour postprandial glucose excursion (mmol/L) [A]			
Baseline → week 26	4.29→2.57	3.97 →4.13	4.24→4.86
Change from baseline	-1.59	-0.04	0.70
Treatment difference	-1.55[-1.96, -1.14][C,E]		0.73 [0.28,1.19][D]
2 hour postprandial glucose excursion (mg/dL) [A]			
Baseline → week 26	112.7→72.7	101.6 →103.9	108.0 →97.2
Change from baseline	-34.7	-3.5	-10.2
Treatment difference	-31.2 [-41.1, -21.2][C,E]		-6.7 [-17.6, 4.3] [D].
2 hour postprandial glucose excursion (mmol/L) [A]			
Baseline → week 26	6.26→4.04	5.64→5.77	5.99→5.40
Change from baseline	-1.93	-0.20	-0.56
Treatment difference	-1.73 [-2.28, -1.18][C,E]		-0.37 [-0.98, -0.24][D]
Body weight (Kg)			
Baseline → week 26	77.3→77.9	77.3→78.2	77.6→78.1
Change from baseline	0.6	0.8	0.7
Treatment difference	-0.2 [-0.6, 0.1][A]		-0.1[-0.5, 0.3][D]
Severe hypoglycaemia [B] **(% of patients)**	5.5 %	5.7 %	4.6 %

Week 26 and change from baseline values are based on the least-squares means (adjusted means).
The 95 % confidence interval is stated in '*[ ]*'.
[A] Meal test
[B] Severe hypoglycaemia is defined as episode requiring assistance of another person due to patient's neurological impairment.

[C] The difference is for mealtime Lyumjev – mealtime Humalog.
[D] The difference is for postmeal Lyumjev – mealtime Humalog.
[E] Statistically significant in favour of mealtime Lyumjev.

Figure 2. Time course of blood glucose excursion during mixed-meal tolerance test at week 26 in patients with type 1 diabetes



PPG = Postprandial glucose
Lyumjev and Humalog administered at mealtime
Lyumjev + 20 = Lyumjev was injected 20 minutes after the start of the meal.
*p < 0.05 for pairwise comparison on Lyumjev versus Humalog
^p < 0.05 for pairwise comparison on Lyumjev +20 versus Humalog
#p < 0.05 for pairwise comparison on Lyumjev +20 versus Lyumjev

Continuous glucose monitoring (CGM) in Type 1 Diabetes – Adults

A subset of patients (N = 269) participated in an evaluation of the 24 hour ambulatory glucose profiles captured with blinded CGM. At the 26 week assessment, patients treated with mealtime Lyumjev demonstrated statistically significant improvement in PPG control during CGM assessment of glucose excursions or incremental area under the curve (AUC) 0 - 2 hours, 0 - 3 hours, and 0 - 4 hours after meals compared to patients treated with Humalog. Patients treated with mealtime Lyumjev reported statistically significantly longer time in range (6 am to midnight) with 603 minutes in range, (3.9 to 10 mmol/L, 71 – 180 mg/dL), and 396 minutes in range (3.9 to 7.8 mmol/L, 71 to 140 mg/dL), 44 and 41 minutes longer than Humalog patients respectively.

Type 2 Diabetes – Adults

PRONTO-T2D was a 26 week, treat-to-target trial that evaluated the efficacy of Lyumjev in 673 patients randomised to either blinded mealtime Lyumjev or to blinded mealtime Humalog, both in combination with a basal insulin (insulin glargine or insulin degludec) in a basal-bolus regimen. . Mealtime Lyumjev or mealtime Humalog was injected 0 - 2 minutes before the meal.
Efficacy results are provided in Table 3 and Figure 3.

58.2 % of patients treated with mealtime Lyumjev and 52.5 % of patients treated with mealtime Humalog reached a target HbA1c of < 7 %.

Basal, bolus and total insulin doses were similar among study arms at the end of the trial.

Table 3 Results from 26 week basal-bolus clinical trial in patients with type 2 diabetes

	Mealtime Lyumjev + basal insulin	**Mealtime Humalog + basal insulin**
Number of randomised subjects (N)	**336**	**337**
HbA_{1c} (%)		
Baseline → week 26	7.28→6.92	7.31→6.86
Change from baseline	-0.38	-0.43
Treatment difference	0.06 [-0.05, 0.16]	
HbA_{1c} (mmol/mol)		
Baseline → week 26	56.0→52.1	56.4→51.5
Change from baseline	-4.1	-4.7
Treatment difference	0.6 [-0.6, 1.8]	
1 hour postprandial glucose excursion (mg/dL)[A]		
Baseline → week 26	76.6→63.1	77.1→74.9
Change from baseline	-13.8	-2.0
Treatment difference	-11.8 [-18.1, -5.5][C]	
1 hour postprandial glucose excursion (mmol/L)[A]		
Baseline → week 26	4.25→3.50	4.28→4.16
Change from baseline	-0.77	-0.11
Treatment difference	-0.66 [-1.01, -0.30][C]	
2 hour postprandial glucose excursion (mg/dL)[A]		
Baseline → week 26	99.3→80.4	99.6→97.8
Change from baseline	-19.0	-1.6
Treatment difference	-17.4 [-25.3, -9.5][C]	
2 hour postprandial glucose excursion (mmol/L)[A]		
Baseline → week 26	5.51→4.47	5.53→5.43
Change from baseline	-1.06	-0.09
Treatment difference	-0.96 [-1.41, -0.52][C]	
Body weight (Kg)		
Baseline → week 26	89.8→91.3	90.0 →91.6
Change from baseline	1.4	1.7
Treatment difference	-0.2 [-0.7, 0.3]	
Severe hypoglycaemia (% of patients)[B]	0.9 %	1.8 %

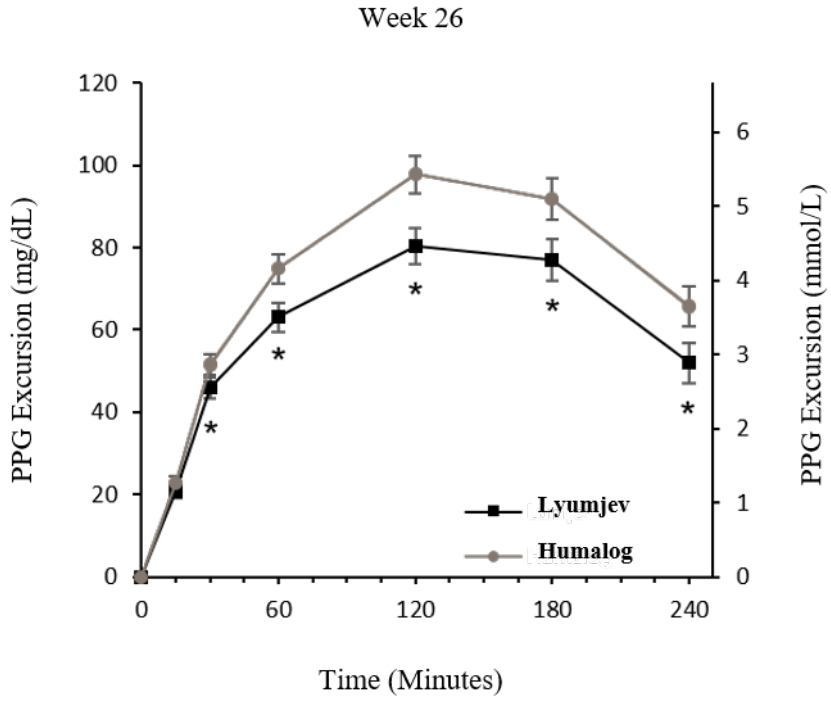
Week 26 and change from baseline values are based on the least-squares means (adjusted means).
The 95 % confidence interval is stated in '*[ ]*'. The difference is for mealtime Lyumjev – mealtime Humalog.

[A] Meal test

[B] Severe hypoglycaemia is defined as episode requiring assistance of another person due to patient's neurological impairment.

[C] Statistically significant in favour of mealtime Lyumjev.

Figure 3. Time course of blood glucose excursion during mixed-meal tolerance test at week 26 in patients with type 2 diabetes



PPG = Postprandial glucose
Lyumjev and Humalog administered at mealtime
Data are LSM (SE), *p < 0.05

Special populations

Elderly

In the two 26 week clinical studies (PRONTO-T1D and PRONTO-T2D), 187 of 1 116 (17 %) Lyumjev treated patients with type 1 diabetes or type 2 diabetes were ≥ 65 years of age and 18 of 1 116 (2 %) were ≥ 75 years of age. No overall differences in safety or effectiveness were observed between elderly patients and younger patients.

5.2 Pharmacokinetic properties

Absorption

Absorption of insulin lispro was accelerated and the duration of exposure was shorter in healthy subjects and patients with diabetes following injection of Lyumjev compared to Humalog. In patients with type 1 diabetes:

- Insulin lispro appeared in circulation approximately 1 minute after injection of Lyumjev, which was five minutes faster than Humalog .
- Time to 50 % maximum concentration was 14 minutes shorter with Lyumjev compared to Humalog.
- Following injection of Lyumjev, there was seven times more insulin lispro in circulation during the first 15 minutes compared to Humalog and three times more insulin lispro during the first 30 minutes compared to Humalog.
- After administration of Lyumjev the time to maximum insulin lispro concentration was achieved at 57 minutes.
- Following injection of Lyumjev there was 41 % less insulin lispro in circulation after 3 hours following injection compared to Humalog.

- The duration of insulin lispro exposure for Lyumjev was 60 minutes shorter compared to Humalog.
- The total insulin lispro exposure (ratio and 95 % CI of 1.03 (0.973, 1.09) and maximum concentration (ratio and 95 % CI of 1.06 (0.97, 1.16) were comparable between Lyumjev and Humalog.

In type 1 patients, the day-to-day variability [CV %] of Lyumjev was 13 % for total insulin lispro exposure (AUC, 0 - 10h) and 23 % for maximum insulin lispro concentration ($C_{max)}$.The absolute bioavailability of insulin lispro after subcutaneous administration of Lyumjev in the abdomen, upper arm and thigh was approximately 65 %. The accelerated absorption of insulin lispro is maintained regardless of injection site (abdomen, upper arm and thigh). No exposure data are available following injection in the buttocks.

Maximum concentration and time to maximum concentration were comparable for the abdomen and upper arm regions; time to maximum concentration was longer and maximum concentration lower for the thigh.

Total insulin lispro exposure and maximum insulin lispro concentration increased proportionally with increasing subcutaneous doses of Lyumjev within the dose range from 7U to 30U.

Comparison of Lyumjev 200 units/mL and Lyumjev 100 units/mL

The results of a study in healthy subjects demonstrated that Lyumjev 200 units/mL is bioequivalent to Lyumjev 100 units/mL following administration of a single 15 unit dose for the area under serum insulin lispro concentration-time curve from time zero to infinity and maximum insulin lispro concentration. The accelerated insulin lispro absorption after administration of 200 units/mL was similar to that observed with Lyumjev 100 units/mL. No dose conversion is required if transferring a patient between the strengths.

Distribution

The geometric mean (% coefficient of variation [CV %]) volume of distribution of insulin lispro (Vd) was 34 L (30 %) after intravenous administration of Lyumjev as a bolus injection of a 15 unit dose in healthy subjects.

Elimination

The geometric mean (CV %) clearance of insulin lispro was 32 L/hour (22 %) and the median half-life of insulin lispro was 44 minutes after intravenous administration of Lyumjev as a bolus injection of a 15 unit dose in healthy subjects.

Special populations

In adult subjects, age, gender, and race did not affect the pharmacokinetics and pharmacodynamics of Lyumjev.

Paediatric population

The pharmacokinetic differences between Lyumjev and Humalog were, overall, similar in children and adolescents as observed in adults. Following a subcutaneous injection, Lyumjev showed an accelerated absorption with a higher early insulin lispro exposure in children (8–11 years) and adolescents (12–17 years) whilst maintaining a similar total exposure, maximum concentration and time to maximum concentration compared to Humalog.

Patients with renal and hepatic impairment

Renal and hepatic impairment is not known to impact the pharmacokinetics of insulin lispro.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development after exposure to insulin lispro.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol
Magnesium chloride hexahydrate
Metacresol
Sodium citrate dihydrate
Treprostinil sodium
Zinc oxide
Water for injections
Hydrochloric acid and sodium hydroxide (for pH adjustment)

6.2 Incompatibilities

This medicinal product must not be mixed with any other insulin or any other medicinal product.

6.3 Shelf life

Before use

2 years

After first use

28 days

6.4 Special precautions for storage

Before use

Store in the refrigerator (2 °C - 8 °C).
Do not freeze.
Store in the original package in order to protect from light.

After first use

Do not refrigerate.
Do not store above 30 °C.
Do not freeze.
Keep the cap on the pen in order to protect from light.

6.5 Nature and contents of container

Type I clear glass cartridges, sealed with disc seals secured with aluminium seals and halobutyl plungers.

The 3 mL cartridges are sealed in a disposable pen injector KwikPen

The medicinal product is packed in a white carton with dark blue bands and dark blue and light blue checked bands and an image of the pen. On the carton and label the insulin strength is highlighted in a box with a yellow background. There is a yellow warning label on the cartridge holder "Use only in this pen, or severe overdose can result". The KwikPen is taupe, the dose knob is taupe with raised ridges on side.

3 mL KwikPen: Packs of 2 pre-filled pens, 5 pre-filled pens or a multipack of 10 (2 packs of 5) pre-filled pens.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Lyumjev should look clear and colourless. It should not be used if it is cloudy, coloured, or has particles or clumps in it.

Lyumjev should not be used if it has been frozen.

A new needle must always be attached before each use. Needles must not be re-used. Needles are not included.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V., Papendorpseweg 83, 3528 BJ Utrecht, The Netherlands.

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1422/013
EU/1/20/1422/014
EU/1/20/1422/015

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24 March 2020

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

ANNEX II

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) of the biological active substance

Eli Lilly and Company, Indianapolis, Indiana, 46285, USA.
Lilly del Caribe, Inc., 12.3 KM 65th Infantry Road, Carolina, Puerto Rico 00985.

Name and address of the manufacturer responsible for batch release

Lilly France S.A.S, Rue du Colonel Lilly, 67640 Fegersheim, France.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – Vial

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 100 units/mL solution for injection in vial
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

Each mL solution contains 100 units of insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 vial of 10 mL
2 vials of 10 mL

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous and intravenous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not freeze.

Store in original package in order to protect from light.

Before use: Store in a refrigerator.

After first use: Do not store above 30 °C. Discard after 28 days.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83, 3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1422/001 1vial
EU/1/20/1422/002 2 vials

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 100 units/mL

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (with blue box) multipack – Vial

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 100 units/mL solution for injection in vial
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

Each mL solution contains 100 units of insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

Multipack: 5 (5 packs of 1) vials of 10 mL.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous and intravenous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not freeze.
Store in original package in order to protect from light.

Before use: Store in a refrigerator.

After first use: Do not store above 30 °C. Discard after 28 days.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83, 3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1422/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 100 units/mL

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON (without blue box) component of a multipack – Vial

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 100 units/mL solution for injection in vial
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

Each mL solution contains 100 units of insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 vial of 10 mL. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous and intravenous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not freeze.

Store in original package in order to protect from light.

Before use: Store in a refrigerator.

After first use: Do not store above 30 °C. Discard after 28 days.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83, 3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

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13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 100 units/mL

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT - Vial

1. NAME OF THE MEDICINAL PRODUCT AND ROUTES OF ADMINISTRATION

Lyumjev 100 units/mL solution for injection
insulin lispro
Subcutaneous and intravenous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON - Cartridges

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 100 units/mL solution for injection in cartridge
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

Each mL solution contains 100 units of insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

2 cartridges of 3 mL
5 cartridges of 3 mL
10 cartridges of 3 mL

5. METHOD AND ROUTES OF ADMINISTRATION

Use these cartridges with a Lilly 3 mL pen only.
Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNINGS, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before use:
Store in a refrigerator.
Do not freeze.
Store in original package in order to protect from light.

After first use:
Do not store above 30 °C.
Do not refrigerate or freeze.
Recap the pen after use in order to protect from light.
Discard after 28 days.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83, 3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1422/004 2 cartridges
EU/1/20/1422/005 5 cartridges
EU/1/20/1422/006 10 cartridges

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 100 units/mL

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT - Cartridges

1. NAME OF THE MEDICINAL PRODUCT AND ROUTES OF ADMINISTRATION

Lyumjev 100 units/mL solution for injection in cartridge
insulin lispro
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – KwikPen.

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 100 units/mL KwikPen solution for injection in pre-filled pen.
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

Each mL solution contains 100 units of insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

2 pens of 3 mL
5 pens of 3 mL

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before use:
Store in a refrigerator.

Do not freeze.
Store in original package in order to protect from light.

After first use:
Do not store above 30 °C.
Do not refrigerate or freeze.
Recap the pen after use in order to protect from light.
Discard after 28 days.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83, 3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1422/007 2 pens
EU/1/20/1422/008 5 pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 100 units/mL KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (with blue box) multipack – KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 100 units/mL KwikPen solution for injection in pre-filled pen
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

Each mL solution contains 100 units of insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

Multipack: 10 (2 packs of 5) pre-filled pens of 3 mL.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before use:
Store in a refrigerator.

Do not freeze.
Store in original package in order to protect from light.

After first use:
Do not store above 30 °C.
Do not refrigerate or freeze.
Recap the pen after use in order to protect from light.
Discard after 28 days

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83, 3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1422/009

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 100 units/mL KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON (without blue box) component of a multipack – KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 100 units/mL KwikPen solution for injection in pre-filled pen
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

Each mL solution contains 100 units of insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

5 pens of 3 mL. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before use:
Store in a refrigerator.

Do not freeze.
Store in original package in order to protect from light.

After first use:
Do not store above 30 °C.
Do not refrigerate or freeze.
Recap the pen after use in order to protect from light.
Discard after 28 days.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83, 3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1422/009

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 100 units/mL KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT - KwikPen

1. NAME OF THE MEDICINAL PRODUCT AND ROUTES OF ADMINISTRATION

Lyumjev 100 units/mL KwikPen solution for injection
insulin lispro
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – Junior KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 100 units/mL Junior KwikPen solution for injection in pre-filled pen.
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

Each mL solution contains 100 units of insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

2 pen of 3 mL.
5 pens of 3 mL.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

The pen delivers 0.5 - 30 units in steps of 0.5 units.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before use:
Store in a refrigerator.
Do not freeze.
Store in original package in order to protect from light.

After first use:
Do not store above 30 °C.
Do not refrigerate or freeze..
Recap the pen after use in order to protect from light.
Discard after 28 days.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83, 3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1422/010 2 pen
EU/1/20/1422/011 5 pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 100 units/mL Junior KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (with blue box) multipack – Junior KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 100 units/mL Junior KwikPen solution for injection in pre-filled pen.
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

Each mL solution contains 100 units of insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

Multipack: 10 (2 packs of 5) pre-filled pens of 3 mL.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

The pen delivers 0.5 - 30 units in steps of 0.5 units.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before use:
Store in a refrigerator.
Do not freeze.
Store in original package in order to protect from light.

After first use:
Do not store above 30 °C.
Do not refrigerate or freeze.
Recap the pen after use in order to protect from light.
Discard after 28 days.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83, 3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1422/012

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 100 units/mL Junior KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON (without blue box) component of a multipack – Junior KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 100 units/mL Junior KwikPen solution for injection in pre-filled pen.
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

Each mL solution contains 100 units of insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

5 pens of 3 mL. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

The pen delivers 0.5 - 30 units in steps of 0.5 units.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before use:
Store in a refrigerator.
Do not freeze.
Store in original package in order to protect from light.

After first use:
Do not store above 30 °C.
Do not refrigerate or freeze.
Recap the pen after use in order to protect from light.
Discard after 28 days

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83, 3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1422/012

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 100 units/mL Junior KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT - Junior KwikPen

1. NAME OF THE MEDICINAL PRODUCT AND ROUTES OF ADMINISTRATION

Lyumjev 100 units/mL Junior KwikPen solution for injection
insulin lispro
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON __ Tempo Pen. Pack of 5.

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 100 units/mL Tempo Pen solution for injection in a pre-filled pen

insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each mL solution contains 100 units insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

5 pens of 3 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before use:
Store in a refrigerator.
Do not freeze.
Store in original package in order to protect from light.

After first use:
Do not store above 30 °C.
Do not refrigerate or freeze.
Recap the pen after use to protect from light.
Discard after 28 days.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83, 3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1422/016 5 pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 100 units/mL Tempo Pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (with blue box) multipack – Tempo Pen

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 100 units/mL Tempo Pen solution for injection in a pre-filled pen

insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each mL solution contains 100 units insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

Multipack: 10 (2 packs of 5) pens of 3 mL.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before use:
Store in a refrigerator.
Do not freeze.
Store in original package in order to protect from light.

