FRONT

For the use only of a Registered Medical Practitioner or Hospital or Laboratory

℞

Insulin Glargine Injection (rDNA)

Basalog one®

बेसल्लौग वन

100 IU/mL, 3 mL Prefilled Pen

Biocon

COMPOSITION
Each mL of prefilled pen contains:
Insulin glargine (rDNA) 100 IU
m-cresol 2.7 mg (as preservative)
Excipients q.s.
(Each 100 units is equivalent to 3.64 mg insulin glargine)
For a full list of excipients, see **List of Excipients** section.

PHARMACEUTICAL FORM
- Solution for injection in a prefilled pen.
- Clear colourless solution.

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

Pharmacodynamic Properties
Insulin glargine is a recombinant human insulin analogue designed to exhibit low solubility at neutral pH. It is completely soluble at the acidic pH of the injection solution (pH 4). Once injected into the subcutaneous tissue, the acidic solution is neutralised to form micro-precipitates from which small amounts of insulin glargine are continuously released, providing a smooth, peakless, predictable concentration vs 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 and can therefore, be considered to exert a similar effect via the insulin receptor.
In clinical pharmacology studies, intravenous insulin glargine and human insulin have 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.

Mechanism of Action
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 muscles and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis in the adipocyte, inhibits proteolysis and enhances protein synthesis.

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 (21AGly-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 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.

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 glycohaemoglobin and the incidence of symptomatic hypoglycaemia 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 and forty-three patients treated with insulin glargine in this study continued treatment with insulin glargine in an uncontrolled extension study with mean duration of follow up to 2 years. No new safety signals were seen during this extended treatment with insulin glargine.

Biocon's Efficacy Data
Efficacy of Biocon's insulin glargine was assessed in a phase 3 study conducted by Biocon Limited to establish safety and non-inferiority (in comparison to reference product), with respect to decrease in glycosylated haemoglobin (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 fasting plasma glucose (FPG), post-prandial glucose (PPG) and 7-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.

Biocon's Safety Data
In a clinical study conducted by Biocon Limited, the adverse events were similar in nature, frequency, and severity as compared to the reference product. Hypoglycaemic events were the most common adverse events in both the treatment groups. Apart from hypoglycaemia, pyrexia was the next most common adverse event with three events in each study arm. Retinal adverse events reported in this study were comparable between the treatment groups. The abnormalities in the laboratory parameters were comparable between the two study arms and all of them were considered not clinically significant. Antibodies against Biocon's insulin glargine were observed with the same frequency as compared to the reference product.

Preclinical Safety Data
Nonclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated-dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction. Animal studies do not indicate direct harmful effects with respect to fertility.

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

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

Insulin glargine should be administered once daily at any time but at the same time each day.

The insulin glargine dose regimen (dose and timing) should be individually adjusted. In patients with type 2 diabetes mellitus, it 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, insulin glargine should only be used in this age group under careful medical supervision.

No clinical study safety data are available in children below 2 years of age.

Initiation of Insulin Glargine Therapy
The recommended starting dose of insulin glargine 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 Insulin Glargine
When changing from a treatment regimen with an intermediate or long-acting insulin to a regimen with insulin glargine, a change of 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 insulin glargine should reduce their daily dose of basal insulin by 20% to 30% during the first week 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 may experience an improved insulin response with insulin glargine because of antibodies to human insulin. Close metabolic monitoring is recommended during transition and in the initial weeks thereafter. With improved metabolic control and resulting in increase of 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 **Special Warnings and Precautions for Use** section).

Method of Administration
Insulin glargine is administered subcutaneously and should not be given intravenously. The prolonged duration of action of insulin glargine is dependent on 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 insulin glargine. The prolonged duration of action of insulin glargine 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.

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

Handling of the prefilled pen
For detailed instructions, refer to the Instruction for Use (IFU), PI provided with the prefilled pen.

Preparation and handling
Insulin glargine should be inspected visually prior to administration. Insulin glargine must only be used if the solution is clear and colourless with no visible particles.

Mixing and diluting
Insulin glargine must not be diluted or mixed with any other insulin or solution.

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).

Insulin glargine 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 **Undesirable Effects** section).

