Basagine®
(Insulin Glargine)

Disposable Pen of 3mL Solution for Injection

بیساجین

DESCRIPTION
Basagine (Insulin Glargine) is a solution for injection used as antidiabetic agent. Insulin Glargine is a biosynthetic long-acting, Human Insulin analogue administered subcutaneously to lower the excess blood-glucose-level. It is synthesized by using recombinant DNA technology and a special laboratory strain of non-pathogenic *Escherichia coli.*
Insulin Glargine differs from Human Insulin in that the amino acid asparagine at position A21 is replaced by glycine and two arginines are added to the C-terminus of the B-chain. Chemically, it is 21^{A}-Gly-30^{b}a-L-Arg-30^{b}b-L-Arg-Human Insulin and has the molecular formula $C_{267}H_{404}N_{72}O_{78}S_6$.

QUALITATIVE AND QUANTITATIVE COMPOSITION
Basagine (Insulin Glargine) Solution for Injection 100Units/mL in Disposable Pen is available for administration as:

Basagine Solution for Injection 100Units/mL
Each mL contains:
Insulin Glargine (rDNA origin).....100Units
(3mL cartridge in disposable pen)

CLINICAL PHARMACOLOGY
Mechanism of action
The primary activity of Insulin Glargine is the regulation of glucose metabolism. It inhibits hepatic glucose production and lowers blood glucose level by enhancing peripheral glucose uptake especially by skeletal muscle and fat. It also inhibits lipolysis in the adipocyte, inhibits proteolysis and enhances protein synthesis.
Insulin Glargine is a Human Insulin analogue designed to have a low solubility at neutral pH. It is completely soluble at the acidic pH of the injection solution (pH 4). After injection into the subcutaneous tissue, the acidic solution is neutralized leading to formation of micro-precipitates from which small amounts of Insulin Glargine are continuously released, providing a smooth, peakless, predictable concentration/time profile with a prolonged duration of action. its analogs lower blood glucose by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis and proteolysis, and enhances protein synthesis.

Pharmacokinetics
Absorption & Bioavailability
Following subcutaneous injection, absorption of Insulin Glargine is slower and more prolonged compared with that of Isophane (NPH) Human Insulin; the serum concentration time profile for Insulin Glargine is relatively constant over 24 hours.
After subcutaneous injection of 0.3 units/kg Insulin Glargine in patients with type I diabetes, a relatively constant concentration/time profile has been demonstrated. The duration of action after abdominal, deltoid, or thigh subcutaneous administration is almost similar. Insulin Glargine injected once daily will reach steady state levels in 2 – 4 days after the first dose.

Metabolism
Insulin Glargine is partly metabolized in the subcutaneous depot at the carboxyl terminus of the B chain to form the active metabolites i.e. M1 (21^{A}-Gly-Insulin) and M2 (21^{A}Gly-des-30^{B}-Thr-Insulin) having similar *in vitro* activity to Insulin.

Special population
Age, Race and Gender
Age, race and gender did not show difference in safety and efficacy between Insulin Glargine and NPH Human Insulin.

Renal & Hepatic Insufficiency
The effect of renal & hepatic insufficiency on the pharmacokinetics of Insulin Glargine has not been studied. However, some studies with Human Insulin have shown increased circulating levels of Insulin in patients with renal & hepatic failure. Careful glucose monitoring and dose adjustments may be necessary in patients with renal & hepatic dysfunction.

THERAPEUTIC INDICATIONS
Basagine (Insulin Glargine) is indicated for once daily subcutaneous administration for the treatment of:
– Adult and Pediatric patients with Type I Diabetes Mellitus.
– Adult patients with Type II Diabetes Mellitus who require Basal (long-acting) Insulin for the control of hyperglycemia.

