PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

BASAGLAR® (solution for injection)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of the solution for injection contains 100 units insulin glargine equivalent to 3,64 mg.

Each cartridge or pen contains 3 ml of solution for injection, equivalent to 300 units.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

Clear and colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of diabetes mellitus in adults, adolescents and children 6 years and older where treatment with insulin is required, as a basal or part of a basal-bolus regimen.

4.2 Posology and method of administration

Posology

BASAGLAR contains insulin glargine, an insulin analogue and has a prolonged duration of action.

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

The BASAGLAR regimen (dose and timing) should be individually adjusted. In patients with type 2 diabetes mellitus, BASAGLAR can also be given together with orally active anti-diabetic medicinal products.

The potency of BASAGLAR is stated in units. These units are exclusive to insulin glargine and are not the same as IU or the units used to express the potency of other insulin analogues (see section 5.1).

Before starting therapy with BASAGLAR Kwikpen (pre-filled pen), patients should read the "User Manual" that accompanies the delivery device, to ensure the correct use thereof.
The BASAGLAR cartridges are to be used only in conjunction with a reusable pen device recommended for the use with Lilly insulin cartridges. The "User Manual" for using the pen must be followed carefully for loading the cartridge, attaching the needle, and administering the insulin injection.

Special population

Elderly populations (≥ 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 reduced insulin metabolism.

Paediatric population

BASAGLAR can be used in children aged 6 years and above.

No clinical study safety data are available in children below 6 years of age.

Switch from other insulins to BASAGLAR

When switching from a treatment regimen with an intermediate or long-acting insulin to a regimen with BASAGLAR, 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).

Switch from twice daily NPH insulin to BASAGLAR

To reduce the risk of nocturnal and early morning hypoglycaemia, patients who are changing their basal insulin regimen from a twice daily NPH insulin to a once daily regimen with BASAGLAR should reduce their daily dose of basal insulin by 20 to 30 % during the first weeks of treatment.

Switch from insulin glargine 300 units/ml to BASAGLAR

BASAGLAR and other products containing insulin glargine 300 units/ml are not bioequivalent and are not directly interchangeable. To reduce the risk of hypoglycaemia, patients who are changing their basal insulin regimen from an insulin regimen with once daily insulin glargine 300 units/ml to a once daily regimen with BASAGLAR should reduce their dose by approximately 20 %.

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.

Close metabolic monitoring is recommended during the switch 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 hypoglycaemia or hyperglycaemia (see section 4.4).

Patients with high insulin doses because of antibodies to human insulin may experience an improved insulin response with BASAGLAR.

Method of administration

BASAGLAR is administered subcutaneously.

BASAGLAR should not be administered intravenously. The prolonged duration of action of insulin glargine 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 BASAGLAR.

Injection sites [~~must~~] should always be rotated within the same region in order to reduce the risk of lipodystrophy and cutaneous amyloidosis (see section 4.4 and 4.8).

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

For further details on handling, see section 6.6.

4.3 Contraindications

BASAGLAR is contraindicated in patients with hypersensitivity to insulin glargine or any of its excipients listed in section 6.6 .

BASAGLAR should not be used in pregnancy and mothers on BASAGLAR should not breastfeed their infants (see section 4.6).

4.4 Special warnings and precautions for use

Diabetic ketoacidosis

BASAGLAR is not the insulin of choice for the treatment of diabetic ketoacidosis. Instead, short-term insulin administered intravenously is recommended in such cases.

Insulin requirements and dose adjustments

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 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.

Hypoglycaemia

Hypoglycaemia is the most frequent adverse reaction of BASAGLAR. The risk of hypoglycaemia increases with intensive glycaemic control.

The timing 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 more 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 must be educated to recognize and manage 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,
- after transfer 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 section 4.5).

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 BASAGLAR 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.

Other factors such as changes in food intake (e.g. amount of food or timing of meals), alcohol intake, exercise, and concomitant medications may also alter the risk of hypoglycaemia.

Injection technique

Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. There is a potential risk of delayed insulin absorption and worsened glycaemic control following insulin injections at sites with these reactions. A sudden change in the injection site to an unaffected area has been reported to result in hypoglycaemia. Blood glucose monitoring is recommended after the change in the injection site, and dose adjustment of antidiabetic medications may be considered.

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.

Insulin antibodies

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 5.1).

