For the use of only a registered medical practitioner or hospital or laboratory

Biocon Biologics

℞

Insulin Glargine Injection IP (rDNA Origin)

100 IU/mL

BASALOG® बेसल्लौग

1 Vial of 3 mL / 5 mL / 10 mL

Insulin Glargine is a recombinant. Human insulin analogue that is a long acting (up to 24 hour duration of action) parenteral blood-glucose-lowering agent.

BASALOG®
(Insulin Glargine (rDNA origin) 100 IU/mL solution for injection in a vial)

COMPOSITION
Each mL contains
Insulin Glargine IP (rDNA Origin) 100 IU
m-Cresol 2.7 mg (as preservative)
Excipients.... q.s.
(Each 100 units is equivalent to 3.64 mg insulin glargine)

PHARMACEUTICAL FORM
Solution for injection in a vial.
Clear colourless solution.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic Properties
Pharmacotherapeutic group: Drugs used in diabetes. Insulins and analogues for injection, long-acting. ATC code: A10AE04

Mechanism of Action
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 insulin glargine 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. Insulin receptor binding: Insulin glargine is very similar to human insulin with respect to insulin receptor binding kinetics. It can, therefore, be considered to mediate the same type of effect via the insulin receptor as insulin.

The primary activity of insulin, including insulin glargine, is regulation of glucose metabolism. Insulin and its analogues lower blood glucose levels by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis in the adipocyte, inhibits proteolysis and enhances protein synthesis.

In clinical pharmacology studies, intravenous insulin glargine and human insulin have been shown to be equipotent when given at the same doses. As with all insulins, the time course of action of insulin glargine may be affected by physical activity and other variables.

In euglycemic clamp studies in healthy subjects or in patients with type1 diabetes, the onset of action of subcutaneous insulin glargine was slower than NPH human insulin. The effect profile of insulin glargine was relatively constant with no pronounced peak and the duration of its effect was prolonged compared to NPH human insulin.

The longer duration of action (up to 24 hours) of insulin glargine is directly related to its slower rate of absorption and supports once daily subcutaneous administration. The time course of action of insulins, including insulin glargine, may vary between individuals and/or within the same individual.

In a clinical study, symptoms of hypoglycaemia or counter-regulatory hormone responses were similar after intravenous insulin glargine and human insulin both in healthy volunteers and patients with type 1 diabetes.

In an another 5 year NPH-controlled study (NPH given bid) in 1024 type 2 diabetic patients in which progression of retinopathy by 3 or more steps on the Early Treatment Diabetic Retinopathy Study (ETDRS) scale was investigated by fundus photography. No significant difference was seen in the progression of diabetic retinopathy when insulin glargine was compared to NPH insulin.

Paediatric population
A 24-week parallel group study was conducted in 125 children with type 1 diabetes mellitus aged 1 to 6 years (61 children from 2 to 5 in the insulin glargine group and 64 children from 1 to 6 in the NPH insulin group), comparing insulin glargine given once daily in the morning to NPH insulin given once or twice daily as basal insulin. Both groups received bolus insulin before meals.

Comparison of the two treatment regimens in terms of hypoglycemia was the primary objective of the study. The composite primary outcome consisted of continuous glucose monitoring excursions below 70mg/dL (3.9mM), confirmed by fingerstick blood glucose (FSBG) measurements, other FSBG measurements <70mg/dL, and episodes of symptomatic hypoglycemia.

The primary aim of demonstrating non-inferiority of insulin glargine to NPH in this composite outcome did not meet the non-inferiority margin. However, the rate of symptomatic hypoglycemia events is the most commonly used and clinically relevant component of the composite outcome. Rates of symptomatic hypoglycemia were numerically lower in the insulin glargine group, both overall (25.5 episodes per patient year, vs 33.0 for NPH) and overnight (2.38 episodes per patient year, vs 3.65 for NPH). Glycohaemoglobin and glucose variabilities were comparable in both treatment groups. No new safety signals were observed in this trial.

In a randomised, controlled clinical study, paediatric patients (age range 6 to 15 years) with type 1 diabetes (n=349) were treated for 28 weeks with a basal-bolus insulin regimen where regular human insulin was used before each meal. Insulin glargine was administered once daily at bedtime and NPH human insulin was administered once or twice daily. Similar effects on glycohemoglobin and the incidence of symptomatic hypoglycemia were observed in both treatment groups, however fasting plasma glucose decreased more from baseline in the insulin glargine group than in the NPH group. There was less severe hypoglycaemia in the insulin glargine group as well. One hundred forty three of the patients treated with insulin glargine in this study continued treatment with insulin glargine in an uncontrolled extension study with mean duration of follow-up of 2 years. No new safety signals were seen during this extended treatment with insulin glargine.