After first use:
Do not store above 30 °C.
Do not refrigerate or freeze.
Recap the pen after use to protect from light.
Discard after 28 days.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83, 3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1422/017

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 100 units/mL Tempo Pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON (without blue box) component of a multipack – Tempo Pen

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 100 units/mL Tempo Pen solution for injection in a pre-filled pen

insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each mL solution contains 100 units insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

5 pens of 3 mL. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before use:
Store in a refrigerator.
Do not freeze.
Store in original package in order to protect from light.

After first use:
Do not store above 30 °C.
Do not refrigerate or freeze.
Recap the pen after use to protect from light.
Discard after 28 days.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83, 3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1422/017

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 100 units/mL Tempo Pen

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT –Tempo Pen

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Lyumjev 100 units/mL Tempo Pen injection
insulin lispro
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – KwikPen.

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 200 units/mL KwikPen solution for injection in pre-filled pen
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

Each mL solution contains 200 units of insulin lispro (equivalent to 6.9 mg)

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

2 pens of 3 mL.
5 pens of 3 mL.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

Use only in this pen, or severe overdose can result.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before use:
Store in a refrigerator.
Do not freeze.
Store in original package in order to protect from light.

After first use:
Do not store above 30 °C.
Do not refrigerate or freeze..
Recap the pen after use in order to protect from light.
Discard after 28 days

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83, 3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1422/013 2 pens
EU/1/20/1422/014 5 pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 200 units/mL KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (with blue box) multipack – KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 200 units/mL KwikPen solution for injection in pre-filled pen
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

Each mL solution contains 200 units of insulin lispro (equivalent to 6.9 mg)

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

Multipack: 10 (2 packs of 5) pre-filled pens of 3 mL.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

Use only in this pen, or severe overdose can result.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before use:
Store in a refrigerator.
Do not freeze.
Store in original package in order to protect from light.

After first use:
Do not store above 30 °C.
Do not refrigerate or freeze.
Recap the pen after use in order to protect from light.
Discard after 28 days.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83, 3528 BJ Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1422/015

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 200 units/mL KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON (without blue box) component of a multipack – KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Lyumjev 200 units/mL KwikPen solution for injection in pre-filled pen
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

Each mL solution contains 200 units of insulin lispro (equivalent to 6.9 mg)

3. LIST OF EXCIPIENTS

Excipients: glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, metacresol, sodium hydroxide, hydrochloric acid, water for injections.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

5 pens of 3 mL. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

Use only in this pen, or severe overdose can result.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before use:
Store in a refrigerator.
Do not freeze.
Store in original package in order to protect from light.

After first use:
Do not store above 30 °C.
Do not refrigerate or freeze.
Recap the pen after use in order to protect from light.
Discard after 28 days.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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EU/1/20/1422/015

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Lyumjev 200 units/mL KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT - KwikPen

1. NAME OF THE MEDICINAL PRODUCT AND ROUTES OF ADMINISTRATION

Lyumjev 200 units/mL KwikPen solution for injection
insulin lispro
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 mL

6. OTHER

Use only in this pen, or severe overdose can result.

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Lyumjev 100 units/ml solution for injection in vial
insulin lispro

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Lyumjev is and what it is used for

Lyumjev 100 units/ml solution for injection in vial contains the active ingredient insulin lispro. Lyumjev is used to treat diabetes mellitus in adults, adolescents and children aged 1 year and above. It is a mealtime insulin that works more quickly than other medicines containing insulin lispro. Lyumjev contains ingredients that speed up absorption of insulin lispro into the body.

Diabetes is a condition in which your body does not make enough insulin or does not use insulin effectively, which results in effects such as high levels of sugar in the blood. Lyumjev is an insulin medicine that is used in the treatment of diabetes and so controls blood sugar. Effective treatment of diabetes, with good control of blood sugar, prevents long-term complications from your diabetes.

Treatment with Lyumjev helps to control blood sugar in the long term and prevent complications from your diabetes. Lyumjev has its maximum effect 1 to 3 hours after injection and the effect lasts for up to 5 hours. You should use Lyumjev at the start of the meal, or up to 20 minutes after starting the meal.

Your doctor may tell you to use Lyumjev as well as a longer- or intermediate-acting insulin. Do not change your insulin unless your doctor tells you to.

2. What you need to know before you use Lyumjev

Do NOT use Lyumjev
- if you think your blood sugar is dropping (**hypoglycaemia**). Further on, this leaflet tells you how to deal with low blood sugar (see section 3 under “If you use more Lyumjev than you should”).
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Lyumjev.

If you cannot see very well you will need help from someone who has been trained to give injections.

- **Low blood sugar** (hypoglycaemia).

Low blood sugar can be serious and untreated hypoglycaemia may even lead to death.
Lyumjev starts to lower blood sugar faster than some other mealtime insulins. If hypoglycaemia occurs, you may experience it earlier after an injection of Lyumjev. If you often have hypoglycaemia or have difficulty recognising it, please discuss this with your doctor or nurse. If your blood sugar levels are well controlled by your current insulin therapy or after long duration of diabetes, you may not feel the warning symptoms when your blood sugar is falling too low.Warning signs are listed later in this leaflet. For symptoms please see "Common problems of diabetes".

You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood sugar often. Making changes to the types of insulin you use may cause your blood sugar to rise or fall too much. It may be necessary to increase the frequency of blood sugar testing if you are at risk of low blood sugars. Your doctor may need to change the doses of your other diabetes medicines.

- **High blood sugar** (hyperglycaemia).

Stopping or not taking enough insulin may lead to high blood sugar (hyperglycaemia) and diabetic ketoacidosis, serious conditions that can even lead to death. For symptoms please see "Common problems of diabetes".

- If you are using an insulin pump and it stops working you will need to fix the problem immediately as this can lead to high blood sugar. You may need to take an injection of Lyumjev using an insulin pen or a syringe if your pump stops working.
- If your insulin treatment is being combined with one of a class of diabetes medicines called thiazolidinediones or glitazones, such as pioglitazone, tell your doctor as soon as possible if you get signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling caused by fluid retention (oedema).
- If you have a serious allergic reaction to insulin or any of the ingredients in Lyumjev, stop using this medicine and contact emergency medical services straight away.
- Always check the pack and the label for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Lyumjev that your doctor has told you to use.
- Keep the carton, or keep a note of the batch number on the carton. If you have a side effect you can then provide that number when you report the advere side effect, see "reporting of side effects".
- Always use a new needle for each injection to prevent infections and blocked needles. If a needle is blocked replace it with a new needle.

- **Skin changes at the injection site.**

The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work well if you inject into a lumpy area (See How to use Lyumjev). Contact your doctor if you are currently injecting into a lumpy area before you start injecting into a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Children and adolescents
This medicine is not recommended for use in children below the age of 1 year.

Other medicines and Lyumjev
Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines. Some medicines affect your blood sugar level - this may mean your insulin dose has to change.

Your blood sugar levels may fall (hypoglycaemia) if you take:

- other medicines for diabetes (oral and injectable)
- sulphonamide antibiotics (for infections)
- acetylsalicylic acid (for pain and mild fever and to prevent blood clotting)
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors)
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril) (for some heart problems or high blood pressure)
- angiotensin II receptor blockers (for high blood pressure or heart problems)
- somatostatin analogues (such as octreotide, which are used to treat a rare condition involving too much growth hormone)

Your blood sugar levels may rise (hyperglycaemia) if you take:

- danazol (for endometriosis)
- the contraceptive pill (birth control pills)
- thyroid hormone replacement therapy (for thyroid problems)
- human growth hormone (for growth hormone deficiency)
- diuretics (for high blood pressure or if you have a build-up of water in your body)
- sympathomimetic agents (for serious allergic reactions or used in some cold remedies)
- corticosteroids (to treat asthma or autoimmune conditions)

Beta-blockers (used for high blood pressure, arrhythmia or angina) make it harder to recognise the warning signs of low blood sugar.

Lyumjev with alcohol
Your blood sugar levels may either rise or fall if you drink alcohol. Therefore the amount of insulin needed may change. You should therefore monitor your blood sugar level more often than usual.

Pregnancy and breast-feeding
If you are planning to have a baby, think you may be pregnant, are pregnant or breast-feeding, ask your doctor, nurse or pharmacist for advice before taking this medicine. The amount of insulin you need usually falls during the first 3 months of pregnancy and increases for the remaining 6 months. After you have had your baby your insulin requirements will likely return to how much you needed before your pregnancy.

There are no restrictions on treatment with Lyumjev during breast-feeding. If you are breast-feeding, you may need to alter your insulin intake or diet.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or using machines). You should contact your doctor about driving if you have:
- frequent episodes of hypoglycaemia
- reduced or absent warning signs of hypoglycaemia

Lyumjev contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

3. How to use Lyumjev

Always use this medicine exactly as described in this leaflet or as your doctor, pharmacist or nurse has told you. Check with them if you are not sure.

They will have told you exactly how much Lyumjev to use, when to use it, and how often. They will also tell you how often to visit your diabetes clinic.

You should always have spare insulin and another injection device in case you need them.

If you are blind or visually impaired you will need help from someone to make your injections.

Your doctor may tell you to use Lyumjev as well as a longer- or intermediate-acting insulin. Inject them separately. Lyumjev should not be mixed with any other insulin.

When to inject Lyumjev
Lyumjev is a mealtime insulin. You should use Lyumjev when you start to eat, or a minute or two before the meal; you also have the option to inject up to 20 minutes after starting the meal.

How much insulin to use
Your doctor will work out your dose based on your blood sugar and body weight and explain
- How much Lyumjev you need at each meal.
- How and when to check your blood sugar level.
- How to change your insulin dose depending on your blood sugar levels.
- What to do if you change your diet, or change how much you exercise, if you are ill or if you are using other medicines.
- If you change the type of insulin you use, you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.

Do not use Lyumjev
- If it does not look like water. Lyumjev must be clear, have no colour and no solid pieces in it. Check each time you inject yourself.
- If Lyumjev has not been stored correctly (see section 5 “How to store Lyumjev”).
- If the plastic cap of the vial is damaged, do not use.

Where to inject Lyumjev
- Inject Lyumjev under the skin (subcutaneous injection).
- Do not inject yourself directly into a vein. Only your physician can administer Lyumjev by the intravenous use. He will only do this under special circumstances such as surgery or if you are ill and your sugar levels are too high.
- Make sure you inject at least 1 cm from the last injection and that you ‘rotate’ the places you inject (upper arm, thigh, buttocks or abdomen), as you have been taught.
- If you need to inject another insulin at the same time as Lyumjev, use a different injection site.

How to inject Lyumjev from a vial
- First wash your hands.
- Before you make an injection, clean your skin as you have been instructed. Clean the rubber stopper on the vial, but do not remove the stopper.
- Use a new, sterile syringe and needle to pierce the rubber stopper and draw in the amount of Lyumjev you want. Your doctor, nurse or clinic will tell you how to do this. **Do not share your needles and syringes.**
- Inject under the skin, as you were taught. After your injection, leave the needle in the skin for 5 seconds to make sure you receive the full dose.

Using Lyumjev in an insulin pump
- Only certain insulin infusion pumps may be used to infuse Lyumjev.

- Carefully follow the instructions supplied with your infusion pump.
- Be sure to use the correct reservoir and catheter for your pump. It is important to use the correct needle length on the filling system to avoid damaging the pump.
- Change the infusion set (tubing and needle) according to the instructions supplied with the infusion set.
- If repeated or severe low blood sugar levels occur, tell your doctor or nurse.
- A pump malfunction or obstruction of the infusion set can result in a rapid rise in sugar levels. If you think Lyumjev is not flowing, follow the pump instructions and if appropriate, notify your doctor or nurse.
- You may need to take an injection of Lyumjev if your pump does not work properly.

After injecting
If you are unsure how much you have injected then check your blood sugar levels before deciding if you need another injection.

If you use more Lyumjev than you should
If you inject too much Lyumjev, or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low (hypoglycaemia) and you can treat yourself, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor or nurse has advised you and have some rest. This will often get you over a low blood sugar or a minor insulin overdose. Check your blood sugar again after 15-20 mins until blood sugar is stabilised.

If you are unable to treat yourself (severe hypoglycaemia) because you feel too dizzy, weak, confused, have difficulty talking, lose consciousness or have a seizure you may need to be treated with glucagon. This can be given by someone who knows how to use it. Eat glucose or sugar after the glucagon. If glucagon does not work, you will have to go to hospital or call emergency services. Ask your doctor to tell you about glucagon.

Tell everyone you spend time with that you have diabetes. Tell them what could happen if your blood sugar gets too low, including the risk of passing out.

Let them know that if you pass out, they must: turn you on your side to avoid choking, get medical help straight away and not give you any food or drink because you may choke.

If you forget to use Lyumjev
If you forget to use your insulin or you use less than you should, or are unsure how much you have injected, your blood sugar may get too high (hyperglycaemia). Check your blood sugar level to decide if an insulin dose is needed. Resume your usual dosing schedule at your next meal.

If you stop using Lyumjev
Do not stop or change your insulin unless your doctor tells you to. If you use less Lyumjev than you should, a high blood sugar may occur.

If high blood sugar (hyperglycaemia) is not treated it can be very serious and cause headaches, nausea, vomiting, abdominal pain, dehydration, unconsciousness, coma or even death (see section 4).

Three simple steps to reduce your risk of hypoglycaemia or hyperglycaemia are:
- Always keep spare syringes and a spare vial of Lyumjev.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Low blood sugar (hypoglycaemia) is very common with insulin treatment (may affect more than 1 in 10 people). It can be very serious. If your blood sugar level falls too much you may become unconscious. Serious hypoglycaemia may cause brain damage and may be life-threatening. If you have symptoms of low blood sugar, act **immediately** to increase your blood sugar level. See section 3 under 'If you use more Lyumjev than you should'.

Allergic reactions are common (may affect up to 1 in 10 people). They may be severe and they may include the following symptoms:

- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you have a serious allergic reaction (including an anaphylactic attack) to insulin or any of the ingredients in Lyumjev, stop using this medicine and contact emergency medical service straight away.

Other side effects include

Very common
Infusion site reactions. Some people get redness, pain, swelling or itching around the area of the insulin infusion. If you have infusion site reactions, tell your doctor

Common
Injection site reactions. Some people get redness, pain, swelling or itching around the area of the insulin injection. This usually clears up in a few minutes to a few weeks without needing to stop Lyumjev. If you have injection site reactions, tell your doctor.

Uncommon (may affect up to 1 in 100 people)
Skin changes at the injection site: If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by the build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Other potential side effects
Swelling in arms or ankles due to fluid retention (oedema), particularly at the start of insulin therapy or during a change in your diabetes medicines.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

Low blood sugar
Low blood sugar (hypoglycaemia) means there is not enough sugar in the blood. This can be caused if:
- you take too much Lyumjev or other insulin;
- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;

- you have an infection or illness (especially diarrhoea or vomiting);
- there is a change in your need for insulin for example if you lose weight; or you have trouble with your kidneys or liver which gets worse.

See section 'If you use more Lyumjev than you should.'

The first symptoms of low blood sugar usually come on quickly and include the following:
- tiredness
- rapid heart beat
- nervousness or shakiness
- feeling sick
- headache
- cold sweat

If you are not confident about recognising your warning symptoms, avoid situations such as driving a car, in which you or others would be put at risk by hypoglycaemia.

High blood sugar (hyperglycaemia) and diabetic ketoacidosis
Hyperglycaemia (too much sugar in the blood) means that the levels of glucose in your body are too high. Hyperglycaemia can be brought about by:
- not taking your insulin;
- using less insulin than your body needs;
- an imbalance between the amount of carbohydrates you eat and the insulin you take; or
- fever, infection or emotional stress.

The early symptoms of hyperglycaemia are;
- being very thirsty
- headache
- feeling sleepy
- urinating more often

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. Additional symptoms include the following:
- nausea and/or vomiting
- abdominal pain
- rapid pulse
- heavy breathing
- moderate or large amounts of urine ketones. Ketones are produced when your body burns fat for energy instead of glucose.

If you have any of these symptoms and high sugars **get medical help immediately.**
See section 'If you forget to use Lyumjev'.

Illness
If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Lyumjev

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Do not freeze.
Keep in the outer carton in order to protect from light.

Before first use
Store in a refrigerator (2 °C to 8 °C).

After first use
Do not store above 30 °C.
Discard after 28 days **even if some of the solution remains.**

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Lyumjev 100 units/ml solution for injection in vial contains
- The active substance is insulin lispro. Each ml solution contains 100 units of insulin lispro. One vial contains 1 000 units of insulin lispro in 10 ml solution.
- The other ingredients are metacresol, glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, water for injections. Sodium hydroxide or hydrochloric acid may have been used to adjust the pH (see the end of section 2 under 'Lyumjev contains sodium').

What Lyumjev looks like and contents of the pack
Lyumjev 100 units/ml, solution for injection is a clear, colourless, aqueous solution in a vial. Each vial contains 1 000 units (10 millilitres). Pack sizes of 1 , 2 or a multipack of 5 × 1 vials. Not all pack sizes may be marketed.

Marketing Authorisation Holder
Eli Lilly Nederland B.V., Papendorpseweg 83, 3528 BJ Utrecht, The Netherlands.

Manufacturer
Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France.

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/.

The following information is intended for heath care professionals only:

Lyumjev 100 units /mL is available in vials if administration of intravenous injection is necessary.

For intravenous use, Lyumjev should be diluted to concentrations of 0.1 to 1.0 unit/mL in 5 % glucose solution for injection or sodium chloride 9 mg/mL (0.9 %) solution for injection. It is recommended

that the system is primed before starting the infusion to the patient.Compatibility has been demonstrated in ethylene-propylene copolymer and polyolefin with polyvinyl chloride bags.

Chemical and physical in-use stability has been demonstrated for 14 days at 2–8 °C and 20 hours at 20–25 °C when protected from light. From a microbiological point of view, the medicinal product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would not normally be longer than 24 hours at 2–8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

Package leaflet: Information for the user

Lyumjev 100 units/ml solution for injection in cartridge
insulin lispro

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Lyumjev is and what it is used for

Lyumjev 100 units/ml solution for injection in a cartridge contains the active ingredient insulin lispro. Lyumjev is used to treat diabetes mellitus in adults,adolescents and children aged 1 year and above. It is a mealtime insulin that works more quickly than other medicines containing insulin lispro. Lyumjev contains ingredients that speed up absorption of insulin lispro into the body.

Diabetes is a condition in which your body does not make enough insulin or does not use insulin effectively, which results in effects such as high levels of sugar in the blood. Lyumjev is an insulin medicinethat is used in the treatment of diabetes and so controls blood sugar. Effective treatment of diabetes, with good control of blood sugar, prevents long-term complications from your diabetes.

Treatment with Lyumjev helps to control blood sugar in the long term and prevent complications from your diabetes. Lyumjev has its maximum effect 1 to 3 hours after injection and the effect lasts for up to 5 hours. You should use Lyumjev at the start of the meal, or up to 20 minutes after starting the meal.

Your doctor may tell you to use Lyumjev as well as a longer- or intermediate-acting insulin. Do not change your insulin unless your doctor tells you to.

2. What you need to know before you use Lyumjev

Do NOT use Lyumjev
- if you think your blood sugar is dropping (**hypoglycaemia**). Further on, this leaflet tells you how to deal with low blood sugar (see section 3 under “If you use more Lyumjev than you should”).
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Lyumjev.

If you cannot see very well you will need help from someone who has been trained to give injections.

- **Low blood sugar** (hypoglycaemia).

Low blood sugar can be serious and untreated hypoglycaemia may even lead to death.
Lyumjev starts to lower blood sugar faster than some other mealtime insulins. If hypoglycaemia occurs, you may experience it earlier after an injection of Lyumjev. If you often have hypoglycaemia or have difficulty recognising it, please discuss this with your doctor or nurse. If your blood sugar levels are well controlled by your current insulin therapy or after long duration of diabetes, you may not feel the warning symptoms when your blood sugar is falling too low.Warning signs are listed later in this leaflet. For symptoms please see "Common problems of diabetes".

You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood sugar often. Making changes to the types of insulin you use may cause your blood sugar to rise or fall too much. It may be necessary to increase the frequency of blood sugar testing if you are at risk of low blood sugars. Your doctor may need to change the doses of your other diabetes medicines.

- **High blood sugar** (hyperglycaemia).

Stopping or not taking enough insulin may lead to high blood sugar (hyperglycaemia) and diabetic ketoacidosis, serious conditions that can even lead to death. For symptoms please see "Common problems of diabetes".

- If your insulin treatment is being combined with one of a class of diabetes medicines called thiazolidinediones or glitazones, such as pioglitazone, tell your doctor as soon as possible if you get signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling caused by fluid retention (oedema).
- If you have a serious allergic reaction to insulin or any of the ingredients in Lyumjev, stop using this medicine and contact emergency medical services straight away.
- Always check the pack and the label for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Lyumjev that your doctor has told you to use.
- Keep the carton, or keep a note of the batch number on the carton. If you have a side effect you can then provide that number when you report the advere side effect, see "reporting of side effects".
- Always use a new needle for each injection to prevent infections and blocked needles. If a needle is blocked replace it with a new needle.

