NovoMix® 30 FlexPen®

100 U/ml

Suspension for injection in a pre-filled pen.

Qualitative and quantitative composition

1 ml of the suspension contains 100 U of soluble insulin aspart*/protamine-crystallised insulin aspart* in the ratio 30/70 (equivalent to 3.5 mg).
1 pre-filled pen contains 3 ml equivalent to 300 U.
*Insulin aspart produced by recombinant DNA technology in *Saccharomyces cerevisiae*.

Pharmaceutical form: White suspension for injection in a pre-filled pen. FlexPen®.

Therapeutic indications: Treatment of patients with diabetes mellitus requiring insulin.

Posology

NovoMix® 30 dosing is individual and determined in accordance with the needs of the patient. Blood glucose monitoring and insulin dose adjustments are recommended to achieve optimal glycaemic control.
In patients with type 2 diabetes, NovoMix® 30 can be given as monotherapy. NovoMix® 30 can also be given in combination with oral antidiabetic drugs if the patient's blood glucose is inadequately controlled with oral antidiabetic drugs alone.

How to start

Insulin naïve patients: For patients with type 2 diabetes, the recommended starting dose of NovoMix® 30 is 6 U at breakfast and 6 U at dinner (evening meal). However, it can also be initiated once daily with 12 U at dinner (evening meal).

How to switch

When transferring a patient from biphasic human insulin to NovoMix® 30, start with the same dose and regimen. Then titrate according to individual needs (see *The following titration guideline*). As with all insulin products, close glucose monitoring is recommended during the transfer and in the initial weeks thereafter.

How to intensify

NovoMix® 30 can be intensified from once daily to twice daily. When using NovoMix® 30 once daily, it is generally recommended to move to twice-daily when reaching 30 units by splitting the dose into equal breakfast and dinner doses (50:50).
From NovoMix® 30 twice daily to thrice daily: The morning dose can be split into morning and lunchtime doses (thrice daily dosing).

How to adjust the dose

- Adjust the dose of NovoMix® 30 on the basis of the lowest pre-meal blood glucose level from the three previous days.
- Always change the mealtime dose preceding the measurement.
- Dose adjustment can be made once a week until target HbA_{1c} is reached.
- The dose should not be increased if hypoglycaemia occurred within these days.
- Adjustment of dosage may be necessary if patients undertake increased physical activity, change their usual diet or during concomitant illness.

The following titration guideline is recommended for dose adjustment:

Pre-meal blood glucose level		NovoMix® 30 dose adjustment
< 4.4 mmol/l	< 80 mg/dl	- 2 U
4.4 – 6.1 mmol/l	80 – 110 mg/dl	0
6.2 – 7.8 mmol/l	111 – 140 mg/dl	+ 2 U
7.9 – 10 mmol/l	141 – 180 mg/dl	+ 4 U
> 10 mmol/l	> 180 mg/dl	+ 6 U

Special populations

As with all insulin products, in special populations, glucose monitoring should be intensified and the insulin aspart dosage adjusted on an individual basis.
Elderly: NovoMix® 30 can be used in elderly patients; however there is limited experience with the use of NovoMix® 30 in combination with OADs in patients older than 75 years.
Renal and hepatic impairment: Renal or hepatic impairment may reduce the patient's insulin requirements.

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Paediatric population: NovoMix® 30 can be used in children and adolescents aged 10 years and above when premixed insulin is preferred. Limited clinical data exists for children aged 6 to 9 years (see *Pharmacodynamic properties*).
No data are available for NovoMix® 30 in children below 6 years of age.

Method of administration

NovoMix® 30 is for subcutaneous administration only.
NovoMix® 30 must not be administered intravenously, as it may result in severe hypoglycaemia. Intramuscular administration should be avoided. NovoMix® 30 is not to be used in insulin infusion pumps.
NovoMix® 30 is administered subcutaneously by injection in the thigh or in the abdominal wall. If convenient, the gluteal or deltoid region may be used. Injection sites should always be rotated within the same region in order to reduce the risk of lipodystrophy. As with all insulin products, the duration of action will vary according to the dose, injection site, blood flow, temperature and level of physical activity.
NovoMix® 30 has a faster onset of action than biphasic human insulin and should generally be given immediately before a meal. When necessary, NovoMix® 30 can be given soon after a meal.