Pharmacokinetic Properties
Absorption
None

Distribution
After subcutaneous injection of insulin glargine in healthy subjects and diabetic patients, the insulin serum concentrations indicated a slower and much more prolonged absorption and a lack of a peak in comparison to human NPH insulin. Concentrations were, thus, consistent with the time profile of the pharmacodynamics activity of insulin glargine. After subcutaneous injection of 0.3IU/kg insulin glargine in diabetic patients, a flat concentration-time glargine in diabetics patients, a flat concentration-time profile has been demonstrated; this is also reflected in the wide range of tmax values (between 1.5 and 22.5 hours compared to NPH (2.5 to 10.0 hours). When given intravenously, the concentration profiles and the apparent elimination half-life of insulin glargine and human insulin were comparable. There were no relevant differences in serum insulin levels after abdominal deltoid or thigh administration of insulin glargine. Insulin glargine has less-intra and inter-individual variability in pharmacokinetic profile compared to human ultralente insulin.

Metabolism
After subcutaneous injection of insulin glargine (reference product) in healthy subjects and diabetics patients, insulin glargine is rapidly metabolized at the carboxy terminus of the Beta chain with formation of two active metabolites M1 (21A-Gly-insulin) and M2 (21A-Gly-des-30B-Thr-insulin). In plasma, the principal circulating compound is the metabolites M1. The exposure to M1 increases with the administered dose of insulin glargine (reference product). The pharmacokinetics and pharmacodynamics findings indicate that the effect of the subcutaneous injection with insulin glargine (reference product) is principally based on exposure to M1 insulin glargine and the metabolite M2 were not detectable in the vast majority of subjects and, when they were detectable their concentration was independent of administered dose of insulin glargine (reference product).

Elimination
None

Special Populations
Age and gender: Information on the effect of age and gender on the pharmacokinetics of insulin glargine is unavailable. However, in large clinical trials, subgroup analysis based on age and gender did not indicate any difference in safety and efficacy in insulin glargine treated patients over the entire study population. The same holds true for NPH treated patients.

Smoking: In clinical trials subgroup analysis showed no difference in safety and efficacy of insulin glargine between the group of smokers and the total study population. The same is true for NPH insulin.

Obesity. In clinical trials subgroup analysis based on BMI showed no differences in safety and efficacy of Insulin glargine in the group of patients compared to the total study population. The same is true for NPH insulin

Paediatric population
Pharmacokinetics in children aged 2 to less than 6 years of age with type 1 diabetes mellitus was assess in one clinical study. Plasma 'trough' levels of insulin glargine and its main metabolites M1 and M2 were measured in children treated with insulin glargine, revealing plasma concentration patterns similar to adults, and providing no evidence for accumulation of insulin glargine or its metabolites with chronic dosing.

Clinical studies-efficacy results
Efficacy of Biocon's insulin glargine was assessed in a phase III study conducted by Biocon Limited to establish safety and non-inferiority (in comparison to reference product), with respect to decrease in HbA1C in patients with type 1 diabetes mellitus.

The results established non-inferiority of Biocon's insulin glargine compared to the reference product, with respect to change in HbA1c. The changes in FPG, PPG and seven-point glucose were comparable between the two study arms. The proportion of patients who achieved target HbA1c <7% was comparable between groups. Mean insulin dose was also comparable between the two arms. Compliance was good during the study, with average compliance >98% for both basal and pre-meal soluble insulin which was comparable for both study arms.

Overall the two study treatments were comparable with respect to efficacy.

A 24-week parallel group study was conducted in 125 children with type 1 diabetes mellitus aged 1 to 6 years (61 children from 2 to 5 in the insulin glargine group and 64 children from 1 to 6 in the NPH insulin group), comparing insulin glargine given once daily in the morning to NPH insulin given once or twice daily as basal insulin. Both groups received bolus insulin before meals. Comparison of the two treatment regimens in terms of hypoglycemia was the primary objective of the study. The composite primary outcome consisted of continuous glucose monitoring excursions below 70mg/dL (3.9mM), confirmed by fingerstick blood glucose (FSBG) measurements, other FSBG measurements <70mg/dL, and episodes of symptomatic hypoglycemia. The primary aim of demonstrating non-inferiority of insulin glargine to NPH in this composite outcome did not meet the non-inferiority margin. However, the rate of symptomatic hypoglycemia events is the most commonly used and clinically relevant component of the composite outcome. Rates of symptomatic hypoglycemia were numerically lower in the insulin glargine group, both overall (25.5 episodes per patient year, vs 33.0 for NPH) and overnight (2.38 episodes per patient year, vs 3.65 for NPH). Glycohaemoglobin and glucose variabilities were comparable in both treatment groups. No new safety signals were observed in this trial.