DOSAGE AND ADMINISTRATION
Important Administration Instructions
- Visually inspect Basagine (Insulin Glargine) disposable pens for particulate matter and discoloration prior to administration. Only use if the solution is clear and colorless with no visible particles.
- Administer Basagine (Insulin Glargine) subcutaneously into the abdominal area, thigh, or deltoid, and rotate injection sites within the same region from one injection to the next to reduce the risk of lipodystrophy and localized cutaneous amyloidosis. Do not inject into areas of lipodystrophy or localized cutaneous amyloidosis.
- During changes to a patient's Insulin regimen, increase the frequency of blood glucose monitoring.
- Do not administer intravenously or via an Insulin pump.
- Do not dilute or mix Basagine (Insulin Glargine) with any other Insulin or solution.
- The instructions for using the pen must be followed carefully for attaching the needle, and administering the Insulin injection.
- If the Insulin pen is damaged or not working properly (due to mechanical defects) it has to be discarded, and a new Insulin pen has to be used.

General Dosing Instructions
- Administer Basagine (Insulin Glargine) subcutaneously once daily at any time of day but at the same time every day.
- Individualize and adjust the dosage of Basagine (Insulin Glargine) based on the patient's metabolic needs, blood glucose monitoring results and glycemic control goal.
- Dosage adjustments may be needed with changes in physical activity, changes in meal patterns (i.e., macronutrient content or timing of food intake), during acute illness, or changes in renal or hepatic function. Dosage adjustments should only be made under medical supervision with appropriate glucose monitoring.
- In patients with type I diabetes, Basagine (Insulin Glargine) must be used concomitantly with short-acting Insulin.

Initiation of Basagine (Insulin Glargine) Therapy
Recommended Starting Dosage in Patients with Type I Diabetes
The recommended starting dosage of Basagine (Insulin Glargine) in patients with type I diabetes is approximately one-third of the total daily Insulin requirements. Use short-acting, premeal Insulin to satisfy the remainder of the daily Insulin requirements.

Recommended Starting Dosage in Patients with Type II Diabetes
The recommended starting dosage of Basagine (Insulin Glargine) in patients with type II diabetes who are not currently treated with Insulin is 0.2 units/kg or up to 10 units once daily.

Switching to Basagine (Insulin Glargine) from Other Insulin Therapies
Dosage adjustments are recommended to lower the risk of hypoglycemia when switching patients to Basagine (Insulin Glargine) from other Insulin therapies. When switching from:
- Once-daily NPH Insulin to once-daily Basagine (Insulin Glargine), the recommended starting Basagine (Insulin Glargine) dosage is the same as the dosage of NPH that is being discontinued.
- Twice-daily NPH Insulin to once-daily Basagine (Insulin Glargine), the recommended starting Basagine (Insulin Glargine) dosage is 80% of the total NPH dosage that is being discontinued.

Pediatric
Safety and efficacy of Basagine (Insulin Glargine) have been established in children aged 2 years and older. The dose regimen (dose and timing) should be individually adjusted.

ADVERSE REACTIONS
Very common: Hypoglycaemia.
Common: Lip hypertrophy and injection site reactions.
Uncommon: Lipoatrophy.
Rare: Allergic reactions, visual impairment, retinopathy and edema.
Very rare: Dysgeusia and myalgia.
Not known: Cutaneous amyloidosis.

CONTRAINDICATIONS
Insulin Glargine is contraindicated:
- In patients with hypersensitivity to Insulin Glargine or to any of the excipients of the product.
- During episodes of hypoglycemia.

