HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use SEMGLEE safely and effectively. See full prescribing information for SEMGLEE.

SEMGLEE™ (insulin glargine injection), for subcutaneous use
Initial U.S. Approval: 2000

----------INDICATIONS AND USAGE----------
SEMGLEE is a long-acting human insulin analog indicated to improve glycemic control in adults and pediatric patients with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus. (1)

Limitations of Use
Not recommended for treating diabetic ketoacidosis. (1)

----------DOSAGE AND ADMINISTRATION----------
- Individualize dosage based on metabolic needs, blood glucose monitoring, glycemic control, type of diabetes, prior insulin use. (2.1, 2.3, 2.4)
- Administer subcutaneously into the abdominal area, thigh, buttocks or upper arms once daily at any time of day, but at the same time every day. (2.1)
- Do not dilute or mix with any other insulin or solution. (2.1)
- Rotate injection sites to reduce the risk of lipodystrophy and localized cutaneous amyloidosis. (2.2)
- Closely monitor glucose when changing to SEMGLEE and during initial weeks thereafter. (2.4)

----------DOSAGE FORMS AND STRENGTHS----------
Injection: 100 units/mL (U-100) available as:
- 10 mL multiple-dose vial (3)
- 3 mL single-patient-use prefilled pen (3)

----------CONTRAINDICATIONS----------
- During episodes of hypoglycemia (4)
- Hypersensitivity to SEMGLEE or one of its excipients (4)

----------WARNINGS AND PRECAUTIONS----------
- *Never share* a SEMGLEE prefilled pen between patients, even if the needle is changed. (5.1)
- *Hyperglycemia or hypoglycemia with changes in insulin regimen:* Make changes to a patient's insulin regimen (e.g., insulin strength, manufacturer, type, injection site or method of administration) under close medical supervision with increased frequency of blood glucose monitoring. (5.2)
- *Hypoglycemia:* May be life-threatening. Increase frequency of glucose monitoring with changes to: insulin dosage, coadministered glucose lowering medications, meal pattern, physical activity; and in patients with renal or hepatic impairment and hypoglycemia unawareness. (5.3, 6.1)
- *Medication Errors:* Accidental mix-ups between insulin products can occur. Instruct patients to check insulin labels before injection. (5.4, 6.3)
- *Hypersensitivity reactions*: Severe, life-threatening, generalized allergy, including anaphylaxis, can occur. Discontinue SEMGLEE. Monitor and treat if indicated. (5.5, 6.1)
- *Hypokalemia:* May be life-threatening. Monitor potassium levels in patients at risk of hypokalemia and treat if indicated. (5.6)
- *Fluid retention and heart failure with concomitant use of thiazolidinediones (TZDs)*: Observe for signs and symptoms of heart failure; consider dosage reduction or discontinuation of TZD if heart failure occurs. (5.7)

----------ADVERSE REACTIONS----------
Adverse reactions commonly associated with insulin glargine products include hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, rash, edema and weight gain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Mylan at 1-877-446-3679 (1-877-4-INFO-RX) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- *Drugs that may increase the risk of hypoglycemia:* antidiabetic agents, ACE inhibitors, angiotensin II receptor blocking agents, disopyramide, fibrates, fluoxetine, monoamine oxidase inhibitors, pentoxifylline, pramlintide, salicylates, somatostatin analog (e.g., octreotide), and sulfonamide antibiotics. (7)
- *Drugs that may decrease the blood glucose lowering effect:* atypical antipsychotics, corticosteroids, danazol, diuretics, estrogens, glucagon, isoniazid, niacin, oral contraceptives, phenothiazines, progestogens (e.g., in oral contraceptives), protease inhibitors, somatropin, sympathomimetic agents (e.g., albuterol, epinephrine, terbutaline), and thyroid hormones. (7)
- *Drugs that may increase or decrease the blood glucose lowering effect:* Alcohol, beta-blockers, clonidine, lithium salts, and pentamidine. (7)
- *Drugs that may blunt the signs and symptoms of hypoglycemia:* beta-blockers, clonidine, guanethidine, and reserpine. (7)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 6/2020

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

SEMGLEE is indicated to improve glycemic control in adults and pediatric patients with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus.

Limitations of Use

SEMGLEE is not recommended for the treatment of diabetic ketoacidosis.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

- Always check insulin labels before administration *[see Warnings and Precautions (5.4)]*.
- Visually inspect SEMGLEE vials and prefilled pens for particulate matter and discoloration prior to administration. Only use if the solution is clear and colorless with no visible particles.
- Prior to initiation of SEMGLEE, train patients on proper use and injection technique.
- Administer SEMGLEE subcutaneously once daily at any time of day but at the same time every day.
- Administer SEMGLEE subcutaneously into the abdominal area, thigh, buttocks or upper arms, and rotate injection sites within the same region from one injection to the next to reduce the risk of lipodystrophy and localized cutaneous amyloidosis. Do not inject into areas of lipodystrophy or localized cutaneous amyloidosis *[see Warnings and Precautions (5.2) and Adverse Reactions (6)]*.
- During changes to a patient's insulin regimen, increase the frequency of blood glucose monitoring *[see Warnings and Precautions (5.2)]*.
- The SEMGLEE prefilled pen dials in 1-unit increments.
- Use SEMGLEE prefilled pen with caution in patients with visual impairment who may rely on audible clicks to dial their dose.
- Do not administer intravenously or via an insulin pump.
- Do not dilute or mix SEMGLEE with any other insulin or solution.

2.2 General Dosing Instructions

- Individualize and adjust the dosage of SEMGLEE based on the individual's metabolic needs, blood glucose monitoring results and glycemic control goal.
- Dosage adjustments may be needed with changes in physical activity, changes in meal patterns (i.e., macronutrient content or timing of food intake), during acute illness, or changes in renal or hepatic function. Dosage adjustments should only be made under medical supervision with appropriate glucose monitoring *[see Warnings and Precautions (5.2)]*.

2.3 Initiation of SEMGLEE Therapy

Type 1 Diabetes

- In patients with type 1 diabetes, SEMGLEE must be used concomitantly with short-acting insulin. The recommended starting dose of SEMGLEE in patients with type 1 diabetes should be approximately one-third of the total daily insulin requirements. Short-acting, premeal insulin should be used to satisfy the remainder of the daily insulin requirements.

Type 2 Diabetes

- The recommended starting dose of SEMGLEE in patients with type 2 diabetes who are not currently treated with insulin is 0.2 units/kg or up to 10 units once daily. One may need to adjust the amount and timing of short-or rapid-acting insulins and dosages of other antidiabetic drugs.

2.4 Changing to SEMGLEE from Other Insulin Therapies

- If changing patients from once-daily insulin glargine injection 300 units/mL to once-daily SEMGLEE, the recommended initial SEMGLEE dose is 80% of the insulin glargine injection 300 units/mL dose that is being discontinued. This dose reduction will lower the likelihood of hypoglycemia *[see Warnings and Precautions (5.3)]*.
- If changing from a treatment regimen with an intermediate or long-acting insulin (other than an insulin glargine injection 100 units/mL) to a regimen with SEMGLEE, a change in the dose of the basal insulin may be required and the amount and timing of the shorter-acting insulins and doses of other antidiabetic drugs may need to be adjusted.
- In patients changing from once-daily NPH insulin to once daily dose of SEMGLEE, the recommended initial SEMGLEE dose is the same as the dose of NPH that is being discontinued.
- If changing patients from twice-daily NPH insulin to once-daily SEMGLEE, the recommended initial SEMGLEE dosage is 80% of the total NPH dose that is being discontinued. This dosage reduction will lower the likelihood of hypoglycemia *[see Warnings and Precautions (5.3)]*.

3 DOSAGE FORMS AND STRENGTHS

Injection: 100 units per mL (U-100) a clear, colorless, solution available as:

- 10 mL multiple-dose vial
- 3 mL single-patient-use prefilled pen

4 CONTRAINDICATIONS

SEMGLEE is contraindicated:

- during episodes of hypoglycemia *[see Warnings and Precautions (5.3)]*.
- in patients with hypersensitivity to insulin glargine or one of its excipients *[see Warnings and Precautions (5.5)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Never Share a SEMGLEE Prefilled Pen, Syringe or Needle Between Patients

SEMGLEE prefilled pens must never be shared between patients, even if the needle is changed. Patients using SEMGLEE vials must never re-use or share needles or syringes with another person. Sharing poses a risk for transmission of blood-borne pathogens.

5.2 Hyperglycemia or Hypoglycemia with Changes in Insulin Regimen

Changes in an insulin regimen (e.g., insulin strength, manufacturer, type, injection site or method of administration) may affect glycemic control and predispose to hypoglycemia *[see Warnings and Precautions (5.3)]* or hyperglycemia. Repeated insulin injections into areas of lipodystrophy or localized cutaneous amyloidosis have been reported to result in hyperglycemia; and a sudden change in the injection site (to an unaffected area) has been reported to result in hypoglycemia *[see Adverse Reactions (6)]*.

Make any changes to a patient's insulin regimen under close medical supervision with increased frequency of blood glucose monitoring. Advise patients who have repeatedly injected into areas of lipodystrophy or localized cutaneous amyloidosis to change the injection site to unaffected areas and closely monitor for hypoglycemia. For patients with type 2 diabetes, dosage adjustments of concomitant antidiabetic products may be needed.

5.3 Hypoglycemia

Hypoglycemia is the most common adverse reaction associated with insulin, including SEMGLEE *[see Adverse Reactions (6.1)]*. Severe hypoglycemia can cause seizures, may be life-threatening or cause death. Hypoglycemia can impair concentration ability and reaction time; this may place an individual and others at risk in situations where these abilities are important (e.g., driving or operating other machinery).

Hypoglycemia can happen suddenly, and symptoms may differ in each individual and change over time in the same individual. Symptomatic awareness of hypoglycemia may be less pronounced in patients with longstanding diabetes, in patients with diabetic nerve disease, in patients using medications that block the sympathetic nervous system (e.g., beta-blockers) *[see Drug Interactions (7)]*, or in patients who experience recurrent hypoglycemia.

<u>Risk Factors for Hypoglycemia</u>

The risk of hypoglycemia generally increases with intensity of glycemic control. The risk of hypoglycemia after an injection is related to the duration of action of the insulin *[see Clinical Pharmacology (12.2)]* and, in general, is highest when the glucose lowering effect of the insulin is maximal. As with all insulin preparations, the glucose lowering effect time course of SEMGLEE may vary in different individuals or at different times in the same individual and depends on many conditions, including the area of injection as well as the injection site blood supply and temperature.

Other factors which may increase the risk of hypoglycemia include changes in meal pattern (e.g., macronutrient content or timing of meals), changes in level of physical activity, or changes to coadministered medication *[see Drug Interactions (7)]*. Patients with renal or hepatic impairment may be at higher risk of hypoglycemia *[see Use in Specific Populations (8.6, 8.7)]*.