Preclinical Safety Data
Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

CLINICAL PARTICULARS

Therapeutic Indications
For the treatment of adults, adolescents and children of 2 years of above with diabetes mellitus, where treatment with insulin is required.

Posology and Method of Administration
Posology
BASALOG® contains insulin glargine, an insulin analogue, and has a prolonged duration of action.

BASALOG® should be administered once daily at any time but at the same time each day.

The **BASALOG®** dose regimen (dose and timing) should be individually adjusted. In patients with type 2 diabetes mellitus, **BASALOG®** can also be given together with orally active antidiabetic medicinal products.

Elderly population (≥65 years old): In the elderly, progressive deterioration of renal function may lead to a steady decrease in insulin requirements.

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 capacity for gluconeogenesis and reduced insulin metabolism.

Paediatric population:

The safety profile for patients ≤18 years of age is similar to the safety profile for patients > 18 years. No clinical study safety data are available in patients below 2 years of age.

Due to limited experience on the efficacy and safety of insulin glargine in children below the age of 2 years, **BASALOG®** should only be used in this age group under careful medical supervision.

Initiation of **BASALOG®** therapy: The recommended starting dose of **BASALOG®** in patients with type 1 diabetes should be approximately one-third of the total daily insulin requirements. Short-acting, pre-meal insulin should be used to satisfy the remainder of the daily insulin requirements.

Based on published information the recommended starting dose on an average is 10 IU once daily and subsequently adjusted according to the patient's need to a total daily dose ranging from 2 to 100 IU, however doses needs to be individualized by the prescriber for a particular patient.

Transition from other insulins to **BASALOG®**: When changing from a treatment regimen with an intermediate or long-acting insulin to a regimen with **BASALOG®**, a change of the dose of the basal insulin may be required and the concomitant antidiabetic treatment may need to be adjusted (dose and timing of additional regular insulins or fast-acting insulin analogues or the dose of oral antidiabetic medicinal products). To reduce the risk of nocturnal and early morning hypoglycaemia, patients who are changing their basal insulin regimen from twice daily NPH insulin to a once daily regimen with **BASALOG®** should reduce their daily dose of basal insulin by 20-30% during the first weeks of treatment. During the first weeks the reduction should, at least partially, be compensated by an increase in mealtime insulin, after this period the regimen should be adjusted individually. As with other insulin analogues, patients with high insulin doses because of antibodies to human insulin may experience an improved insulin response with **BASALOG®**. Close metabolic monitoring is recommended during the transition and in the initial weeks thereafter. With improved metabolic control and resulting increase in insulin sensitivity a further adjustment in dose regimen may become necessary. Dose adjustment may also be required, for example, if the patient's weight or life-style changes, change of timing of insulin dose or other circumstances arise that increase susceptibility to hypo or hyperglycaemia (see section Special Warnings and Precautions for Use).

Method of administration
BASALOG® is administered subcutaneously.

BASALOG® should not be administered intravenously. The prolonged duration of action of **BASALOG®** is dependent on its injection into subcutaneous tissue. Intravenous administration of the usual subcutaneous dose could result in severe hypoglycaemia.

There are no clinically relevant differences in serum insulin or glucose levels after abdominal, deltoid or thigh administration of **BASALOG®** . The prolonged duration of action of **BASALOG®** is dependent on injection into subcutaneous space. As with all insulins, injection sites within an injection area (abdomen, thigh, or deltoid) must be rotated from one injection to the next.

In published clinical studies, there was no relevant difference in insulin glargine absorption after abdominal, deltoid, or thigh subcutaneous administration. As for all insulins, the rate of absorption, and consequently the onset and duration of action, may be affected by exercise and other variables.

BASALOG® must not be mixed with any other insulin or diluted. Mixing or diluting can change its time/action profile and mixing can cause precipitation.