PRECAUTIONS
- Insulin Glargine prefilled pens must never be shared between patients, even if the needle is changed. Sharing poses a risk for transmission of blood-borne pathogens.
- Changes in an Insulin regimen (e.g., Insulin strength, manufacturer, type, injection site or method of administration) may affect glycemic control and predispose to hypoglycemia or hyperglycemia. Repeated Insulin injections into areas of lipodystrophy or localized cutaneous amyloidosis have been reported to result in hyperglycemia; and a sudden change in the injection site (to unaffected area) has been reported to result in hypoglycemia.
- Make any changes to a patient's Insulin regimen under close medical supervision with increased frequency of blood glucose monitoring. Advise patients who have repeatedly injected into areas of lipodystrophy or localized cutaneous amyloidosis to change the injection site to unaffected areas and closely monitor for hypoglycemia. For patients with type II diabetes, dosage adjustments of concomitant oral and antidiabetic products may be needed.
- Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with Insulins, including Insulin Glargine. If hypersensitivity reactions occur, discontinue Insulin Glargine; treat per standard of care and monitor until symptoms and signs resolve.
- All Insulins, 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).
- Thiazolidinediones (TZDs), which are peroxisome proliferator-activated receptor (PPAR)-gamma agonists, can cause dose-related fluid retention, when used in combination with Insulin. Fluid retention may lead to or exacerbate heart failure. Patients treated with Insulin, including Insulin Glargine, and a PPAR-gamma agonist 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 the PPAR-gamma agonist must be considered.
- The time of occurrence of hypoglycemia depends on the action profile of the Insulins used and may, therefore, change when the treatment regimen is changed. Due to more sustained Basal Insulin supply with Insulin Glargine, less nocturnal but more early morning hypoglycaemia can be expected.
- Glucose monitoring is essential for all patients receiving Insulin therapy. Changes to an Insulin regimen should be made cautiously and only under medical supervision.
- In case of insufficient glucose control or a tendency to hyperglycemic or hypoglycemic episodes, the patient's adherence to the prescribed treatment regimen, injection sites, proper injection technique and all other relevant factors must be reviewed before the consideration of dose adjustment.
- Insulin requirements may be altered during illness or emotional disturbance, these situations may necessitate intensified metabolic monitoring and possibly, further special measures (e.g., dose adjustment, urine tests for ketones).
- As with all Insulins, the time course of Insulin Glargine action may vary in different individuals or at different times in the same individual and the rate of absorption are dependent on blood supply, temperature and physical activity. All factors increasing such risk require particularly close monitoring and may necessitate dose adjustment.
- Insulin administration may cause Insulin antibodies to form. In rare cases, the presence of such Insulin antibodies may necessitate adjustment of the Insulin dose.
- Insulin Glargine is not the Insulin of choice for the treatment of diabetic ketoacidosis. Instead, intravenous Regular Insulin is recommended in these cases.
- In patients with renal impairment, Insulin requirement may be diminished because of reduced Insulin metabolism. In the elderly, progressive deterioration of renal function may lead to a steady decrease in Insulin requirements.
- In patients with diabetes and severe hepatic impairment, Insulin requirements may be diminished due to reduced capacity of gluconeogenesis and reduced Insulin metabolism.
- The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia or hyperglycemia. Patients should be advised to take precautions to avoid hypoglycaemia whilst driving or operating machines.
- Caution should be exercised when Insulin Glargine is administered to elderly patients. In elderly patients with diabetes, the initial dosing, dosage increments, and maintenance dosage should be conservative to avoid hypoglycemic reactions. Hypoglycemia may be difficult to recognize in elderly patients.

Pregnancy
There are no well-controlled clinical studies conducted to monitor the use of Insulin Glargine in pregnant women. It is essential for patients with pre-existing or gestational diabetes to maintain good metabolic control before conception and throughout pregnancy. Insulin requirements may decrease during the first trimester, generally increase during the second and third trimesters, and rapidly decline after delivery. Careful blood glucose control is essential in such patients.

Nursing Mothers
It is unknown whether Insulin Glargine is excreted in significant amount in human milk. Because many drugs including Human Insulin, are excreted in human milk, caution should be exercised when Insulin Glargine is administered to nursing women. Use of Insulin Glargine is compatible with breastfeeding, but women with diabetes who are lactating may require adjustments of their Insulin doses.