Contraindications

Hypersensitivity to insulin aspart or any of the excipients (see *List of excipients*).

Special warnings and precautions for use

Before travelling between different time zones, the patient should seek the doctor's advice since this may mean that the patient has to take the insulin and meals at different times.

Hyperglycaemia (high blood sugar)

Inadequate dosing or discontinuation of treatment, especially in type 1 diabetes, may lead to hyperglycaemia and diabetic ketoacidosis. Usually the first symptoms of hyperglycaemia develop gradually over a period of hours or days. They include thirst, increased frequency of urination, nausea, vomiting, drowsiness, flushed dry skin, dry mouth, loss of appetite as well as acetone odour of breath. In type 1 diabetes, untreated hyperglycaemic events eventually lead to diabetic ketoacidosis, which is potentially lethal.

Hypoglycaemia (low blood sugar)

Omission of a meal or unplanned strenuous physical exercise may lead to hypoglycaemia. Hypoglycaemia may occur if the insulin dose is too high in relation to the insulin requirement (see *Undesirable effects* and *Overdose*).
Compared with biphasic human insulin, NovoMix® 30 may have a more pronounced glucose lowering effect up to 6 hours after injection. This may have to be compensated for in the individual patient, through adjustment of insulin dose and/or food intake. Patients, whose blood glucose control is greatly improved, e.g. by intensified insulin therapy, may experience a change in their usual warning symptoms of hypoglycaemia, and should be advised accordingly. Usual warning symptoms may disappear in patients with longstanding diabetes.
Tighter control of glucose levels can increase the potential for hypoglycaemic episodes and therefore require special attention during dose intensification as outlined in *Posology*.
Since NovoMix® 30 should be administered in immediate relation to a meal, the rapid onset of action should therefore be considered in patients with concomitant diseases or medication where a delayed absorption of food might be expected.
Concomitant illness, especially infections and feverish conditions, usually increases the patient's insulin requirements.
Concomitant diseases of the kidney, liver or affecting the adrenal, pituitary or thyroid gland can require changes in the insulin dose.
When patients are transferred between different types of insulin products, the early warning symptoms of hypoglycaemia may change or become less pronounced than those experienced with their previous insulin.

Transfer from other insulin products

Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand (manufacturer), type, origin (human insulin, insulin analogue) and/or method of manufacture may result in the need for a change in dosage. Patients transferred to NovoMix® 30 from another type of insulin may require an increased number of daily injections or a change in dosage from that used with their usual insulin products. If an adjustment is needed, it may occur with the first dose or during the first few weeks or months.

Injection site reactions

As with any insulin therapy, injection site reactions may occur and include pain, redness, hives, inflammation, bruising, swelling and itching. Continuous rotation of the injection site within a given area reduces the risk of developing these reactions. Reactions usually resolve in a few days to a few weeks. On rare occasions, injection site reactions may require discontinuation of NovoMix® 30.

Combination of thiazolidinediones and insulin medicinal products

Cases of congestive heart failure have been reported when thiazolidinediones were used in combination with insulin, especially in patients with risk factors for development of congestive heart failure. This should be kept in mind if treatment with the combination of thiazolidinediones and insulin medicinal products is considered. If the combination is used, patients should be observed for signs and symptoms of congestive heart failure, weight gain and oedema. Thiazolidinediones should be discontinued if any deterioration in cardiac symptoms occurs.

Insulin antibodies

Insulin administration may cause insulin antibodies to form. In rare cases, the presence of such insulin antibodies may necessitate adjustment of the insulin dose in order to correct a tendency to hyper- or hypoglycaemia.

Interaction with other medicinal products and other forms of interaction

A number of medicinal products are known to interact with the glucose metabolism.
The following substances may reduce the patient's insulin requirements:
Oral antidiabetic products, monoamine oxidase inhibitors (MAOIs), beta-blockers, angiotensin converting enzyme (ACE) inhibitors, salicylates, anabolic steroids and sulfonamides.
The following substances may increase the patient's insulin requirements:
Oral contraceptives, thiazides, glucocorticoids, thyroid hormones, sympathomimetics, growth hormone and danazol. Beta-blocking agents may mask the symptoms of hypoglycaemia. Octreotide/lanreotide may either increase or decrease the insulin requirement.
Alcohol may intensify or reduce the hypoglycaemic effect of insulin.