Instructions to be given to the patient

Before injecting this insulin,

1. Wash hands with soap and water.
2. Disinfect the rubber stopper with an alcohol swab.
3. Look at the vial and the insulin. The insulin should be clear and colourless. Do not roll or shake the vial. Shaking right before the dose is drawn into the syringe may cause bubbles or foam.
4. Draw air into the syringe, in the same amount as the volume of insulin to be injected.
5. Inject the air into the vial, push the needle through the rubber stopper and press the plunger.
6. Turn the vial and syringe upside down.
7. Draw the correct dose of insulin into the syringe.
8. Pull the needle out of the vial.
9. Make sure that there is no air left in the syringe: point the needle upwards and push the air out.
10. Check you have the right dose.
11. Inject the insulin into the subcutaneous tissue.

Contraindications
Hypersensitivity to the active substance or to any of the excipients.

Special Warnings and Precautions for Use
All insulin products, including insulin glargine (reference product), 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).

BASALOG® is not the insulin of choice for the treatment of diabetic ketoacidosis. Instead, regular insulin administered intravenously is recommended in such cases.

In case of insufficient glucose control or a tendency to hyper-or hypoglycaemic episodes, the patient's adherence to the prescribed treatment regimen, injection sites and proper injection technique and all other relevant factors must be reviewed before dose adjustment is considered.

Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand (manufacturer), type (regular, NPH, lente, long-acting, etc.), origin (animal, human, human insulin analogue) and/or method of manufacture may result in the need for a change in dose.

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. (See section **Undesirable Effects).**

Hypoglycaemia: The time of occurrence of hypoglycaemia 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 **BASALOG®**, less nocturnal but early morning hypoglycaemia can be expected.

Particular caution should be exercised, and intensified blood glucose monitoring is advisable in patients in whom hypoglycaemic episodes might be of particular clinical relevance, such as in patients with significant stenoses of the coronary arteries or of the blood vessels supplying the brain (risk of cardiac or cerebral complications of hypoglycaemia) as well as in patients with proliferative retinopathy, particularly if not treated with photocoagulation (risk of transient amaurosis following hypoglycaemia).

Patients should be aware of circumstances where warning symptoms of hypoglycaemia are diminished. The warning symptoms of hypoglycaemia may be changed, be less pronounced or be absent in certain risk groups. These include patients:

- in whom an autonomic neuropathy is present,
- with a long history of diabetes,
- suffering from a psychiatric illness,
- receiving concurrent treatment with certain other medicinal products (see section **Drug Interactions).**

Such situations may result in severe hypoglycaemia (and possibly loss of consciousness) prior to the patient's awareness of hypoglycaemia. The prolonged effect of subcutaneous insulin glargine may delay recovery from hypoglycaemia. If normal or decreased values for glycated haemoglobin are noted, the possibility of recurrent, unrecognised (especially nocturnal) episodes of hypoglycaemia must be considered.

Adherence of the patient to the dose and dietary regimen, correct insulin administration and awareness of hypoglycaemia symptoms are essential to reduce the risk of hypoglycaemia. Factors increasing the susceptibility to hypoglycaemia require particularly close monitoring and may necessitate dose adjustment. These include:

- change in the injection area,
- improved insulin sensitivity (e.g., by removal of stress factors),
- unaccustomed, increased or prolonged physical activity,
- intercurrent illness (e.g. vomiting, diarrhoea),
- inadequate food intake,
- missed meals,
- alcohol consumption,
- certain uncompensated endocrine disorders, (e.g. in hypothyroidism and in anterior pituitary or adrenocortical insufficiency),
- concomitant treatment with certain other medicinal products.

BASALOG® contains metacresol, which may cause allergic reactions.

Intercurrent illness: Intercurrent illness requires intensified metabolic monitoring. In many cases urine tests for ketones are indicated, and often it is necessary to adjust the insulin dose. The insulin requirement is often increased. Patients with type 1 diabetes must continue to consume at least a small amount of carbohydrates on a regular basis; even if they are able to eat only little or no food, or are vomiting etc. and they must never omit insulin entirely.

Drug Interactions
A number of substances affect glucose metabolism and may require dose adjustment of insulin glargine.

Substances that may enhance the blood-glucose-lowering effect and increase susceptibility to hypoglycaemia include oral antidiabetic medicinal products, angiotensin converting enzyme (ACE) inhibitors, disopyramide, fibrates, fluoxetine, monoamine oxidase (MAO) inhibitors, pentoxifylline, propoxyphene, salicylates and sulfonamide antibiotics.

Substances that may reduce the blood-glucose-lowering effect include corticosteroids, danazol, diazoxide, diuretics, glucagon, isoniazid, oestrogens and progestogens, phenothiazine derivatives, somatropin, sympathomimetic medicinal products (e.g. epinephrine [adrenaline], 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 hypoglycaemia, which may sometimes be followed by hyperglycaemia.