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 insulin glargine, 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 glycaemic control is markedly improved
- in whom hypoglycaemia develops gradually
- who are elderly
- who are transferred from animal insulin to human insulin
- 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 Drug Interactions section).

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 (eg, by removal of stress factors), unaccustomed, increased or prolonged physical activity, intercurrent illness (eg, vomiting, diarrhoea), inadequate food intake, missed meals, alcohol consumption, certain uncompensated endocrine disorders, (eg, in hypothyroidism and in anterior pituitary or adrenocortical insufficiency), concomitant treatment with certain other medicinal products.

Hypersensitivity and allergic reactions
Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulin products.

BASALOG One® contains metacresol, which may cause allergic reactions.

Renal impairment
Due to its long duration of action, insulin glargine is not recommended during periods of rapidly declining renal function because of the risk for prolonged hypoglycaemia. Although studies have not been performed in patients with diabetes and renal impairment, a reduction in the insulin glargine dose may be required in patients with renal impairment because of reduced insulin metabolism, similar to observations found with other insulins.

Hepatic impairment
Due to its long duration of action, insulin glargine is not recommended during periods of rapidly declining hepatic function because of the risk for prolonged hypoglycaemia. Although studies have not been performed in patients with diabetes and hepatic impairment, a reduction in the insulin glargine dose may be required in patients with hepatic impairment because of reduced capacity for gluconeogenesis and reduced insulin metabolism, similar to observations found with other insulins.

Intercurrent illness
Intercurrent illnesses requires intensive 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 in conditions where they are vomiting and they must never omit insulin entirely.

Fluid retention and heart failure with concomitant use of peroxisome proliferator-activated receptor (PPAR)-gamma agonists
Thiazolidinediones (TZDs), which are peroxisome proliferator-activated receptor (PPAR)-gamma agonists, 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 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.

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 sulphonamide 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 (eg, epinephrine [adrenaline], salbutamol, terbutaline), thyroid hormones, atypical antipsychotic medicinal products (eg, 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.

Pregnancy and Lactation
Pregnancy
No clinical data on insulin glargine exposed during 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 on pregnancy, no malformations, nor foeto- or neonatal toxicity.

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 insulin glargine 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.

Lactation
It is unknown whether insulin glargine is excreted in human milk. No metabolic effects of ingested insulin glargine on the breastfed newborn or 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.

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 hyperglycaemia or, as a result of visual impairment. This may constitute a risk in situations where these abilities are of special importance
(eg, 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 commonly (>1/10)*
  Metabolism and nutrition disorders: hypoglycaemia.
- *Side effects reported commonly (>1/100 to <1/10)*
  Skin and subcutaneous tissue disorders: lipohypertrophy.
  General disorders and administration site conditions: injection site reactions.
- *Side effects reported uncommonly (≥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 neuroglycopaenia 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, intensive 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 safetyprofile 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, and water for injection.

Incompatibilities
Insulin glargine 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.

Dosage: As directed by Physician

Storage and Precautions
Always store the pen with the cap on, to avoid any contamination.

Before use: **Store the prefilled pen in the refrigerator at 2°C to 8°C (36°F - 46°F). Do not freeze.**

During use: Once you take the pen out of the refrigerator, allow it to reach room temperature (to around 30°C) naturally. Cold insulin is painful to inject.

℞
Insulin Glargine Injection (rDNA)
Basalog one®
बेसल्लौग वन
100 IU/mL, 3 mL Prefilled Pen
Biocon

BF1177/04

After first use, store the pen at room temperature up to 30°C (86°F). Use the pen within 28 days from the date of first use. (Do not refrigerate)

Protect from excessive heat and sunlight.

Keep out of reach of children

Special Precautions for Disposal and Other Handling
Insulin glargine 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 **BASALOG One®** before use. It must only be used if the solution is clear, colourless, with no visible solid particles. Since insulin glargine 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 3 mL prefilled pen.

Presentation: 1 Prefilled pen of 3mL Cartridge

Pack Sizes: 1×3 mL

Currently available in 3 mL pack only.

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

® - Registered trademark

Leaflet revised **June 2019**

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.