- **Skin changes at the injection site.**

The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work well if you inject into a lumpy area (See How to use Lyumjev). Contact your doctor if you are currently injecting into a lumpy area before you start injecting into a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Children and adolescents
This medicine is not recommended for use in children below the age of 1 year.

Other medicines and Lyumjev
Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines. Some medicines affect your blood sugar level - this may mean your insulin dose has to change.

Your blood sugar levels may fall (hypoglycaemia) if you take:

- other medicines for diabetes (oral and injectable)
- sulphonamide antibiotics (for infections)
- acetylsalicylic acid (for pain and mild fever and to prevent blood clotting)
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors)
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril) (for some heart problems or high blood pressure)
- angiotensin II receptor blockers (for high blood pressure or heart problems)
- somatostatin analogues (such as octreotide, which are used to treat a rare condition involving too much growth hormone)

Your blood sugar levels may rise (hyperglycaemia) if you take:

- danazol (for endometriosis)
- the contraceptive pill (birth control pills)
- thyroid hormone replacement therapy (for thyroid problems)
- human growth hormone (for growth hormone deficiency)
- diuretics (for high blood pressure or if you have a build-up of water in your body)
- sympathomimetic agents (for serious allergic reactions or used in some cold remedies)
- corticosteroids (to treat asthma or autoimmune conditions)

Beta-blockers (used for high blood pressure, arrhythmia or angina) make it harder to recognise the warning signs of low blood sugar.

Lyumjev with alcohol
Your blood sugar levels may either rise or fall if you drink alcohol. Therefore the amount of insulin needed may change. You should therefore monitor your blood sugar level more often than usual.

Pregnancy and breast-feeding
If you are planning to have a baby, think you may be pregnant, are pregnant or breast-feeding, ask your doctor, nurse or pharmacist for advice before taking this medicine. The amount of insulin you need usually falls during the first 3 months of pregnancy and increases for the remaining 6 months. After you have had your baby your insulin requirements will likely return to how much you needed before your pregnancy.

There are no restrictions on treatment with Lyumjev during breast-feeding. If you are breast-feeding, you may need to alter your insulin intake or diet.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or using machines). You should contact your doctor about driving if you have:
- frequent episodes of hypoglycaemia
- reduced or absent warning signs of hypoglycaemia

Lyumjev contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

3. How to use Lyumjev

Always use this medicine exactly as described in this leaflet or as your doctor, pharmacist or nurse has told you. Check with them if you are not sure.

They will have told you exactly how much Lyumjev to use, when to use it, and how often. They will also tell you how often to visit your diabetes clinic.

To prevent the possible transmission of disease, each cartridge must be used by you only, even if the needle on the pen is changed.

You should always have spare insulin and another injection device in case you need them.

If you are blind or visually impaired you will need help from someone to make your injections.

Your doctor may tell you to use Lyumjev as well as a longer- or intermediate-acting insulin. Inject them separately. Lyumjev should not be mixed with any other insulin.

When to inject Lyumjev
Lyumjev is a mealtime insulin. You should use Lyumjev when you start to eat, or a minute or two before the meal; you also have the option to inject up to 20 minutes after starting the meal.

How much insulin to use
Your doctor will work out your dose based on your blood sugar and body weight and explain
- How much Lyumjev you need at each meal.
- How and when to check your blood sugar level.
- How to change your insulin dose depending on your blood sugar levels.
- What to do if you change your diet, or change how much you exercise, if you are ill or if you are using other medicines.
- If you change the type of insulin you use, you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.

Do not use Lyumjev
- If it does not look like water. Lyumjev must be clear, have no colour and no solid pieces in it. Check each time you inject yourself.
- If Lyumjev has not been stored correctly (see section 5 “How to store Lyumjev”).
- If the cartridge is damaged in any way, do not use.

Getting the pen ready to use
- First wash your hands. Disinfect the rubber membrane of the cartridge.
- **You must only use Lyumjev cartridges in Lilly insulin pens. Please make sure that Lyumjev or Lilly cartridges are mentioned in the leaflet accompanying your pen. The 3 ml cartridge only fits the 3 ml pen.**
- Follow the instructions that come with the pen. Put the cartridge into the pen.
- Use a new needle. (Needles are not included).
- Prime every time. The pen must be primed until you see insulin at the needle tip before each injection to make sure the pen is ready to dose. If you do not prime, you may get the wrong dose.

Injecting Lyumjev
- Before you make an injection, clean your skin.
- Inject under the skin (subcutaneous injection), as you were taught by your physician or nurse.
- After your injection, leave the needle in the skin for 5 seconds to make sure you receive the full dose. Make sure you inject at least 1 cm from the last injection and that you ‘rotate’ the places you inject (upper arm, thigh, buttocks or abdomen).
- If you do not have enough insulin in the pen to complete your dose, make a note of how much you still need to take. Prime a new pen and inject the remaining dose.
- If you need to inject another insulin at the same time as Lyumjev, use a different injection site.
- Do not inject directly into a vein.

After injecting
- As soon as you have done the injection, take the needle off the pen using the outer needle cap. This will keep the Lyumjev sterile and prevent leaking. It will also stop air going back into the pen and the needle clogging up. **Do not share your needles. Do not share your pen.** Replace the cap on your pen. Leave the cartridge in the pen.
- If you are unsure how much you have injected then check your blood sugar levels before deciding if you need another injection.

Further injections
- Every time you plan to make an injection use a new needle. Before every injection, prime the pen to clear any large air bubbles.
- Once the cartridge is empty, do not use it again.

If you use more Lyumjev than you should
If you inject too much Lyumjev, or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low (hypoglycaemia) and you can treat yourself, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor or nurse has advised you and have some rest. This will often get you over a low blood sugar or a minor insulin overdose. Check your blood sugar again after 15-20 mins until blood sugar is stabilised.

If you are unable to treat yourself (severe hypoglycaemia) because you feel too dizzy, weak, confused, have difficulty talking, lose consciousness or have a seizure you may need to be treated with glucagon. This can be given by someone who knows how to use it. Eat glucose or sugar after the glucagon. If glucagon does not work, you will have to go to hospital or call emergency services. Ask your doctor to tell you about glucagon.

Tell everyone you spend time with that you have diabetes. Tell them what could happen if your blood sugar gets too low, including the risk of passing out.
Let them know that if you pass out, they must: turn you on your side to avoid choking, get medical help straight away and not give you any food or drink because you may choke.

If you forget to use Lyumjev
If you forget to use your insulin or you usee less than you should, or are unsure how much you have injected, your blood sugar may get too high (hyperglycaemia). Check your blood sugar level to decide if an insulin dose is needed. Resume your usual dosing schedule at your next meal.

If you stop using Lyumjev
Do not stop or change your insulin unless your doctor tells you to. If you use less Lyumjev than you should, a high blood sugar may occur.

If high blood sugar (hyperglycaemia) is not treated it can be very serious and cause headaches, nausea, vomiting, abdominal pain, dehydration, unconsciousness, coma or even death (see section 4).

Three simple steps to reduce your risk of hypoglycaemia or hyperglycaemia are:
- Always keep a spare pen and cartridges, in case you lose your pen or cartridges or they get damaged.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Low blood sugar (hypoglycaemia) is very common with insulin treatment (may affect more than 1 in 10 people). It can be very serious. If your blood sugar level falls too much you may become unconscious. Serious hypoglycaemia may cause brain damage and may be life-threatening. If you have symptoms of low blood sugar, act **immediately** to increase your blood sugar level. See section 3 under 'If you use more Lyumjev than you should'.

Allergic reactions are common (may affect up to 1 in 10 people). They may be severe and they may include the following symptoms:

- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you have a serious allergic reaction (including an anaphylactic attack) to insulin or any of the ingredients in Lyumjev, stop using this medicine and contact emergency medical service straight away.

Other side effects include

Common
Injection site reactions. Some people get redness, pain, swelling or itching around the area of the insulin injection. This usually clears up in a few minutes to a few weeks without needing to stop Lyumjev. If you have injection site reactions, tell your doctor.

Uncommon (may affect up to 1 in 100 people)
Skin changes at the injection site: If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by the build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Other potential side effects
Swelling in arms or ankles due to fluid retention (oedema) particularly at the start of insulin therapy or during a change in your diabetes medicines.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

Low blood sugar
Low blood sugar (hypoglycaemia) means there is not enough sugar in the blood. This can be caused if:
- you take too much Lyumjev or other insulin;
- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;
- you have an infection or illness (especially diarrhoea or vomiting);
- there is a change in your need for insulin for example if you lose weight; or you have trouble with your kidneys or liver which gets worse.

See section "If you use more Lyumjev than you should".

The first symptoms of low blood sugar usually come on quickly and include the following:

- tiredness
- rapid heart beat
- nervousness or shakiness
- feeling sick
- headache
- cold sweat

If you are not confident about recognising your warning symptoms, avoid situations such as driving a car, in which you or others would be put at risk by hypoglycaemia.

High blood sugar (hyperglycaemia) and diabetic ketoacidosis
Hyperglycaemia (too much sugar in the blood) means that the levels of glucose in your body are too high. Hyperglycaemia can be brought about by:
- not taking your insulin;
- using less insulin than your body needs;
- an imbalance between the amount of carbohydrates you eat and the insulin you take; or
- fever, infection or emotional stress.

The early symptoms of hyperglycaemia are;
- being very thirsty
- headache
- feeling sleepy
- urinating more often

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. Additional symptoms include the following:
- nausea and/or vomiting
- abdominal pain
- rapid pulse
- heavy breathing
- moderate or large amounts of urine ketones. Ketones are produced when your body burns fat for energy instead of glucose.

If you have any of these symptoms and high sugars **get medical help immediately.**
See section 'If you forget to use Lyumjev'.

Illness
If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Lyumjev

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Before first use
Store in a refrigerator (2 °C to 8 °C).
Do not freeze.

Keep in the outer carton in order to protect from light.

After first use (after cartridge insertion into the pen)
Do not store above 30 °C.
Do not freeze.
Do not refrigerate.

The pen with the inserted cartridge should not be stored with the needle attached.
Keep the cap on the pen in order to protect from light.
Discard after 28 days **even if some of the solution remains**.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Lyumjev 100 units/ml solution for injection in cartridge contains
- The active substance is insulin lispro. Each ml solution contains 100 units of insulin lispro. One cartridge contains 300 units of insulin lispro in 3 ml solution.
- The other ingredients are metacresol, glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, water for injections. Sodium hydroxide or hydrochloric acid may have been used to adjust the pH (see the end of section 2 under 'Lyumjev contains sodium').

What Lyumjev looks like and contents of the pack
Lyumjev 100 units/ml, solution for injection is a clear, colourless, aqueous solution in a cartridge. Each cartridge contains 300 units (3 millilitres). Pack sizes of 2, 5 or 10 cartridges. Not all pack sizes may be marketed.

Marketing Authorisation Holder
Eli Lilly Nederland B.V., Papendorpseweg 83, 3528 BJ Utrecht, The Netherlands.

Manufacturer
Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France.

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/.

Package leaflet: Information for the user

Lyumjev 100 units/ml KwikPen solution for injection in pre-filled pen
insulin lispro

Each KwikPen delivers 1 to 60 units in steps of 1 units.

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Lyumjev KwikPen is and what it is used for

Lyumjev 100 units/ml KwikPen solution for injection in pre-filled pen contains the active ingredient insulin lispro. Lyumjev is used to treat diabetes mellitus in adults, adolescents and children aged 1 year and above. It is a mealtime insulin that works more quickly than other medicines containing insulin lispro. Lyumjev contains ingredients that speed up absorption of insulin lispro into the body.

Diabetes is a condition in which your body does not make enough insulin or does not use insulin effectively, which results in effects such as high levels of sugar in the blood. Lyumjev is an insulin medicinethat is used in the treatment of diabetes and so controls blood sugar. Effective treatment of diabetes, with good control of blood sugar, prevents long-term complications from your diabetes.

Treatment with Lyumjev helps to control blood sugar in the long term and prevent complications from your diabetes. Lyumjev has its maximum effect 1 to 3 hours after injection and the effect lasts for up to 5 hours. You should use Lyumjev at the start of the meal, or up to 20 minutes after starting the meal.

Your doctor may tell you to use Lyumjev as well as a longer- or intermediate-acting insulin. Do not change your insulin unless your doctor tells you to.

The Lyumjev 100 units/ml KwikPen is a disposable pre-filled pen containing 3 ml (300 units, 100 units/ml) of insulin lispro. One KwikPen contains multiple doses of insulin. The KwikPen dials 1 unit at a time. **The number of units are displayed in the dose window, always check this before your injection.** You can give from 1 to 60 units in a single injection. **If your dose is more than 60 units, you will need to give yourself more than one injection.**

2. What you need to know before you use Lyumjev KwikPen

Do NOT use Lyumjev KwikPen
- if you think your blood sugar is dropping (**hypoglycaemia**). Further on, this leaflet tells you how to deal with low blood sugar (see section 3 under "If you use more Lyumjev than you should").
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Lyumjev.

If you cannot see very well you will need help from someone who has been trained to give injections.

- **Low blood sugar** (hypoglycaemia).

Low blood sugar can be serious and untreated hypoglycaemia may even lead to death.
Lyumjev starts to lower blood sugar faster than some other mealtime insulins. If hypoglycaemia occurs, you may experience it earlier after an injection of Lyumjev. If you often have hypoglycaemia or have difficulty recognising it, please discuss this with your doctor or nurse. If your blood sugar levels are well controlled by your current insulin therapy or after long duration of diabetes, you may not feel the warning symptoms when your blood sugar is falling too low.Warning signs are listed later in this leaflet. For symptoms please see "Common problems of diabetes".

You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood sugar often. Making changes to the types of insulin you use may cause your blood sugar to rise or fall too much. It may be necessary to increase the frequency of blood sugar testing if you are at risk of low blood sugars. Your doctor may need to change the doses of your other diabetes medicines.

- **High blood sugar** (hyperglycaemia).

Stopping or not taking enough insulin may lead to high blood sugar (hyperglycaemia) and diabetic ketoacidosis, serious conditions that can even lead to death. For symptoms please see "Common problems of diabetes".

- If your insulin treatment is being combined with one of a class of diabetes medicines called thiazolidinediones or glitazones, such as pioglitazone, tell your doctor as soon as possible if you get signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling caused by fluid retention (oedema).
- If you have a serious allergic reaction to insulin or any of the ingredients in Lyumjev, stop using this medicine and contact emergency medical services straight away.
- Always check the pack and the label for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Lyumjev that your doctor has told you to use.
- Keep the carton, or keep a note of the batch number on the carton. If you have a side effect you can then provide that number when you report the advere side effect, see "reporting of side effects".
- Always use a new needle for each injection to prevent infections and blocked needles. If a needle is blocked replace it with a new needle.

- **Skin changes at the injection site.**

The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work well if you inject into a lumpy area (See How to use Lyumjev KwikPen). Contact your doctor if you are currently injecting into a lumpy area before you start injecting into a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Children and adolescents
This medicine is not recommended for use in children below the age of 1 year.

Other medicines and Lyumjev
Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines. Some medicines affect your blood sugar level - this may mean your insulin dose has to change.

Your blood sugar levels may fall (hypoglycaemia) if you take:

- other medicines for diabetes (oral and injectable)
- sulphonamide antibiotics (for infections)
- acetylsalicylic acid (for pain and mild fever and to prevent blood clotting)
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors)
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril) (for some heart problems or high blood pressure)
- angiotensin II receptor blockers (for high blood pressure or heart problems)
- somatostatin analogues (such as octreotide, which are used to treat a rare condition involving too much growth hormone)

Your blood sugar levels may rise (hyperglycaemia) if you take:

- danazol (for endometriosis)
- the contraceptive pill (birth control pills)
- thyroid hormone replacement therapy (for thyroid problems)
- human growth hormone (for growth hormone deficiency)
- diuretics (for high blood pressure or if you have a build-up of water in your body)
- sympathomimetic agents (for serious allergic reactions or used in some cold remedies)
- corticosteroids (to treat asthma or autoimmune conditions)

Beta-blockers (used for high blood pressure, arrhythmia or angina) make it harder to recognise the warning signs of low blood sugar.

Lyumjev with alcohol
Your blood sugar levels may either rise or fall if you drink alcohol. Therefore the amount of insulin needed may change. You should therefore monitor your blood sugar level more often than usual.

Pregnancy and breast-feeding
If you are planning to have a baby, think you may be pregnant, are pregnant or breast-feeding, ask your doctor, nurse or pharmacist for advice before taking this medicine. The amount of insulin you need usually falls during the first 3 months of pregnancy and increases for the remaining 6 months. After you have had your baby your insulin requirements will likely return to how much you needed before your pregnancy.

There are no restrictions on treatment with Lyumjev during breast-feeding. If you are breast-feeding, you may need to alter your insulin intake or diet.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or using machines). You should contact your doctor about driving if you have:
- frequent episodes of hypoglycaemia
- reduced or absent warning signs of hypoglycaemia

Lyumjev KwikPen contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use Lyumjev KwikPen

Always use this medicine exactly as described in this leaflet or as your doctor, pharmacist or nurse has told you. Check with them if you are not sure.

They will have told you exactly how much Lyumjev to use, when to use it, and how often. They will also tell you how often to visit your diabetes clinic.

To prevent the possible transmission of disease, each pen must be used by you only, even if the needle is changed.

You should always have spare insulin and another injection device in case you need them.

If you are blind or visually impaired you will need help from someone to make your injections.

Your doctor may tell you to use Lyumjev as well as a longer- or intermediate-acting insulin. Inject them separately. Lyumjev should not be mixed with any other insulin.

When to inject Lyumjev
Lyumjev is a mealtime insulin. You should use Lyumjev when you start to eat, or a minute or two before the meal; you also have the option to inject up to 20 minutes after starting the meal.

How much insulin to use
Your doctor will work out your dose based on your blood sugar and body weight and explain
- How much Lyumjev you need at each meal.
- How and when to check your blood sugar level.
- How to change your insulin dose depending on your blood sugar levels.
- What to do if you change your diet, or change how much you exercise, if you are ill or if you are using other medicines.
- If you change the type of insulin you use, you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.

Do not use Lyumjev
- If it does not look like water. Lyumjev must be clear, have no colour and no solid pieces in it. Check each time you inject yourself.
- If Lyumjev has not been stored correctly (see section 5 "How to store Lyumjev").
- If the pen is damaged in any way, do not use.

Getting the KwikPen ready to use (Please see instructions for use)
- First wash your hands.
- Read the instructions on how to use your pre-filled insulin pen. Please follow the instructions carefully. Here are some reminders.
- Use a new needle. (Needles are not included).
- Prime your KwikPen before each use. This checks that insulin comes out and clears the air bubbles from your KwikPen. There may still be some small air bubbles left in the pen. Small air bubbles are normal and will not affect your dose.
- The number of units are displayed in the dose window, always check this before your injection.

Injecting Lyumjev
- Before you make an injection, clean your skin.
- Inject under the skin (subcutaneous injection), as you were taught by your physician or nurse.

- After your injection, leave the needle in the skin for 5 seconds to make sure you receive the full dose. Make sure you inject at least 1 cm from the last injection and that you 'rotate' the places you inject (upper arm, thigh, buttocks or abdomen).
- If you do not have enough insulin in the pen to complete your dose, make a note of how much you still need to take. Prime a new pen and inject the remaining dose.
- If you need to inject another insulin at the same time as Lyumjev, use a different injection site.
- Do not inject directly into a vein.

After injecting
- As soon as you have done the injection, unscrew the needle from the KwikPen using the outer needle cap. This will keep the insulin sterile and stop it leaking. It also stops air entering the pen and your needle clogging. **Do not share your needles**. **Do not share your pen**. Replace the cap on your pen.
- If you are unsure how much you have injected then check your blood sugar levels before deciding if you need another injection.

Further injections
- Every time you use a KwikPen you must use a new needle. Before every injection, clear any air bubbles. You can see how much insulin is left by holding the KwikPen with the needle pointing up.
- Once the KwikPen is empty, do not use it again.

If you use more Lyumjev than you should
If you inject too much Lyumjev, or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low (hypoglycaemia) and you can treat yourself, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor or nurse has advised you and have some rest. This will often get you over a low blood sugar or a minor insulin overdose. Check your blood sugar again after 15-20 mins until blood sugar is stabilised.

If you are unable to treat yourself (severe hypoglycaemia) because you feel too dizzy, weak, confused, have difficulty talking, lose consciousness or have a seizure you may need to be treated with glucagon. This can be given by someone who knows how to use it. Eat glucose or sugar after the glucagon. If glucagon does not work, you will have to go to hospital or call emergency services. Ask your doctor to tell you about glucagon.

Tell everyone you spend time with that you have diabetes. Tell them what could happen if your blood sugar gets too low, including the risk of passing out.
Let them know that if you pass out, they must: turn you on your side to avoid choking, get medical help straight away and not give you any food or drink because you may choke.