Pregnancy and lactation

There is limited clinical experience with NovoMix® 30 in pregnancy. NovoMix® 30 has not been investigated in pregnant women. However, data from two randomised controlled clinical trials (157 and 14 insulin aspart-exposed pregnancies respectively, in basal-bolus regimen) do not indicate any adverse effect of insulin aspart on pregnancy or on the health of the foetus/newborn when compared to soluble human insulin (see *Pharmacodynamic properties*). In addition, the data from a clinical trial including 27 women with gestational diabetes randomised to treatment with insulin aspart vs. soluble human insulin (insulin aspart: 14; soluble human insulin: 13) showed similar safety profiles between treatments.
In general, intensified blood glucose control and monitoring of pregnant women with diabetes are recommended throughout pregnancy and when contemplating pregnancy. Insulin requirements usually fall in the first trimester and increase subsequently during the second and third trimesters. After delivery, insulin requirements normally return rapidly to pre-pregnancy values.
There are no restrictions on treatment with NovoMix® 30 during lactation. Insulin treatment of the breast-feeding mother presents no risk to the baby. However, the NovoMix® 30 dosage may need to be adjusted.

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 operating machinery).
Patients should be advised to take precautions to avoid hypoglycaemia while driving or operating a machine. This is particularly important in those who have reduced or absent awareness of the warning signs of hypoglycaemia or have frequent episodes of hypoglycaemia. The advisability of driving or operating a machine should be considered in these circumstances.

Undesirable effects

a. Summary of the safety profile

Adverse reactions observed in patients using NovoMix® are mainly due to the pharmacologic effect of insulin.
The most frequently reported adverse reaction during treatment is hypoglycaemia. The frequencies of hypoglycaemia vary with patient population, dose regimens and level of glycaemic control, please see section c below.
At the beginning of the insulin treatment, refraction anomalies, oedema and injection site reactions (pain, redness, hives, inflammation, bruising, swelling and itching at the injection site) may occur. These reactions are usually of transitory nature. Fast improvement in blood glucose control may be associated with acute painful neuropathy, which is usually reversible.
Intensification of insulin therapy with abrupt improvement in glycaemic control may be associated with temporary worsening of diabetic retinopathy, while long-term improved glycaemic control decreases the risk of progression of diabetic retinopathy.

b. Tabulated list of adverse reactions

Adverse reactions listed below are based on clinical trial data and classified according to MedDRA System Organ Class. Frequency categories are defined according to the following convention: 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); not known (cannot be estimated from the available data).

Immune system disorders	Uncommon – Urticaria, rash, eruptions
	Very rare – Anaphylactic reactions*
Metabolism and nutrition disorders	Very common – Hypoglycaemia*
Nervous system disorders	Rare – Peripheral neuropathy (painful neuropathy)
Eye disorders	Uncommon – Refraction disorders
	Uncommon – Diabetic retinopathy
Skin and subcutaneous tissue disorders	Uncommon – Lipodystrophy*
General disorders and administration site conditions	Uncommon – Injection site reactions
	Uncommon – Oedema

* see section c

c. Description of selected adverse reactions

Anaphylactic reactions
The occurrence of generalised hypersensitivity reactions (including generalised skin rash, itching, sweating, gastrointestinal upset, angioneurotic oedema, difficulties in breathing, palpitation and reduction in blood pressure) is very rare but can potentially be life-threatening.

Hypoglycaemia
The most frequently reported adverse reaction is hypoglycaemia. It may occur if the insulin dose is too high in relation to the insulin requirement. Severe hypoglycaemia may lead to unconsciousness and/or convulsions and may result in temporary or permanent impairment of brain function or even death. The symptoms of hypoglycaemia usually occur suddenly. They may include cold sweats, cool pale skin, fatigue, nervousness or tremor, anxiousness, unusual tiredness or weakness, confusion, difficulty in concentration, drowsiness, excessive hunger, vision changes, headache, nausea and palpitation.
In clinical trials, the frequency of hypoglycaemia varied with patient population, dose regimens and level of glycaemic control. During clinical trials the overall rates of hypoglycaemia did not differ between patients treated with insulin aspart compared to human insulin.

Lipodystrophy
Lipodystrophy is reported as uncommon. Lipodystrophy may occur at the injection site.