BACK

For the use only of a Registered Medical Practitioner or Hospital or Laboratory

℞

Insulin Glargine Injection (rDNA)

Basalog one®

बेसल्लोग वन

100 IU/mL, 3 mL Prefilled Pen

Biocon

INSTRUCTIONS FOR USE:

Insulin Glargine Injection (rDNA) 3 mL Prefilled Pen (100 IU/mL)

BASALOG One® is a prefilled, disposable pen injector containing 300 units of insulin glargine (rDNA Origin). Please read all the instructions carefully before using **BASALOG One®** (hereafter "pen"). If you are unable to read or follow all of the instructions completely on your own, seek the help of someone who has been trained to use the pen.

Please follow these instructions every time you use the pen. If you do not follow these instructions each time you use the pen, you may either get too much or too little insulin. This may affect your blood glucose level.

Before You Use the Pen for the First Time:

Check that the carton is sealed with an intact hologram. After opening the carton check that the pen looks new and undamaged. Otherwise, call the customer service helpline number provided on the carton.

Storage:

- ☑ Before first use, **store the cartons containing the pen in the refrigerator at 2°C - 8°C (36°F - 46°F).** DO NOT freeze.
- ☑ Once you take a pen out of the refrigerator, allow it to reach room temperature (around 30°C) naturally before first use. Cold insulin is painful to inject.
- ☑ Always store the pen with the cap on, to avoid any contamination.
- ☑ After first use, store the pen at room temperature up to 30°C (86°F).
- ☑ Use the pen within **28 days** from first use. **Dispose of the pen after 28 days.**

⚠ **DO NOT** refrigerate the pen after first use. Store at room temperature between uses.

⚠ **NEVER** leave the needle attached to the pen during storage. This could lead to contamination or needle blockage.

Each Time You Use the Pen:

1. **Wash your hands** with soap and water before you handle the pen.
2. **Check the pen's label** to ensure that you are taking the correct type of insulin. The pen has a purple label and a purple injection button.
3. **Check the expiration date** given on the pen's label.
4. **Check the appearance** of the drug in the cartridge. This is important especially if you take more than one type of insulin.
5. **DO NOT** use the pen if the drug in the cartridge appears cloudy, colored or has visible particles.
6. **ALWAYS use a new Sterile disposable Hypodermic needle** for each injection.
7. **Select the injection location** as recommended by your Health Care Professional (HCP).
8. **ALWAYS** put the pen cap back on the pen after use, and store the pen at room temperature in a cool, dry place.

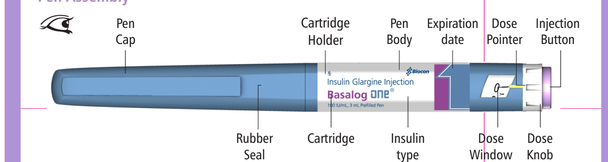
Required Supplies

Make sure you have the following items:

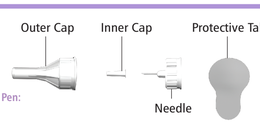
☑ Pen ☑ Sterile disposable hypodermic needle* ☑ 2 Alcohol Wipes*

NO PRINT PANEL

Pen Assembly



Needle



Needles Compatible with this Pen:

- BD UltraFine 31G, 5mm
- BD UltraFine 32G, 4mm
- Novofine 32G, 6mm
- Terumo Nanopass 33G, 5mm

Alcohol wipes: x2

* Not provided with the pen.

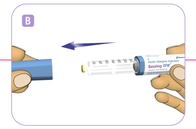
Step-By-Step Instructions

Preparing the Pen:

A 1. Inspect the pen:
Check the purple-colored label present on the pen for:
a. Correct insulin type
b. Expiration date

Check the Insulin through the cartridge holder for:
a. Clear and colourless appearance of the solution
b. Absence of cracks, breakage, or solution leakage

B 1. Hold the pen body with one hand.
2. With the other hand, pull off the pen cap.
3. Keep the pen cap aside for later use (in **Step Q**).

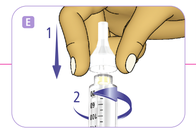


C 1.Remove an alcohol wipe from its package.
2.Wipe the rubber seal at the front end of the cartridge with the alcohol wipe.
☑ **Note:** Use of an alcohol wipe reduces chances of infection.