<u>Risk Mitigation Strategies for Hypoglycemia</u>

Patients and caregivers must be educated to recognize and manage hypoglycemia. Self-monitoring of blood glucose plays an essential role in the prevention and management of hypoglycemia. In patients at higher risk for hypoglycemia and patients who have reduced symptomatic awareness of hypoglycemia, increased frequency of blood glucose monitoring is recommended.

5.4 Medication Errors

Accidental mix-ups between long-acting insulin products and other insulins, particularly rapid-acting insulins, have been reported. To avoid medication errors between SEMGLEE and other insulins, instruct patients to always check the insulin label before each injection *[see Adverse Reactions (6.3)]*.

5.5 Hypersensitivity and Allergic Reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulin products, including SEMGLEE. If hypersensitivity reactions occur, discontinue SEMGLEE; treat per standard of care and monitor until symptoms and signs resolve *[see Adverse Reactions (6.1)]*. SEMGLEE is contraindicated in patients who have had hypersensitivity reactions to insulin glargine or one of the excipients *[see Contraindications (4)]*.

5.6 Hypokalemia

All insulin products, including SEMGLEE, 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).

5.7 Fluid Retention and Heart Failure with Concomitant Use of 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 SEMGLEE, 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.

6 ADVERSE REACTIONS

The following adverse reactions are discussed elsewhere:

- Hypoglycemia *[see Warnings and Precautions (5.3)]*
- Medication Errors *[see Warnings and Precautions (5.4)]*
- Hypersensitivity and allergic reactions *[see Warnings and Precautions (5.5)]*
- Hypokalemia *[see Warnings and Precautions (5.6)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trial of another drug and may not reflect the rates observed in practice.

The data in Table 1 reflect the exposure of 280 patients with type 1 diabetes to SEMGLEE with mean exposure duration of 50 weeks. The type 1 diabetes study population had the following characteristics: the majority of patients were male, 60.2%, mean age was 42 years, the majority of patients were Caucasian, 94.6%, mean BMI was 26.5 kg/m^2, mean duration of diabetes prior to entry into the study was 19 years, mean HbA1c at baseline was 7.4%.

The data in Table 2 reflect the exposure of 276 patients with type 2 diabetes to SEMGLEE with mean exposure duration of 22 weeks. The type 2 diabetes study population had the following characteristics: the majority of patients were male, 55.7%, mean age was 55 years, more than half, 52.7%, of the patients were Caucasian, 26.6% were Hispanic, and 9.8% were Black, mean BMI was 31.5 kg/m^2, the mean duration of diabetes prior to entry into the study was 12 years, mean HbA1c at baseline was 8.1%.

Common adverse reactions (ARs) were defined as those occurring in ≥5% of SEMGLEE treated patients in clinical trials. Common ARs (other than hypoglycemia) from the type 1 diabetes mellitus and type 2 diabetes mellitus trials are listed in Table 1 and Table 2, respectively.

Table 1: Adverse Reactions Occurring in ≥ 5% of Adult Patients with Type 1 Diabetes Treated with SEMGLEE in a 52-Week Trial

	SEMGLEE + Insulin Lispro, % **(n= 280)**
Upper respiratory tract infection	10
Nasopharyngitis	9

Table 2: Adverse Reactions Occurring in ≥ 5% of Adult Patients with Type 2 Diabetes Treated with SEMGLEE in a 24-Week Trial

	SEMGLEE + Oral Diabetic Medication, % **(n= 276)**
Upper respiratory tract infection	6

The frequencies of adverse reactions during another insulin glargine product clinical trial of 5 years duration in patients with type 2 diabetes mellitus are listed in Table 3.

Table 3: Adverse Reactions Occurring in ≥ 10% of Adult Patients with Type 2 Diabetes in a 5 Year Trial

	Another Insulin Glargine Product, % **(n = 514)**
Upper respiratory tract infection	29
Edema peripheral	20
Hypertension	20
Influenza	19
Sinusitis	19
Cataract	18
Bronchitis	15
Arthralgia	14
Pain in extremity	13
Back pain	13
Cough	12
Urinary tract infection	11
Diarrhea	11
Depression	11
Headache	10

The frequencies of adverse reactions during another insulin glargine product clinical trial of 28 weeks duration in children and adolescents with type 1 diabetes mellitus are listed in Table 4.

Table 4: Adverse Reactions (with Frequency ≥ 5% and the Same or Higher with Another Insulin Glargine Product, 100 units/mL, than Comparator) in a 28-week Clinical Trial of Pediatric Patients with Type 1 Diabetes

	Another Insulin Glargine Product, % **(n = 174)**
Rhinitis	5

Severe Hypoglycemia

Hypoglycemia is the most commonly observed adverse reaction in patients using insulin, including SEMGLEE *[see Warnings and Precautions (5.3)]*. The rates of reported hypoglycemia depend on the

definition of hypoglycemia used, diabetes type, insulin dose, intensity of glucose control, background therapies, and other intrinsic and extrinsic patient factors. For these reasons, comparing rates of hypoglycemia in clinical trials for SEMGLEE with the incidence of hypoglycemia for other products may be misleading and also, may not be representative of hypoglycemia rates that will occur in clinical practice.

In SEMGLEE trials, an episode of hypoglycemia was classified as severe if it required the assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions and resulted in neurological recovery, regardless of the availability of a blood glucose measurement. The incidence of severe symptomatic hypoglycemia in patients receiving SEMGLEE with type 1 diabetes mellitus and type 2 diabetes mellitus *[see Clinical Studies (14)]* was 4% at 52 weeks and 0% at 24 weeks, respectively.

In a clinical trial with another insulin glargine product, severe symptomatic hypoglycemia was defined as an event with symptoms consistent with hypoglycemia requiring the assistance of another person and associated with either a blood glucose below 50 mg/dL (≤ 56 mg/dL in the 5-year trial and ≤ 36 mg/dL in the ORIGIN trial) or prompt recovery after oral carbohydrate, intravenous glucose or glucagon administration. The incidence of severe symptomatic hypoglycemia in children and adolescents age 6 to 15 years with type 1 diabetes *[see Clinical Studies (14)]* was 23% at 26 weeks. Table 5 displays the proportion of patients experiencing severe symptomatic hypoglycemia in another insulin glargine product and Standard Care groups in the ORIGIN Trial *[see Clinical Studies (14)]*.

Table 5: Severe Symptomatic Hypoglycemia in the ORIGIN Trial

	ORIGIN Trial (Median duration of follow-up: 6.2 years)	
	Another Insulin Glargine Product N = 6231	**Standard Care N = 6273**
Percent of patients	6	2

Allergic Reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, generalized skin reactions, angioedema, bronchospasm, hypotension, and shock may occur with any insulin, including SEMGLEE and may be life threatening.

Injection Site Reactions

Patients taking SEMGLEE may experience injection site reactions, including redness, pain, itching, urticaria, edema, and inflammation. In clinical studies in adult patients, there was a higher incidence of injection site pain in patients treated with another insulin glargine product (2.7%) compared to NPH insulin-treated patients (0.7%). The incidence of injection site reactions in patients receiving SEMGLEE was 0.7% at 24 weeks.

Insulin Initiation and Intensification of Glucose Control

Intensification or rapid improvement in glucose control has been associated with a transitory, reversible ophthalmologic refraction disorder, worsening of diabetic retinopathy, and acute painful peripheral neuropathy. However, long-term glycemic control decreases the risk of diabetic retinopathy and neuropathy.

Lipodystrophy
Long term use of insulin, including SEMGLEE, can cause lipodystrophy at the site of repeated insulin injections. Lipodystrophy includes lipohypertrophy (thickening of adipose tissue) and lipoatrophy (thinning of adipose tissue) and may affect insulin absorption *[see Dosage and Administration (2.1)]*.

Peripheral Edema
Insulin, including SEMGLEE, may cause sodium retention and edema. The incidence of peripheral edema in patients receiving SEMGLEE was 1.4% in the type 1 diabetes mellitus trial and 0.7% in the type 2 diabetes mellitus trial.

Weight Gain
Weight gain can occur with insulin therapy, including SEMGLEE, and has been attributed to the anabolic effects of insulin. The average weight gain in patients receiving SEMGLEE was 1 kg at 52 weeks in the type 1 diabetes mellitus trial and 0.7 kg at 24 weeks in the type 2 diabetes mellitus trial.

6.2 Immunogenicity
As with all therapeutic proteins, insulin administration may cause anti-insulin antibodies to form. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay and may be influenced by several factors such as: assay methodology, sample handling, timing of sample collection, concomitant medication, and underlying disease. For these reasons, comparison of the incidence of antibodies to SEMGLEE with the incidence of antibodies in other studies or to other products may be misleading. The presence of such insulin antibodies may increase or decrease the efficacy of insulin and may require adjustment of the insulin dose.

In a 52 weeks study of type 1 diabetes mellitus patients, changes from baseline in terms of anti-drug antibody (ADA) percentage binding and the incidence of ADA (positive or negative response) for total ADAs and insulin cross-reactive ADAs, were similar in patients who received SEMGLEE compared with another insulin glargine product.

In a 24 weeks study of type 2 diabetes mellitus patients, immunogenicity profiles were comparable between patients who received SEMGLEE or another insulin glargine product, with most patients showing negative responses for total ADAs and insulin cross-reactive ADAs. Immunogenicity profiles were also similar between insulin-naïve and insulin non-naïve patients in the study.

6.3 Postmarketing Experience
The following adverse reactions have been identified during postapproval use of another insulin glargine product. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Medication errors have been reported in which other insulin products, particularly rapid-acting insulins, have been accidentally administered instead of insulin glargine.

Localized cutaneous amyloidosis at the injection site has occurred. Hyperglycemia has been reported with repeated insulin injections into areas of localized cutaneous amyloidosis; hypoglycemia has been reported with a sudden change to an unaffected injection site.