Overdose

A specific overdose for insulin cannot be defined, however, hypoglycaemia may develop over sequential stages if too high doses relative to the patient's requirement are administered:

- Mild hypoglycaemic episodes can be treated by oral administration of glucose or sugary products. It is therefore recommended that the diabetic patient always carries sugar-containing products.
- Severe hypoglycaemic episodes, where the patient has become unconscious, can be treated with glucagon (0.5 to 1 mg) given intramuscularly or subcutaneously by a trained person, or with glucose given intravenously by a healthcare professional. Glucose must be given intravenously if the patient does not respond to glucagon within 10 to 15 minutes. Upon regaining consciousness, administration of oral carbohydrates is recommended for the patient in order to prevent a relapse.

Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in diabetes. Insulins and analogues for injection, intermediate- or long-acting combined with fast-acting. ATC code: A10AD05.
NovoMix® 30 is a biphasic suspension of soluble insulin aspart (rapid-acting insulin analogue) and insulin aspart crystallised with protamine (intermediate-acting insulin analogue). The suspension contains rapid-acting and intermediate-acting insulin aspart in the ratio 30/70. Insulin aspart is equipotent to human insulin on a molar basis.

Mechanism of action

The blood glucose lowering effect of insulin aspart is due to the facilitated uptake of glucose following binding of insulin to receptors on muscle and fat cells and to the simultaneous inhibition of glucose output from the liver.
When NovoMix® 30 is injected subcutaneously, the onset of action will occur within 10 to 20 minutes of injection. The maximum effect is exerted between 1 and 4 hours after injection. The duration of action is up to 24 hours.
In a 3-month trial comparing NovoMix® 30 with biphasic human insulin 30 administration before breakfast and dinner in patients with type 1 and type 2 diabetes, NovoMix® 30 resulted in significantly lower postprandial blood glucose after both meals (breakfast and dinner).
A meta-analysis including nine trials in patients with type 1 and type 2 diabetes showed that compared to biphasic human insulin 30, administration of NovoMix® 30 before breakfast and dinner resulted in significantly better postprandial blood glucose control (average prandial glucose increments over breakfast, lunch and dinner). While fasting blood glucose was higher in patients treated with NovoMix® 30, the overall glycaemic control measured by glycosylated haemoglobin was similar.
In one study, 341 patients with type 2 diabetes were randomised to treatment with NovoMix® 30 either alone or in combination with metformin, or to metformin together with sulfonylurea. HbA_{1c} after 16 weeks of treatment - did not differ between patients with NovoMix® 30 combined with metformin and patients with metformin plus sulfonylurea. In this trial 57% of the patients had baseline HbA_{1c} above 9%; in these patients treatment with NovoMix® 30 in combination with metformin resulted in significantly lower HbA_{1c} than metformin in combination with sulfonylurea.
In one study, patients with type 2 diabetes, insufficiently controlled on oral hypoglycaemic agents alone, were randomised to treatment with twice daily NovoMix® 30 (117 patients) or once daily insulin glargine (116 patients). After 28 weeks treatment following the dosing guideline, the mean reduction in HbA_{1c} was 2.8% with NovoMix® 30 (mean at baseline = 9.7%). With NovoMix® 30, 66% and 42% of the patients reached HbA_{1c} levels below 7% and 6.5%, respectively, and mean FPG was reduced by about 7 mmol/l (from 14.0 mmol/l at baseline to 7.1 mmol/l).
In patients with type 2 diabetes, a meta-analysis showed a reduced risk of overall nocturnal hypoglycaemic episodes and major hypoglycaemia with NovoMix® 30 compared to biphasic human insulin 30. The risk of overall daytime hypoglycaemic episodes was higher in patients treated with NovoMix® 30.
Paediatric population: A 16-week clinical trial comparing postprandial glycaemic control of meal-related NovoMix® 30 with meal-related human insulin/biphasic human insulin 30 and bedtime NPH insulin was performed in 167 subjects aged 10 to 18 years. Mean HbA_{1c} remained similar to baseline throughout the trial in both treatment groups, and there was no difference in hypoglycaemia rate with NovoMix® 30 or biphasic human insulin 30.
In a smaller (54 subjects) and younger (age range 6 to 12 years) population, treated in a double-blind, cross-over trial (12 weeks on each treatment) the rate of hypoglycaemic episodes and the postprandial glucose increase was significantly lower with NovoMix® 30 compared to biphasic human insulin 30. Final HbA_{1c} was significantly lower in the biphasic human insulin 30 treated group compared with NovoMix® 30.
Elderly: The pharmacodynamic properties of NovoMix® 30 have not been investigated in the elderly. However, a randomised, double-blind cross-over PK/PD trial comparing insulin aspart with soluble human insulin was performed in elderly patients with type 2 diabetes (19 patients aged 65-83 years, mean age 70 years). The relative differences in the pharmacodynamic properties (GIR_{max}, $AUC_{GIR,\ 0\text{-}120\ min}$) between insulin aspart and soluble human insulin in the elderly were similar to those seen in healthy subjects and in younger subjects with diabetes.

Pharmacokinetic properties

In insulin aspart substitution of amino acid proline with aspartic acid at position B28 reduces the tendency to form hexamers as observed with human insulin. The insulin aspart in the soluble phase of NovoMix® 30 comprises 30% of the total insulin; this is absorbed more rapidly from the subcutaneous layer than the soluble insulin component of biphasic human insulin. The remaining 70% is in crystalline form as protamine-crystallised insulin aspart; this has a prolonged absorption profile similar to human NPH insulin.
The maximum serum insulin concentration is, on average, 50% higher with NovoMix® 30 than with biphasic human insulin 30. The time to maximum concentration is, on average, half of that for biphasic human insulin 30.
In healthy volunteers, a mean maximum serum concentration of 140 ± 32 pmol/l was reached about 60 minutes after a subcutaneous dose of 0.20 U/kg body weight. The mean half-life ($t_{1/2}$) of NovoMix® 30, reflecting the absorption rate of the protamine bound fraction, was about 8-9 hours. Serum insulin levels returned to baseline 15-18 hours after a subcutaneous dose. In type 2 diabetic patients, the maximum concentration was reached about 95 minutes after dosing, and concentrations well above zero for not less than 14 hours post-dosing were measured.
Elderly: The pharmacokinetic properties of NovoMix® 30 have not been investigated in the elderly patients. However, the relative differences in pharmacokinetic properties between insulin aspart and soluble human insulin in elderly subjects (65-83 years, mean age 70 years) with type 2 diabetes, were similar to those observed in healthy subjects and in younger subjects with diabetes. A decreased absorption rate was observed in elderly subjects, resulting in a later t_{max} (82 (interquartile range: 60-120) minutes), whereas C_{max} was similar to that observed in younger subjects with type 2 diabetes and slightly lower than in subjects with type 1 diabetes.
Renal and hepatic impairment: The pharmacokinetics of NovoMix® 30 has not been investigated in patients with renal or hepatic impairment.
Paediatric population: The pharmacokinetics of NovoMix® 30 has not been investigated in children or adolescents. However, the pharmacokinetic and pharmacodynamic properties of soluble insulin aspart have been investigated in children (6-12 years) and adolescents (13-17 years) with type 1 diabetes. Insulin aspart was rapidly absorbed in both age groups, with similar t_{max} as in adults. However, C_{max} differed between the age groups, stressing the importance of the individual titration of insulin aspart.

Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction.
In *in vitro* tests, including binding to insulin and IGF-1 receptor sites and effects on cell growth, insulin aspart behaved in a manner that closely resembled human insulin. Studies also demonstrate that the dissociation of binding to the insulin receptor of insulin aspart is equivalent to human insulin.

List of excipients

Glycerol, phenol, metacresol, zinc chloride, disodium phosphate dihydrate, sodium chloride, protamine sulfate, hydrochloric acid/sodium hydroxide (for pH adjustment) and water for injections.

Special precautions for storage

Storage when not in use: Store in a refrigerator (2°C – 8°C). Keep away from the cooling element. Do not freeze.
The expiry date is printed on the label and carton.
After removing NovoMix® 30 FlexPen® from the refrigerator, it is recommended to allow NovoMix® 30 FlexPen® to reach room temperature before resuspending the insulin as instructed for the first time use.
Storage during use or when carried as a spare: NovoMix® 30 FlexPen® that is being used or carried as a spare is not to be kept in the refrigerator. It can be kept at room temperature (below 30°C) for up to 4 weeks.
Keep the pen cap on FlexPen® in order to protect from light. NovoMix® 30 must be protected from excessive heat and light.

