Basagine™

بيساجين

[Insulin Glargine]

Solution for Injection
100 Units/mL
For Subcutaneous use only

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 & QUANTITATIVE COMPOSITION

BASAGINE (Insulin Glargine) is available as solution for injection for subcutaneous administration as:

BASAGINE Injection 100 Units/mL
Each mL contains:
Insulin Glargine (rDNA Origin)..... 100 Units

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 neutralised 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.

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 1 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 (21A-Gly-des-30^{B}-Thr-insulin) having similar *invitro* 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 rDNA Origin 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 & ADMINISTRATION

Adults

BASAGINE (Insulin Glargine) is a human insulin analogue. Its potency is approximately the same as human insulin. It exhibits a relatively constant glucose-lowering profile over 24 hours that permits once-daily dosing.

BASAGINE (Insulin Glargine) may be administered at any time during the day. BASAGINE (Insulin Glargine) should be administered subcutaneously once a day at the same time every day. The desired levels as well as the doses and timing of antidiabetic medications must be determined individually. Blood glucose monitoring is recommended for all patients with diabetes.

BASAGINE (Insulin Glargine) may be prescribed with either a short-acting insulin or an oral anti-diabetic.

Pediatric

BASAGINE (Insulin Glargine) can be safely administered to pediatric patients $\geq$ 6 years of age. The dose recommended is the same as directed for adults.

Change Over to BASAGINE

If changing from a treatment regimen with intermediate or long acting insulin with BASAGINE (Insulin Glargine), the amount and timing of short acting insulin or fast-acting insulin analogue or the dose of any oral antidiabetes drug may need to be adjusted.

- If transferring patients from once-daily NPH insulin to once-daily BASAGINE (Insulin Glargine), the recommended initial BASAGINE (Insulin Glargine) dose is the same as the dose of NPH that is being discontinued.
- If transferring patients from twice-daily NPH insulin to once-daily BASAGINE (Insulin Glargine), the recommended initial BASAGINE (Insulin Glargine) dose is 80% of the total NPH dose that is being discontinued. This dose reduction will lower the likelihood of hypoglycemia.

Administration

BASAGINE (Insulin Glargine) should be administered subcutaneously only and should not be administered intravenously. BASAGINE (Insulin Glargine) must not be mixed or diluted with any other form of insulin. Mixing or diluting can change its time/action profile and mixing can cause precipitation. The prolonged duration of activity of BASAGINE (Insulin Glargine) is dependent on injection into subcutaneous space.

ADVERSE REACTIONS

Very Common:

Hypoglycemia is the most frequently occurring undesirable effect of insulin therapy that a patient with diabetes may suffer.

Common:
Lipohypertrophy, injection site reactions such as redness, pain, itching, swelling or inflammation.

Uncommon:
Lipoatrophy.

Rare:
Allergic reaction, visual impairment, retinopathy, edema (insulin may cause sodium retention and edema particularly if previously poor metabolic control is improved by intensified insulin therapy).

Very Rare:
Myalgia, dysgeusia.

CONTRAINDICATIONS
BASAGINE (Insulin Glargine) must not be used in patients hypersensitive to insulin glargine or any of its excipients.

PRECAUTIONS
- 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 hyperglycaemic or hypoglycaemic 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.

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.

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.

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 at temperature between 2°C to 8°C in a refrigerator. Do not freeze.
Protect from heat and sunlight.
Once opened, the vial may be used for up to four weeks when stored below 25°C. Do not use beyond this period. Use only if the solution is clear, colourless, with no solid particles visible and of a water-like consistency. The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED
BASAGINE (Insulin Glargine) Solution for Injection 100 Units/mL is available as 1 vial of 3mL.

Keep out of reach of children.

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

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Manufactured by:
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29-30/27, K.I.A., Karachi, Pakistan

L00-200005079