7 DRUG INTERACTIONS
Table 8 includes clinically significant drug interactions with SEMGLEE.

Table 8: Clinically Significant Drug Interactions with SEMGLEE

Drugs that May Increase the Risk of Hypoglycemia	
Drugs:	Antidiabetic agents, ACE inhibitors, angiotensin II receptor blocking agents, disopyramide, fibrates, fluoxetine, monoamine oxidase inhibitors, pentoxifylline, pramlintide, salicylates, somatostatin analogs (e.g., octreotide), and sulfonamide antibiotics
Intervention:	Dose reductions and increased frequency of glucose monitoring may be required when SEMGLEE is coadministered with these drugs.
Drugs that May Decrease the Blood Glucose Lowering Effect of SEMGLEE	
Drugs:	Atypical antipsychotics (e.g., olanzapine and clozapine), corticosteroids, danazol, diuretics, estrogens, glucagon, isoniazid, niacin, oral contraceptives, phenothiazines, progestogens (e.g., in oral contraceptives), protease inhibitors, somatropin, sympathomimetic agents (e.g., albuterol, epinephrine, terbutaline), and thyroid hormones.
Intervention:	Dose increases and increased frequency of glucose monitoring may be required when SEMGLEE is coadministered with these drugs.
Drugs that May Increase or Decrease the Blood Glucose Lowering Effect of SEMGLEE	
Drugs:	Alcohol, beta-blockers, clonidine, and lithium salts. Pentamidine may cause hypoglycemia, which may sometimes be followed by hyperglycemia.
Intervention:	Dose adjustment and increased frequency of glucose monitoring may be required when SEMGLEE is coadministered with these drugs.
Drugs that May Blunt Signs and Symptoms of Hypoglycemia	
Drugs:	beta-blockers, clonidine, guanethidine, and reserpine
Intervention:	Increased frequency of glucose monitoring may be required when SEMGLEE is coadministered with these drugs.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Published studies with use of insulin glargine during pregnancy have not reported a clear association with insulin glargine and adverse developmental outcomes *(see Data).* There are risks to the mother and fetus associated with poorly controlled diabetes in pregnancy *(see Clinical Considerations).*

Rats and rabbits were exposed to insulin glargine in animal reproduction studies during organogenesis, respectively 50 times and 10 times the human subcutaneous dose of 0.2 units/kg/day. Overall, the effects of insulin glargine did not generally differ from those observed with regular human insulin *(see Data).*

The estimated background risk of major birth defects is 6% to 10% in women with pregestational diabetes with an HbA1c >7 and has been reported to be as high as 20% to 25% in women with a HbA1c >10. The estimated background risk of miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-associated maternal and/or embryo-fetal risk

Poorly controlled diabetes in pregnancy increases the maternal risk for diabetic ketoacidosis, preeclampsia, spontaneous abortions, preterm delivery, and delivery complications. Poorly controlled diabetes increases the fetal risk for major birth defects, stillbirth, and macrosomia-related morbidity.

Data

Human Data

Published data do not report a clear association with insulin glargine and major birth defects, miscarriage, or adverse maternal or fetal outcomes when insulin glargine is used during pregnancy. However, these studies cannot definitely establish the absence of any risk because of methodological limitations including small sample size and some lacking comparator groups.

Animal Data

Subcutaneous reproduction and teratology studies have been performed with insulin glargine and regular human insulin in rats and Himalayan rabbits. Insulin glargine was given to female rats before mating, during mating, and throughout pregnancy at doses up to 0.36 mg/kg/day, which is approximately 50 times the recommended human subcutaneous starting dose of 0.2 units/kg/day (0.007 mg/kg/day), on a mg/kg basis. In rabbits, doses of 0.072 mg/kg/day, which is approximately 10 times the recommended human subcutaneous starting dose of 0.2 units/kg/day on a mg/kg basis, were administered during organogenesis. The effects of insulin glargine did not generally differ from those observed with regular human insulin in rats or rabbits. However, in rabbits, five fetuses from two litters of the high-dose group exhibited dilation of the cerebral ventricles. Fertility and early embryonic development appeared normal.

8.2 Lactation

Risk Summary

There are either no or only limited data on the presence of insulin glargine in human milk, the effects on breastfed infant, or the effects on milk production. Endogenous insulin is present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for SEMGLEE, and any potential adverse effects on the breastfed child from SEMGLEE or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of SEMGLEE to improve glycemic control in pediatric patients with type 1 diabetes mellitus have been established in pediatric patients. The use of SEMGLEE for this indication is based upon an adequate and well-controlled trial of another insulin glargine product in pediatric patients age 6 to 15 years with type 1 diabetes and additional data in adults with type 1 diabetes *[see Clinical Studies (14.2)]*.

In the pediatric clinical trial, pediatric patients with type 1 diabetes had a higher incidence of severe symptomatic hypoglycemia compared to the adults in trials with type 1 diabetes *[see Adverse Reactions (6.1)]*.

The safety and effectiveness of SEMGLEE in pediatric patients younger than 6 years of age with type 1 diabetes and pediatric patients with type 2 diabetes have not been established.

8.5 Geriatric Use

In clinical studies of patients with type 1 and type 2 diabetes who were treated with another insulin glargine product, 15% of patients were ≥ 65 years of age and 2% were ≥ 75 years of age. The only difference in safety or effectiveness in the subpopulation of patients ≥ 65 years of age compared to the entire study population was a higher incidence of cardiovascular events typically seen in an older population in the insulin glargine and NPH treatment groups.

Nevertheless, caution should be exercised when SEMGLEE is administered to geriatric patients. In elderly patients with diabetes, the initial dosing, dose increments, and maintenance dosage should be conservative to avoid hypoglycemia. Hypoglycemia may be difficult to recognize in the elderly.

8.6 Renal Impairment

The effect of renal impairment on the pharmacokinetics of SEMGLEE has not been studied. Some studies with human insulin have shown increased circulating levels of insulin in patients with renal failure. Frequent glucose monitoring and dose adjustment may be necessary for SEMGLEE in patients with renal impairment *[see Warnings and Precautions (5.3)]*.

8.7 Hepatic Impairment

The effect of hepatic impairment on the pharmacokinetics of SEMGLEE has not been studied. Frequent glucose monitoring and dose adjustment may be necessary for SEMGLEE in patients with hepatic impairment *[see Warnings and Precautions (5.3)]*.

8.8 Obesity

In clinical trials, subgroup analyses based on BMI did not show differences in safety and efficacy between SEMGLEE and another insulin glargine product.

10 OVERDOSAGE

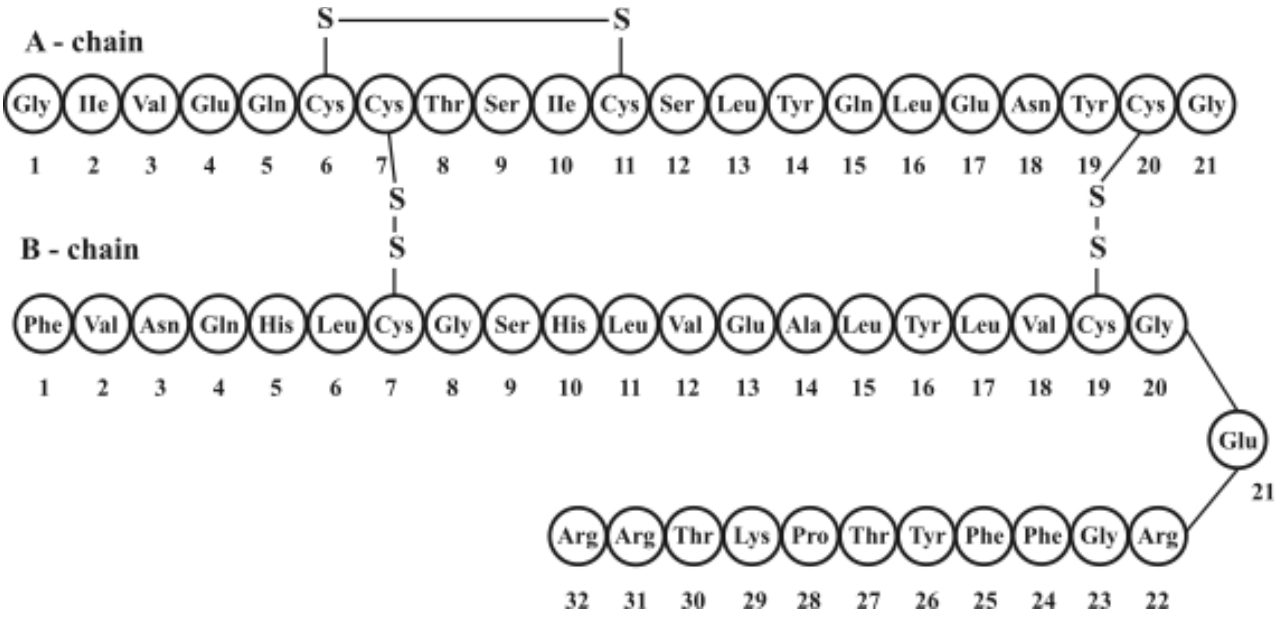
Excess insulin administration may cause hypoglycemia and hypokalemia *[see Warnings and Precautions (5.3, 5.6)]*. Mild episodes of hypoglycemia can usually be treated with oral glucose. Adjustments in drug dosage, meal patterns, or exercise may be needed.

More severe episodes of hypoglycemia with coma, seizure, or neurologic impairment may be treated with intramuscular/subcutaneous glucagon or concentrated intravenous glucose. Sustained carbohydrate intake and observation may be necessary because hypoglycemia may recur after apparent clinical recovery. Hypokalemia must be corrected appropriately.

11 DESCRIPTION

SEMGLEE contains insulin glargine as a sterile solution for subcutaneous use. Insulin glargine is a recombinant human long-acting insulin analog *[see Clinical Pharmacology (12)]*. SEMGLEE is produced by recombinant DNA technology utilizing a recombinant yeast strain, *Pichia pastoris*, as the production organism. Insulin glargine differs from human insulin in that the amino acid asparagine at

position A21 is replaced by glycine and two arginines are added to the C-terminus of the B-chain. Chemically, insulin glargine is 21^{A}-Gly-30^{B}a-L-Arg-30^{B}b-L-Arg-human insulin and has the empirical formula $C_{267}H_{404}N_{72}O_{78}S_{6}$ and a molecular weight of 6063. Insulin glargine has the following structural formula:



SEMGLEE consists of insulin glargine dissolved in a clear, colorless, sterile solution. Each milliliter contains 100 units (3.64 mg) insulin glargine.

The 10 mL SEMGLEE vial contains the following inactive ingredients per mL: 30 mcg zinc, 20 mg glycerol 85%, 20 mcg polysorbate-20, 2.7 mg *m*-Cresol and water for injection.

The 3 mL SEMGLEE prefilled pen contains the following inactive ingredients per mL: 30 mcg zinc, 20 mg glycerol 85%, 2.7 mg *m*-Cresol and water for injection.

The pH is adjusted by addition of aqueous solutions of hydrochloric acid and sodium hydroxide. SEMGLEE has a pH of approximately 4.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

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

12.2 Pharmacodynamics

The pharmacodynamic profile for SEMGLEE was determined after subcutaneous administration of a single 0.5 U/kg dose in a euglycemic clamp study conducted in 116 type 1 diabetes patients. The median time to maximum effect of SEMGLEE (measured by the peak rate of glucose infusion) was approximately 11.3 hours. The pharmacodynamic profile of SEMGLEE following subcutaneous injection demonstrated sustained glucose lowering activity over 24 hours with no pronounced peak. The

arithmetic mean area under the glucose infusion rate curve (AUC GIR 0-24h) and maximum glucose infusion rate were 1423 mg/kg and 1.8 mg/kg/min, respectively.

The time course of action of insulins, including SEMGLEE, may vary between individuals and within the same individual.

12.3 Pharmacokinetics

Absorption

After subcutaneous injection of a single 0.5 U/kg dose of SEMGLEE in a euglycemic clamp study conducted in 116 type 1 diabetes patients, the M1 active metabolite plasma concentration profile indicated a prolonged absorption and a relatively constant concentration/time profile over 24 hours.