DRUG INTERACTIONS
A number of drugs affect glucose metabolism and may require dose adjustment and particularly close monitoring of Insulin Glargine.
- Drugs that may enhance the blood-glucose -lowering effect and increase susceptibility to hypoglycaemia include oral antidiabetic agents, angiotensin converting enzyme (ACE) inhibitors, disopyramide, fibrates, fluoxetine, monoamine oxidase (MAO) inhibitors, pentoxifylline, propoxyphene, salicylates and sulfonamide antibiotics.
- Drugs that may reduce the blood-glucose-lowering effect include corticosteroids, danazol, diazoxide, diuretics, glucagon, isoniazid, estrogens and progestogens, phenothiazine derivatives, somatropin, sympathomimetic agents (e.g., epinephrine, salbutamol, terbutaline), thyroid hormones, atypical antipsychotic medicinal products (e.g., clozapine and olanzapine) and protease inhibitors.
- Beta-blockers, clonidine, lithium salts or alcohol may either potentiate or weaken the blood-glucose-lowering effect of Insulin. Pentamidine may cause hypoglycemia, which may sometimes be followed by hyperglycemia.
- The sign of hypoglycemia may be reduced or absent in patients taking sympatholytic drugs such as beta blockers, clonidine, guanethidine and reserpine.

OVERDOSAGE
Symptoms
Insulin Glargine overdose may lead to severe and sometimes long-term and life-threatening hypoglycemia.

Treatment
Mild episodes of hypoglycemia can usually be treated with oral carbohydrates. Adjustments in dosage 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 intramuscular/subcutaneous glucagon or concentrated intravenous glucose. Sustained carbohydrate intake and observation may be necessary because hypoglycemia may recur after apparent clinical recovery.

STORAGE
Store in a refrigerator at 2°C - 8°C.
Protect from heat and light.
Do not freeze.
After first opening, the pen may be stored for a maximum of 4 weeks under the temperature condition of not more than 25°C.
The pen in use must not be stored in the refrigerator.
The pen cap must be put back on the pen after each injection in order to protect from light.

HOW SUPPLIED
Basagine (Insulin Glargine) Solution for Injection 100Units/mL is available as Disposable Pen of 3mL.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Manufactured by:
Gan & Lee Pharmaceuticals,
No.8 Nanfeng West 1st Street, Huoxian, Tongzhou District, Beijing, China.

Manufactured for:
Getz pharma (PVT) LIMITED
www.getzpharma.com
29-30/27, K.I.A., Karachi, Pakistan

Basagine® (Insulin Glargine) INSTRUCTION MANUAL

بیساجین ہدایات نامہ

STEP 1 Checking the Basagine Pen

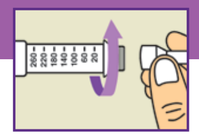
پہلا مرحلہ: بیساجین (Basagine) پین کی جانچ کریں

1 Pull off the pen cap.

1- پین کے ڈھکن کو ہٹادیں۔

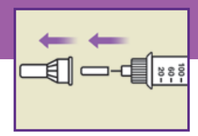
2 Check that insulin is clear.

2- چیک کریں کہ انسولین سلوشن صاف ہے۔



3 Keep the needle straight and screw it on to the pen until fix. Do not over-tighten.

3- سوئی کو سیدھا رکھیں اور اسے ٹھیک سے پین پر لگائیں۔ زیادہ مضبوطی سے بند مت کریں۔



4 Pull off the needle cap and keep it for later use.

4- سوئی کے ڈھکن کو ہٹادیں اور اسے بعد میں استعمال کے لیے رکھ لیں۔

5 Make sure that there is no air bubble in the insulin. Select 2 units by turning the dose selector until the dose pointer is at the 2 mark.

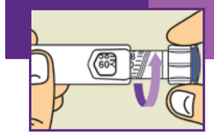
5- اس بات کو یقینی بنائیں کہ انسولین میں کوئی ہوا کا بلبلہ نہیں ہے۔ 2 یونٹس مقدار کے لیے ڈوز سلیکٹر کو اتنا گھمایئے کہ ڈوز پوائنٹر 2 کے نشان پر آجائے۔

6 Press the injection button all the way in to check if insulin comes out of the needle tip. You may have to perform the safety test (repeat step 5&6) 1 to 5 times before insulin comes out of the needle tip. The dose selector display will turn to '0'.