In addition, under the influence of sympatholytic medicinal products such as beta-blockers, clonidine, guanethidine and reserpine, the signs of adrenergic counter-regulation may be reduced or absent.

Fluid retention and heart failure with concomitant use of **PPAR-gamma** agonists

Thiazolidinediones (TZDs), which are peroxisome proliferator-activated receptor (PPAR)-gamma agonist including pioglitazone, 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 Basalog Refil, and 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 PPAR-gamma agonist must be considered.

Pregnancy and Lactation
Pregnancy: For insulin glargine no clinical data on exposed pregnancies from controlled clinical trials are available. A moderate amount of data on pregnant women (between 300-1000 pregnancy outcomes) exposed to marketed insulin glargine indicate no adverse effects of insulin glargine on pregnancy and no malformative nor feto/neonatal toxicity of insulin glargine.

Animal data do not indicate reproductive toxicity.

Patients with diabetes should be advised to inform their health care professional if they are pregnant or are contemplating pregnancy.

The use of **BASALOG®** may be considered during pregnancy, if necessary.

It is essential for patients with pre-existing or gestational diabetes to maintain good metabolic control throughout pregnancy. Insulin requirements may decrease during the first trimester and generally increase during the second and third trimesters. Immediately after delivery, insulin requirements decline rapidly (increased risk of hypoglycaemia). Careful monitoring of glucose control is essential.

Breastfeeding: It is unknown whether insulin glargine is excreted in human milk. No metabolic effects of ingested insulin glargine on the breastfed newborn/infant are anticipated since insulin glargine as a peptide is digested into amino acids in the human gastrointestinal tract. Breastfeeding women may require adjustments in insulin dose and diet.

Fertility: Animal studies do not indicate direct harmful effects with respect to fertility.

Effects on Ability to Drive and Use Machines
The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia or hyperglycemia or, 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 operating machines).

Patients should be advised to take precautions to avoid hypoglycaemia whilst driving. It should be considered whether it is advisable to drive or operate machines in these circumstances.

Undesirable Effects
Hypoglycaemia, in general the most frequent adverse reaction of insulin therapy, may occur if the insulin dose is too high in relation to the insulin requirement.

The following related adverse reactions from clinical investigations are listed below by system organ class and in order of decreasing incidence
Side effects reported very common (≥1/10) Metabolism and nutrition disorders: Hypoglycaemia
Side effects reported common (≥1/100 to <1/10) Skin and subcutaneous tissue disorders: lipohypertrophy
General disorders and administration site conditions: injection site reactions
Side effects reported uncommon (≥1/1,000 to <1/100) Skin and subcutaneous tissue disorders: lipoatrophy
Side effects reported rare (≥1/10,000 to <1/1,000)
Immune system disorders: Allergic reactions
Eye disorders: visual impairment, retinopathy
General disorders and administration site conditions: Oedema
Side effects reported very rare (<1/10,000)

Nervous system disorders: Dysgeusia

Musculoskeletal and connective tissue disorders: Myalgia

Metabolism and nutrition disorders: Severe hypoglycaemic attacks, especially if recurrent, may lead to neurological damage. Prolonged or severe hypoglycaemic episodes may be life-threatening. In many patients, the signs and symptoms of neuroglycopenia are preceded by signs of adrenergic counter-regulation. Generally, the greater and more rapid the decline in blood glucose, the more marked is the phenomenon of counter-regulation and its symptoms.

Immune system disorders: Immediate-type allergic reactions to insulin are rare. Such reactions to insulin (including insulin glargine) or the excipients may, for example, be associated with generalised skin reactions, angio-oedema, bronchospasm, hypotension and shock, and may be life-threatening. Insulin administration may cause insulin antibodies to form. In clinical studies, antibodies that cross-react with human insulin and insulin glargine were observed with the same frequency in both NPH-insulin and insulin glargine treatment groups. 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.

Eye disorders: A marked change in glycaemic control may cause temporary visual impairment, due to temporary alteration in the turgidity and refractive index of the lens. Long-term improved glycaemic control decreases the risk of progression of diabetic retinopathy. However, intensification of insulin therapy with abrupt improvement in glycaemic control may be associated with temporary worsening of diabetic retinopathy. In patients with proliferative retinopathy, particularly if not treated with photocoagulation, severe hypoglycaemic episodes may result in transient amaurosis.