The median time to maximum M1 plasma concentration was 12 hours after injection. The mean plasma observed area under the concentration-time curve for M1 from time zero to 24 hours and peak plasma concentration were 10.5 ng*hr/mL and 0.64 ng/mL, respectively.

Elimination

Metabolism

A metabolism study in humans indicates that insulin glargine is partly metabolized at the carboxyl terminus of the B chain in the subcutaneous depot to form two active metabolites with *in vitro* activity similar to that of human insulin, M1 (21^{A}-Gly-insulin) and M2 (21^{A}-Gly-des30^{B}-Thr-insulin). Unchanged drug and these degradation products are also present in the circulation.

Specific Populations

Age, Race, and Gender

Effect of age, race, and gender on the pharmacokinetics of SEMGLEE has not been evaluated.

Obesity

Effect of Body Mass Index (BMI) on the pharmacokinetics of SEMGLEE has not been evaluated.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

In mice and rats, standard two-year carcinogenicity studies with another insulin glargine product were performed at doses up to 0.455 mg/kg, which was for the rat approximately 65 times the recommended human subcutaneous starting dose of 0.2 units/kg/day (0.007 mg/kg/day) on a mg/kg basis. Histiocytomas were found at injection sites in male rats and mice in acid vehicle containing groups and are considered a response to chronic tissue irritation and inflammation in rodents. These tumors were not found in female animals, in saline control, or insulin comparator groups using a different vehicle.

Another insulin glargine product was not mutagenic in tests for detection of gene mutations in bacteria and mammalian cells (Ames and HGPRT-test) and in tests for detection of chromosomal aberrations (cytogenetics *in vitro* in V79 cells and *in vivo* in Chinese hamsters).

In a combined fertility and prenatal and postnatal study of another insulin glargine product in male and female rats at subcutaneous doses up to 0.36 mg/kg/day, which was approximately 50 times the recommended human subcutaneous starting dose of 0.2 units/kg/day (0.007 mg/kg/day) maternal toxicity due to dose-dependent hypoglycemia, including some deaths, was observed. Consequently, a reduction of the rearing rate occurred in the high-dose group only. Similar effects were observed with NPH insulin.

14 CLINICAL STUDIES

14.1 Overview of Clinical Studies

Following are the results of studies conducted with SEMGLEE and with another insulin glargine product in adult and pediatric patients with type 1 diabetes mellitus and adults with type 2 diabetes mellitus.

14.2 Clinical Studies in Adult and Pediatric Patients with Type 1 Diabetes

A 24 weeks multicenter, open-label, randomized, active-controlled study to evaluate the glucose lowering effect of once-daily SEMGLEE compared to that of once-daily administration of another insulin glargine product, 100 units/mL, in combination with mealtime insulin lispro was conducted in patients with type 1 diabetes. Mean age was 42 years, the majority of patients were Caucasian, 94.6%, mean BMI was 26.5 kg/m^2, mean duration of diabetes prior to entry into the study was 19 years, the mean exposure of 280 patients to SEMGLEE during the study was 50 weeks. At week 24, treatment with SEMGLEE was found to be non-inferior to that achieved with comparator insulin glargine product with regard to the mean change in HbA1c over 24 weeks of treatment.

Table 9: Adult Type 1 Diabetes Mellitus, SEMGLEE plus Mealtime Insulin versus Another Insulin Glargine Product plus Mealtime Insulin

Baseline to 24 weeks HbA1c (%)	**SEMGLEE + Insulin lispro (N=280)**	**Another Insulin Glargine Product + Insulin lispro (N=278)**
Baseline (mean)	7.37	7.39
Change (adjusted mean)[a]	0.11	0.08
Difference from comparator and 95% CI[a]	0.03 (-0.06, 0.12)	

[a] Analysis of Covariance including all post-baseline data regardless of rescue or treatment discontinuation. Missing Week 24 data were multiply-imputed with a mean for each subject equal to their respective baseline value.

In two clinical studies (Studies A and B), patients with type 1 diabetes (Study A; n = 585, Study B n = 534) were randomized to 28 weeks of basal-bolus treatment with another insulin glargine product, 100 units/mL, or NPH insulin. Regular human insulin was administered before each meal. This other insulin glargine product was administered at bedtime. NPH insulin was administered either as once daily at bedtime or in the morning and at bedtime when used twice daily.

In Study A, the average age was 39.2 years. The majority of patients were White (99%) and 55.7% were male. The mean BMI was approximately 24.9 kg/m^2. The mean duration of diabetes was 15.5 years.

In Study B, the average age was 38.5 years. The majority of patients were White (95.3%) and 50.6% were male. The mean BMI was approximately 25.8 kg/m^2. The mean duration of diabetes was 17.4 years.

In another clinical study (Study C), patients with type 1 diabetes (n = 619) were randomized to 16 weeks of basal-bolus treatment with another insulin glargine product, 100 units/mL, or NPH insulin. Insulin lispro was used before each meal. This other insulin glargine product was administered once daily at bedtime and NPH insulin was administered once or twice daily. The average age was 39.2 years. The majority of patients were White (96.9%) and 50.6% were male. The mean BMI was approximately 25.6 kg/m^2. The mean duration of diabetes was 18.5 years.

In these 3 studies, another insulin glargine product, 100 units/mL and NPH insulin had similar effects on HbA1c (Table 10).

Table 10: Type 1 Diabetes Mellitus–Adult

Treatment duration **Treatment in combination with**	**Study A** **28 weeks** **Regular insulin**		**Study B** **28 weeks** **Regular insulin**		**Study C** **16 weeks** **Insulin lispro**	
	Another Insulin Glargine Product	**NPH**	**Another Insulin Glargine Product**	**NPH**	**Another Insulin Glargine Product**	**NPH**
Number of subjects treated	292	293	264	270	310	309
HbA1c						
Baseline HbA1c Adjusted mean change at trial end	8.0 +0.2	8.0 +0.1	7.7 -0.2	7.7 -0.2	7.6 -0.1	7.7 -0.1
Treatment Difference (95% CI)	+0.1 (0.0;+0.2)		+0.1 (-0.1;+0.2)		0.0 (-0.1;+0.1)	
Fasting blood glucose (mg/dL)						
Baseline mean	167	166	166	175	175	173
Adj. mean change from baseline	-21	-16	-20	-17	-29	-12

Type 1 Diabetes – Pediatric (see Table 11): In a randomized, controlled clinical study (Study D), pediatric 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. Other insulin glargine product was administered once daily at bedtime and NPH insulin was administered once or twice daily. The average age was 11.7 years. The majority of patients were White (96.8%) and 51.9% were male. The mean BMI was approximately 18.9 kg/m^2. The mean duration of diabetes was 4.8 years. Similar effects on HbA1c (Table 11) were observed in both treatment groups.

Table 11: Type 1 Diabetes Mellitus–Pediatric

Treatment duration **Treatment in combination with**	**Study D** **28 weeks** **Regular insulin**	
	Another Insulin Glargine Product + Regular Insulin	**NPH+ Regular Insulin**
Number of subjects treated	174	175
HbA1c		
Baseline mean	8.5	8.8
Change from baseline (adjusted mean)	+0.3	+0.3
Difference from NPH (adjusted mean)	0.0	
(95% CI)	(-0.2; +0.3)	
Fasting blood glucose (mg/dL)		
Baseline mean	194	191

Mean change from baseline	-23	-12

14.3 Clinical Studies in Adults with Type 2 Diabetes

A 24 weeks multicenter, open-label, randomized, active-controlled study to evaluate the glucose lowering effect of once-daily SEMGLEE compared to that of once-daily administration of another insulin glargine product, 100 units/mL, both administered in combination with oral antidiabetic drugs, was conducted in patients with type 2 diabetes. Mean age was 55 years, more than half, 52.7%, of the patients were Caucasian, 26.6% were Hispanic, and 9.8% were Black, mean BMI was 31.5 kg/m^2, the mean duration of diabetes prior to entry into the study was 12 years, the mean exposure of 276 patients to SEMGLEE during the study was 22 weeks. At week 24, treatment with SEMGLEE was found to be non-inferior to that achieved with comparator insulin glargine product with regard to the reduction in HbA1c over 24 weeks of treatment.

Table 12: Adult Type 2 Diabetes Mellitus SEMGLEE plus Oral Antidiabetic Medication versus Comparator Insulin Glargine Product plus Oral Antidiabetic Medication

Baseline to 24 weeks HbA1c (%)	**SEMGLEE + Oral Antidiabetic Medication (N=277)**	**Comparator Insulin Glargine Product, 100 units/mL + Oral Antidiabetic Medication (N=283)**
Baseline (mean)	8.09	8.10
Change (adjusted mean)[a]	-0.37	-0.42
Difference from comparator and 95% CI[a]	0.05 (-0.11, 0.21)	

[a] Analysis of Covariance including all post-baseline data regardless of rescue or treatment discontinuation. Missing Week 24 data were multiply-imputed with a mean for each subject equal to their respective baseline value.

In a randomized, controlled clinical study (Study E) (n = 570), another insulin glargine product, 100 units/mL was evaluated for 52 weeks in combination with oral anti-diabetic medications (a sulfonylurea, metformin, acarbose, or combinations of these drugs). The average age was 59.5 years. The majority of patients were White (92.8%) and 53.7% were male. The mean BMI was approximately 29.1 kg/m^2. The mean duration of diabetes was 10.3 years. This other insulin glargine product administered once daily at bedtime was as effective as NPH insulin administered once daily at bedtime in reducing HbA1c and fasting glucose (Table 13).

In a randomized, controlled clinical study (Study F), in patients with type 2 diabetes not using oral anti-diabetic medications (n = 518), a basal-bolus regimen of another insulin glargine product, 100 units/mL once daily at bedtime or NPH insulin administered once or twice daily was evaluated for 28 weeks. Regular human insulin was used before meals, as needed. The average age was 59.3 years. The majority of patients were White (80.7%) and 60% were male. The mean BMI was approximately 30.5 kg/m^2. The mean duration of diabetes was 13.7 years. This other insulin glargine product had similar effectiveness as either once-or twice-daily NPH insulin in reducing HbA1c and fasting glucose (Table 13).

In a randomized, controlled clinical study (Study G), patients with type 2 diabetes were randomized to 5 years of treatment with another insulin glargine product, 100 units/mL once-daily or twice-daily NPH insulin. For patients not previously treated with insulin, the starting dose of this other insulin glargine product or NPH insulin was 10 units daily. Patients who were already treated with NPH insulin either continued on the same total daily NPH insulin dose or started this other insulin glargine product at a

dose that was 80% of the total previous NPH insulin dose. The primary endpoint for this study was a comparison of the progression of diabetic retinopathy by 3 or more steps on the Early Treatment Diabetic Retinopathy Study (ETDRS) scale. HbA1c change from baseline was a secondary endpoint. Similar glycemic control in the 2 treatment groups was desired in order to not confound the interpretation of the retinal data. Patients or study personnel used an algorithm to adjust this other insulin glargine product and NPH insulin doses to a target fasting plasma glucose ≤ 100 mg/dL. After this other insulin glargine product or NPH insulin dose was adjusted, other anti-diabetic agents, including premeal insulin were to be adjusted or added. The average age was 55.1 years. The majority of patients were White (85.3%) and 53.9% were male. The mean BMI was approximately 34.3 kg/m^2. The mean duration of diabetes was 10.8 years. This other insulin glargine product group had a smaller mean reduction from baseline in HbA1c compared to the NPH insulin group, which may be explained by the lower daily basal insulin doses in this other insulin glargine product group (Table 13).