If you forget to use Lyumjev
If you forget to use your insulin or you use less than you should, or are unsure how much you have injected, your blood sugar may get too high (hyperglycaemia). Check your blood sugar level to decide if an insulin dose is needed. Resume your usual dosing schedule at your next meal.

If you stop using Lyumjev
Do not stop or change your insulin unless your doctor tells you to. If you use less Lyumjev than you should, a high blood sugar may occur.

If high blood sugar (hyperglycaemia) is not treated it can be very serious and cause headaches, nausea, vomiting, abdominal pain, dehydration, unconsciousness, coma or even death (see section 4).

Three simple steps to reduce your risk of hypoglycaemia or hyperglycaemia are:
- Always keep a spare pen in case you lose your KwikPen or it gets damaged.

- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Low blood sugar (hypoglycaemia) is very common with insulin treatment (may affect more than 1 in 10 people). It can be very serious. If your blood sugar level falls too much you may become unconscious. Serious hypoglycaemia may cause brain damage and may be life-threatening. If you have symptoms of low blood sugar, act **immediately** to increase your blood sugar level. See section 3 under 'If you use more Lyumjev than you should'.

Allergic reactions are common (may affect up to 1 in 10 people). They may be severe and they may include the following symptoms:

- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you have a serious allergic reaction (including an anaphylactic attack) to insulin or any of the ingredients in Lyumjev, stop using this medicine and contact emergency medical service straight away.

Other side effects include

Common
Injection site reactions. Some people get redness, pain, swelling or itching around the area of the insulin injection. This usually clears up in a few minutes to a few weeks without needing to stop Lyumjev. If you have injection site reactions, tell your doctor.

Uncommon (may affect up to 1 in 100 people)
Skin changes at the injection site: If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by the build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Other potential side effects
Swelling in arms or ankles due to fluid retention (oedema) particularly at the start of insulin therapy or during a change in your diabetes medicines.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

Low blood sugar
Low blood sugar (hypoglycaemia) means there is not enough sugar in the blood. This can be caused if:
- you take too much Lyumjev or other insulin;

- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;
- you have an infection or illness (especially diarrhoea or vomiting);
- there is a change in your need for insulin for example if you lose weight; or you have trouble with your kidneys or liver which gets worse.

See section "If you use more Lyumjev than you should".

The first symptoms of low blood sugar usually come on quickly and include the following:

- tiredness
- rapid heart beat
- nervousness or shakiness
- feeling sick
- headache
- cold sweat

If you are not confident about recognising your warning symptoms, avoid situations such as driving a car, in which you or others would be put at risk by hypoglycaemia.

High blood sugar (hyperglycaemia) and diabetic ketoacidosis
Hyperglycaemia (too much sugar in the blood) means that the levels of glucose in your body are too high. Hyperglycaemia can be brought about by:

- not taking your insulin;
- using less insulin than your body needs;
- an imbalance between the amount of carbohydrates you eat and the insulin you take; or
- fever, infection or emotional stress.

The early symptoms of hyperglycaemia are;

- being very thirsty
- headache
- feeling sleepy
- urinating more often

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. Additional symptoms include the following:

- nausea and/or vomiting
- abdominal pain
- rapid pulse
- heavy breathing
- moderate or large amounts of urine ketones. Ketones are produced when your body burns fat for energy instead of glucose.

If you have any of these symptoms and high sugars **get medical help immediately.**
See section 'If you forget to use Lyumjev'.

Illness
If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Lyumjev KwikPen

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Before first use
Store in a refrigerator (2 °C to 8 °C).
Do not freeze.
Keep in the outer carton in order to protect from light.

After first use
Do not store above 30 °C.
Do not freeze.
Do not refrigerate.

The KwikPen should not be stored with the needle attached. Keep the cap on the pen in order to protect from light.
Discard after 28 days **even if some of the solution remains**.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Lyumjev 100 units/ml KwikPen solution for injection contains
- The active substance is insulin lispro. Each ml solution contains 100 units of insulin lispro. One KwikPen contains 300 units of insulin lispro in 3 ml solution.
- The other ingredients are metacresol, glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, water for injections. Sodium hydroxide or hydrochloric acid may have been used to adjust the pH (see the end of section 2 under 'Lyumjev KwikPen contains sodium').

What Lyumjev KwikPen looks like and contents of the pack
Lyumjev KwikPen solution for injection is a clear, colourless, aqueous solution in a pre-filled pen. Each pre-filled pen contains 300 units (3 millilitres).

Pack sizes of 2, 5 or a multipack of 2 x 5 pre-filled pens. Not all pack sizes may be marketed.

The Lyumjev KwikPen is taupe. The dose knob is blue with raised ridges on side. The label is blue and white. Each Lyumjev KwikPen delivers 1 to 60 units in steps of 1 unit.

Marketing Authorisation Holder
Eli Lilly Nederland B.V., Papendorpseweg 83, 3528 BJ Utrecht, The Netherlands.

Manufacturer
Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France.

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/.

Instructions for Use

Lyumjev 100 units/mL KwikPen solution for injection in pre-filled pen
insulin lispro

PLEASE READ THESE INSTRUCTIONS BEFORE USE

Read the instructions for use before you start taking Lyumjev and each time you get another Lyumjev KwikPen. There may be new information. This information does not take the place of talking to your healthcare professional about your medical condition or your treatment.

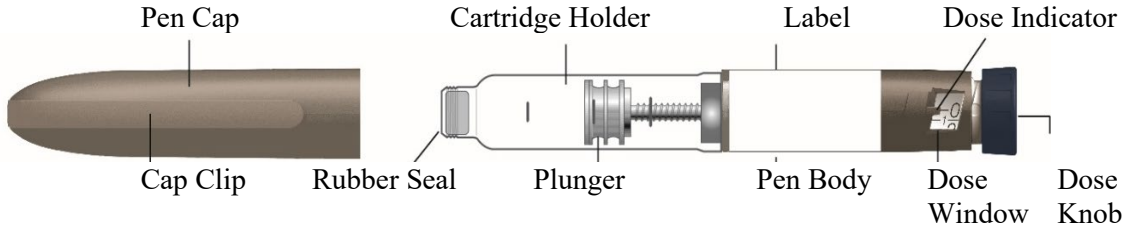
Do not share your Lyumjev KwikPen with other people, even if the needle has been changed. Do not reuse or share needles with other people. You may give other people a serious infection or get a serious infection from them.

Lyumjev 100 units/mL KwikPen ("Pen") is a disposable pre-filled pen containing 3 mL (300 units, 100 units/mL) of insulin lispro solution for injection.

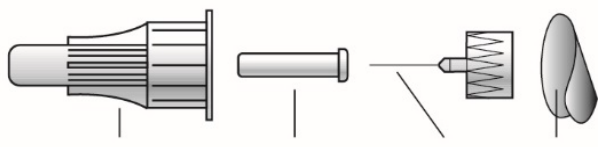
- Your healthcare professional will tell you how many units to give as your dose and how to inject your prescribed dose of insulin.
- You can give yourself more than 1 dose from the Pen.
- Each turn of the dose knob dials 1 unit of insulin. You can give from 1 to 60 units in a single injection.
- If your dose is more than 60 units, you will need to give yourself more than 1 injection. Always check the number in the dose window to make sure you dialed the correct dose.
- The plunger only moves a little with each injection, and you may not notice that it moves. The plunger will only reach the end of the cartridge when you have used all 300 units in the Pen.

People who are blind or have vision problems should not use the Pen without help from a person trained to use the Pen.

Lyumjev KwikPen Parts



Pen Needle Parts
(Needles Not Included)



Dose Knob

Outer Needle Shield	Inner Needle Shield	Needle	Paper Tab

How to recognize your Lyumjev KwikPen

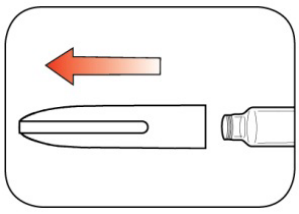
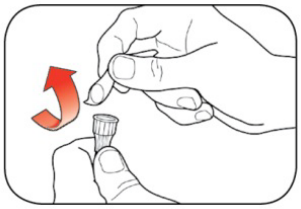
- Pen colour: Taupe
- Dose Knob: Blue, with raised ridges on side
- Label: Blue and white

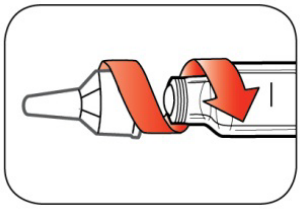
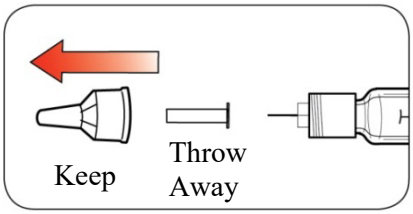
Supplies needed to give your injection

- Lyumjev KwikPen
- KwikPen compatible needle (BD [Becton, Dickinson and Company] Pen needles recommended)
- Swab or gauze

Preparing your Pen

- Wash your hands with soap and water.
- Check the Pen to make sure you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
- **Do not** use your Pen past the expiry date printed on the label or for more than 28 days after you first start using the Pen.
- Always use a **new needle** for each injection to help prevent infections and blocked needles.

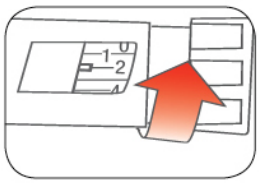
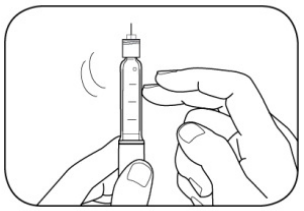
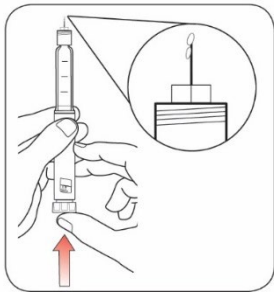
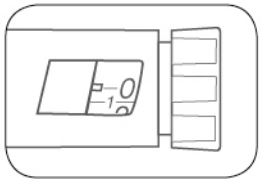
Step 1: • Pull the Pen cap straight off. – **Do not** remove the Pen label. • Wipe the rubber seal with a swab.	
Step 2: • Check the liquid in the Pen. • Lyumjev should look clear and colourless. **Do not** use if it is cloudy, coloured, or has particles or clumps in it.	
Step 3: • Select a new needle. • Pull off the paper tab from the outer needle shield.	

Step 4: • Push the capped needle straight onto the Pen and twist the needle on until it is tight.	
Step 5: • Pull off the outer needle shield. **Do not** throw it away. • Pull off the inner needle shield and throw it away.	

Priming your Pen

Prime before each injection.

- Priming your Pen means removing the air from the needle and cartridge that may collect during normal use and ensures that your Pen is working correctly.
- If you **do not** prime before each injection, you may get too much or too little insulin.

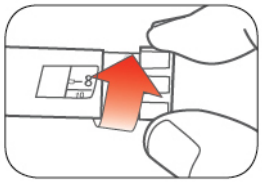
Step 6: • To prime your Pen, turn the dose knob to select 2 units.	
Step 7: • Hold your Pen with the needle pointing up. Tap the cartridge holder gently to collect air bubbles at the top.	
Step 8: • Continue holding your Pen with the needle pointing up. Push the dose knob in until it stops and "**0**" is seen in the dose window. Hold the dose knob in and **count to 5 slowly**. You should see insulin at the tip of the needle. – If you **do not** see insulin, repeat priming steps 6 to 8, but not more than 4 times. – If you **still do not** see insulin, change the needle and repeat priming steps 6 to 8. Small air bubbles are normal and will not affect your dose.	 

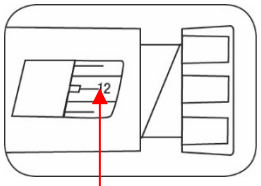
Selecting your dose

- You can give from 1 to 60 units in a single injection.
- If your dose is more than 60 units, you will need to give more than 1 injection.
  - If you need help with dividing up your dose the right way, ask your healthcare professional.
  - Use a new needle for each injection and repeat the priming steps.

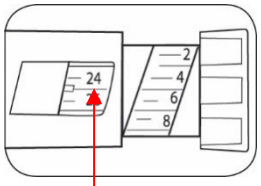
Step 9:

- Turn the dose knob to select the number of units you need to inject. The dose indicator should line up with your dose.
  - The Pen dials 1 unit at a time.
  - The dose knob clicks as you turn it.
  - **Do not** dial your dose by counting the clicks. You may dial the wrong dose. This may lead to getting too much insulin or not enough insulin.
  - The dose can be corrected by turning the dose knob in either direction until the correct dose lines up with the dose indicator.
  - The **even** numbers are printed on the dial. The example to the right shows 12 units.
  - The **odd** numbers, after the number 1, are shown as full lines between the numbers. The example to the right shows 25 units.
- **Always check the number in the dose window to make sure you have dialed the correct dose.**





Example: 12 units shown in the dose window



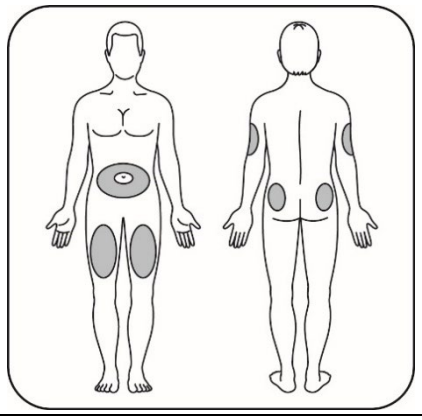
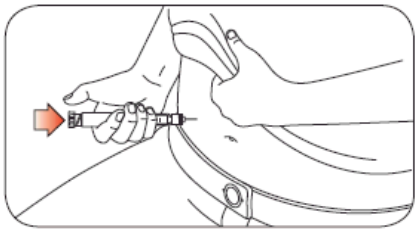
Example: 25 units shown in the dose window

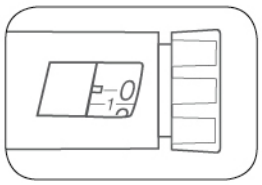
- The Pen will not let you dial more than the number of units left in the Pen.
- If you need to inject more than the number of units left in the Pen, you may either:
  - inject the amount left in your Pen and then use a new Pen to give the rest of your dose,

  or
  - get a new Pen and inject the full dose.
- It is normal to see a small amount of insulin left in the Pen that you cannot inject.

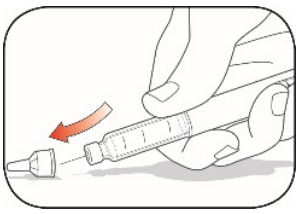
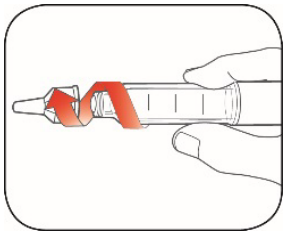
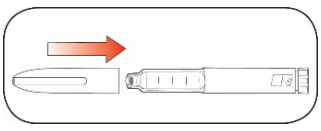
Giving your injection

- Inject your insulin as your healthcare professional has shown you.
- Change (rotate) your injection site for each injection.
- **Do not** try to change your dose while injecting.

Step 10: • Choose your injection site. Lyumjev is injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs or upper arms. • Wipe your skin with a swab, and let your skin dry before you inject your dose.	
Step 11: • Insert the needle into your skin. • Push the dose knob all the way in. • Continue to hold the dose knob in and **slowly count to 5** before removing the needle.  **Do not** try to inject your insulin by turning the dose knob. You will **not** receive your insulin by turning the dose knob.	

Step 12: • Pull the needle out of your skin. – A drop of insulin at the needle tip is normal. It will not affect your dose. • Check the number in the dose window. – If you see “0” in the dose window, you have received the full amount you dialed. – If you do not see “0” in the dose window, you did not receive your full dose. **Do not** redial. Insert the needle into your skin and finish your injection. – If you **still** do not think you received the full amount you dialed for your injection, **do not start over or repeat that injection**. Monitor your blood glucose as instructed by your healthcare professional. – If you normally need to give 2 injections for your full dose, be sure to give your second injection. The plunger only moves a little with each injection, and you may not notice that it moves. If you see blood after you take the needle out of your skin, press the injection site lightly with a piece of gauze or a swab. **Do not** rub the area.	

After your injection

Step 13: • Carefully replace the outer needle shield.	
Step 14: • Unscrew the capped needle and dispose of it as described below (see **Disposing of Pens and needles** section). • **Do not** store the Pen with the needle attached to prevent leaking, blocking the needle, and air from entering the Pen.	
Step 15: • Replace the Pen cap by lining up the cap clip with the dose indicator and pushing straight on.	

Disposing of Pens and needles

- Put used needles in a sharps container or a hard plastic container with a secure lid. **Do not** throw needles directly into your household waste.
- **Do not** recycle the filled sharps container.
- Ask your healthcare professional about options to dispose of the Pen and the sharps container properly.
- The directions regarding needle handling are not intended to replace local, healthcare professional or institutional policies.

Troubleshooting

- If you cannot remove the Pen cap, gently twist the cap back and forth, and then pull the cap straight off.
- If the dose knob is hard to push:

– pushing the dose knob more slowly will make it easier to inject.

– your needle may be blocked. Put on a new needle and prime the Pen.

– you may have dust, food, or liquid inside the Pen. Throw the Pen away and get a new Pen.

If you have any questions or problems with your Lyumjev 100 units/mL KwikPen, call your healthcare professional for help or contact your local Lilly affiliate.

Document Revision Date:

Package leaflet: Information for the user

Lyumjev 100 units/ml Junior KwikPen solution for injection in pre-filled pen
insulin lispro

Each Junior KwikPen delivers 0.5 to 30 units in steps of 0.5 units.

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Lyumjev Junior KwikPen is and what it is used for

Lyumjev 100 units/ml Junior KwikPen solution for injection in pre-filled pen contains the active ingredient insulin lispro. Lyumjev is used to treat diabetes mellitus in adults, adolescents and children aged 1 year and above. It is a mealtime insulin that works more quickly than other medicines containing insulin lispro. Lyumjev contains ingredients that speed up absorption of insulin lispro into the body.

Diabetes is a condition in which your body does not make enough insulin or does not use insulin effectively, which results in effects such as high levels of sugar in the blood. Lyumjev is an insulin medicinethat is used in the treatment of diabetes and so controls blood sugar. Effective treatment of diabetes, with good control of blood sugar, prevents long-term complications from your diabetes.

Treatment with Lyumjev helps to control blood sugar in the long term and prevent complications from your diabetes. Lyumjev has its maximum effect 1 to 3 hours after injection and the effect lasts for up to 5 hours. You should use Lyumjev at the start of the meal, or up to 20 minutes after starting the meal.

Your doctor may tell you to use Lyumjev as well as a longer- or intermediate-acting insulin. Do not change your insulin unless your doctor tells you to.

Lyumjev 100 units/ml Junior KwikPen is a disposable pre-filled pen containing 3 ml (300 units, 100 units/ml) of insulin lispro. One KwikPen contains multiple doses of insulin. The KwikPen dials half unit (0.5 unit) at a time. **The number of units are displayed in the dose window, always check this before your injection.** You can give from 0.5 unit to 30 units in a single injection. **If your dose is more than 30 units, you will need to give yourself more than one injection.**

2. What you need to know before you use Lyumjev Junior KwikPen

Do NOT use Lyumjev Junior KwikPen
- if you think your blood sugar is dropping (**hypoglycaemia**). Further on this leaflet tells you how to deal with low blood sugar (see section 3 under "If you use more Lyumjev than you should").
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Lyumjev.

If you cannot see very well you will need help from someone who has been trained to give injections.

- **Low blood sugar** (hypoglycaemia).

Low blood sugar can be serious and untreated hypoglycaemia may even lead to death.
Lyumjev starts to lower blood sugar faster than some other mealtime insulins. If hypoglycaemia occurs, you may experience it earlier after an injection of Lyumjev. If you often have hypoglycaemia or have difficulty recognising it, please discuss this with your doctor or nurse. If your blood sugar levels are well controlled by your current insulin therapy or after long duration of diabetes, you may not feel the warning symptoms when your blood sugar is falling too low.Warning signs are listed later in this leaflet. For symptoms please see "Common problems of diabetes".

You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood sugar often. Making changes to the types of insulin you use may cause your blood sugar to rise or fall too much. It may be necessary to increase the frequency of blood sugar testing if you are at risk of low blood sugars. Your doctor may need to change the doses of your other diabetes medicines.

- **High blood sugar** (hyperglycaemia).

Stopping or not taking enough insulin may lead to high blood sugar (hyperglycaemia) and diabetic ketoacidosis, serious conditions that can even lead to death. For symptoms please see "Common problems of diabetes".