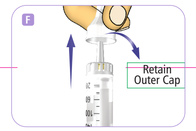
Attaching a New Needle:

D 1.Take a new sterile disposable hypodermic needle.
2.Hold the outer needle cap with one hand.
3.With the other hand, pull off the protective tab from the outer needle cap.
⚠ **Caution:** DO NOT use the needle if the protective tab is damaged or missing. The needle may not be sterile.

E 1.Hold the pen body facing upwards with one hand.
2.With the other hand, attach the outer needle cap straight on to the cartridge holder as shown (1).
⚠ **Caution:** DO NOT try to attach the outer needle cap in a tilted manner. This can bend or damage the needle.
3. Screw the outer needle cap in the clockwise direction, till it feels securely fixed on the pen (2).



F 1. With a gentle pull, remove the outer needle cap.
2. **Keep** the **outer** needle cap. It is required to safely remove the needle later (in **Step P**).

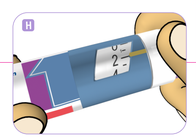


G 1. Carefully pull off and **throw away** the **inner** needle cap.
⚠ **Caution:** DO NOT re-use the inner needle cap to cover the needle. You may accidentally injure yourself. Only use the outer needle cap to cover the needle (in **Step P**).

Priming the Pen Needle with 2 Units:

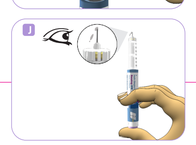
H 1. Turn the white-colored dose knob to set **2 units**.
- "2" must be visible in the dose window, and align with the pointer on the pen body.
- You will hear a "CLICK" for each unit dialled.

☑**Note: If** you turn past 2 units, then simply turn back the dose knob in the opposite direction to correct the dose.
⚠**Important: Always prime the pen needle before each injection.**



I 1.Hold the pen body facing upwards with one hand.
2.**Tap the cartridge** holder gently with your finger.
This helps any large air bubbles present to rise to the top of the cartridge.
☑**Note:** Small bubbles may still be visible, and will not pose any problem.

J 1. Hold the pen body facing **upwards** with one hand.
2. With your thumb, **press** the injection button in untill it stops moving and the dose window shows "0".
3. Keep the injection button **pressed down.**
4. Priming is complete when you observe drops of insulin at the tip of the needle.



☑ Note: If you do not see drops at the needle tip, repeat Steps H to J for a maximum of 4 times.
- After 4 attempts, if insulin drops are still not visible at the needle-tip, it is likely that the needle is clogged.
- Proceed directly to Step P to remove the needle. Then, return to Step D to attach the new needle and repeat priming (Step H).
- If the problem still persists, report the faulty pen by calling the customer service helpline number and use a new pen.

☑ **Always prime the pen needle before each injection** to check insulin flow and avoid incomplete dose.

Setting the Dose:

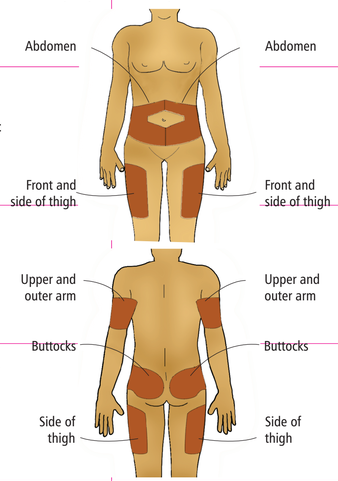
K 1. Check that the dose window shows "**0**".
2. Look at the cartridge holder scale to **estimate** the insulin units left in the cartridge. If enough medication is not available in the cartridge, use a new pen to inject your required dose.
3. Turn the dose knob to set **the** required dose. The number in the dose window must align with the pointer on the pen body.

☑**Note:**
- Ensure that you hear "CLICK" as you set the desired dose.
- The pen does not allow you to dial a dose beyond the units available within the cartridge.
- Do not force the dose knob to turn beyond 80 units. 80 units **is the** maximum **dose that yo**u can inject in a single injection.

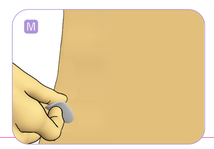
⚠**Caution:** DO NOT push the injection button when turning the dose knob (during dose setting)

Select and Clean Injection Site:

L 1.Select the injection location as recommended by your Health Care Professional.
☑**Note:** Preferred injection locations on your body are both your arms, hips, thighs, and lower abdomen. It is advised to rotate your injection site for each injection.