Table 13: Type 2 Diabetes Mellitus–Adult

Treatment duration **Treatment in combination with**	**Study E** **52 weeks** **Oral agents**		**Study F** **28 weeks** **Regular insulin**		**Study G** **5 years** **Regular insulin**	
	Another Insulin Glargine Product	**NPH**	**Another Insulin Glargine Product**	**NPH**	**Another Insulin Glargine Product**	**NPH**
Number of subjects treated	289	281	259	259	513	504
HbA1c						
Baseline mean	9.0	8.9	8.6	8.5	8.4	8.3
Adjusted mean change from baseline	-0.5	-0.4	-0.4	-0.6	-0.6	-0.8
Another Insulin Glargine Product, 100 units/mL – NPH	-0.1		+0.2		+0.2	
95% CI for Treatment difference	(-0.3; +0.1)		(0.0; +0.4)		(+0.1; +0.4)	
Fasting blood glucose (mg/dL)						
Baseline mean	179	180	164	166	190	180
Adj. mean change from baseline	-49	-46	-24	-22	-45	-44

Another Insulin Glargine Product, 100 units/mL, Timing of Daily Dosing (see Table 14): The safety and efficacy of other insulin glargine product administered pre-breakfast, pre-dinner, or at bedtime were evaluated in a randomized, controlled clinical study in patients with type 1 diabetes (study H, n = 378). Patients were also treated with insulin lispro at mealtime. The average age was 40.9 years. All patients were White (100%) and 53.7% were male. The mean BMI was approximately 25.3 kg/m^2. The mean duration of diabetes was 17.3 years. This other insulin glargine product administered at different times of the day resulted in similar reductions in HbA1c compared to that with bedtime administration (see Table 14). In these patients, data are available from 8-point home glucose monitoring. The maximum mean blood glucose was observed just prior to injection of this other insulin glargine product regardless of time of administration.

In this study, 5% of patients in this other insulin glargine product-breakfast arm discontinued treatment because of lack of efficacy. No patients in the other two arms discontinued for this reason. The safety and efficacy of this other insulin glargine product administered pre-breakfast or at bedtime were also evaluated in a randomized, active-controlled clinical study (Study I, n = 697) in patients with type 2

diabetes not adequately controlled on oral anti-diabetic therapy. All patients in this study also received glimepiride 3 mg daily. The average age was 60.8 years. The majority of patients were White (96.6%) and 53.7% were male. The mean BMI was approximately 28.7 kg/m^2. The mean duration of diabetes was 10.1 years. This other insulin glargine product given before breakfast was at least as effective in lowering HbA1c as this other insulin glargine product given at bedtime or NPH insulin given at bedtime (see Table 14).

Table 14: Another Insulin Glargine Product, 100 units/mL, Timing of Daily Dosing in Type 1 (Study H) and Type 2 (Study I) Diabetes Mellitus

Treatment duration Treatment in Combination with:	**Study H 24 weeks Insulin lispro**			**Study I 24 weeks Glimepiride**		
	Another Insulin Glargine Product Breakfast	**Another Insulin Glargine Product Dinner**	**Another Insulin Glargine Product Bedtime**	**Another Insulin Glargine Product Breakfast**	**Another Insulin Glargine Product Bedtime**	**NPH Bedtime**
Number of subjects treated*	112	124	128	234	226	227
HbA1c						
Baseline mean	7.6	7.5	7.6	9.1	9.1	9.1
Mean change from baseline	-0.2	-0.1	0.0	-1.3	-1.0	-0.8

*** Intent-to-treat ***Not applicable**

Five-Year Trial Evaluating the Progression of Retinopathy: Retinopathy was evaluated in the clinical studies with another insulin glargine product, 100 units/mL, by analysis of reported retinal adverse events and fundus photography. The numbers of retinal adverse events reported for this other insulin glargine product and NPH insulin treatment groups were similar for patients with type 1 and type 2 diabetes.

Another insulin glargine product, 100 units/mL, was compared to NPH insulin in a 5-year randomized clinical trial that evaluated the progression of retinopathy as assessed with fundus photography using a grading protocol derived from the Early Treatment Diabetic Retinopathy Scale (ETDRS). Patients had type 2 diabetes (mean age 55 years) with no (86%) or mild (14%) retinopathy at baseline. Mean baseline HbA1c was 8.4%. The primary outcome was progression by 3 or more steps on the ETDRS scale at study endpoint. Patients with pre-specified post-baseline eye procedures (pan-retinal photocoagulation for proliferative or severe nonproliferative diabetic retinopathy, local photocoagulation for new vessels, and vitrectomy for diabetic retinopathy) were also considered as 3-step progressors regardless of actual change in ETDRS score from baseline. Retinopathy graders were blinded to treatment group assignment. The results for the primary endpoint are shown in Table 15 for both the per-protocol and Intent-to-Treat populations and indicate similarity of this other insulin glargine product to NPH in the progression of diabetic retinopathy as assessed by this outcome.

Table 15: Number (%) of Patients with 3 or More Step Progression on ETDRS Scale at Endpoint

	Another Insulin Glargine Product (%)	**NPH (%)**	**Difference [a,b] (SE)**	**95% CI for difference**

Per-protocol	53/374 (14.2%)	57/363 (15.7%)	-2.0% (2.6%)	-7.0% to +3.1%
Intent-to-Treat	63/502 (12.5%)	71/487 (14.6%)	-2.1% (2.1%)	-6.3% to +2.1%

a: Difference = Another Insulin Glargine Product, 100 units/mL – NPH
b: Using a generalized linear model (SAS GENMOD) with treatment and baseline HbA1c strata (cutoff 9.0%) as the classified independent variables, and with binomial distribution and identity link function

The Origin Study: The Outcome Reduction with Initial Glargine Intervention trial (i.e., ORIGIN) was an open-label, randomized, 2-by-2, factorial design study. One intervention in ORIGIN compared the effect of another insulin glargine product, 100 units/mL, to standard care on major adverse cardiovascular outcomes in 12,537 participants ≥ 50 years of age with abnormal glucose levels [i.e., impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT)] or early type 2 diabetes mellitus and established cardiovascular (i.e., CV) disease or CV risk factors at baseline.

The objective of the trial was to demonstrate that use of this other insulin glargine product use could significantly lower the risk of major cardiovascular outcomes compared to standard care. Two coprimary composite cardiovascular endpoints were used in ORIGIN. The first coprimary endpoint was the time to first occurrence of a major adverse cardiovascular event defined as the composite of CV death, nonfatal myocardial infarction and nonfatal stroke. The second coprimary endpoint was the time to the first occurrence of CV death or nonfatal myocardial infarction or nonfatal stroke or revascularization procedure or hospitalization for heart failure.

Participants were randomized to either this other insulin glargine product (N = 6264) titrated to a goal fasting plasma glucose of ≤ 95 mg/dL or to standard care (N = 6273). Anthropometric and disease characteristics were balanced at baseline. The mean age was 64 years and 8% of participants were 75 years of age or older. The majority of participants were male (65%). Fifty nine percent were Caucasian, 25% were Latin, 10% were Asian and 3% were Black. The median baseline BMI was 29 kg/m^2. Approximately 12% of participants had abnormal glucose levels (IGT and/or IFG) at baseline and 88% had type 2 diabetes. For patients with type 2 diabetes, 59% were treated with a single oral antidiabetic drug, 23% had known diabetes but were on no antidiabetic drug and 6% were newly diagnosed during the screening procedure. The mean HbA1c (SD) at baseline was 6.5% (1.0). Fifty-nine percent of participants had had a prior cardiovascular event and 39% had documented coronary artery disease or other cardiovascular risk factors.

Vital status was available for 99.9% and 99.8% of participants randomized to this other insulin glargine product and standard care respectively at end of trial. The median duration of follow-up was 6.2 years [range: 8 days to 7.9 years]. The mean HbA1c (SD) at the end of the trial was 6.5% (1.1) and 6.8% (1.2) in this other insulin glargine product and standard care group respectively. The median dose of this other insulin glargine product at end of trial was 0.45 U/kg. Eighty-one percent of patients randomized to this other insulin glargine product were using this other insulin glargine product at end of the study. The mean change in body weight from baseline to the last treatment visit was 2.2 kg greater in this other insulin glargine group than in the standard care group.

Overall, the incidence of major adverse cardiovascular outcomes was similar between groups (see Table 16). All-cause mortality was also similar between groups.

Table 16: Cardiovascular Outcomes in ORIGIN -Time to First Event Analyses

	Another Insulin Glargine Product N = 6264	**Standard Care N = 6273**	**Another Insulin Glargine Product vs Standard Care**

	n (Events per 100 PY)	n (Events per 100 PY)	Hazard Ratio (95% CI)
Coprimary endpoints			
CV death, nonfatal myocardial infarction, or nonfatal stroke	1041 (2.9)	1013 (2.9)	1.02 (0.94, 1.11)
CV death, nonfatal myocardial infarction, or nonfatal stroke, hospitalization for heart failure or revascularization procedure	1792 (5.5)	1727 (5.3)	1.04 (0.97, 1.11)
Components of coprimary endpoints			
CV death	580	576	1.00 (0.89, 1.13)
Myocardial Infarction (fatal or nonfatal)	336	326	1.03 (0.88, 1.19)
Stroke (fatal or nonfatal)	331	319	1.03 (0.89, 1.21)
Revascularizations	908	860	1.06 (0.96, 1.16)
Hospitalization for heart failure	310	343	0.90 (0.77, 1.05)

In the ORIGIN trial, the overall incidence of cancer (all types combined) or death from cancer (Table 17) was similar between treatment groups.

Table 17: Cancer Outcomes in ORIGIN -Time to First Event Analyses

	Another Insulin Glargine Product N = 6264	**Standard Care N = 6273**	**Another Insulin Glargine Product vs Standard Care**
	n (Events per 100 PY)	n (Events per 100 PY)	Hazard Ratio (95% CI)
Cancer endpoints			
Any cancer event (new or recurrent)	559 (1.56)	561 (1.56)	0.99 (0.88, 1.11)
New cancer events	524 (1.46)	535 (1.49)	0.96 (0.85, 1.09)
Death due to Cancer	189 (0.51)	201 (0.54)	0.94 (0.77, 1.15)

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

SEMGLEE (insulin glargine injection) is supplied as a clear, colorless, solution 100 units/mL (U-100) available as:

SEMGLEE	**Total Volume**	**Concentration**	**Total Units Available in Presentation**	**Dose Increment**	**NDC Number**	**Package Size**
multiple-dose vial	10 mL	100 units/mL	1,000 units	n/a	49502-195-80	1 vial
	3 mL	100 units/mL	300 units	1 unit	49502-196-71	1 pen

single-patient-use prefilled pen					49502-196-73	3 pens
					49502-196-75	5 pens

The SEMGLEE prefilled pen dials in 1-unit increments.