- If your insulin treatment is being combined with one of a class of diabetes medicines called thiazolidinediones or glitazones, such as pioglitazone, tell your doctor as soon as possible if you get signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling caused by fluid retention (oedema).
- If you have a serious allergic reaction to insulin or any of the ingredients in Lyumjev, stop using this medicine and contact emergency medical services straight away.
- Always check the pack and the label for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Lyumjev that your doctor has told you to use.
- Keep the carton, or keep a note of the batch number on the carton. If you have a side effect you can then provide that number when you report the advere side effect, see "reporting of side effects".
- Always use a new needle for each injection to prevent infections and blocked needles. If a needle is blocked replace it with a new needle.

- **Skin changes at the injection site.**

The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work well if you inject into a lumpy area (See How to use Lyumjev Junior KwikPen). Contact your doctor if you are currently injecting into a lumpy area before you start injecting into a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Children and adolescents
This medicine is not recommended for use in children below the age of 1 year.

Other medicines and Lyumjev
Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines. Some medicines affect your blood sugar level - this may mean your insulin dose has to change.

Your blood sugar levels may fall (hypoglycaemia) if you take:

- other medicines for diabetes (oral and injectable)
- sulphonamide antibiotics (for infections)
- acetylsalicylic acid (for pain and mild fever and to prevent blood clotting)
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors)
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril) (for some heart problems or high blood pressure)
- angiotensin II receptor blockers (for high blood pressure or heart problems)
- somatostatin analogues (such as octreotide, which are used to treat a rare condition involving too much growth hormone)

Your blood sugar levels may rise (hyperglycaemia) if you take:

- danazol (for endometriosis)
- the contraceptive pill (birth control pills)
- thyroid hormone replacement therapy (for thyroid problems)
- human growth hormone (for growth hormone deficiency)
- diuretics (for high blood pressure or if you have a build-up of water in your body)
  sympathomimetic agents (for serious allergic reactions or used in some cold remedies)
- corticosteroids (to treat asthma or autoimmune conditions)

Beta-blockers (used for high blood pressure, arrhythmia or angina) make it harder to recognise the warning signs of low blood sugar.

Lyumjev with alcohol
Your blood sugar levels may either rise or fall if you drink alcohol. Therefore the amount of insulin needed may change. You should therefore monitor your blood sugar level more often than usual.

Pregnancy and breast-feeding
If you are planning to have a baby, think you may be pregnant, are pregnant or breast-feeding, ask your doctor, nurse or pharmacist for advice before taking this medicine. The amount of insulin you need usually falls during the first 3 months of pregnancy and increases for the remaining 6 months. After you have had your baby your insulin requirements will likely return to how much you needed before your pregnancy.

There are no restrictions on treatment with Lyumjev during breast-feeding. If you are breast-feeding, you may need to alter your insulin intake or diet.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or using machines). You should contact your doctor about driving if you have:
- frequent episodes of hypoglycaemia
- reduced or absent warning signs of hypoglycaemia

Lyumjev Junior KwikPen contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use Lyumjev Junior KwikPen

Always use this medicine exactly as described in this leaflet or as your doctor, pharmacist or nurse has told you. Check with them if you are not sure.

They will have told you exactly how much Lyumjev to use, when to use it, and how often. They will also tell you how often to visit your diabetes clinic.

To prevent the possible transmission of disease, each pen must be used by you only, even if the needle is changed.

You should always have spare insulin and another injection device in case you need them.

If you are blind or visually impaired you will need help from someone to make your injections.

Your doctor may tell you to use Lyumjev as well as a longer- or intermediate-acting insulin. Inject them separately. Lyumjev should not be mixed with any other insulin.

When to inject Lyumjev
Lyumjev is a mealtime insulin. You should use Lyumjev when you start to eat, or a minute or two before the meal; you also have the option to inject up to 20 minutes after starting the meal.

How much insulin to use
Your doctor will work out your dose based on your blood sugar and body weight and explain
- How much Lyumjev you need at each meal.
- How and when to check your blood sugar level.
- How to change your insulin dose depending on your blood sugar levels.
- What to do if you change your diet, or change how much you exercise, if you are ill or if you are using other medicines.
- If you change the type of insulin you use, you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.

Do not use Lyumjev
- If it does not look like water. Lyumjev must be clear, have no colour and no solid pieces in it. Check each time you inject yourself.
- If Lyumjev has not been stored correctly (see section 5 "How to store Lyumjev").
- If the pen is damaged in any way, do not use.

Getting the Lyumjev Junior KwikPen ready to use (Please see instructions for use)
- First wash your hands.
- Read the instructions on how to use your pre-filled insulin pen. Please follow the instructions carefully. Here are some reminders.
- Use a new needle. (Needles are not included).
- Prime your Lyumjev Junior KwikPen before each use. This checks that insulin comes out and clears the air bubbles from your Lyumjev Junior KwikPen. There may still be some small air bubbles left in the pen. Small air bubbles are normal and will not affect your dose.
- The number of units are displayed in the dose window, always check this before your injection.

Injecting Lyumjev
- Before you make an injection, clean your skin.
- Inject under the skin (subcutaneous injection), as you were taught by your physician or nurse.

- After your injection, leave the needle in the skin for 5 seconds to make sure you receive the full dose. Make sure you inject at least 1 cm from the last injection and that you 'rotate' the places you inject (upper arm, thigh, buttocks or abdomen).
- If you do not have enough insulin in the pen to complete your dose, make a note of how much you still need to take. Prime a new pen and inject the remaining dose.
- If you need to inject another insulin at the same time as Lyumjev, use a different injection site.
- Do not inject directly into a vein.

After injecting
- As soon as you have done the injection, unscrew the needle from the Lyumjev Junior KwikPen using the outer needle cap. This will keep the insulin sterile and stop it leaking. It also stops air entering the pen and your needle clogging. **Do not share your needles**. **Do not share your pen**. Replace the cap on your pen.
- If you are unsure how much you have injected then check your blood sugar levels before deciding if you need another injection.

Further injections
- Every time you use a Lyumjev Junior KwikPen you must use a new needle. Before every injection, clear any air bubbles. You can see how much insulin is left by holding the Lyumjev Junior KwikPen with the needle pointing up.
- Once the Lyumjev Junior KwikPen is empty, do not use it again.

If you use more Lyumjev than you should
If you inject too much Lyumjev, or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low (hypoglycaemia) and you can treat yourself, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor or nurse has advised you and have some rest. This will often get you over a low blood sugar or a minor insulin overdose. Check your blood sugar again after 15-20 mins until blood sugar is stabilised.

If you are unable to treat yourself (severe hypoglycaemia) because you feel too dizzy, weak, confused, have difficulty talking, lose consciousness or have a seizure you may need to be treated with glucagon. This can be given by someone who knows how to use it. Eat glucose or sugar after the glucagon. If glucagon does not work, you will have to go to hospital or call emergency services. Ask your doctor to tell you about glucagon.

Tell everyone you spend time with that you have diabetes. Tell them what could happen if your blood sugar gets too low, including the risk of passing out.
Let them know that if you pass out, they must: turn you on your side to avoid choking, get medical help straight away and not give you any food or drink because you may choke.

If you forget to use Lyumjev
If you forget to use your insulin or you use less than you should, or are unsure how much you have injected, your blood sugar may get too high (hyperglycaemia). Check your blood sugar level to decide if an insulin dose is needed. Resume your usual dosing schedule at your next meal.

If you stop using Lyumjev
Do not stop or change your insulin unless your doctor tells you to. If you use less Lyumjev than you should, a high blood sugar may occur.

If high blood sugar (hyperglycaemia) is not treated it can be very serious and cause headaches, nausea, vomiting, abdominal pain, dehydration, unconsciousness, coma or even death (see section 4).

Three simple steps to reduce your risk of hypoglycaemia or hyperglycaemia are:
- Always keep a spare pen in case you lose your Lyumjev Junior KwikPen or it gets damaged.

- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Low blood sugar (hypoglycaemia) is very common with insulin treatment (may affect more than 1 in 10 people). It can be very serious. If your blood sugar level falls too much you may become unconscious. Serious hypoglycaemia may cause brain damage and may be life-threatening. If you have symptoms of low blood sugar, act **immediately** to increase your blood sugar level. See section 3 under 'If you use more Lyumjev than you should'.

Allergic reactions are common (may affect up to 1 in 10 people). They may be severe and they may include the following symptoms:

- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you have a serious allergic reaction (including an anaphylactic attack) to insulin or any of the ingredients in Lyumjev, stop using this medicine and contact emergency medical service straight away.

Other side effects include

Common
Injection site reactions. Some people get redness, pain, swelling or itching around the area of the insulin injection. This usually clears up in a few minutes to a few weeks without needing to stop Lyumjev. If you have injection site reactions, tell your doctor.

Uncommon (may affect up to 1 in 100 people)
Skin changes at the injection site: If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by the build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Other potential side effects
Swelling in arms or ankles due to fluid retention (oedema) particularly at the start of insulin therapy or during a change in your diabetes medicines.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

Low blood sugar
Low blood sugar (hypoglycaemia) means there is not enough sugar in the blood. This can be caused if:
- you take too much Lyumjev or other insulin;

- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;
- you have an infection or illness (especially diarrhoea or vomiting);

there is a change in your need for insulin for example if you lose weight; or you have trouble with your kidneys or liver which gets worse.See section 'If you use more Lyumjev than you should.'

The first symptoms of low blood sugar usually come on quickly and include the following:

- tiredness
- rapid heart beat
- nervousness or shakiness
- feeling sick
- headache
- cold sweat

If you are not confident about recognising your warning symptoms, avoid situations such as driving a car, in which you or others would be put at risk by hypoglycaemia.

High blood sugar (hyperglycaemia) and diabetic ketoacidosis
Hyperglycaemia (too much sugar in the blood) means that the levels of glucose in your body are too high. Hyperglycaemia can be brought about by:
- not taking your insulin;
- using less insulin than your body needs;
- an imbalance between the amount of carbohydrates you eat and the insulin you take; or
- fever, infection or emotional stress.

The early symptoms of hyperglycaemia are;
- being very thirsty
- headache
- feeling sleepy
- urinating more often

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. Additional symptoms include the following:
- nausea and/or vomiting
- abdominal pain
- rapid pulse
- heavy breathing
- moderate or large amounts of urine ketones. Ketones are produced when your body burns fat for energy instead of glucose.

If you have any of these symptoms and high sugars **get medical help immediately.**
See section 'If you forget to use Lyumjev'.

Illness
If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Lyumjev Junior KwikPen

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Before first use
Store in a refrigerator (2 °C to 8 °C).
Do not freeze.
Keep in the outer carton in order to protect from light.

After first use
Do not store above 30 °C.
Do not freeze.
Do not refrigerate.

The Lyumjev Junior KwikPen should not be stored with the needle attached. Keep the cap on the pen in order to protect from light.
Discard after 28 days **even if some of the solution remains**.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Lyumjev 100 units/ml Junior KwikPen solution for injection contains
- The active substance is insulin lispro. Each ml solution contains 100 units of insulin lispro. One Lyumjev Junior KwikPen contains 300 units of insulin lispro in 3 ml solution.
- The other ingredients are metacresol, glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, water for injections. Sodium hydroxide or hydrochloric acid may have been used to adjust the pH (see the end of section 2 under 'Lyumjev Junior KwikPen contains sodium').

What Lyumjev 100 units/ml Junior KwikPen looks like and contents of the pack
Lyumjev 100 units/ml Junior KwikPen solution for injection is a clear, colourless, aqueous solution in a pre-filled pen. Each pre-filled pen contains 300 units (3 millilitres).

Pack sizes of 2, 5 or a multipack of 2 x 5 pre-filled pens. Not all pack sizes may be marketed.

The Lyumjev Junior KwikPen is taupe. The dose knob is peach with raised ridges on the end and side. The label is white with a peach colour bar, and peach, light blue and dark blue colour band Each Lyumjev Junior KwikPen delivers 0.5 to 30 units in steps of 0.5 units.

Marketing Authorisation Holder
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Manufacturer
Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France.

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This leaflet was last revised in

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/.

Instructions for Use

Lyumjev 100 units/mL Junior KwikPen solution for injection in pre-filled pen
insulin lispro

PLEASE READ THESE INSTRUCTIONS BEFORE USE

Read the instructions for use before you start taking Lyumjev and each time you get another Lyumjev Junior KwikPen. There may be new information. This information does not take the place of talking to your healthcare professional about your medical condition or your treatment.

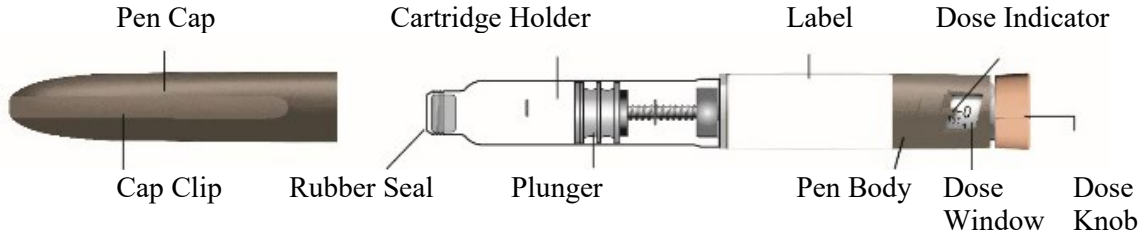
Do not share your Lyumjev Junior KwikPen with other people, even if the needle has been changed. Do not reuse or share needles with other people. You may give other people a serious infection or get a serious infection from them.

Lyumjev 100 units/mL Junior KwikPen ("Pen") is a disposable pre-filled pen containing 3 mL (300 units, 100 units/mL) of insulin lispro solution for injection.

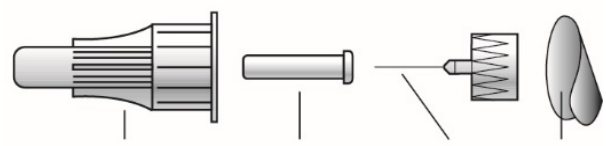
- Your healthcare professional will tell you how many units to give as your dose and how to inject your prescribed dose of insulin.
- You can give yourself more than 1 dose from the Pen.
- Each turn of the dose knob dials half (0.5 unit) of insulin. You can give from half (0.5 unit) to 30 units in a single injection.
- If your dose is more than 30 units, you will need to give yourself more than 1 injection. Always check the number in the dose window to make sure you dialed the correct dose.
- The plunger only moves a little with each injection, and you may not notice that it moves. The plunger will only reach the end of the cartridge when you have used all 300 units in the Pen.

People who are blind or have vision problems should not use the Pen without help from a person trained to use the Pen.

Lyumjev Junior KwikPen Parts



Pen Needle Parts
(Needles Not Included)



Dose Knob

Outer Needle Shield | Inner Needle Shield | Needle | Paper Tab

How to recognize your Lyumjev Junior KwikPen

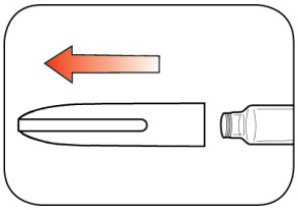
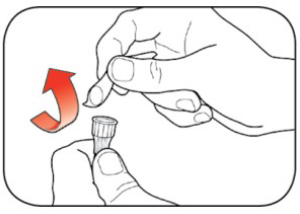
- Pen colour: Taupe
- Dose knob: Peach, with raised ridges on end and side
- Label: White with a peach colour bar, and peach, light blue and dark blue colour band

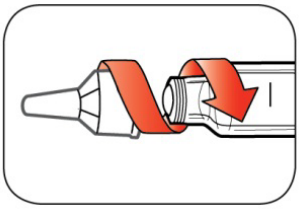
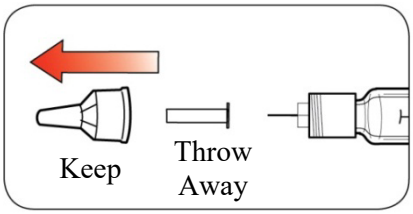
Supplies needed to give your injection

- Lyumjev Junior KwikPen
- KwikPen compatible needle (BD [Becton, Dickinson and Company] Pen needles recommended)
- Swab or gauze

Preparing your Pen

- Wash your hands with soap and water.
- Check the Pen to make sure you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
- **Do not** use your Pen past the expiry date printed on the label or for more than 28 days after you first start using the Pen.
- Always use a **new needle** for each injection to help prevent infections and blocked needles.

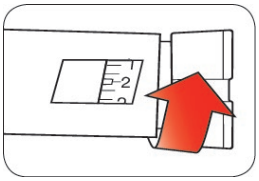
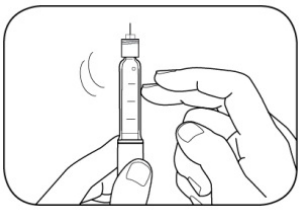
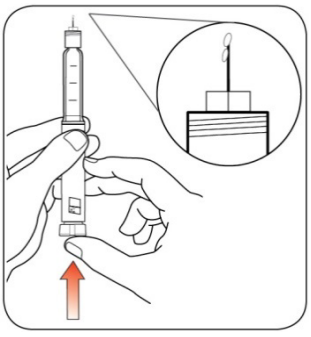
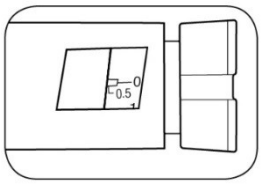
Step 1: • Pull the Pen cap straight off. – **Do not** remove the Pen label. • Wipe the rubber seal with a swab.	
Step 2: • Check the liquid in the Pen. • Lyumjev should look clear and colourless. **Do not** use if it is cloudy, coloured, or has particles or clumps in it.	
Step 3: • Select a new needle. • Pull off the paper tab from the outer needle shield.	

Step 4: • Push the capped needle straight onto the Pen and twist the needle on until it is tight.	
Step 5: • Pull off the outer needle shield. **Do not** throw it away. • Pull off the inner needle shield and throw it away.	

Priming your Pen

Prime before each injection.

- Priming your Pen means removing the air from the needle and cartridge that may collect during normal use and ensures that your Pen is working correctly.
- If you **do not** prime before each injection, you may get too much or too little insulin.

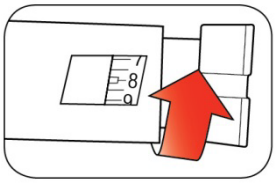
Step 6: • To prime your Pen, turn the dose knob to select 2 units.	
Step 7: • Hold your Pen with the needle pointing up. Tap the cartridge holder gently to collect air bubbles at the top.	
Step 8: • Continue holding your Pen with the needle pointing up. Push the dose knob in until it stops and "**0**" is seen in the dose window. Hold the dose knob in and **count to 5 slowly**. You should see insulin at the tip of the needle. – If you **do not** see insulin, repeat priming steps 6 to 8, but not more than 4 times. – If you **still do not** see insulin, change the needle and repeat priming steps 6 to 8. Small air bubbles are normal and will not affect your dose.	 

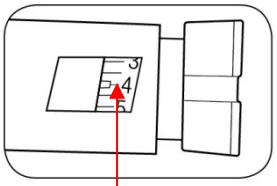
Selecting your dose

- You can give from half unit (0.5 unit) to 30 units in a single injection.
- If your dose is more than 30 units, you will need to give more than 1 injection.
  - If you need help with dividing up your dose the right way, ask your healthcare professional.
  - Use a new needle for each injection and repeat the priming steps.
  - If you usually need more than 30 units, ask your healthcare professional if a different Lyumjev KwikPen would be better for you.

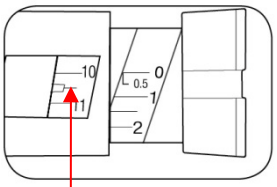
Step 9:

- Turn the dose knob to select the number of units you need to inject. The dose indicator should line up with your dose.
  - The Pen dials half unit (0.5 unit) at a time.
  - The dose knob clicks as you turn it.
  - **Do not** dial your dose by counting the clicks. You may dial the wrong dose. This may lead to getting too much insulin or not enough insulin.
  - The dose can be corrected by turning the dose knob in either direction until the correct dose lines up with the dose indicator.
  - The **whole unit** numbers are printed on the dial. The example to the right shows 4 units.
  - The **half units** are shown as lines between the whole unit numbers. The example to the right shows 10.5 units.
- **Always check the number in the dose window to make sure you have dialed the correct dose.**





Example: 4 units shown in the dose window



Example: 10 ½ (10.5) units shown in the dose window

- The Pen will not let you dial more than the number of units left in the Pen.
- If you need to inject more than the number of units left in the Pen, you may either:
  - inject the amount left in your Pen and then use a new Pen to give the rest of your dose,

  or
  - get a new Pen and inject the full dose.
- It is normal to see a small amount of insulin left in the Pen that you cannot inject.

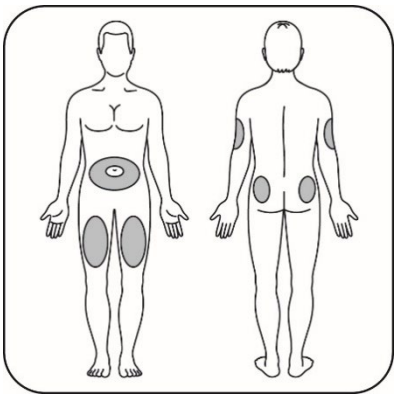
Giving your injection

- Inject your insulin as your healthcare professional has shown you.