Medication errors

Medication errors have been reported in which other insulins, particularly short-acting insulins, have been accidentally administered instead of insulin glargine. The insulin label must always be checked before each injection to avoid medication errors between BASAGLAR and other insulins.

Thiazolidinediones (TZDs) used in combination with Insulin

TZDs e.g. pioglitazone in combination with insulin are associated with an increased risk of oedema and heart failure; especially in patients with underlying cardiac disease.

Sodium content

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e., essentially 226 “sodium-free”.

4.5 Interaction with other medicines and other forms of interaction

A number of medicines affect glucose metabolism and may require insulin dose adjustment.

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

Medicines that may decrease the blood-glucose-lowering effect of BASAGLAR include corticosteroids, niacin, danazol, diazoxide, diuretics, glucagon, isoniazid, oestrogens, progestogens, phenothiazine derivatives, somatropin, sympathomimetic agents (e.g.

epinephrine (adrenaline), salbutamol, terbutaline), thyroid hormones, atypical antipsychotic medications (e.g. olanzapine and clozapine), and protease inhibitors.

Beta-blockers, clonidine, lithium salts, and 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 medicines such as beta-blockers, clonidine, guanethidine and reserpine, the signs of adrenergic counter-regulation may be reduced or absent.

4.6 Fertility, pregnancy and lactation

BASAGLAR should not be used in pregnancy and mothers on BASAGLAR should not breastfeed their infants.

4.7 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, for example, as a result if visual impairment. This may constitute a risk in situations where these abilities are of special importance, (e.g. driving a car or using machinery).

Patients should be advised to take precautions to avoid hypoglycaemia whilst driving. This is particularly important in those who have reduced or absent awareness of the warning symptoms of hypoglycaemia or have frequent episodes of hypoglycaemia. It should be considered whether it is advisable to drive or operate machines in these circumstances.

4.8 Undesirable effects

a. Summary of safety profile

Hypoglycaemia (very common), 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 (see section 4.4).

b. Tabulated list of adverse reactions

The following related adverse reactions investigations are listed in Table 1 as MedDRA preferred term by system organ class and in order of decreasing incidence (very common: ≥ 1/10; common: ≥ 1/100 to < 1/10; uncommon: ≥ 1/1 000 to < 1/100; rare: ≥ 1/10 000 to < 1/1 000; very rare: < 1/10 000) and not known (cannot be estimated from available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1: The frequency of adverse reactions of BASAGLAR

	Very common	**Common**	**Uncommon**	**Rare**	**Very rare**	**Not known**
Immune system disorders						
Allergic reactions				X		
Metabolism and nutrition disorders						
Hypoglycaemia	X					
Nervous system disorders						
Dysgeusia					X	
Eyes disorders						
Visual impairment				X		
Retinopathy				X		
Skin and subcutaneous tissue disorders						

Lipohypertrophy		X				
Lipoatrophy			X			
Cutaneous amyloidosis						X
Musculoskeletal and connective tissue disorders						
Myalgia					X	
General disorders and administration site conditions						
Injection site reactions		X				
Oedema				X		

c. Description of selected adverse reactions

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.

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

Lipodystrophy and cutaneous amyloidosis may occur at the injection site and delay insulin absorption. Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions (see section 4.4).

General disorders and administration site conditions

Injection site reactions include redness, pain, itching, urticaria, oedema, and inflammation. Most minor reactions to insulins at the injection site usually resolve in a few days to a few weeks.

BASAGLAR, may cause sodium retention and oedema, particularly if previously poor metabolic control is improved by intensified insulin therapy.

Antibody production

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

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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Alternately, report suspected adverse events to the company at: ade_za@lilly.com.

4.9 Overdose

Symptoms

BASAGLAR 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 21.1 Insulin preparation

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 designated 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 formulation of micro-precipitates from which small amounts of insulin glargine are continuously released, providing a relatively constant concentration/time profile over 24 hours with no pronounced peaks.

Pharmacodynamic effects

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.

The time course of action of insulin glargine may be affected by physical activity and other variables.

The prolonged duration of action of subcutaneous insulin glargine is directly related to its slower rate of absorption and supports once daily administration. The time course of action of insulin and insulin analogues such as insulin glargine may vary considerably in different individuals or within the same individual.

Symptoms of hypoglycaemia or counter-regulatory hormone responses were similar after intravenous glargine and human insulin.