6- انجکشن بٹن کو دبا کر اچھی طرح سے اس بات کی یقین دہانی کرلیں کہ انسولین سوئی سے نکل آئے۔ اس حفاظتی ٹیسٹ (مرحلہ نمبر 5 اور 6) کو 1 سے 5 مرتبہ دہرائیں یہاں تک کہ انسولین سوئی کی نوک سے باہر آجائے۔ ڈوز سلیکٹر کا ڈسپلے 0 پر آجائے گا۔

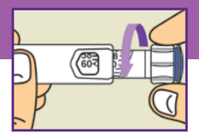
STEP 2 Selecting your Dose

دوسرا مرحلہ: خوراک کا انتخاب



1 Select the number of units you need to inject by turning the dose selector until your required dose lines up with the dose pointer. Remember that 60 units is the maximum dose you can deliver in one injection.

1- جس مقدار میں آپ کو انسولین چاہیے اسکے لیے ڈوز سلیکٹر کو اس وقت تک گھمایئے جب تک آپ کی مطلوبہ مقدار ڈوز پوائنٹر کی سیدھ میں نہ آجائے۔ یاد رکھیے کہ ایک مرتبہ انجکشن سے انسولین لینے کی زیادہ سے زیادہ مقدار 60 یونٹس ہیں۔



2 If you select a different dose than you need, simply turn back the dose selector until the correct dose lines up with the dose pointer.

2- اگر مطلوبہ مقدار سے مختلف مقدار کا انتخاب ہوجائے تو ایسی صورت میں ڈوز سلیکٹر اس وقت تک واپس گھمایئے جب تک صحیح مقدار ڈوز پوائنٹر کی سیدھ میں نہ آجائے۔

STEP 3 Making your injection

Follow the injection technique recommended by your healthcare professional.

تیسرا مرحلہ: انجکشن لگانے کا طریقہ

اپنے معالج کے تجویز کردہ انجکشن لگانے کے طریقے پر عمل کریں۔

1 To inject, press the injection button completely in, until you hear or feel a click. Leave the needle under the skin for at least 10 seconds.

This ensures that the selected insulin dose is delivered. Withdraw the needle. You have completed your injection and the selected insulin dose has been delivered. The dose selector display will show '0'.

1- انجکشن لگانے کے لیے انجکشن بٹن کو مکمل طور پر دبایئے یہاں تک کہ آپ کو کلک کی آواز سنائی دے یا محسوس ہو۔ سوئی کو کم از کم 10 سیکنڈ کے لیے جلد کے اندر چھوڑ دیں۔

یہ عمل اس بات کو یقینی بناتا ہے کہ انسولین کی مطلوبہ مقدار آپ کے جسم میں پہنچ گئی ہے۔ سوئی کو جلد سے باہر نکالیں۔ اب ڈوز سلیکٹر '0' دکھا رہا ہوگا۔

2 After you have withdrawn the needle, a few droplets of insulin may appear at the needle tip. This is normal and has no effect on the dose delivered.

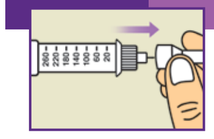
2- سوئی نکالنے کے بعد انسولین کے چند قطرے سوئی کی نوک پر نظر آسکتے ہیں یہ عام بات ہے اور اس سے جسم میں پہنچنے والی انسولین کی مقدار پر کوئی اثر نہیں پڑتا ہے۔

STEP 4 Replacing used Needle

Immediately after the injection:

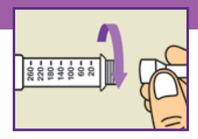
چوتھا مرحلہ: استعمال شدہ سوئی کو تبدیل کرنا

انجکشن لگانے کے فوراً بعد:



1 Carefully replace the needle cap onto the needle.

1- سوئی کے ڈھکن کو احتیاط سے واپس سوئی پر لگادیں۔



2 Hold the Pen holder and unscrew the needle. Dispose off the needle properly as instructed by your healthcare professional.

2- پین ہولڈر کو پکڑیں اور سوئی کو گھما کر نکالیں۔ اپنے معالج کی ہدایت کے مطابق سوئی کو درست طریقے سے ضائع کردیں۔

3 Always firmly replace the pen cap after use.

3- استعمال کے بعد پین کے ڈھکن کو ہمیشہ واپس پین پر اچھی طرح لگادیں۔

Getz pharma