- Change (rotate) your injection site for each injection.
- **Do not** try to change your dose while injecting.

<table>
<tr>
<td>Step 10:
• Choose your injection site.

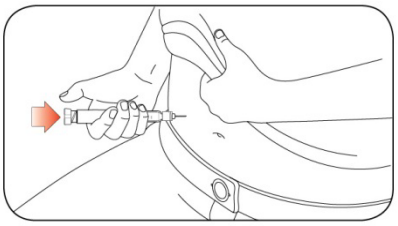
Lyumjev is injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs or upper arms.

• Wipe your skin with a swab, and let your skin dry before you inject your dose.</td>
<td>  </td>
</tr>
<tr>
<td>Step 11:
• Insert the needle into your skin.

• Push the dose knob all the way in.

• Continue to hold the dose knob in and slowly count to 5 before removing the needle.

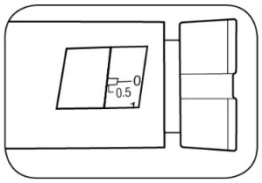
Do not try to inject your insulin by turning the dose knob. You will not receive your insulin by turning the dose knob.</td>
<td>  </td>
</tr>
</table>

Step 12:

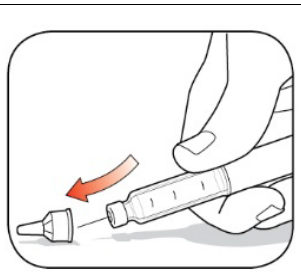
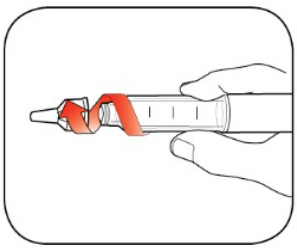
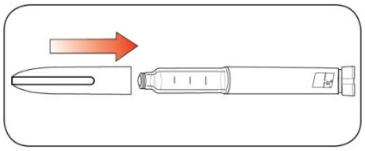
- Pull the needle out of your skin.
  - A drop of insulin at the needle tip is normal. It will not affect your dose.
- Check the number in the dose window.
  - If you see “0” in the dose window, you have received the full amount you dialed.
  - If you do not see “0” in the dose window, you did not receive your full dose. **Do not** redial. Insert the needle into your skin and finish your injection.
  - If you **still** do not think you received the full amount you dialed for your injection, **do not start over or repeat that injection**. Monitor your blood glucose as instructed by your healthcare professional.
  - If you normally need to give 2 injections for your full dose, be sure to give your second injection.

The plunger only moves a little with each injection, and you may not notice that it moves.

If you see blood after you take the needle out of your skin, press the injection site lightly with a piece of gauze or a swab. **Do not** rub the area.



After your injection

Step 13: • Carefully replace the outer needle shield.	
Step 14: • Unscrew the capped needle and dispose of it as described below (see **Disposing of Pens and needles** section). • **Do not** store the Pen with the needle attached to prevent leaking, blocking the needle, and air from entering the Pen.	
Step 15: • Replace the Pen cap by lining up the cap clip with the dose indicator and pushing straight on.	

Disposing of Pens and needles

- Put used needles in a sharps container or a hard plastic container with a secure lid. **Do not** throw needles directly into your household waste.
- **Do not** recycle the filled sharps container.
- Ask your healthcare professional about options to dispose of the Pen and the sharps container properly.
- The directions regarding needle handling are not intended to replace local, healthcare professional or institutional policies.

Troubleshooting

- If you cannot remove the Pen cap, gently twist the cap back and forth, and then pull the cap straight off.
- If the dose knob is hard to push:
  - pushing the dose knob more slowly will make it easier to inject.
  - your needle may be blocked. Put on a new needle and prime the Pen.
  - you may have dust, food, or liquid inside the Pen. Throw the Pen away and get a new Pen.

If you have any questions or problems with your Lyumjev 100 units/mL Junior KwikPen, call your healthcare professional for help or contact your local Lilly affiliate.

Document Revision Date:

Package leaflet: Information for the user

Lyumjev 100 units/ml Tempo Pen solution for injection in pre-filled pen
insulin lispro

Each Tempo Pen delivers 1 to 60 units in steps of 1 units.

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Lyumjev Tempo Pen is and what it is used for

Lyumjev 100 units/ml Tempo Pen solution for injection in pre-filled pen contains the active ingredient insulin lispro. Lyumjev is used to treat diabetes mellitus in adults, adolescents and children aged 1 year and above. It is a mealtime insulin that works more quickly than other medicines containing insulin lispro. Lyumjev contains ingredients that speed up absorption of insulin lispro into the body.

Diabetes is a condition in which your body does not make enough insulin or does not use insulin effectively, which results in effects such as high levels of sugar in the blood. Lyumjev is an insulin medicine that is used in the treatment of diabetes and so controls blood sugar. Effective treatment of diabetes, with good control of blood sugar, prevents long-term complications from your diabetes.

Treatment with Lyumjev helps to control blood sugar in the long term and prevent complications from your diabetes. Lyumjev has its maximum effect 1 to 3 hours after injection and the effect lasts for up to 5 hours. You should use Lyumjev at the start of the meal, or up to 20 minutes after starting the meal.

Your doctor may tell you to use Lyumjev as well as a longer- or intermediate-acting insulin. Do not change your insulin unless your doctor tells you to.

The Lyumjev 100 units/ml Tempo Pen is a disposable pre-filled pen containing 3 ml (300 units, 100 units/ml) of insulin lispro. One Tempo Pen contains multiple doses of insulin. The Tempo Pen dials 1 unit at a time. **The number of units are displayed in the dose window, always check this before your injection.** You can give from 1 to 60 units in a single injection. **If your dose is more than 60 units, you will need to give yourself more than one injection.**

2. What you need to know before you use Lyumjev Tempo Pen

Do NOT use Lyumjev Tempo Pen
- if you think your blood sugar is dropping (**hypoglycaemia**). Further on, this leaflet tells you how to deal with low blood sugar (see section 3 under "If you use more Lyumjev than you should").
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Lyumjev.

If you cannot see very well you will need help from someone who has been trained to give injections.

- **Low blood sugar** (hypoglycaemia).

Low blood sugar can be serious and untreated hypoglycaemia may even lead to death.
Lyumjev starts to lower blood sugar faster than some other mealtime insulins. If hypoglycaemia occurs, you may experience it earlier after an injection of Lyumjev. If you often have hypoglycaemia or have difficulty recognising it, please discuss this with your doctor or nurse. If your blood sugar levels are well controlled by your current insulin therapy or after long duration of diabetes, you may not feel the warning symptoms when your blood sugar is falling too low.Warning signs are listed later in this leaflet. For symptoms please see "Common problems of diabetes".

You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood sugar often. Making changes to the types of insulin you use may cause your blood sugar to rise or fall too much. It may be necessary to increase the frequency of blood sugar testing if you are at risk of low blood sugars. Your doctor may need to change the doses of your other diabetes medicines.

- **High blood sugar** (hyperglycaemia).

Stopping or not taking enough insulin may lead to high blood sugar (hyperglycaemia) and diabetic ketoacidosis, serious conditions that can even lead to death. For symptoms please see "Common problems of diabetes".

- If your insulin treatment is being combined with one of a class of diabetes medicines called thiazolidinediones or glitazones, such as pioglitazone, tell your doctor as soon as possible if you get signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling caused by fluid retention (oedema).
- If you have a serious allergic reaction to insulin or any of the ingredients in Lyumjev, stop using this medicine and contact emergency medical services straight away.
- Always check the pack and the label for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Lyumjev that your doctor has told you to use.
- Keep the carton, or keep a note of the batch number on the carton. If you have a side effect you can then provide that number when you report the advere side effect, see "reporting of side effects".
- Always use a new needle for each injection to prevent infections and blocked needles. If a needle is blocked replace it with a new needle.

- **Skin changes at the injection site.**

The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work well if you inject into a lumpy area (See How to use Lyumjev Tempo Pen). Contact your doctor if you are currently injecting into a lumpy area before you start injecting into a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

The Tempo Pen contains a magnet. If you have a medical device fitted, such as a heart pacemaker, this may not work correctly if the Tempo Pen is held too close. The magnetic field extends to approximately 1.5 cm.

Children and adolescents
This medicine is not recommended for use in children below the age of 1 year.

Other medicines and Lyumjev
Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines. Some medicines affect your blood sugar level - this may mean your insulin dose has to change.

Your blood sugar levels may fall (hypoglycaemia) if you take:

- other medicines for diabetes (oral and injectable)
- sulphonamide antibiotics (for infections)
- acetylsalicylic acid (for pain and mild fever and to prevent blood clotting)
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors)
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril) (for some heart problems or high blood pressure)
- angiotensin II receptor blockers (for high blood pressure or heart problems)
- somatostatin analogues (such as octreotide, which are used to treat a rare condition involving too much growth hormone)

Your blood sugar levels may rise (hyperglycaemia) if you take:

- danazol (for endometriosis)
- the contraceptive pill (birth control pills)
- thyroid hormone replacement therapy (for thyroid problems)
- human growth hormone (for growth hormone deficiency)
- diuretics (for high blood pressure or if you have a build-up of water in your body)
- sympathomimetic agents (for serious allergic reactions or used in some cold remedies)
- corticosteroids (to treat asthma or autoimmune conditions)

Beta-blockers (used for high blood pressure, arrhythmia or angina) make it harder to recognise the warning signs of low blood sugar.

Lyumjev with alcohol
Your blood sugar levels may either rise or fall if you drink alcohol. Therefore the amount of insulin needed may change. You should therefore monitor your blood sugar level more often than usual.

Pregnancy and breast-feeding
If you are planning to have a baby, think you may be pregnant, are pregnant or breast-feeding, ask your doctor, nurse or pharmacist for advice before taking this medicine. The amount of insulin you need usually falls during the first 3 months of pregnancy and increases for the remaining 6 months. After you have had your baby your insulin requirements will likely return to how much you needed before your pregnancy.

There are no restrictions on treatment with Lyumjev during breast-feeding. If you are breast-feeding, you may need to alter your insulin intake or diet.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or using machines). You should contact your doctor about driving if you have:
- frequent episodes of hypoglycaemia

- reduced or absent warning signs of hypoglycaemia

Lyumjev Tempo Pen contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use Lyumjev Tempo Pen

Always use this medicine exactly as described in this leaflet or as your doctor, pharmacist or nurse has told you. Check with them if you are not sure.

They will have told you exactly how much Lyumjev to use, when to use it, and how often. They will also tell you how often to visit your diabetes clinic.

To prevent the possible transmission of disease, each pen must be used by you only, even if the needle is changed.

You should always have spare insulin and another injection device in case you need them.

If you are blind or visually impaired you will need help from someone to make your injections.

Your doctor may tell you to use Lyumjev as well as a longer- or intermediate-acting insulin. Inject them separately. Lyumjev should not be mixed with any other insulin.

The Tempo Pen is designed to work with the Tempo Smart Button. The optional additional feature Tempo Smart Button is a product available for the Tempo Pen, which may be used for transmitting dose information to a mobile application. The Tempo Pen can be used with or without the Tempo Smart Button attached. See instructions provided with the Tempo Smart Button and the mobile application for further information.

When to inject Lyumjev
Lyumjev is a mealtime insulin. You should use Lyumjev when you start to eat, or a minute or two before the meal; you also have the option to inject up to 20 minutes after starting the meal.

How much insulin to use
Your doctor will work out your dose based on your blood sugar and body weight and explain
- How much Lyumjev you need at each meal.
- How and when to check your blood sugar level.
- How to change your insulin dose depending on your blood sugar levels.
- What to do if you change your diet, or change how much you exercise, if you are ill or if you are using other medicines.
- If you change the type of insulin you use, you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.

Do not use Lyumjev
- If it does not look like water. Lyumjev must be clear, have no colour and no solid pieces in it. Check each time you inject yourself.
- If Lyumjev has not been stored correctly (see section 5 "How to store Lyumjev").
- If the pen is damaged in any way, do not use.

Getting the Tempo Pen ready to use (Please see instructions for use)
- First wash your hands.
- Read the instructions on how to use your pre-filled insulin pen. Please follow the instructions carefully. Here are some reminders.
- Use a new needle. (Needles are not included).

- Prime your Tempo Pen before each use. This checks that insulin comes out and clears the air bubbles from your Tempo Pen. There may still be some small air bubbles left in the pen. Small air bubbles are normal and will not affect your dose.
- The number of units are displayed in the dose window, always check this before your injection.

Injecting Lyumjev
- Before you make an injection, clean your skin.
- Inject under the skin (subcutaneous injection), as you were taught by your physician or nurse.
- After your injection, leave the needle in the skin for 5 seconds to make sure you receive the full dose. Make sure you inject at least 1 cm from the last injection and that you 'rotate' the places you inject (upper arm, thigh, buttocks or abdomen).
- If you do not have enough insulin in the pen to complete your dose, make a note of how much you still need to take. Prime a new pen and inject the remaining dose.
- If you need to inject another insulin at the same time as Lyumjev, use a different injection site.
- Do not inject directly into a vein.

After injecting
- As soon as you have done the injection, unscrew the needle from the Tempo Pen using the outer needle cap. This will keep the insulin sterile and stop it leaking. It also stops air entering the pen and your needle clogging. **Do not share your needles**. **Do not share your pen**. Replace the cap on your pen.
- If you are unsure how much you have injected then check your blood sugar levels before deciding if you need another injection.

Further injections
- Every time you use a Tempo Pen you must use a new needle. Before every injection, clear any air bubbles. You can see how much insulin is left by holding the Tempo Pen with the needle pointing up.
- Once the Tempo Pen is empty, do not use it again.

If you use more Lyumjev than you should
If you inject too much Lyumjev, or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low (hypoglycaemia) and you can treat yourself, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor or nurse has advised you and have some rest. This will often get you over a low blood sugar or a minor insulin overdose. Check your blood sugar again after 15-20 mins until blood sugar is stabilised.

If you are unable to treat yourself (severe hypoglycaemia) because you feel too dizzy, weak, confused, have difficulty talking, lose consciousness or have a seizure you may need to be treated with glucagon. This can be given by someone who knows how to use it. Eat glucose or sugar after the glucagon. If glucagon does not work, you will have to go to hospital or call emergency services. Ask your doctor to tell you about glucagon.

Tell everyone you spend time with that you have diabetes. Tell them what could happen if your blood sugar gets too low, including the risk of passing out.
Let them know that if you pass out, they must: turn you on your side to avoid choking, get medical help straight away and not give you any food or drink because you may choke.

If you forget to use Lyumjev
If you forget to use your insulin, or you use less than you should, or are unsure how much you have injected, your blood sugar may get too high (hyperglycaemia). Check your blood sugar level to decide if an insulin dose is needed. Resume your usual dosing schedule at your next meal.

If you stop using Lyumjev
Do not stop or change your insulin unless your doctor tells you to. If you use less Lyumjev than you should, a high blood sugar may occur.

If high blood sugar (hyperglycaemia) is not treated it can be very serious and cause headaches, nausea, vomiting, abdominal pain, dehydration, unconsciousness, coma or even death (see section 4).

Three simple steps to reduce your risk of hypoglycaemia or hyperglycaemia are:
- Always keep a spare pen in case you lose your Tempo Pen or it gets damaged.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Low blood sugar (hypoglycaemia) is very common with insulin treatment (may affect more than 1 in 10 people). It can be very serious. If your blood sugar level falls too much you may become unconscious. Serious hypoglycaemia may cause brain damage and may be life-threatening. If you have symptoms of low blood sugar, act **immediately** to increase your blood sugar level. See section 3 under 'If you use more Lyumjev than you should'.

Allergic reactions are common (may affect up to 1 in 10 people). They may be severe and they may include the following symptoms:

- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you have a serious allergic reaction (including an anaphylactic attack) to insulin or any of the ingredients in Lyumjev, stop using this medicine and contact emergency medical service straight away.

Other side effects include

Common
Injection site reactions. Some people get redness, pain, swelling or itching around the area of the insulin injection. This usually clears up in a few minutes to a few weeks without needing to stop Lyumjev. If you have injection site reactions, tell your doctor.

Uncommon (may affect up to 1 in 100 people)
Skin changes at the injection site: If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by the build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Other potential side effects
Swelling in arms or ankles due to fluid retention (oedema) particularly at the start of insulin therapy or during a change in your diabetes medicines.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

Low blood sugar
Low blood sugar (hypoglycaemia) means there is not enough sugar in the blood. This can be caused if:
- you take too much Lyumjev or other insulin;
- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;
- you have an infection or illness (especially diarrhoea or vomiting);
- there is a change in your need for insulin for example if you lose weight; or you have trouble with your kidneys or liver which gets worse.

See section "If you use more Lyumjev than you should".

The first symptoms of low blood sugar usually come on quickly and include the following:

- tiredness
- rapid heart beat
- nervousness or shakiness
- feeling sick
- headache
- cold sweat

If you are not confident about recognising your warning symptoms, avoid situations such as driving a car, in which you or others would be put at risk by hypoglycaemia.

High blood sugar (hyperglycaemia) and diabetic ketoacidosis
Hyperglycaemia (too much sugar in the blood) means that the levels of glucose in your body are too high. Hyperglycaemia can be brought about by:
- not taking your insulin;
- using less insulin than your body needs;
- an imbalance between the amount of carbohydrates you eat and the insulin you take; or
- fever, infection or emotional stress.

The early symptoms of hyperglycaemia are;
- being very thirsty
- headache
- feeling sleepy
- urinating more often

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. Additional symptoms include the following:
- nausea and/or vomiting
- abdominal pain
- rapid pulse
- heavy breathing
- moderate or large amounts of urine ketones. Ketones are produced when your body burns fat for energy instead of glucose.

If you have any of these symptoms and high sugars **get medical help immediately.**
See section 'If you forget to use Lyumjev'.

Illness
If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Lyumjev Tempo Pen

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Before first use
Store in a refrigerator (2 °C to 8 °C).
Do not freeze.
Keep in the outer carton in order to protect from light.

After first use
Do not store above 30 °C.
Do not freeze.
Do not refrigerate.

The Tempo Pen should not be stored with the needle attached. Keep the cap on the pen in order to protect from light.
Discard after 28 days **even if some of the solution remains**.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Lyumjev 100 units/ml Tempo Pen solution for injection contains
- The active substance is insulin lispro. Each ml solution contains 100 units of insulin lispro. One Tempo Pen contains 300 units of insulin lispro in 3 ml solution.
- The other ingredients are metacresol, glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, water for injections. Sodium hydroxide or hydrochloric acid may have been used to adjust the pH (see the end of section 2 under 'Lyumjev Tempo Pen contains sodium').
- The Tempo Pen contains a magnet (see section 2, "Warnings and precautions").

What Lyumjev Tempo Pen looks like and contents of the pack
Lyumjev Tempo Pen solution for injection is a clear, colourless, aqueous solution in a pre-filled pen. Each pre-filled pen contains 300 units (3 millilitres).

Pack sizes of 5 or a multipack of 2 x 5 pre-filled pens. Not all pack sizes may be marketed.

The Lyumjev Tempo Pen is taupe. The dose knob is blue with raised ridges around the entire side. The label is blue, green and white. Each Lyumjev Tempo Pen delivers 1 to 60 units in steps of 1 unit.

Marketing Authorisation Holder
Eli Lilly Nederland B.V., Papendorpseweg 83, 3528 BJ Utrecht, The Netherlands.

Manufacturer
Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France.

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/.

Instructions for Use

Lyumjev 100 units/mL Tempo Pen solution for injection in pre-filled pen
insulin lispro

PLEASE READ THESE INSTRUCTIONS BEFORE USE

Read the instructions for use before you start using Lyumjev and each time you get another Lyumjev Tempo Pen. There may be new information. This information does not take the place of talking to your healthcare professional about your medical condition or your treatment.

Lyumjev 100 units/mL Tempo Pen ("Pen") is a disposable pre-filled pen containing 3 mL (300 units, 100 units/mL) of insulin lispro solution for injection.

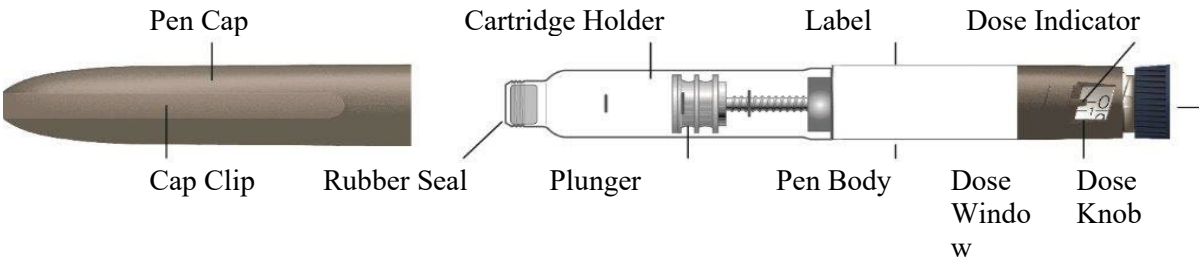
- Your healthcare professional will tell you how many units to give as your dose and how to inject your prescribed dose of insulin.
- You can give yourself more than 1 dose from the Pen.
- Each turn of the dose knob dials 1 unit of insulin. You can give from 1 to 60 units in a single injection.
- If your dose is more than 60 units, you will need to give yourself more than 1 injection. Always check the number in the dose window to make sure you dialed the correct dose.
- The plunger only moves a little with each injection, and you may not notice that it moves. The plunger will only reach the end of the cartridge when you have used all 300 units in the Pen.