5.2 Pharmacokinetic properties

Absorption

After subcutaneous injection of insulin glargine in healthy subjects and patients with diabetes, the insulin serum concentrations indicated a slow, prolonged absorption and a relatively constant concentration profile over 24 hours with no pronounced peak.

Biotransformation and Elimination

After subcutaneous injection of insulin glargine in diabetic patients, insulin glargine is metabolised at the carboxyl terminus of the Beta chain with formation of two active metabolites M1 (21A-Gly-insulin) and M2 (21A-Gly-des-30B-Thr-insulin).
The *in vitro* activity of M1 and M2 were similar to that of insulin. Unchanged medicine and these degradation products are also present in the circulation.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Zinc oxide

Metacresol

Glycerol

Hydrochloric acid (for pH adjustment)

Sodium hydroxide (for pH adjustment)

Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years

Shelf life after first use

The medicinal product may be stored for a maximum of 28 days up to 30°C and away from direct heat or direct light.

Pens in use must not be stored in the refrigerator.

The pen cap must be put back on the pen after each injection in order to protect from light.

6.4 Special precautions for storage

Before use

Store in a refrigerator between 2 °C – 8 °C.

Do not freeze.

Do not store BASAGLAR next to the freezer compartment or a freezer pack.

Keep in original container until required for use in order to protect from light.

In Use

Once in-use store at or below 30 °C for a period up to 28 days. The unused portion must be discarded. Protect from light.

Keep out of reach of children.

6.5 Nature and contents of container

Cartridge: 3 ml solution in a cartridge (type 1 colourless glass) with a plunger (grey chlorobutyl rubber) and a disc seal (laminate of red polyisoprene and cream bromobutyl or grey chlorobutyl rubber) with aluminium seal. Cartridges are packed into blisters. Blisters are packed into an outer cardboard carton. Cartridges are to be used only in conjunction with a reusable pen device recommended for the use with Lilly insulin cartridges. Packs of 1, 2, 5 and multipacks containing 10 cartridges (2 packs of 5 cartridges) are available. Not all pack sizes may be marketed.

Pre-filled pen: 3 ml solution in a cartridge (type 1 colourless glass) with a plunger (grey chlorobutyl rubber) and a disc seal (laminate of red polyisoprene and cream bromobutyl or grey chlorobutyl rubber) with aluminium seal. The cartridge is sealed in a disposable pen injector. Pre-filled pens are packed in an outer cardboard carton. Packs of 1, 2, 5

and multipacks containing 10 pens (2 packs of 5 pens) are available. Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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

Insulin pen

The BASAGLAR cartridges are to be used only in conjunction with a Lilly reusable insulin pen (see section 4.4).

The pen should be used as recommended in the information provided with the device.

The instructions for using the pen must be followed carefully for loading the cartridge, attaching the needle, and administering the insulin injection.

Empty pens must never be reused and must be properly discarded.

To prevent the possible transmission of disease, each pen must be used by one patient only.

If the insulin pen is damaged or not working properly (due to mechanical defects) it has to be discarded, and a new insulin pen has to be used.

Cartridge

Inspect the cartridge before use. It must only be used if the solution is clear, colourless, with no solid particles visible, and if it is of water-like consistency. Since BASAGLAR is a solution, it does not require re-suspension before use. Air bubbles must be removed from the cartridge before injection (see instructions for using the pen).

To prevent the possible transmission of disease, each pen must be used by one patient only.

Empty cartridges must not be refilled and must be properly discarded. Insulin label must always be checked before each injection to avoid medication errors between insulin glargine and other insulins (see section 4.4).

7. HOLDER OF CERTIFICATE OF REGISTRATION:

Eli Lilly (S.A.) (Pty) Limited

First Floor, Golden Oak House, Ballyoaks Office Park,

35 Ballyclare Drive

Bryanston, 2021

Johannesburg

South Africa

8. REGISTRATION NUMBER(S)

49/21.1/0708

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

18 February 2016

10. DATE OF REVISION OF THE TEXT

15 January 2025

Registration Details for Botswana		
Basaglar cartridge	BOT1703125	Schedule 2
Basaglar KwikPen	BOT1703126	Schedule 2
Please report any suspected ADRs to BoMRA through e-reporting https://primaryreporting.who-umc.org/BW and e-mail reportadr@bomra.co.bw.		
Registration Details for Namibia		
Basaglar Solution for injection 100IU/ml	Reg. No.: 17/21.1/0014	Schedule: NS2