Dispense in the original sealed carton with the enclosed Instructions for Use.

Needles are not included in the packs.
BD Ultra-Fine™ needles are compatible with this pen.

16.2 Storage

Dispense in the original sealed carton with the enclosed Instructions for Use.

Do not store SEMGLEE in the freezer and do not allow to freeze. Discard SEMGLEE if it has been frozen. Protect SEMGLEE from direct heat and light.

Storage conditions are summarized in the following table:

	Not in-use (unopened) **Refrigerated (2° to 8°C [36° to 46°F])**	**Not in-use (unopened)** **Room Temperature (up to 30°C [86°F])**	**In-use (opened)** **(see temperature Below)**
10 mL multiple-dose vial	Until expiration date	28 days	28 days Refrigerated (2° to 8°C [36° to 46°F]) or room temperature (up to 30°C [86°F])
3 mL single-patient-use prefilled pen	Until expiration date	28 days	28 days Room temperature (up to 30°C [86°F]) only (Do not refrigerate)

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Never Share a SEMGLEE Prefilled Pen or Syringe Between Patients

Advise patients that they must never share a SEMGLEE prefilled pen with another person, even if the needle is changed. Advise patients using SEMGLEE vials not to re-use or share needles or syringes with another person. Sharing carries a risk for transmission of blood-borne pathogens *[see Warnings and Precautions (5.1)]*.

Hyperglycemia or Hypoglycemia

Inform patients that hypoglycemia is the most common adverse reaction with insulin. Inform patients of the symptoms of hypoglycemia. Inform patients that the ability to concentrate and react may be impaired as a result of hypoglycemia. This may present a risk in situations where these abilities are especially important, such as driving or operating other machinery. Advise patients who have frequent

hypoglycemia or reduced or absent warning signs of hypoglycemia to use caution when driving or operating machinery *[see Warnings and Precautions (5.3)]*.

Advise patients that changes in insulin regimen can predispose to hyperglycemia or hypoglycemia and that changes in insulin regimen should be made under close medical supervision *[see Warnings and Precautions (5.2)]*.

Medications Errors

Instruct patients to always check the insulin label before each injection *[see Warnings and Precautions (5.4)]*.

Administration

Advise patients that SEMGLEE must NOT be diluted or mixed with any other insulin or solution and that SEMGLEE must only be used if the solution is clear and colorless with no particles visible *[see Dosage and Administration (2.1)]*.

Patient Information
SEMGLEE™ (Sehm-GLEE)
(insulin glargine injection) for subcutaneous use, 100 units/mL (U-100)

Do not share your syringes with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

What is SEMGLEE?

- SEMGLEE is a long-acting man-made insulin used to control high blood sugar in adults with diabetes mellitus.
- SEMGLEE is not for use to treat diabetic ketoacidosis.
- It is not known if SEMGLEE is safe and effective in children less than 6 years of age with type 1 diabetes.
- It is not known if SEMGLEE is safe and effective in children with type 2 diabetes.

Do not use SEMGLEE if you:

- are having an episode of low blood sugar (hypoglycemia).
- have an allergy to insulin glargine or any of the ingredients in SEMGLEE. See the end of this Patient Information leaflet for a complete list of ingredients in SEMGLEE.

Before using SEMGLEE, tell your healthcare provider about all your medical conditions including if you:

- have liver or kidney problems.
- take other medicines, especially ones called TZDs (thiazolidinediones).
- have heart failure or other heart problems. If you have heart failure, it may get worse while you take TZDs with SEMGLEE.
- are pregnant, planning to become pregnant, or are breastfeeding**.** It is not known if SEMGLEE may harm your unborn baby or breastfeeding baby.

Tell your healthcare provider about all the medicines you take including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Before you start using SEMGLEE, talk to your healthcare provider about low blood sugar and how to manage it.

How should I use SEMGLEE?

- Read the detailed **Instructions for Use** that come with your SEMGLEE insulin**.**
- Use SEMGLEE exactly as your healthcare provider tells you to. Your healthcare provider should tell you how much SEMGLEE to use and when to use it.
- Know the amount of SEMGLEE you use. **Do not** change the amount of SEMGLEE you use unless your healthcare provider tells you to.
- Check your insulin label each time you give your injection to make sure you are using the correct insulin.
- **Do not** re-use needles. Always use a new needle for each injection. Re-use of needles increases your risk of having blocked needles, which may cause you to get the wrong dose of SEMGLEE. Using a new needle for each injection lowers your risk of getting an infection.
- You may take SEMGLEE at any time during the day but you must take it at the same time every day.
- Only use SEMGLEE that is clear and colorless. **Do not** use SEMGLEE if it is cloudy or slightly colored, or if you see particles in the solution.
- SEMGLEE is injected under the skin (subcutaneously) of your thigh, buttocks, upper arms, or stomach area (abdomen).
- Do not use SEMGLEE in an insulin pump or inject SEMGLEE into your vein (intravenously).
- **Change (rotate) your injection sites within the area you choose with each dose** to reduce your risk of getting pits in skin or thickened skin (lipodystrophy) and skin with lumps (localized cutaneous amyloidosis) at the injection sites.
  - **Do not** use the exact spot for each injection.
  - **Do not** inject where the skin has pits, is thickened, or has lumps.
  - **Do not** inject where the skin is tender, bruised, scaly or hard, or into scars or damaged skin.
- **Do not** mix SEMGLEE with any other type of insulin or liquid medicine.
- **Check your blood sugar levels.** Ask your healthcare provider what your blood sugar should be and when you should check your blood sugar levels.
- **Keep SEMGLEE and all medicines out of the reach of children.**

Your dose of SEMGLEE may need to change because of:

- a change in level of physical activity or exercise, weight gain or loss, increased stress, illness, change in diet, or because of the medicines you take.

What should I avoid while using SEMGLEE?

While using SEMGLEE do not:

- drive or operate heavy machinery, until you know how SEMGLEE affects you.
- drink alcohol or use over-the-counter medicines that contain alcohol.

What are the possible side effects of SEMGLEE and other insulins?

SEMGLEE may cause serious side effects that can lead to death, including:

- **low blood sugar (hypoglycemia).** Signs and symptoms that may indicate low blood sugar include:

o dizziness or light-headedness, sweating, confusion, headache, blurred vision, slurred speech, shakiness, fast heartbeat, anxiety, irritability or mood change, hunger.

- **severe allergic reaction (whole body reaction). Get medical help right away if you have any of these signs or symptoms of a severe allergic reaction:**
  o a rash over your whole body, trouble breathing, a fast heartbeat, or sweating.
- **low potassium in your blood (hypokalemia).**
- **heart failure.** Taking certain diabetes pills called TZDs (thiazolidinediones) with SEMGLEE may cause heart failure in some people. This can happen even if you have never had heart failure or heart problems before. If you already have heart failure it may get worse while you take TZDs with SEMGLEE. Your healthcare provider should monitor you closely while you are taking TZDs with SEMGLEE. Tell your healthcare provider if you have any new or worse symptoms of heart
  failure including:
  o shortness of breath, swelling of your ankles or feet, sudden weight gain.
  Treatment with TZDs and SEMGLEE may need to be changed or stopped by your healthcare provider if you have new or worse heart failure.

Get emergency medical help if you have: trouble breathing, shortness of breath, fast heartbeat, swelling of your face, tongue, or throat, sweating, extreme drowsiness, dizziness, confusion.

The most common side effects of SEMGLEE include:

- low blood sugar (hypoglycemia), weight gain, allergic reactions, injection site reactions, skin thickening or pits at the injection site (lipodystrophy), itching, rash and swelling.

These are not all the possible side effects of SEMGLEE. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of SEMGLEE.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use SEMGLEE for a condition for which it was not prescribed. Do not give SEMGLEE to other people, even if they have the same symptoms that you have. It may harm them.

You can ask your pharmacist or healthcare provider for information about SEMGLEE that is written for health professionals.

What are the ingredients in SEMGLEE?

- **Active ingredient:** insulin glargine
- **10 mL vial inactive ingredients:** zinc, glycerol 85%, polysorbate-20, *m*-Cresol, and water for injection. Hydrochloric acid and sodium hydroxide may be added to adjust the pH.

For more information, call Mylan at 1-877-446-3679 (1-877-4-INFO-RX).
Manufactured for: Mylan Specialty L.P., Morgantown, WV 26505 U.S.A.
Manufactured by: Biocon Sdn. Bhd., Johor – 79200, Malaysia

This Patient Information has been approved by the U.S. Food and Drug Administration

Approved: 6/2020
MA:B:PIV:INGLIJ:RX7

Instructions for Use
SEMGLEE™ (Sehm-GLEE)
(insulin glargine injection) for subcutaneous use
10 mL Vial (100 Units/mL, U-100)

Read this Instructions for Use before you start taking SEMGLEE and each time you get a new SEMGLEE vial. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

Your healthcare provider should show you or a caregiver how to use SEMGLEE the right way before you use it for the first time.

Do not share your SEMGLEE syringes with other people even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

Supplies needed to give your injection:
- a SEMGLEE 10 mL vial
- a U-100 insulin syringe and needle
- alcohol wipes
- 1 sharps container for throwing away used needles and syringes. See "**Disposing of used needles and syringes**" at the end of these instructions

Preparing your SEMGLEE dose:
- Wash your hands with soap and water or with alcohol.
- Check the SEMGLEE label to make sure you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
- Check the insulin to make sure it is clear and colorless. **Do not** use SEMGLEE if it is colored or cloudy, or if you see particles in the solution.
- **Do not** use SEMGLEE after the expiration date stamped on the label or 28 days after you first use it.
- **Always use a syringe that is marked for U-100 insulin.** If you use a syringe other than a U-100 insulin syringe, you may get the wrong dose of insulin.
- **Always use a new syringe or needle for each injection. Do not reuse or share your syringes or needles with other people. You may give other people a serious infection or get a serious infection from them.**

Step 1:

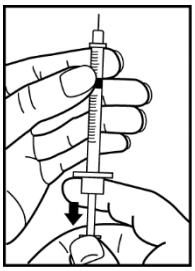
If you are using a new vial, remove the protective cap. Do not remove the rubber stopper.

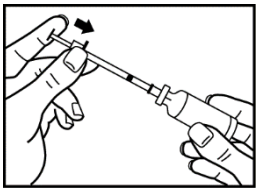
Step 2:

Wipe the top of the vial with an alcohol wipe. You do not have to shake the vial of SEMGLEE before use.

Step 3:

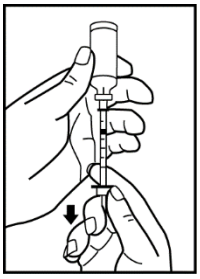
Draw air into the syringe equal to your insulin dose. Put the needle through the rubber top of the vial and push the plunger to inject the air into the vial.