Skin and subcutaneous tissue disorders: As with any insulin therapy, lipodystrophy may occur at the injection site and delay local insulin absorption. Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions.

General disorders and administration site conditions: Injection site reactions include redness, pain, itching, hives, swelling, or inflammation. Most minor reactions to insulins at the injection site usually resolve in a few days to a few weeks. Rarely, insulin may cause sodium retention and oedema particularly if previously poor metabolic control is improved by intensified insulin therapy.

Paediatric population:
In general, the safety profile for children and adolescents (≤18 years of age) is similar to the safety profile for adults. The adverse reaction reports received from post marketing surveillance included relatively more frequent injection site reactions (injection site pain, injection site reaction) and skin reactions (rash, urticaria) in children and adolescents (≤18 years of age) than in adults.

Clinical study safety data are not available for children under 2 years.

Medication errors have been reported in which other insulins, particulary short acting insulins have been accidentally administered instead of insulin glargine.

Overdose
Symptoms: Insulin overdose may lead to severe and sometimes long-term and life-threatening hypoglycaemia.

Management: Mild episodes of hypoglycaemia 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 intramuscular/subcutaneous glucagon or concentrated intravenous glucose. Sustained carbohydrate intake and observation may be necessary because hypoglycaemia may recur after apparent clinical recovery.

PHARMACEUTICAL PARTICULARS

List of Excipients
Glycerol, Metacresol, Zinc chloride, Hydrochloric acid, Sodium hydroxide, Water for Injections IP.

Incompatibilities
BASALOG® must not be mixed with other medicinal products. It is important to ensure that syringes do not contain traces of any other material.

Shelf Life
Please refer to carton/label.

Storage and Precautions
Before use: **Store in a refrigerator (2°C - 8°C).**

Do not store BASALOG® in or too near the freezer section or cooling element.

Do not freeze.

During use: **Do not refrigerate. BASALOG® vials that are in use can be kept at room temperature below 30°C (86°F) up to 28 days.**

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

Protect from excessive heat and sunlight.

Special Precautions for Disposal and Other Handling

BASALOG® must not be mixed with any other insulin or diluted. Mixing or diluting can change its time/action profile and mixing can cause precipitation.

Inspect the vial before use. It must only be used if the solution is clear, colourless, with no visible solid particles. Since **BASALOG®** is a solution; it does not require re-suspension before use.

Nature and Contents of Container
Insulin Glargine Injection (rDNA Origin) 100 IU/mL is packed in 5mL clear tubular (USP Type I) glass vials closed with bromobutyl rubber stoppers.

Pack sizes:
Available in 3 mL / 5 mL vials

Marketed by:
Biocon Biologics Limited
Biocon House, Semicon Park, Electronics City, Phase - II, Bengaluru - 560 100, India.

® - Registered trademark

Leaflet Revised - **June 2021**

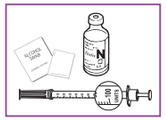
In case of any product related complaints or adverse events related to Biocon products, Call Toll Free No.: **1800-102-9465** or visit our website www.biocon.com and fill voluntary reporting form available under 'Report Adverse Events/Side Effects and Product Complaints' and send the duly filled form to us at **drugsafety@biocon.com.** For general queries regarding diabetes and its management, Call Toll Free No.: **1800-425-7667**.

References
1.http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000284/WC500036082.pdf
2.https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/021081s063lbl.pdf
3.https://www.medicines.org.uk/emc/PIL.18417.latest.pdf

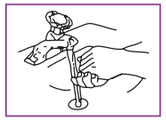
Note: Unless otherwise stated, material contained herein related to studies, tests, treatment and applications are taken from publicly available information.

BF/LL/41158/01

Drawing and Self-Injecting Insulin



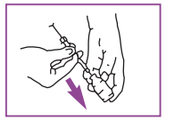
1. Get Supplies



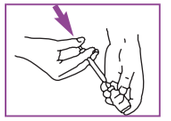
2. Wash hands

3. Wipe top of bottle

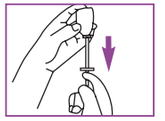
4. Pull plunger down to appropriate number of units as advised by the physician



5. Push needle into bottle



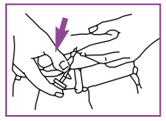
6. Push plunger down



7. Pull plunger down to appropriate number of units as advised by the physician

8. Pick injection site Wipe with Alcohol Swab

9. Pinch up skin Push needle into skin Push plunger in



10. Pull needle out

11. Dispose syringe safely Check your town rules