The Tempo Pen is designed to work with the Tempo Smart Button. The Tempo Smart Button is an optional product that can be attached to the Tempo Pen dose knob and aids in transmitting Lyumjev dose information from the Tempo Pen to a compatible mobile application. The Tempo Pen injects insulin with or without the Tempo Smart Button attached. Your Tempo Smart Button must be attached to a Tempo Pen to record or transfer dose data. Push the Tempo Smart Button straight down on the dose knob until you hear a snap or feel the Tempo Smart Button snap into place. To transmit data to the mobile application, follow the instructions provided with the Tempo Smart Button and the instructions with the mobile application.

Do not share your Lyumjev Tempo Pen with other people, even if the needle has been changed. Do not reuse or share needles with other people. You may give other people a serious infection or get a serious infection from them.

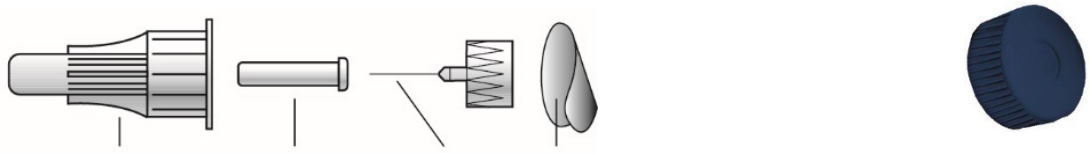
People who are blind or have vision problems should not use the Pen without help from a person trained to use the Pen.

Lyumjev Tempo Pen Parts



Pen Needle Parts (Needles Not Included)

Dose Knob



Outer Needle Shield | Inner Needle Shield | Needle | Paper Tab

How to recognize your Lyumjev Tempo Pen

- Pen colour: Taupe
- Dose Knob: Blue, with raised ridges around the entire side
- Label: Blue, green and white

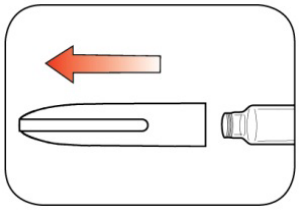
Supplies needed to give your injection

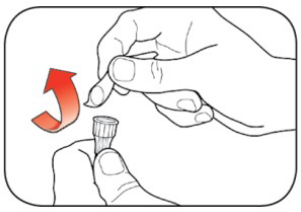
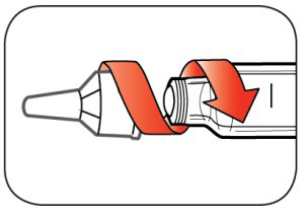
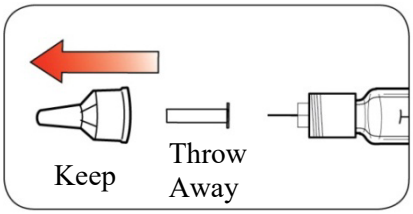
- Lyumjev Tempo Pen
- Tempo Pen compatible needle (BD [Becton, Dickinson and Company] Pen needles recommended)
- Swab or gauze

Needles, swab or gauze are not included.

Preparing your Pen

- Wash your hands with soap and water.
- Check the Pen to make sure you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
- **Do not** use your Pen past the expiry date printed on the label or for more than 28 days after you first start using the Pen.
- Always use a **new needle** for each injection to help prevent infections and blocked needles.

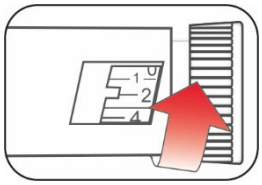
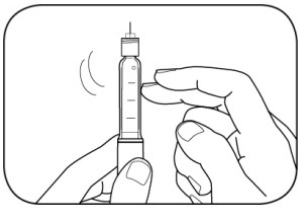
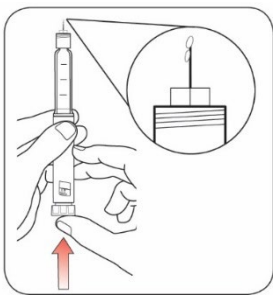
Step 1: • Pull the Pen cap straight off. – **Do not** remove the Pen label. • Wipe the rubber seal with a swab.	
Step 2: • Check the liquid in the Pen. • Lyumjev should look clear and colourless. **Do not** use if it is cloudy, coloured, or has particles or clumps in it.	

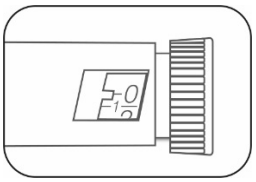
Step 3: • Select a new needle. • Pull off the paper tab from the outer needle shield.	
Step 4: • Push the capped needle straight onto the Pen and twist the needle on until it is tight.	
Step 5: • Pull off the outer needle shield. **Do not** throw it away. • Pull off the inner needle shield and throw it away.	

Priming your Pen

Prime before each injection.

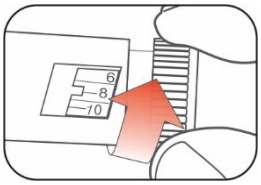
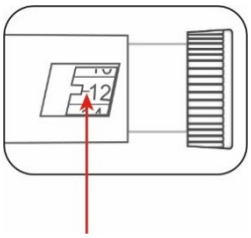
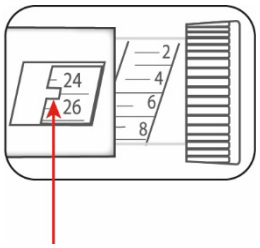
- Priming your Pen means removing the air from the needle and cartridge that may collect during normal use and ensures that your Pen is working correctly.
- If you **do not** prime before each injection, you may get too much or too little insulin.

Step 6: • To prime your Pen, turn the dose knob to select 2 units.	
Step 7: • Hold your Pen with the needle pointing up. Tap the cartridge holder gently to collect air bubbles at the top.	
Step 8: • Continue holding your Pen with the needle pointing up. Push the dose knob in until it stops and "**0**" is seen in the dose window. Hold the dose knob in and **count to 5 slowly**. You should see insulin at the tip of the needle. – If you **do not** see insulin, repeat priming steps 6 to 8, but not more than 4 times.	

– If you **still do not** see insulin, change the needle and repeat priming steps 6 to 8. Small air bubbles are normal and will not affect your dose.	

Selecting your dose

- You can give from 1 to 60 units in a single injection.
- If your dose is more than 60 units, you will need to give more than 1 injection.
  - If you need help with dividing up your dose the right way, ask your healthcare professional.
  - Use a new needle for each injection and repeat the priming steps.

Step 9: • Turn the dose knob to select the number of units you need to inject. The dose indicator should line up with your dose. – The Pen dials 1 unit at a time. – The dose knob clicks as you turn it. – **Do not** dial your dose by counting the clicks. You may dial the wrong dose. This may lead to getting too much insulin or not enough insulin. – The dose can be corrected by turning the dose knob in either direction until the correct dose lines up with the dose indicator. – The **even** numbers are printed on the dial. The example to the right shows 12 units. – The **odd** numbers, after the number 1, are shown as full lines between the numbers. The example to the right shows 25 units. • **Always check the number in the dose window to make sure you have dialed the correct dose.**	  Example: 12 units shown in the dose window  Example: 25 units shown in the dose window

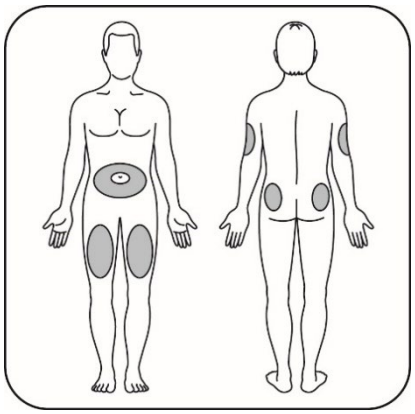
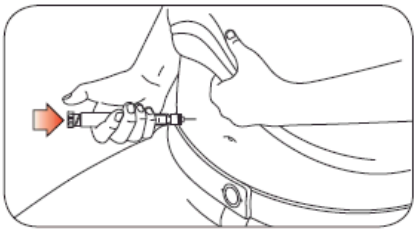
- The Pen will not let you dial more than the number of units left in the Pen.
- If you need to inject more than the number of units left in the Pen, you may either:
  - inject the amount left in your Pen and then use a new Pen to give the rest of your dose,

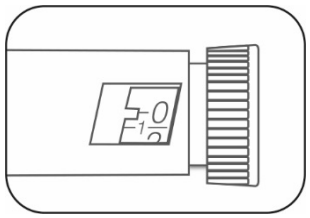
  or
  - get a new Pen and inject the full dose.

- It is normal to see a small amount of insulin left in the Pen that you cannot inject.

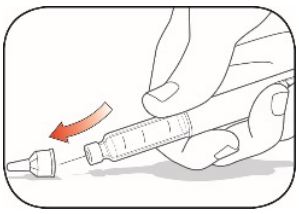
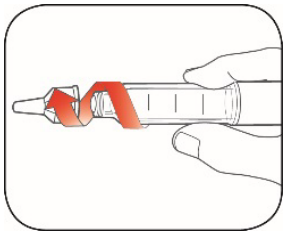
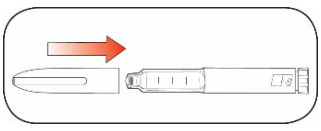
Giving your injection

- Inject your insulin as your healthcare professional has shown you.
- Change (rotate) your injection site for each injection.
- **Do not** try to change your dose while injecting.

Step 10: • Choose your injection site. Lyumjev is injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs or upper arms. • Wipe your skin with a swab, and let your skin dry before you inject your dose.	
Step 11: • Insert the needle into your skin. • Push the dose knob all the way in. • Continue to hold the dose knob in and **slowly count to 5** before removing the needle.  **Do not** try to inject your insulin by turning the dose knob. You will **not** receive your insulin by turning the dose knob.	

Step 12: • Pull the needle out of your skin. – A drop of insulin at the needle tip is normal. It will not affect your dose. • Check the number in the dose window. – If you see “0” in the dose window, you have received the full amount you dialed. – If you do not see “0” in the dose window, you did not receive your full dose. **Do not** redial. Insert the needle into your skin and finish your injection. – If you **still** do not think you received the full amount you dialed for your injection, **do not start over or repeat that injection**. Monitor your blood glucose as instructed by your healthcare professional. – If you normally need to give 2 injections for your full dose, be sure to give your second injection. The plunger only moves a little with each injection, and you may not notice that it moves. If you see blood after you take the needle out of your skin, press the injection site lightly with a piece of gauze or a swab. **Do not** rub the area.	

After your injection

Step 13: • Carefully replace the outer needle shield.	
Step 14: • Unscrew the capped needle and dispose of it as described below (see **Disposing of Pens and needles** section). • **Do not** store the Pen with the needle attached to prevent leaking, blocking the needle, and air from entering the Pen.	
Step 15: • Replace the Pen cap by lining up the cap clip with the dose indicator and pushing straight on.	

Disposing of Pens and needles

- Put used needles in a sharps container or a hard plastic container with a secure lid. **Do not** throw needles directly into your household waste.
- **Do not** recycle the filled sharps container.
- Ask your healthcare professional about options to dispose of the Pen and the sharps container properly.
- The directions regarding needle handling are not intended to replace local, healthcare professional or institutional policies.

Troubleshooting

- If you cannot remove the Pen cap, gently twist the cap back and forth, and then pull the cap straight off.
- If the dose knob is hard to push:

– pushing the dose knob more slowly will make it easier to inject.

– your needle may be blocked. Put on a new needle and prime the Pen.

– you may have dust, food, or liquid inside the Pen. Throw the Pen away and get a new Pen. You may need to get a prescription from your healthcare professional.

If you have any questions or problems with your Lyumjev 100 units/mL Tempo Pen, call your healthcare professional for help or contact your local Lilly affiliate.

Document Revision Date:

Package leaflet: Information for the user

Lyumjev 200 units/ml KwikPen solution for injection in pre-filled pen
insulin lispro

Each KwikPen delivers 1 to 60 units in steps of 1 units

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Lyumjev 200 units/ml KwikPen is and what it is used for

Lyumjev 200 units/ml KwikPen solution for injection in pre-filled pen contains the active ingredient insulin lispro. Lyumjev is used to treat diabetes in adults. It is a mealtime insulin that works more quickly than other medicines containing insulin lispro. Lyumjev contains ingredients that speed up absorption of insulin lispro into the body.

Diabetes is a condition in which your body does not make enough insulin or does not use insulin effectively, which results in effects such as high levels of sugar in the blood. Lyumjev is an insulin medicinethat is used in the treatment of diabetes and so controls blood sugar. Effective treatment of diabetes, with good control of blood sugar, prevents long-term complications from your diabetes.

Treatment with Lyumjev helps to control blood sugar in the long term and prevent complications from your diabetes. Lyumjev has its maximum effect 1 to 3 hours after injection and the effect lasts for up to 5 hours. You should use Lyumjev at the start of the meal, or up to 20 minutes after starting the meal.

Your doctor may tell you to use Lyumjev as well as a longer- or intermediate-acting insulin. Do not change your insulin unless your doctor tells you to.

Lyumjev 200 units/ml KwikPen is a disposable pre-filled pen containing 3 ml (600 units, 200 units/ml) of insulin lispro. One KwikPen contains multiple doses of insulin. The KwikPen dials 1 unit at a time. **The number of units are displayed in the dose window, always check this before your injection.** You can give from 1 to 60 units in a single injection. **If your dose is more than 60 units, you will need to give yourself more than one injection.**

2. What you need to know before you use Lyumjev 200 units/ml KwikPen

Do NOT use Lyumjev 200 units/ml KwikPen

- if you think your blood sugar is dropping (**hypoglycaemia**). Further on this leaflet tells you how to deal with low blood sugar (see section 3 under "If you use more Lyumjev than you should").
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

- **The Lyumjev 200 units/ml solution for injection in your pre-filled pen (the KwikPen) should ONLY be injected with this pre-filled pen. Do not transfer the insulin lispro from your Lyumjev 200 units/ml KwikPen to a syringe**. The markings on the insulin syringe will not measure your dose correctly. A severe overdose can result, causing low blood sugar which may put your life in danger. Do not transfer insulin from your Lyumjev 200 units/ml KwikPen to any other insulin delivery devices like insulin infusion pumps.

Talk to your doctor, pharmacist or nurse before using Lyumjev.

If you cannot see very well you will need help from someone who has been trained to give injections.

- **Low blood sugar** (hypoglycaemia).

Low blood sugar can be serious and untreated hypoglycaemia may even lead to death.
Lyumjev starts to lower blood sugar faster than some other mealtime insulins. If hypoglycaemia occurs, you may experience it earlier after an injection of Lyumjev. If you often have hypoglycaemia or have difficulty recognising it, please discuss this with your doctor or nurse. If your blood sugar levels are well controlled by your current insulin therapy or after long duration of diabetes, you may not feel the warning symptoms when your blood sugar is falling too low.Warning signs are listed later in this leaflet. For symptoms please see "Common problems of diabetes".

You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood sugar often. Making changes to the types of insulin you use may cause your blood sugar to rise or fall too much. It may be necessary to increase the frequency of blood sugar testing if you are at risk of low blood sugars. Your doctor may need to change the doses of your other diabetes medicines.

- **High blood sugar** (hyperglycaemia).

Stopping or not taking enough insulin may lead to high blood sugar (hyperglycaemia) and diabetic ketoacidosis, serious conditions that can even lead to death. For symptoms please see "Common problems of diabetes".

- If your insulin treatment is being combined with one of a class of diabetes medicines called thiazolidinediones or glitazones, such as pioglitazone, tell your doctor as soon as possible if you get signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling caused by fluid retention (oedema).
- If you have a serious allergic reaction to insulin or any of the ingredients in Lyumjev, stop using this medicine and contact emergency medical services straight away.
- Always check the pack and the label for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Lyumjev that your doctor has told you to use.
- Keep the carton, or keep a note of the batch number on the carton. If you have a side effect you can then provide that number when you report the advere side effect, see "reporting of side effects".
- Always use a new needle for each injection to prevent infections and blocked needles. If a needle is blocked replace it with a new needle.

- **Skin changes at the injection site.**

The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work well if you inject into a lumpy area (See How to use Lyumjev 200 units/ml KwikPen). Contact your doctor if you are currently injecting into a lumpy area before you start injecting into a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Children and adolescents
This medicine should not be used in children or adolescents, since there is no experience with this medicine in children and adolescents under 18 years of age.

Other medicines and Lyumjev
Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines. Some medicines affect your blood sugar level - this may mean your insulin dose has to change.

Your blood sugar levels may fall (hypoglycaemia) if you take:

- other medicines for diabetes (oral and injectable)
- sulphonamide antibiotics (for infections)
- acetylsalicylic acid (for pain and mild fever and to prevent blood clotting)
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors)
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril) (for some heart problems or high blood pressure)
- angiotensin II receptor blockers (for high blood pressure or heart problems)
- somatostatin analogues (such as octreotide, which are used to treat a rare condition involving too much growth hormone)

Your blood sugar levels may rise (hyperglycaemia) if you take:

- danazol (for endometriosis)
- the contraceptive pill (birth control pills)
- thyroid hormone replacement therapy (for thyroid problems)
- human growth hormone (for growth hormone deficiency)
- diuretics (for high blood pressure or if you have a build-up of water in your body)
  sympathomimetic agents (for serious allergic reactions or used in some cold remedies)
- corticosteroids (to treat asthma or autoimmune conditions)

Beta-blockers (used for high blood pressure, arrhythmia or angina) make it harder to recognise the warning signs of low blood sugar.

Lyumjev with alcohol
Your blood sugar levels may either rise or fall if you drink alcohol. Therefore the amount of insulin needed may change. You should therefore monitor your blood sugar level more often than usual.

Pregnancy and breast-feeding
If you are planning to have a baby, think you may be pregnant, are pregnant or breast-feeding, ask your doctor, nurse or pharmacist for advice before taking this medicine. The amount of insulin you need usually falls during the first 3 months of pregnancy and increases for the remaining 6 months. After you have had your baby your insulin requirements will likely return to how much you needed before your pregnancy.

There are no restrictions on treatment with Lyumjev during breast-feeding. If you are breast-feeding, you may need to alter your insulin intake or diet.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or using machines). You should contact your doctor about driving if you have:
- frequent episodes of hypoglycaemia
- reduced or absent warning signs of hypoglycaemia

Lyumjev 200 units/ml KwikPen contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use Lyumjev 200 units/ml KwikPen

Always use this medicine exactly as described in this leaflet or as your doctor, pharmacist or nurse has told you. Check with them if you are not sure.

They will have told you exactly how much Lyumjev to use, when to use it, and how often. They will also tell you how often to visit your diabetes clinic.

To prevent the possible transmission of disease, each pen must be used by you only, even if the needle is changed.

Do not use Lyumjev 200 units/ml KwikPen solution for injection in an insulin infusion pump.

You should always have spare insulin and another injection device in case you need them.

If you are blind or visually impaired you will need help from someone to make your injections.

Your doctor may tell you to use Lyumjev as well as a longer- or intermediate-acting insulin. Inject them separately. Lyumjev should not be mixed with any other insulin.

When to inject Lyumjev
Lyumjev is a mealtime insulin. You should use Lyumjev when you start to eat, or a minute or two before the meal; you also have the option to inject up to 20 minutes after starting the meal.

How much insulin to use
Your doctor will work out your dose based on your blood sugar and body weight and explain
- How much Lyumjev you need at each meal.
- How and when to check your blood sugar level.
- How to change your insulin dose depending on your blood sugar levels.
- What to do if you change your diet, or change how much you exercise, if you are ill or if you are using other medicines.
- If you change the type of insulin you use, you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.

Do not use Lyumjev
- If it does not look like water. Lyumjev must be clear, have no colour and no solid pieces in it. Check each time you inject yourself.
- If Lyumjev has not been stored correctly (see section 5 "How to store Lyumjev").
- If the pen is damaged in any way, do not use.

Getting the Lyumjev 200 units/ml KwikPen ready to use (Please see instructions for use)
- First wash your hands.
- Read the instructions on how to use your pre-filled insulin pen. Please follow the instructions carefully. Here are some reminders.