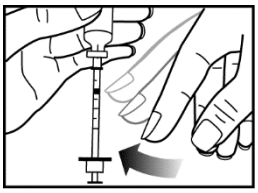
Step 4:

Leave the syringe in the vial and turn both upside down. Hold the syringe and vial firmly in 1 hand. Make sure the tip of the needle is in the insulin. With your free hand, pull the plunger to withdraw the correct dose into the syringe.



Step 5:

Before you take the needle out of the vial, check the syringe for air bubbles. If bubbles are in the syringe, hold the syringe straight up and tap the side of the syringe until the bubbles float to the top. Push the bubbles out with the plunger and draw insulin back in until you have the correct dose.



Step 6:

Remove the needle from the vial. Do not let the needle touch anything. You are now ready to inject.

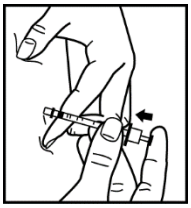
Giving your SEMGLEE injection:

- Inject your insulin exactly as your healthcare provider has shown you.
- Inject your insulin under the skin (subcutaneously) of your thigh, buttocks, upper arms, or stomach area (abdomen).
- **Change (rotate) your injection site within the area you choose for each dose** to reduce your risk of getting pits in the skin or thickened skin (lipodystrophy) and skin with lumps (localized cutaneous amyloidosis) at the injection sites.
- Do not inject where the skin has pits, is thickened, or has lumps.
- Do not inject where the skin is tender, bruised, scaly or hard, or into scars or damaged skin.

Step 7:

Choose your injection site. Wipe the skin with an alcohol wipe to clean the injection site. Let the injection site dry before you inject your dose.

Step 8:
- Pinch the skin.
- Insert the needle in the way your healthcare provider showed you.
- Release the skin.
- Slowly push in the plunger of the syringe all the way, making sure you have injected all the insulin.
- Leave the needle in the skin for about 10 seconds.



Step 9:
- Pull the needle straight out of your skin.
- Gently press the injection site for several seconds. **Do not** rub the area.
- **Do not** recap the used needle. Recapping the needle can lead to a needle stick injury.

Disposing of used needles and syringes:

- Put your used needles and syringes in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and syringes in your household trash.

- If you do not have a FDA-cleared sharps container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,

- leak resistant, and
- properly labeled to warn of hazardous waste inside the container.

- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.

- **Do not** dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. **Do not** recycle your used sharps disposal container.

How should I store SEMGLEE?

- Store unused SEMGLEE vials in the refrigerator between 36° to 46°F (2° to 8°C) until the expiration date. If your unopened SEMGLEE vial is stored at room temperature up to 86°F (30°C), it should be thrown away after 28 days.
- Store in-use (opened) SEMGLEE vials in a refrigerator or at room temperature up to 86°F (30°C).
- The SEMGLEE vials you are using should be thrown away after 28 days, even if it still has insulin left in it.
- **Do not** freeze SEMGLEE.
- Keep SEMGLEE out of direct heat and light.
- If a vial has been frozen or overheated, throw it away.

This Instructions for Use has been approved by the U.S. Food and Drug Administration. Approved: 6/2020

MA:B:IFUV:INGLIJ:RX7

Patient Information
SEMGLEE™ (Sehm-GLEE)
(insulin glargine injection) for subcutaneous use, 100 units/mL (U-100)

Do not share your SEMGLEE pen with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

What is SEMGLEE?

- SEMGLEE is a long-acting man-made insulin used to control high blood sugar in adults with diabetes mellitus.
- SEMGLEE is not for use to treat diabetic ketoacidosis.
- It is not known if SEMGLEE is safe and effective in children less than 6 years of age with type 1 diabetes.
- It is not known if SEMGLEE is safe and effective in children with type 2 diabetes.

Do not use SEMGLEE if you:

- are having an episode of low blood sugar (hypoglycemia).
- have an allergy to insulin glargine or any of the ingredients in SEMGLEE. See the end of this Patient Information leaflet for a complete list of ingredients in SEMGLEE.

Before using SEMGLEE, tell your healthcare provider about all your medical conditions including if you:

- have liver or kidney problems.
- take other medicines, especially ones called TZDs (thiazolidinediones).
- have heart failure or other heart problems. If you have heart failure, it may get worse while you take TZDs with SEMGLEE.
- are pregnant, planning to become pregnant, or are breastfeeding**.** It is not known if SEMGLEE may harm your unborn baby or breastfeeding baby.

Tell your healthcare provider about all the medicines you take including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Before you start using SEMGLEE, talk to your healthcare provider about low blood sugar and how to manage it.

How should I use SEMGLEE?

- Read the detailed **Instructions for Use** that come with your SEMGLEE single-patient-use prefilled pen**.**
- Use SEMGLEE exactly as your healthcare provider tells you to. Your healthcare provider should tell you how much SEMGLEE to use and when to use it.
- Know the amount of SEMGLEE you use. **Do not** change the amount of SEMGLEE you use unless your healthcare provider tells you to.
- Check your insulin label each time you give your injection to make sure you are using the correct insulin.
- Only use SEMGLEE that is clear and colorless**. Do not** use SEMGLEE if it is cloudy or slightly colored, or if you see particles in the solution.
- SEMGLEE comes in a single-patient-use prefilled pen that you must use to give your SEMGLEE. The dose counter on your pen shows your dose of SEMGLEE. Do not make any dose changes unless your healthcare provider tells you to.
- **Do not** re-use needles. Always use a new needle for each injection. Re-use of needles increases your risk of having blocked needles, which may cause you to get the wrong dose of SEMGLEE. Using a new needle for each injection lowers your risk of getting an infection.
- You may take SEMGLEE at any time during the day but you must take it at the same time every day.
- SEMGLEE is injected under the skin (subcutaneously) of your thigh, buttocks, upper arms, or stomach area (abdomen).
- **Do not** use SEMGLEE in an insulin pump or inject SEMGLEE into your vein (intravenously).
- **Change (rotate) your injection sites within the area you choose with each dose** to reduce your risk of getting pits in skin or thickened skin (lipodystrophy) and skin with lumps (localized cutaneous amyloidosis) at the injection sites.
  - **Do not** use the exact spot for each injection.
  - **Do not** inject where the skin has pits, is thickened, or has lumps.
  - **Do not** inject where skin is tender, bruised, scaly or hard, or into scars or damaged skin.
- **Do not** mix SEMGLEE with any other type of insulin or liquid medicine.
- **Check your blood sugar levels.** Ask your healthcare provider what your blood sugar should be and when you should check your blood sugar levels.

Keep SEMGLEE and all medicines out of the reach of children.

Your dose of SEMGLEE may need to change because of:

- a change in level of physical activity or exercise, weight gain or loss, increased stress, illness, change in diet, or because of the medicines you take.

What should I avoid while using SEMGLEE?
While using SEMGLEE do not:

- drive or operate heavy machinery, until you know how SEMGLEE affects you.
- drink alcohol or use over-the-counter medicines that contain alcohol.

What are the possible side effects of SEMGLEE and other insulins?
SEMGLEE may cause serious side effects that can lead to death, including:

- **low blood sugar (hypoglycemia).** Signs and symptoms that may indicate low blood sugar include:
  - o dizziness or light-headedness, sweating, confusion, headache, blurred vision, slurred speech, shakiness, fast heartbeat, anxiety, irritability or mood change, hunger.
- **severe allergic reaction (whole body reaction). Get medical help right away if you have any of these signs or symptoms of a severe allergic reaction:**
  - o a rash over your whole body, trouble breathing, a fast heartbeat, or sweating.
- **low potassium in your blood (hypokalemia).**
- **heart failure.** Taking certain diabetes pills called TZDs (thiazolidinediones) with SEMGLEE may cause heart failure in some people. This can happen even if you have never had heart failure or heart problems before. If you already have heart failure it may get worse while you take TZDs with SEMGLEE. Your healthcare provider should monitor you closely while you are taking TZDs with SEMGLEE. Tell your healthcare provider if you have any new or worse symptoms of heart failure including:
  - o shortness of breath, swelling of your ankles or feet, sudden weight gain.

  Treatment with TZDs and SEMGLEE may need to be changed or stopped by your healthcare provider if you have new or worse heart failure.

Get emergency medical help if you have: trouble breathing, shortness of breath, fast heartbeat, swelling of your face, tongue, or throat, sweating, extreme drowsiness, dizziness, confusion.

The most common side effects of SEMGLEE include:

- low blood sugar (hypoglycemia), weight gain, allergic reactions, injection site reactions, skin thickening or pits at the injection site (lipodystrophy), itching, rash, and swelling.

These are not all the possible side effects of SEMGLEE. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of SEMGLEE.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use SEMGLEE for a condition for which it was not prescribed. Do not give SEMGLEE to other people even if they have the same symptoms that you have. It may harm them.
You can ask your healthcare provider or pharmacist for information about SEMGLEE that is written for health professionals.

What are the ingredients in SEMGLEE?

- **Active ingredient:** insulin glargine
- **3 mL prefilled pen inactive ingredients:** zinc, glycerol 85%, *m*-Cresol, and water for injection. Hydrochloric acid and sodium hydroxide may be added to adjust the pH.

For more information, call Mylan at 1-877-446-3679 (1-877-4-INFO-RX).
Manufactured for: Mylan Specialty L.P., Morgantown, WV 26505 U.S.A.
Manufactured by: Biocon Biologics India Limited, Bengaluru – 560 099 India

This Patient Information has been approved by the U.S. Food and Drug Administration

Approved: 6/2020
IN:B:PIP:INGLIJ:RX7

Patient Information
SEMGLEE™ (Sehm-GLEE)
(insulin glargine injection) for subcutaneous use, 100 units/mL (U-100)

Do not share your SEMGLEE pen with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

What is SEMGLEE?

- SEMGLEE is a long-acting man-made insulin used to control high blood sugar in adults with diabetes mellitus.
- SEMGLEE is not for use to treat diabetic ketoacidosis.
- It is not known if SEMGLEE is safe and effective in children less than 6 years of age with type 1 diabetes.
- It is not known if SEMGLEE is safe and effective in children with type 2 diabetes.

Do not use SEMGLEE if you:

- are having an episode of low blood sugar (hypoglycemia).
- have an allergy to insulin glargine or any of the ingredients in SEMGLEE. See the end of this Patient Information leaflet for a complete list of ingredients in SEMGLEE.

Before using SEMGLEE, tell your healthcare provider about all your medical conditions including if you:

- have liver or kidney problems.
- take other medicines, especially ones called TZDs (thiazolidinediones).
- have heart failure or other heart problems. If you have heart failure, it may get worse while you take TZDs with SEMGLEE.
- are pregnant, planning to become pregnant, or are breastfeeding**.** It is not known if SEMGLEE may harm your unborn baby or breastfeeding baby.

Tell your healthcare provider about all the medicines you take including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Before you start using SEMGLEE, talk to your healthcare provider about low blood sugar and how to manage it.