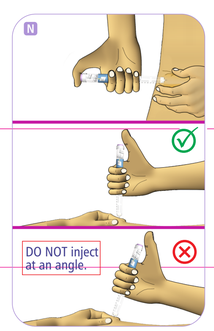


M 2. Clean the skin with an alcohol wipe, at the spot where you want to inject.



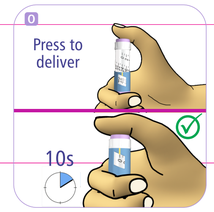
Injecting the Dose:

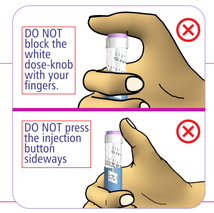
N 3. **Pinch the skin** between your fingers and insert the needle in a single continuous motion, as instructed by your Health Care Professional.
⚠ **Caution:** DO NOT inject with the needle at an angle.



O 1. Place your **thumb or finger** on the injection button.
2. **Press** the injection button all the way in. The white dose-knob will turn and you will hear "Clicks" as you press down.
3. **WAIT!** Hold the injection button pressed in for an additional **10 seconds** after the dose window shows "**0**". This pause ensures that all of the medication is delivered.

⚠ **Caution:**
- **DO NOT** press the injection button sideways or block the white dose-knob with your fingers. This will prevent you from injecting the medication.
- If you don't keep the injection button pressed for 10 seconds after "0" is displayed in the dose window, it could result in an inaccurate dose and you may see drops of insulin at the injection site or at the needle tip.

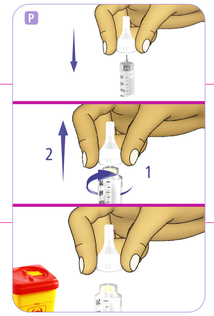




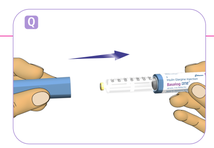
Needle Removal and Disposal:

P 1. Take the outer needle cap that you had saved in Step F.
2. Hold the outer needle cap from its base and carefully cover the needle without touching it.
3. Squeeze the base of the outer needle cap while unscrewing the needle in a counter clockwise (left) direction (1). Keep twisting until the needle can be separated from the pen (2).
4. Discard this needle safely, as instructed by your Health Care Professional or as per local regulations in your country.

☑ Note: It may take several twists to release the needle.



Q 1. Replace the pen cap and store the pen at room temperature (under 86°F or 30°C) for next use. NEVER store with a used needle attached.



Required Storage:

- ☑ Always store the pen with the cap on, to avoid any contamination.
- ☑ After first use, store the pen at room temperature up to 86°F (30°C).
- ☑ Use the pen within **28 days** from first use. **Dispose of the pen after 28 days.**

⚠ **DO NOT** refrigerate the pen after first use. Store at room temperature between uses.

⚠ **NEVER** leave the needle attached to the pen during storage. This could lead to contamination or needle blockage.

Care and Disposal:

- ☑ Always carry a spare insulin prefilled pen injector as recommended by your Health Care Professional, as a precautionary measure, in case your pen is lost or damaged.
- ☑ Always use a new sterile disposable hypodermic needle for each injection.
- ☑ Keep the pen away from moisture, dust, direct sunlight and places where the temperature may get too high or too low.
- ☑ If you feel that the pen is damaged, call on the Customer Service Helpline No. provided on the carton.
- ☑ Discard an empty pen without the needle attached, as instructed by your Health Care Professional.
- ☑ You can clean the outside of your pen by wiping it with a damp cloth.

⚠ DO NOT soak or wash your pen as this may damage it. Do not use alcohol, hydrogen peroxide, bleach or any other solvent to clean the pen. Also, do not apply lubricants such as oil, as this could damage the pen.

⚠ DO NOT share your pen with others. This pen is intended and recommended for use by one person only.

⚠ Keep your pen and needles out of sight and reach of children.

⚠ DO NOT attempt to repair the pen by yourself. Remove the needle as described in Step P, make a note of the problem, and return the pen to the manufacturer. Use a new pen instead.

⚠ Your pen is designed to work accurately and safely. It must be handled with care. Avoid dropping the pen, as this can cause cartridge breakage or can damage the pen.