- Use a new needle. (Needles are not included).
- Prime your Lyumjev 200 units/ml KwikPen before each use. This checks that insulin comes out and clears the air bubbles from your Lyumjev 200 units/ml KwikPen. There may still be some small air bubbles left in the pen. Small air bubbles are normal and will not affect your dose.
- The number of units are displayed in the dose window, always check this before your injection.

Injecting Lyumjev
- Before you make an injection, clean your skin.
- Inject under the skin (subcutaneous injection), as you were taught by your physician or nurse.
- After your injection, leave the needle in the skin for 5 seconds to make sure you receive the full dose. Make sure you inject at least 1 cm from the last injection and that you 'rotate' the places you inject (upper arm, thigh, buttocks or abdomen).
- If you do not have enough insulin in the pen to complete your dose, make a note of how much you still need to take. Prime a new pen and inject the remaining dose.
- If you need to inject another insulin at the same time as Lyumjev, use a different injection site.
- Do not inject directly into a vein.

After injecting
- As soon as you have done the injection, unscrew the needle from the Lyumjev 200 units/ml KwikPen using the outer needle cap. This will keep the insulin sterile and stop it leaking. It also stops air entering the pen and your needle clogging. **Do not share your needles**. **Do not share your pen.** Replace the cap on your pen.
- If you are unsure how much you have injected then check your blood sugar levels before deciding if you need another injection.

Further injections
- Every time you use a Lyumjev 200 units/ml KwikPen you must use a new needle. Before every injection, clear any air bubbles. You can see how much insulin is left by holding the Lyumjev 200 units/ml KwikPen with the needle pointing up.
- Once the Lyumjev 200 units/ml KwikPen is empty, do not use it again.

If you use more Lyumjev than you should
If you inject too much Lyumjev, or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low (hypoglycaemia) and you can treat yourself, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor or nurse has advised you and have some rest. This will often get you over a low blood sugar or a minor insulin overdose. Check your blood sugar again after 15-20 mins until blood sugar is stabilised.

If you are unable to treat yourself (severe hypoglycaemia) because you feel too dizzy, weak, confused, have difficulty talking, lose consciousness or have a seizure you may need to be treated with glucagon. This can be given by someone who knows how to use it. Eat glucose or sugar after the glucagon. If glucagon does not work, you will have to go to hospital or call emergency services. Ask your doctor to tell you about glucagon.

Tell everyone you spend time with that you have diabetes. Tell them what could happen if your blood sugar gets too low, including the risk of passing out.
Let them know that if you pass out, they must: turn you on your side to avoid choking, get medical help straight away and not give you any food or drink because you may choke.

If you forget to use Lyumjev
If you forget to use your insulin or you use less than you should, or are unsure how much you have injected, your blood sugar may get too high (hyperglycaemia). Check your blood sugar level to decide if an insulin dose is needed. Resume your usual dosing schedule at your next meal.

If you stop using Lyumjev
Do not stop or change your insulin unless your doctor tells you to. If you use less Lyumjev than you should, a high blood sugar may occur.

If high blood sugar (hyperglycaemia) is not treated it can be very serious and cause headaches, nausea, vomiting, abdominal pain, dehydration, unconsciousness, coma or even death (see section 4).

Three simple steps to reduce your risk of hypoglycaemia or hyperglycaemia are:
- Always keep a spare pen in case you lose your Lyumjev 200 units/ml KwikPen or it gets damaged.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Low blood sugar (hypoglycaemia) is very common with insulin treatment (may affect more than 1 in 10 people). It can be very serious. If your blood sugar level falls too much you may become unconscious. Serious hypoglycaemia may cause brain damage and may be life-threatening. If you have symptoms of low blood sugar, act **immediately** to increase your blood sugar level. See section 3 under 'If you use more Lyumjev than you should'.

Allergic reactions are common (may affect up to 1 in 10 people). They may be severe and they may include the following symptoms:

- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you have a serious allergic reaction (including an anaphylactic attack) to insulin or any of the ingredients in Lyumjev, stop using this medicine and contact emergency medical service straight away.

Other side effects include

Common
Injection site reactions. Some people get redness, pain, swelling or itching around the area of the insulin injection. This usually clears up in a few minutes to a few weeks without needing to stop Lyumjev. If you have injection site reactions, tell your doctor.

Uncommon (may affect up to 1 in 100 people)
Skin changes at the injection site: If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by the build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Other potential side effects
Swelling in arms or ankles due to fluid retention (oedema) particularly at the start of insulin therapy or during a change in your diabetes medicines.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

Low blood sugar
Low blood sugar (hypoglycaemia) means there is not enough sugar in the blood. This can be caused if:
- you take too much Lyumjev or other insulin;
- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;
- you have an infection or illness (especially diarrhoea or vomiting);
- there is a change in your need for insulin for example if you lose weight; or you have trouble with your kidneys or liver which gets worse.

See section 'If you use more Lyumjev than you should'

The first symptoms of low blood sugar usually come on quickly and include the following:

- tiredness
- rapid heart beat
- nervousness or shakiness
- feeling sick
- headache
- cold sweat

If you are not confident about recognising your warning symptoms, avoid situations such as driving a car, in which you or others would be put at risk by hypoglycaemia.

High blood sugar (hyperglycaemia) and diabetic ketoacidosis
Hyperglycaemia (too much sugar in the blood) means that the levels of glucose in your body are too high. Hyperglycaemia can be brought about by:
- not taking your insulin;
- using less insulin than your body needs;
- an imbalance between the amount of carbohydrates you eat and the insulin you take; or
- fever, infection or emotional stress.

The early symptoms of hyperglycaemia are;
- being very thirsty
- headache
- feeling sleepy
- urinating more often

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. Additional symptoms include the following:
- nausea and/or vomiting
- abdominal pain
- rapid pulse
- heavy breathing
- moderate or large amounts of urine ketones. Ketones are produced when your body burns fat for energy instead of glucose.

If you have any of these symptoms and high sugars **get medical help immediately.**
See section 'If you forget to use Lyumjev'.

Illness
If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Lyumjev 200 units/ml KwikPen

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Keep in the outer carton in order to protect from light.

Before first use
Store in a refrigerator (2 °C to 8 °C).
Do not freeze.

After first use
Do not store above 30 °C.
Do not freeze.
Do not refrigerate.

The Lyumjev 200 units/ml KwikPen should not be stored with the needle attached. Keep the cap on the pen in order to protect from light
Discard after 28 days **even if some of the solution remains**.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Lyumjev 200 units/ml KwikPen solution for injection contains
- The active substance is insulin lispro. Each ml solution contains 200 units of insulin lispro. One Lyumjev 200 units/ml KwikPen contains 600 units of insulin lispro in 3 ml solution.
- The other ingredients are metacresol, glycerol, magnesium chloride hexahydrate, sodium citrate dihydrate, treprostinil sodium, zinc oxide, water for injections. Sodium hydroxide or hydrochloric acid may have been used to adjust the pH (see the end of section 2 under 'Lyumjev 200 units/ml KwikPen contains sodium').

What Lyumjev 200 units/ml KwikPen looks like and contents of the pack
Lyumjev 200 units/ml KwikPen solution for injection is a clear, colourless, aqueous solution in a pre-filled pen. Each pre-filled pen contains 600 units (3 millilitres). Pack sizes of 2 or 5 or a multipack of 10 (2 x 5) pre-filled pens. Not all pack sizes may be marketed.

The Lyumjev 200 units/ml KwikPen is taupe. The dose knob is taupe with raised ridges on side. The label is white with a blue colour bar and checkerboard design. On the carton and label the insulin strength is highlighted in a box with a yellow background.

The yellow warning label on cartridge holder reminds you to "Use only in this pen, or severe overdose can result."

Each Lyumjev 200 units/ml KwikPen delivers 1 to 60 units in steps of 1 unit.

Marketing Authorisation Holder
Eli Lilly Nederland B.V., Papendorpseweg 83, 3528 BJ Utrecht, The Netherlands.

Manufacturer
Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France.

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/.

Instructions for Use

Lyumjev 200 units/mL KwikPen solution for injection in pre-filled pen
insulin lispro

PLEASE READ THESE INSTRUCTIONS BEFORE USE

Read the instructions for use before you start taking Lyumjev and each time you get another Lyumjev KwikPen. There may be new information. This information does not take the place of talking to your healthcare professional about your medical condition or your treatment.

Do not share your Lyumjev KwikPen with other people, even if the needle has been changed. Do not reuse or share needles with other people. You may give other people a serious infection or get a serious infection from them.

Lyumjev 200 units/mL KwikPen ("Pen") is a disposable pre-filled pen containing 3 mL (600 units, 200 units/mL) of insulin lispro solution for injection.

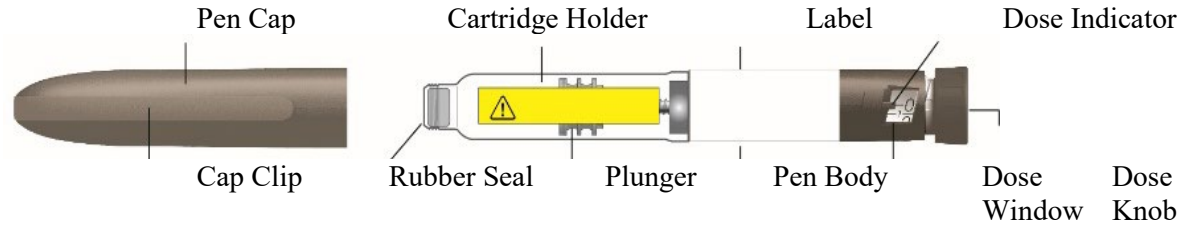
- Your healthcare professional will tell you how many units to give as your dose and how to inject your prescribed dose of insulin.
- You can give yourself more than 1 dose from the Pen.
- Each turn of the dose knob dials 1 unit of insulin. You can give from 1 to 60 units in a single injection.
- If your dose is more than 60 units, you will need to give yourself more than 1 injection. Always check the number in the dose window to make sure you dialed the correct dose.
- The plunger only moves a little with each injection, and you may not notice that it moves. The plunger will only reach the end of the cartridge when you have used all 600 units in the Pen.

This Pen is designed to allow you to give more doses than other pens you may have used in the past. Dial your usual dose as instructed by your healthcare professional.

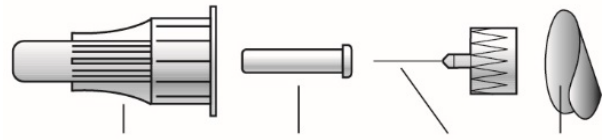
Lyumjev KwikPen is available in two strengths, 100 units/mL and 200 units/mL. Inject Lyumjev 200 units/mL only with your Pen. Do not transfer insulin from your Pen to another insulin delivery device. Syringes and insulin pumps will not measure 200 units/mL of insulin correctly. A severe overdose can result, causing very low blood sugar which may put your life in danger.

People who are blind or have vision problems should not use the Pen without help from a person trained to use the Pen.

Lyumjev KwikPen Parts



Pen Needle Parts
(Needles Not Included)



Dose Knob

How to recognize your Lyumjev KwikPen

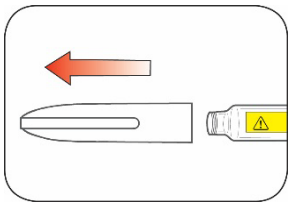
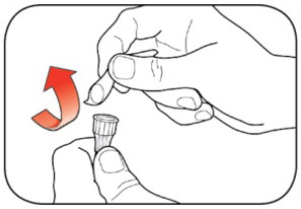
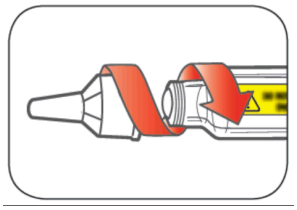
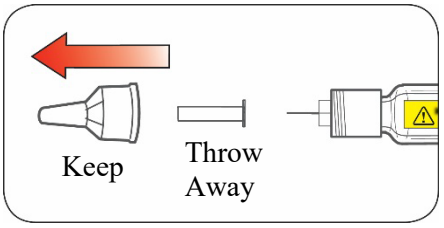
- Pen colour: Taupe
- Dose Knob: Taupe, with raised ridges on side
- Label: White with a blue colour bar and checkerboard design. Yellow warning on cartridge holder.

Supplies needed to give your injection

- Lyumjev KwikPen
- KwikPen compatible needle (BD [Becton, Dickinson and Company] Pen needles recommended)
- Swab or gauze

Preparing your Pen

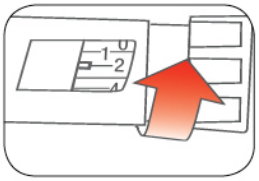
- Wash your hands with soap and water.
- Check the Pen to make sure you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
- **Do not** use your Pen past the expiry date printed on the label or for more than 28 days after you first start using the Pen.
- Always use a **new needle** for each injection to help prevent infections and blocked needles.

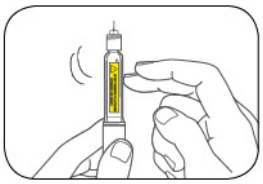
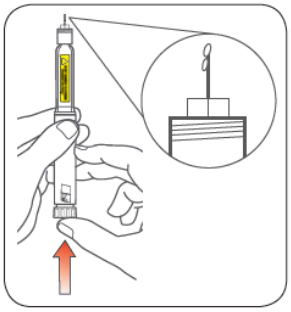
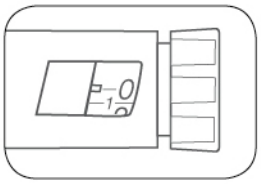
Step 1: • Pull the Pen cap straight off. – **Do not** remove the Pen label. • Wipe the rubber seal with a swab.	 
Step 2: • Check the liquid in the Pen. • Lyumjev should look clear and colourless. **Do not** use if it is cloudy, coloured, or has particles or clumps in it.	
Step 3: • Select a new needle. • Pull off the paper tab from the outer needle shield.	
Step 4: • Push the capped needle straight onto the Pen and twist the needle on until it is tight.	
Step 5: • Pull off the outer needle shield. **Do not** throw it away. • Pull off the inner needle shield and throw it away.	

Priming your Pen

Prime before each injection.

- Priming your Pen means removing the air from the needle and cartridge that may collect during normal use and ensures that your Pen is working correctly.
- If you **do not** prime before each injection, you may get too much or too little insulin.

Step 6: • To prime your Pen, turn the dose knob to select 2 units.	

Step 7: • Hold your Pen with the needle pointing up. Tap the cartridge holder gently to collect air bubbles at the top.	
Step 8: • Continue holding your Pen with the needle pointing up. Push the dose knob in until it stops and "**0**" is seen in the dose window. Hold the dose knob in and **count to 5 slowly**. You should see insulin at the tip of the Needle. – If you **do not** see insulin, repeat priming steps 6 to 8, but not more than 8 times. – If you **still do not** see insulin, change the needle and repeat priming steps 6 to 8. Small air bubbles are normal and will not affect your dose.	 

Selecting your dose

This Pen has been designed to deliver the dose that is shown in the dose window. Dial your usual dose as instructed by your healthcare professional.

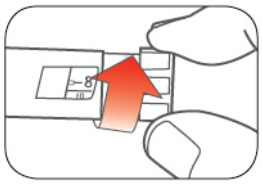
- You can give from 1 to 60 units in a single injection.
- If your dose is more than 60 units, you will need to give more than 1 injection.

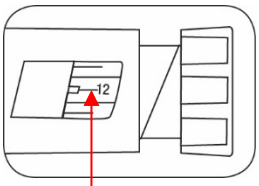
– If you need help dividing up your dose the right way, ask your healthcare professional.

– Use a new needle for each injection and repeat the priming steps.

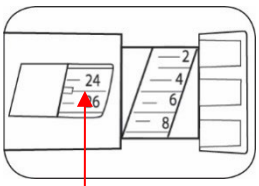
Step 9:

- Turn the dose knob to select the number of units you need to inject. The dose indicator should line up with your dose.
  - The Pen dials 1 unit at a time.
  - The dose knob clicks as you turn it.
  - **Do not** dial your dose by counting the clicks. You may dial the wrong dose. This may lead to getting too much insulin or not enough insulin.
  - The dose can be corrected by turning the dose knob in either direction until the correct dose lines up with the dose indicator.
  - The **even** numbers are printed on the dial. The example to the right shows 12 units.
  - The **odd** numbers, after the number 1, are shown as full lines between the numbers. The example to the right shows 25 units.
- **Always check the number in the dose window to make sure you have dialed the correct dose.**





Example: 12 units shown in the dose window



Example: 25 units shown in the dose window

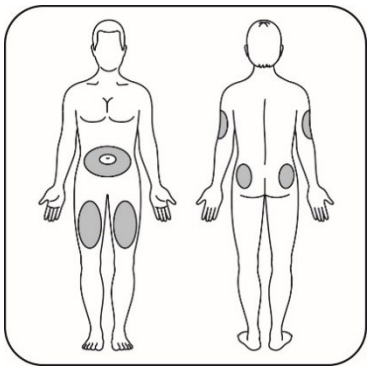
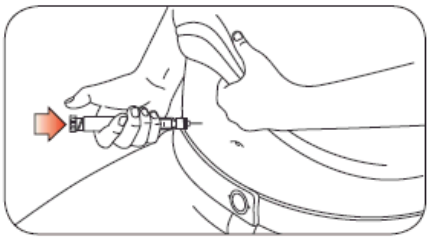
- The Pen will not let you dial more than the number of units left in the Pen.
- If you need to inject more than the number of units left in the Pen, you may either:
  - inject the amount left in your Pen and then use a new Pen to give the rest of your dose,

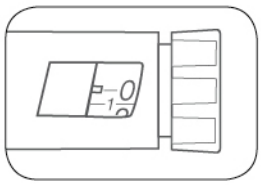
  or

  - get a new Pen and inject the full dose.
- It is normal to see a small amount of insulin left in the Pen that you cannot inject. **Do not transfer this to a syringe. Severe overdose can result.**

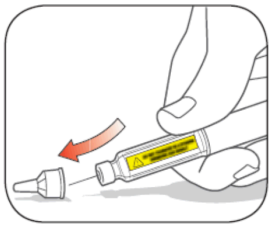
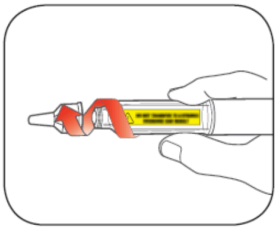
Giving your injection

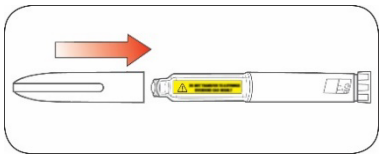
- Inject your insulin as your healthcare professional has shown you.
- Change (rotate) your injection site for each injection.
- **Do not** try to change your dose while injecting.

Step 10: • Choose your injection site. Lyumjev is injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs or upper arms. • Wipe your skin with a swab, and let your skin dry before you inject your dose.	
Step 11: • Insert the needle into your skin. • Push the dose knob all the way in. • Continue to hold the dose knob in and **slowly count to 5** before removing the needle.  **Do not** try to inject your insulin by turning the dose knob. You will **not** receive your insulin by turning the dose knob.	

Step 12: • Pull the needle out of your skin. – A drop of insulin at the needle tip is normal. It will not affect your dose. • Check the number in the dose window. – If you see “0” in the dose window, you have received the full amount you dialed. – If you do not see “0” in the dose window, you did not receive your full dose. **Do not** redial. Insert the needle into your skin and finish your injection. – If you **still** do not think you received the full amount you dialed for your injection, **do not start over or repeat that injection**. Monitor your blood glucose as instructed by your healthcare professional. – If you normally need to give 2 injections for your full dose, be sure to give your second injection. The plunger only moves a little with each injection, and you may not notice that it moves. If you see blood after you take the needle out of your skin, press the injection site lightly with a piece of gauze or a swab. **Do not** rub the area.	

After your injection

Step 13: • Carefully replace the outer needle shield.	
Step 14: • Unscrew the capped needle and dispose of it as described below (see **Disposing of Pens and needles** section). • **Do not** store the Pen with the needle attached to prevent leaking, blocking the needle, and air from entering the Pen.	

Step 15: • Replace the Pen cap by lining up the cap clip with the dose indicator and pushing straight on.	

Disposing of Pens and needles

- Put used needles in a sharps container or a hard plastic container with a secure lid. **Do not** throw needles directly into your household waste.
- **Do not** recycle the filled sharps container.
- Ask your healthcare professional about options to dispose of the Pen and the sharps container properly.
- The directions regarding needle handling are not intended to replace local, healthcare professional or institutional policies.

Troubleshooting

- If you cannot remove the Pen cap, gently twist the cap back and forth, and then pull the cap straight off.
- If the dose knob is hard to push:
  - pushing the dose knob more slowly will make it easier to inject.
  - your needle may be blocked. Put on a new needle and prime the Pen.
  - you may have dust, food, or liquid inside the Pen. Throw the Pen away and get a new Pen.

If you have any questions or problems with your Lyumjev 200 units/mL KwikPen, call your healthcare professional for help or contact your local Lilly affiliate.

Document Revision Date: