Basalin

Insulin Glargine

Package and drug specifications

- Each Basalin injection pen contains 300 IU of Insulin Glargine in 3 mL (100 IU/mL)
- Five pre-filled pens containing solution for injection in a package

Qualitative composition

Sterile solution, clear, colorless and free of any visible particles in pre-filled pen

Tips to be advised to the patient

- The patient's ability to concentrate and react may be impaired as a result of hypoglycemia or hyperglycemia or, for example, as a result of visual impairment. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or using machines).Tell your doctor or pharmacist if you have any side effects.
- Tell your doctor or pharmacist if you have any side effects.
- Insulin overdose may lead to severe and sometimes long-term and life-threatening hypoglycemia. Mild episodes of hypoglycemia can usually be treated with oral carbohydrates. Adjustments in dose of the medicinal product, meal patterns, or physical activity may be needed. More severe episodes with coma, seizure, or neurologic impairment may be treated with glucagon or concentrated intravenous glucose. If you accidentally use more than the recommended amount, visit your doctor or healthcare provider immediately.
- If you forget to take a dose of the drug, your blood glucose level may rise. If so, call your doctor as soon as you are reminded and do not administer an extra dose or increase in dose to make up for the missed dose.
- This medicine is prescribed for your current condition. So do not use it in similar cases or advice to others.
- It is recommended that when using this drug, the name and serial number of the product is recorded in order to maintain the records of the manufacturing series used.

- Basalin pens should never be shared between patients, even if the needle is replaced. Sharing carries a risk for transmission of blood-borne infections.

Therapeutic indications

- To improve glycemic control in adults with type 1 diabetes mellitus and type 2 diabetes mellitus
- To improve glycemic control in children 6 years and older with type 1 diabetes mellitus

Dosing and method of administration

- **Adult**

- Initial dosage in type 1 diabetes mellitus: Approximately one-third to one-half of the total daily insulin requirements. Rapid acting or short acting insulin should be used to complete the balance (approximately two-thirds to one-half) of the daily insulin requirements.
- Initial dosage in type 2 diabetes mellitus: 0.2 units/kg once daily or up to 10 units/day initially is recommended.
- Dosage adjustments: Adjust dose according to blood glucose measurements.

- **Pediatric (6 years and older)**

- Initial dosage in type 1 diabetes mellitus: Approximately one-third of the total daily insulin requirements. Rapid acting or short acting insulin should also be used to complete the balance (approximately two-thirds) of the daily insulin requirements.
- Dosage adjustments: Adjust dose according to blood glucose measurements.

- **Conversion to Basalin from other insulins**

- Converting from once-daily NPH insulin: May be substituted on an equivalent unit-per-unit basis.
- Converting from twice-daily NPH insulin: Use 80% of the total daily dose of NPH initially; administer once daily; adjust dosage according to patient blood glucose response.

- **Conversion between Toujeo and Basalin**

- Conversion from once-daily Toujeo: Use 80% of the dose of Toujeo initially; administer once daily; adjust dosage according to patient blood glucose response.
- Conversion from once-daily Basalin to Toujeo: May be substituted on an equivalent unit-per-unit basis initially; however, generally a higher daily dosage of Toujeo will be required to achieve the same level of glycemic control as with Basalin.

- **Elderly patients (>65 years old)**

  In the elderly, progressive deterioration of renal function may lead to a steady decrease in insulin requirements and also the initial dosing, dose increments, and maintenance dosage should be conservative to avoid hypoglycemic reactions.
- **Renal impairment**

  In patients with renal impairment, insulin requirements may be diminished due to reduced insulin metabolism.
- **Hepatic impairment**

  In patients with hepatic impairment, insulin requirements may be diminished due to reduced capacity for gluconeogenesis and reduced insulin metabolism.
- **Pediatrics**

  The safety and efficacy of insulin glargine in children under 6 years of age have not been established.

Contraindications

- Sensitivity to the drug and its ingredients
- During episodes of hypoglycemia

Warning and precautions

- **Hyperglycemia or Hypoglycemia with Changes in Insulin Regimen**

Changes in insulin strength, manufacturer, type, or method of administration may affect glycemic control and predispose to hypoglycemia or hyperglycemia. These changes should be made cautiously and only under close medical supervision, and the frequency of blood glucose monitoring should be increased. For patients with type 2 diabetes, dosage adjustments of concomitant oral and antidiabetic products may be needed.

- **Hypoglycemia**

Hypoglycemia is the most common adverse reaction associated with insulin, including Insulin Glargine. Severe hypoglycemia can cause seizures, may be life-threatening or cause death. Hypoglycemia can impair concentration ability and reaction time; this may place an individual and others at risk in situations where these abilities are important (e.g., driving or operating other machinery). Hypoglycemia can happen suddenly and symptoms may differ in each individual and

change over time in the same individual. Symptomatic awareness of hypoglycemia may be less pronounced in patients with longstanding diabetes, in patients with diabetic nerve disease, in patients using medications that block the sympathetic nervous system (e.g., beta-blockers) or in patients who experience recurrent hypoglycemia.

Risk Factors for Hypoglycemia

The risk of hypoglycemia after an injection is related to the duration of action of the insulin and, in general, is highest when the glucose lowering effect of the insulin is maximal. As with all insulin preparations, the glucose lowering effect time course of Insulin Glargine may vary in different individuals or at different times in the same individual and depends on many conditions, including the area of injection as well as the injection site blood supply and temperature. Other factors which may increase the risk of hypoglycemia include changes in meal pattern (e.g., macronutrient content or timing of meals), changes in level of physical activity, or changes to coadministered medication. Patients with renal or hepatic impairment may be at higher risk of hypoglycemia.

Risk Mitigation Strategies for Hypoglycemia

Patients and caregivers must be educated to recognize and manage hypoglycemia. Self-monitoring of blood glucose plays an essential role in the prevention and management of hypoglycemia. In patients at higher risk for hypoglycemia and patients who have reduced symptomatic awareness of hypoglycemia, increased frequency of blood glucose monitoring is recommended. The long-acting effect of Insulin Glargine may delay recovery from hypoglycemia.

- **Hypersensitivity and Allergic Reactions**

Severe, life-threatening, generalized allergy, including anaphylaxis, generalized skin reactions, angioedema, bronchospasm, hypotension and shock may occur with insulin glargine. If hypersensitivity reactions occur, discontinue Insulin Glargine; treat per standard of care and monitor until symptoms and signs resolve.

- **Hypokalemia**

All insulin products, including Insulin Glargine, cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia. Untreated hypokalemia may cause respiratory paralysis, ventricular arrhythmia, and death. Monitor potassium levels in patients at

risk for hypokalemia, if indicated (e.g., patients using potassium-lowering medications, patients taking medications sensitive to serum potassium concentrations).

- **Fluid Retention and Heart Failure with Concomitant Use of Thiazolidinediones**

Thiazolidinediones 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, including Insulin Glargine, and Thiazolidinediones should be observed for signs and symptoms of heart failure. If heart failure develops, it should be managed according to current standards of care, and discontinuation or dose reduction of Thiazolidinediones must be considered.

- **Diabetic ketoacidosis**

Should not be used in patients with diabetic ketoacidosis; use an IV rapid acting or shot acting insulin is preferred.

- **Thyroid effects**

Hyperthyroidism may cause an increase in the renal clearance of insulin. Therefore, patients may need more insulin to control their diabetes. Hypothyroidism may delay insulin turnover, requiring less insulin to control diabetes.

- **Travel**

Dosing may need to change if traveling across time zones.

- **Weight gain**

May occur with insulin therapy and has been attributed to the anabolic effects of insulin and the decrease of glucosuria.

- **Sodium retention and edema**

Insulin may cause sodium retention and edema.

- **Lipoatrophy**

Lipoatrophy is the breakdown of adipose tissue at the insulin injection site, causing a depression in the skin and possibly delaying insulin absorption. It may be the result of an immune response or when less pure insulins are administered.

- **Lipohypertrophy**

Lipohypertrophy is the result of repeated insulin injection into the same site. Injection to the same site over a 2 to 4 week period may result in subcutaneous fat accumulation that may interfere with insulin absorption from the site. This condition may be avoided by rotating the injection site.

- **Localized reaction**

Localized reactions and generalized myalgia have been reported with the use of Metacresol as an injectable excipient.

- **Antibody production**

All insulin products can elicit the formation of insulin antibodies. The presence of such insulin antibodies may increase or decrease the efficacy of insulin and may require adjustment of the insulin dose.

- **Medication Errors**

Accidental mix-ups among insulin products, particularly between long-acting insulins and rapid-acting insulins, have been reported. To avoid medication errors between Insulin Glargine and other insulins, instruct patients to always check the insulin label before each injection.

Use in pregnancy and lactation

- **Use in pregnancy**

The pregnancy category of this drug is C. Inform your doctor if you are planning to become pregnant, or if you are already pregnant. Your insulin dose may need to be changed during pregnancy and after giving birth. Particularly careful control of your diabetes, and prevention of hypoglycemia, is important for the health of your baby.

- **Use in lactation**

Insulin glargine is permitted during lactation. If you are breast-feeding consult your doctor as you may require adjustments in your insulin doses and your diet.

Undesirable effects

"Any medication along with the therapeutic effects may also cause some unwanted side effects, although not all of these effects are seen in one person, consult your doctor or pharmacist if you have any of the following side effects."

- **Very common (probability of occurrence more than 10 %):**

- Metabolism and nutrition disorders: Hypoglycemia
- Vascular disorders: Hypertension
- Cardiac disorders: Peripheral edema

- Psychiatric disorders: Depression
- Gastrointestinal disorders: Diarrhea
- Infections and infestations: Urinary tract infection, Influenza
- Respiratory, thoracic and mediastinal disorders: Sinusitis, Bronchitis, Cough
- Immune system disorders: Antibody development
- Eye disorders: Cataract
- Musculoskeletal and connective tissue disorders: Back pain, Limb pain, Arthralgia

- **Common (probability of occurrence of 1 – 10 %):**

- General disorders and administration site conditions: Injection site reactions, Lipohypertrophy
- Eye disorders: Retinal vascular disease
- Nervous system disorders: Headache
- Respiratory, thoracic and mediastinal disorders: Upper respiratory tract infection Nasopharyngitis, Pharyngitis, Rhinitis

- **Uncommon (probability of occurrence 0.1 – 1 %):**

- General disorders and administration site conditions: Lipoatrophy
- Metabolism and nutrition disorders: Hypokalemia, Sodium retention

- **Rare (probability of occurrence 0.01 – 0.1 %):**

- Immune system disorders: Allergic reactions
- Eye disorders: Visual impairment, Retinopathy
- Metabolism and nutrition disorders: Edema

- **Very rare (probability of occurrence less than 0.01 %):**

- Musculoskeletal and connective tissue disorders: Myalgia
- Nervous system disorders: Dysgeusia

Drug interactions

- **The levels/effects of Insulin Glargine may be decreased by following drugs:**
  Hyperglycemia-Associated Agents, Quinolones, Ritodrine, Thiazide and Thiazide-like diuretics, Atypical antipsychotics (such as olanzapine and clozapine), Corticosteroids, Danazol, Estrogens, Glucagon, Isoniazid, Niacin, Oral contraceptives, Phenothiazines, Progestins, Protease inhibitors (such as indinavir), Somatropin, Sympathomimetic products (such as albuterol, epinephrine, terbutaline) and thyroid hormones (such as levothyroxine and liothyronine).
- **The levels/effects of Insulin Glargine may be increased by following drugs:**
  Alpha-lipoic acid, Androgens (Exception Danazol), Antidiabetic agents, Beta-blockers, Dipeptidyl peptidase-IV inhibitors, Direct acting antiviral agents (Sofosbuvir, Daclatasvir and Ledipasvir), Edetate calcium disodium, Glucagon-like peptide-1 agonists (Liraglutide),

Guanethidine, Maitake, Metreleptin, Monoamine oxidase inhibitors (Selegiline, Tranylcypromine), Pegvisomant, Pioglitazone, Pramlintide, Prothionamide, Quinolones, Salicylates, Selective serotonine reuptake inhibitors, Sodium-glucose cotransporter 2 inhibitors (Empagliflozine), Disopyramide, Fibrates, ACE inhibitors, Pentoxifylline, Propoxyphene, Somatostatin analogs (such as octreotide), Sulfonamides

- **The levels/effects of Insulin Glargine may be increased or decreased by following drugs:** Alcohol, Clonidine, Lithium salts, Pentamidine
- **The levels/effects of following drugs may be increased by Insulin Glargine:** Hypoglycemia-associated agents, Rosiglitazone
- **The levels/effects of following drugs may be decreased by Insulin Glargine:** Macimorelin

Mechanism of action

Insulin lowers blood glucose levels by stimulating peripheral glucose uptake, especially by muscle and skeletal fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis in adipocytes, inhibits proteolysis and enhances protein synthesis. Insulin secreted by pancreatic beta cells is the major hormone required for proper utilization of glucose in normal metabolic processes. This compound is composed of two amino acids A (acidic) and B (basic) that are linked by disulfide bonds.

Ingredients

Metacresol, Glycerol, Zinc chloride, Water for injection

Guide for preparation, injection and preservation of the Basalin

Read carefully the instructions below before taking the medicine subcutaneously.

- Basalin contains 300 units of insulin glargine in 3 mL.
- Basalin should be administered once daily and consistently at the same time each day.
- Do not mix and dilute insulin glargine with other insulin and solutions.
- Your doctor will decide if you are able to inject medicine for yourself. Your doctor, pharmacist and nurse will explain how to inject. If you have not received the necessary training for the injection, do not inject it alone.
- If you use similar drugs in the form of a pen, carefully check the pen name and label to ensure that it contains insulin glargine. Then read the description and photos of the various parts of the pen and needle.
- Always use needle with a number from 29 to 32 G and a length of 6 mm.

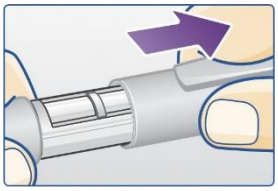
Prepare your pen

1. Remove the pen from the refrigerator and wait for some time to reach the ambient temperature.

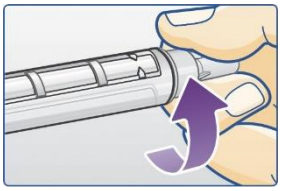
2. Wash your hands thoroughly with warm water and soap.

3. Check the pen carefully before you use it. Do not take medication if any cracks or fractures are visible in the pen and the visible particle in the medication compartment.

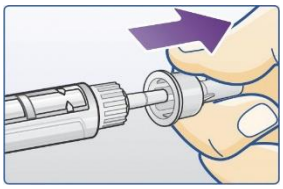
4. Pull off the pen cap.



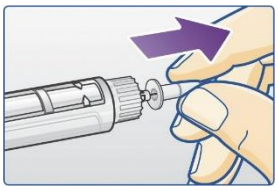
5. Pull off the paper tab from a new disposable needle. Screw the needle straight and tightly onto your pen.



6. Pull off the outer needle cap and keep it for later. You will need it after the injection, to safely remove the needle from the pen.



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



▲ Always use a new needle for each injection. This reduces the risk of contamination, infection, leakage of insulin, blocked needles and inaccurate dosing.

▲ Be careful not to bend or damage the needle.

▲ Never try to put the inner cap back on the needle. You may stick yourself with the needle.

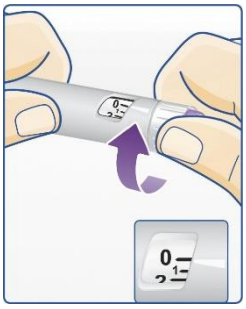
▲ A drop of solution may appear at the needle tip. This is normal, but you must still check the flow, if you use a new pen for the first time.

▲ Do not inject cold insulin glargine,

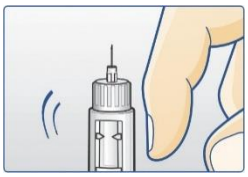
Check the flow

- Check the flow before your first injection with each new pen. If your pen is already in use, go to 'Select your dose'.

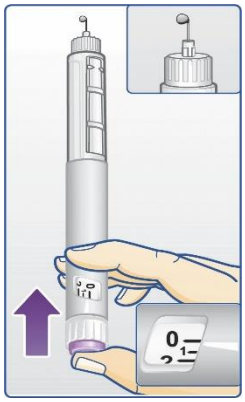
8. Turn the dose selector until 1 unit lines up with the pointer.



9. Hold the pen with the needle pointing up. Tap the cartridge gently with your finger a few times. This will make any air bubbles collect at the top of the cartridge. Some small bubbles may remain in the cartridge.



10. Keep the needle pointing up and press the dose button until 0 mg lines up with the pointer. A drop of insulin should appear at the needle tip. If no drop appears, repeat steps 8 and 9 up to four times. If there is still no drop of insulin, change the needle and repeat steps 8 and 9 once more. Do not use the pen if a drop of insulin still does not appear. This indicates the pen is defective and you must use a new pen.



▲ If you are sure that the pen is broken, call Pooyesh Darou Biopharmaceutical Company.

▲ Never press the dose button before attaching a needle.

▲ If you have dropped your pen against a hard surface or suspect that something is wrong with it, always put on a new disposable needle and check the flow before you inject.

Select your dose

- Always check the pointer lines up with 0 mg.

11. Turn the dose selector until your needed dose lines up with the pointer.

If you selected a wrong dose by mistake, simply change it by turning the dose selector backwards or forwards until the right dose lines up with the pointer.

Be careful not to press the dose button when turning the dose selector backwards, as insulin may come out.

If the dose selector stops before your needed dose lines up with the pointer, there is not enough insulin left for a full dose. In this case, either you can inject what is remaining in the pen and complete your dose with a new pen or use a new pen for your full dose.
▲ The dose selector clicks when you turn it. Do not use these clicks to select your dose. Do not use the cartridge scale to measure how much insulin to inject. It is not accurate enough.

Select injection site

12. You can do injections at any of the following areas:

- The middle and front of the thighs
- One third of the lower and back of the arm (Only if someone else is injected for you)
- On the abdomen 5 cm away from the navel

▲ Do not touched the injection area before injection

▲ Avoid injection in areas where redness, inflammation or bruising occur

▲ Do not injected in areas with ulcers or cuts and stretches

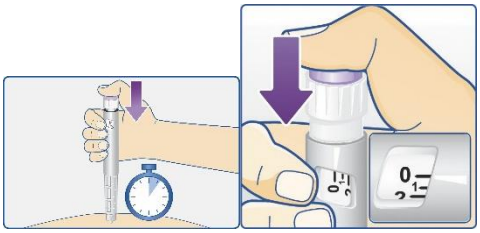
Inject your dose

13. Clean the injection site with an alcoholic pad.

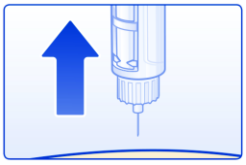
14. Hold the pen with one hand and with the other hand; create a small bulge in the desired place for injection.

15. Place the pen with a 90 degree angle in the center of the bulge and apply the needle to the bottom.

16. Press the dose button to inject until 0 mg lines up with the pointer. Keep the dose button pressed down and leave the needle under the skin for at least 10 seconds. This is to make sure that you get your full dose.



17. Pull out the needle.



▲ Be careful not to touch the display sideways when you inject. This is because it may block the injection.

▲ A small drop of blood or drug from the injection site is not worrying.

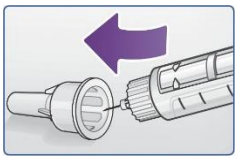
▲ After pulling out the needle, you may see a drop insulin at the needle tip. This is normal and does not affect your dose and in the next injection, keep needle longer in the skin.

▲ Caregivers must be very careful when handling used needles to prevent needle injury and cross-infection.

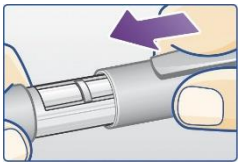
▲ Change (rotate) your injection sites within the area you choose for each dose to prevent lipodystrophy.

After your injection

18. Guide the needle tip into the outer needle cap.



19. When the needle is covered, carefully push the outer needle cap completely on. Then unscrew the needle. Dispose of it carefully and put the pen cap back on and place it in the fridge for later use, in the package.



▲ Always remove the needle after each injection and store your pen without a needle attached.

▲ When the pen is empty, carefully dispose of it without a needle attached.

Storage conditions of Basalin

- Keep the new and unused pens in the refrigerator at 2 to 8 ˚C and protect from frost.
- Store the pen in use in the refrigerator (2 to 8 ˚C) or out of the refrigerator (below 30 ˚C).
- Discard the remaining medicine in the pen after 28 days.
- After each use, put the pen cap on it.
- Keep the medicine away from light and in the original package.
- Avoid placing the drug in the vicinity of direct sunlight or using any heat source such as hot water to deliver the medicine to the ambient temperature.
- Avoid taking an expired medicine. The expiry date is shown on the original packaging and pen label. The expiration date is the last day of the month.
- Do not try to repair your pen or pull it apart.
- Keep your pen away from dust, dirt and liquids.
- Clean the pen with a mild detergent on a moistened cloth.
- Do not wash, soak or lubricate your pen. It may damage your pen.
- Never share your pen or your needles with other people.
- Keep out of sight and reach children.