Nature and contents of container

3 ml suspension cartridge (type 1 glass) with a plunger (bromobutyl) and a rubber closure (bromobutyl/polyisoprene) contained in a pre-filled multidose disposable pen made of polypropylene in a carton. The cartridge contains a glass ball to facilitate resuspension. Pack sizes of 5 and 10 pre-filled pens. Not all pack sizes may be marketed.

Special precautions for disposal and other handling

Needles and NovoMix® 30 FlexPen® must not be shared. The cartridge must not be refilled.
NovoMix® 30 must not be used if the resuspended liquid does not appear uniformly white and cloudy. The necessity of resuspending the NovoMix® 30 FlexPen® suspension immediately before use is to be stressed to the patient.
NovoMix® 30 which has been frozen must not be used.
The patient should be advised to discard the needle after each injection.

Produced by

Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark

INSTRUCTIONS FOR USE FOR THE PATIENT

Do not use NovoMix® 30

- **If you are allergic (hypersensitive)** to insulin aspart or any of the other ingredients in NovoMix® 30 (see *List of excipients*).
- **If you suspect hypoglycaemia** (low blood sugar) is starting (see *Hypoglycaemia*).
- **In insulin infusion pumps.**
- **If FlexPen® is dropped, damaged or crushed.**
- **If it has not been stored correctly** or if it has been frozen.
- **If the resuspended insulin does not appear uniformly white and cloudy.**
- **If, after re-suspension clumps** of material are present or if solid white particles stick to the bottom or the wall of the cartridge.

Before using NovoMix® 30

- **Check the label to make sure** it is the right type of insulin.
- **Always use a new needle** for each injection to prevent contamination.
- **Needles and NovoMix® 30 FlexPen® must not be shared.**

NovoMix® 30 is for injection under the skin

(subcutaneously). Never inject your insulin directly into a vein (intravenously) or muscle (intramuscularly).
With each injection, change the injection site within the particular area of skin that you use. This reduces the risk of developing lumps or skin pitting. The best places to give yourself an injection are: the front of your waist (abdomen); your buttocks; the front of your thighs or upper arms. The insulin will work more quickly if you inject around the waist. You should always measure your blood sugar regularly.

How to handle NovoMix® 30 FlexPen®

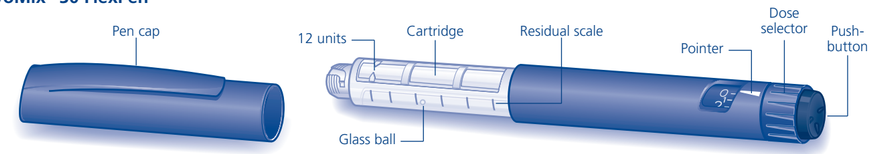
Read and follow the included NovoMix® 30 FlexPen® instructions for use carefully.

NovoMix® 30 suspension for injection in a pre-filled pen. FlexPen® INSTRUCTIONS FOR USE FOR THE PATIENT

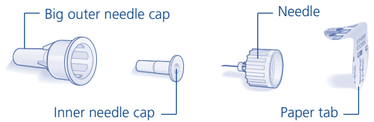
Please read the following instructions carefully before using your NovoMix® 30 FlexPen®.

Your FlexPen® is a unique dial-a-dose insulin pen. You can select doses from 1 to 60 units in increments of 1 unit. FlexPen® is designed to be used with NovoFine® or NovoTwist® disposable needles up to a length of 8 mm. As a precautionary measure, always carry a spare insulin delivery device in case your FlexPen® is lost or damaged.

NovoMix® 30 FlexPen®



Needle (example)



Maintenance

Your FlexPen® is designed to work accurately and safely. It must be handled with care. If it is dropped, damaged or crushed, there is a risk of insulin leakage.

You can clean the exterior of your FlexPen® by wiping it with a medicinal swab. Do not soak, wash or lubricate it as it may damage the pen.

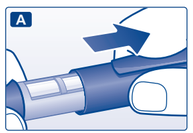
Do not refill your FlexPen®.

Preparing your NovoMix® 30 FlexPen®

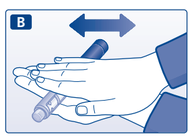
Check the label to make sure that your FlexPen® contains the correct type of insulin. Before your first injection with a new FlexPen®, you must resuspend the insulin:

A Let the insulin reach room temperature before you use it. This makes it easier to resuspend.

Pull off the pen cap.



B Roll the pen between your palms 10 times – it is important that the pen is kept horizontal.

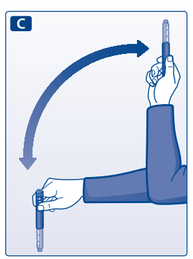


C Then move the pen up and down 10 times between the two positions as shown, so the glass ball moves from one end of the cartridge to the other.

Repeat rolling and moving the pen until the liquid does appear uniformly white and cloudy.

For every following injection move the pen up and down between the two positions at least 10 times until the liquid does appear uniformly white and cloudy.

After you have resuspended the insulin, complete all the following steps of injection without delay.



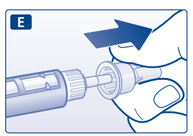
⚠ Always check there are at least 12 units of insulin left in the cartridge to allow resuspension. If there are less than 12 units left, use a new FlexPen®.

Attaching a needle

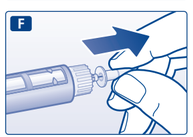
D Remove the paper tab from a new disposable needle.

Screw the needle straight and tightly onto your FlexPen®.

E Pull off the big outer needle cap and keep it for later.



F Pull off the inner needle cap and dispose of it.

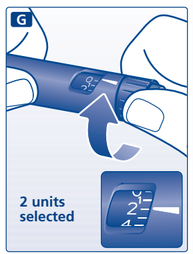


⚠ Always use a new needle for each injection to prevent contamination.
⚠ Be careful not to bend or damage the needle before use.
⚠ To reduce the risk of unexpected needle sticks, never put the inner needle cap back on when you have removed it from the needle.

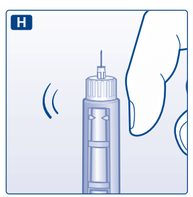
Checking the insulin flow

Prior to each injection, small amounts of air may collect in the cartridge during normal use. To avoid injection of air and ensure proper dosing:

G Turn the dose selector to select 2 units.



H Hold your FlexPen® with the needle pointing upwards and tap the cartridge gently with your finger a few times to make any air bubbles collect at the top of the cartridge.



I Keeping the needle upwards, press the push-button all the way in. The dose selector returns to 0.

A drop of insulin should appear at the needle tip. If not, change the needle and repeat the procedure no more than 6 times.

If a drop of insulin still does not appear, the pen is defective, and you must use a new one.

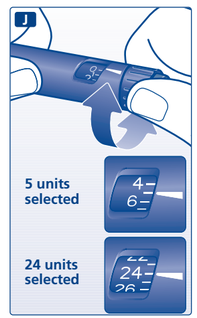
Selecting your dose

Check that the dose selector is set at 0.

J Turn the dose selector to select the number of units you need to inject.

The dose can be corrected either up or down by turning the dose selector in either direction until the correct dose lines up with the pointer. When turning the dose selector, be careful not to push the push-button as insulin will come out.

You cannot select a dose larger than the number of units left in the cartridge.



⚠ Do not use the residual scale to measure your dose of insulin.

Making the injection

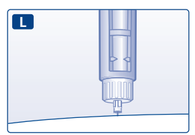
Insert the needle into your skin. Use the injection technique shown by your doctor or nurse.

K Inject the dose by pressing the push-button all the way in until 0 lines up with the pointer. Be careful only to push the push-button when injecting.

Turning the dose selector will not inject insulin.

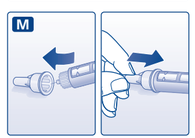
L Keep the push-button fully depressed and let the needle remain under the skin for at least 6 seconds. This will make sure you get the full dose.

Withdraw the needle from the skin, then release the pressure on the push-button.



M Lead the needle into the big outer needle cap without touching it. When the needle is covered, carefully push the big outer needle cap completely on and then unscrew the needle.

Dispose of it carefully and put the pen cap back on.



⚠ Always remove the needle after each injection and store your FlexPen® without the needle attached. Otherwise the liquid may leak out which can cause inaccurate dosing.
⚠ Caregivers should be most careful when handling used needles to avoid needle sticks.
⚠ Dispose of the used FlexPen® carefully without the needle attached.
⚠ Needles and NovoMix® 30 FlexPen® must not be shared.