How should I use SEMGLEE?

- Read the detailed **Instructions for Use** that come with your SEMGLEE single-patient-use prefilled pen**.**
- Use SEMGLEE exactly as your healthcare provider tells you to. Your healthcare provider should tell you how much SEMGLEE to use and when to use it.
- Know the amount of SEMGLEE you use. **Do not** change the amount of SEMGLEE you use unless your healthcare provider tells you to.
- Check your insulin label each time you give your injection to make sure you are using the correct insulin.
- Only use SEMGLEE that is clear and colorless**. Do not** use SEMGLEE if it is cloudy or slightly colored, or if you see particles in the solution.
- SEMGLEE comes in a single-patient-use prefilled pen that you must use to give your SEMGLEE. The dose counter on your pen shows your dose of SEMGLEE. Do not make any dose changes unless your healthcare provider tells you to.
- **Do not** re-use needles. Always use a new needle for each injection. Re-use of needles increases your risk of having blocked needles, which may cause you to get the wrong dose of SEMGLEE. Using a new needle for each injection lowers your risk of getting an infection.
- You may take SEMGLEE at any time during the day but you must take it at the same time every day.
- SEMGLEE is injected under the skin (subcutaneously) of your thigh, buttocks, upper arms, or stomach area (abdomen).
- **Do not** use SEMGLEE in an insulin pump or inject SEMGLEE into your vein (intravenously).
- **Change (rotate) your injection sites within the area you choose with each dose** to reduce your risk of getting pits in skin or thickened skin (lipodystrophy) and skin with lumps (localized cutaneous amyloidosis) at the injection sites.
  - **Do not** use the exact spot for each injection.
  - **Do not** inject where the skin has pits, is thickened, or has lumps.
  - **Do not** inject where skin is tender, bruised, scaly or hard, or into scars or damaged skin.
- **Do not** mix SEMGLEE with any other type of insulin or liquid medicine.
- **Check your blood sugar levels.** Ask your healthcare provider what your blood sugar should be and when you should check your blood sugar levels.

Keep SEMGLEE and all medicines out of the reach of children.

Your dose of SEMGLEE may need to change because of:

- a change in level of physical activity or exercise, weight gain or loss, increased stress, illness, change in diet, or because of the medicines you take.

What should I avoid while using SEMGLEE?
While using SEMGLEE do not:

- drive or operate heavy machinery, until you know how SEMGLEE affects you.
- drink alcohol or use over-the-counter medicines that contain alcohol.

What are the possible side effects of SEMGLEE and other insulins?
SEMGLEE may cause serious side effects that can lead to death, including:

- **low blood sugar (hypoglycemia).** Signs and symptoms that may indicate low blood sugar include:
  - o dizziness or light-headedness, sweating, confusion, headache, blurred vision, slurred speech, shakiness, fast heartbeat, anxiety, irritability or mood change, hunger.
- **severe allergic reaction (whole body reaction). Get medical help right away if you have any of these signs or symptoms of a severe allergic reaction:**
  - o a rash over your whole body, trouble breathing, a fast heartbeat, or sweating.
- **low potassium in your blood (hypokalemia).**
- **heart failure.** Taking certain diabetes pills called TZDs (thiazolidinediones) with SEMGLEE may cause heart failure in some people. This can happen even if you have never had heart failure or heart problems before. If you already have heart failure it may get worse while you take TZDs with SEMGLEE. Your healthcare provider should monitor you closely while you are taking TZDs with SEMGLEE. Tell your healthcare provider if you have any new or worse symptoms of heart failure including:
  - o shortness of breath, swelling of your ankles or feet, sudden weight gain.

  Treatment with TZDs and SEMGLEE may need to be changed or stopped by your healthcare provider if you have new or worse heart failure.

Get emergency medical help if you have: trouble breathing, shortness of breath, fast heartbeat, swelling of your face, tongue, or throat, sweating, extreme drowsiness, dizziness, confusion.

The most common side effects of SEMGLEE include:

- low blood sugar (hypoglycemia), weight gain, allergic reactions, injection site reactions, skin thickening or pits at the injection site (lipodystrophy), itching, rash, and swelling.

These are not all the possible side effects of SEMGLEE. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of SEMGLEE.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use SEMGLEE for a condition for which it was not prescribed. Do not give SEMGLEE to other people even if they have the same symptoms that you have. It may harm them.

You can ask your healthcare provider or pharmacist for information about SEMGLEE that is written for health professionals.

What are the ingredients in SEMGLEE?

- **Active ingredient:** insulin glargine
- **3 mL prefilled pen inactive ingredients:** zinc, glycerol 85%, *m*-Cresol, and water for injection. Hydrochloric acid and sodium hydroxide may be added to adjust the pH.

For more information, call Mylan at 1-877-446-3679 (1-877-4-INFO-RX).
Manufactured for: Mylan Specialty L.P., Morgantown, WV 26505 U.S.A.
Manufactured by: Biocon Sdn. Bhd., Johor – 79200, Malaysia

This Patient Information has been approved by the U.S. Food and Drug Administration

Approved: 6/2020
MA:B:PIP:INGLIJ:RX7

INSTRUCTIONS FOR USE

Semglee™ (Sehm-GLEE)

(insulin glargine injection)

For Single Patient Use Only

100 units/mL (U-100)

1 Prefilled pen with 3 mL cartridge

Read this Instructions for Use carefully before using SEMGLEE single-patient-use prefilled pen and each time you get another pen. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment. If you are unable to read or follow all of the instructions on your own, ask for help from someone trained to use this pen.

Your healthcare provider should show you or a caregiver how to use SEMGLEE the right way before you use it for the first time.

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 sugar level.

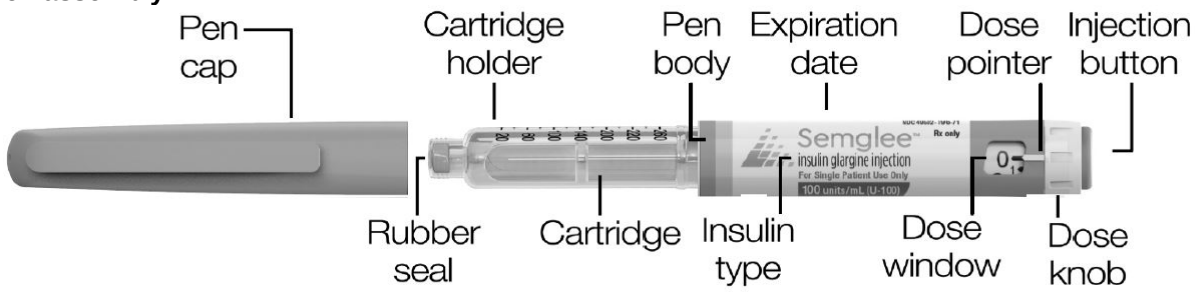
SEMGLEE is a disposable single-patient-use prefilled pen injector that contains a total of 300 units of insulin glargine. Each pen contains more than one dose of medicine. You can select doses from 1 to 80 units in steps of 1 unit. If your prescribed dose is more than 80 units, you will need to give yourself more than 1 injection.

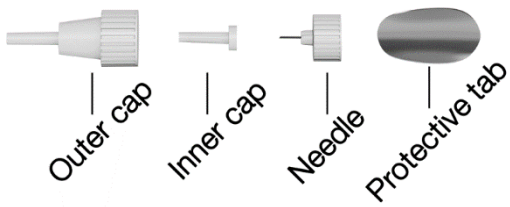
Do not share your SEMGLEE prefilled pen with other people, even if the needle has been changed. You may give other people a serious infection or get a serious infection from them.

People who are blind or have vision problems should not use SEMGLEE prefilled pen without help from a person trained to use SEMGLEE prefilled pen.

Before you use the pen for the first time check that the SEMGLEE disposable prefilled pen injector carton is sealed and that the sticker sealing the carton is not broken. After opening the carton look at the pen to make sure that it looks new and is not broken.

Pen assembly





BD Ultra-Fine needles are compatible with SEMGLEE.

Needles are sold separately.

Required Supplies

- SEMGLEE single-patient-use prefilled pen
- Needle compatible with this pen
- Alcohol wipes
- A sharps container to throw away used needles. See “Step 8 Needle disposal” at the end of this Instructions for Use.

Storage

Unused Pens

- Before using the pen, store the cartons containing the pen in the refrigerator between 36°F to 46°F (2°C to 8°C) until the expiration date. If your unused pen is stored at room temperature up to 86°F (30°C), it should be thrown away after 28 days.
- **Do not** freeze the pen.

In-use Pen

- When using a new pen that has been stored in the refrigerator, take the pen out of the refrigerator. Rest it on a flat surface and wait for it to reach room temperature.
- While using the pen, store it at room temperature up to 86°F (30°C). **Do not** put the pen back in the refrigerator after using it.
- Always store the pen with the pen cap on to prevent contamination. **Do not** leave the needle attached to the pen during storage or re-use needles. You should safely throw away any used needles. See “Step 8 Needle disposal” at the end of this Instructions for Use.
- The pen that you are using should be thrown away 28 days after removing it from the refrigerator, even if the pen has insulin left in it.

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

Always use a new sterile needle for each injection as this helps stop blocked needles and prevents infections.

Each time you use the pen

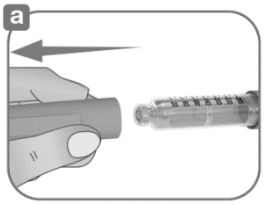
- Wash your hands with soap and water before using your pen.
- Check the pen label to make sure that it is the correct type of insulin. The pen has a purple and white label and a purple injection button.

- Check the expiration date on the pen label. **Do not** use the pen after the expiration date.
- Check that the medicine in the pen cartridge looks clear and colorless. **Do not** use the pen if the medicine in the cartridge looks cloudy, colored or if you can see particles.
- Always use a new sterile disposable needle for each injection.
- Use an injection site that your healthcare provider has shown you.

Step 1. Prepare your pen

A Inspect the pen. Check the purple and white label on the pen to make sure:
- It is the correct insulin type.
- The expiration date has not passed.

B Hold the pen body with 1 hand. With the other hand pull off the pen cap. Put the pen cap off to the side to be used later (See Figure a).

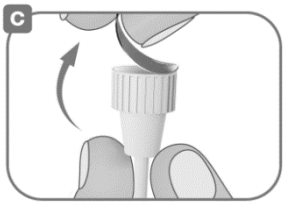


C Check the insulin through the cartridge holder to make sure:
- The insulin looks clear and colorless.
- There are no cracks, breaks or leaks around the cartridge holder.

D Wipe the rubber seal (at the front of the cartridge) with a new alcohol wipe (See Figure b).

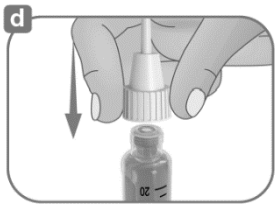
Step 2. Attach a new needle

A Take a new sterile disposable needle and peel off the protective tab (See Figure c). **Do not** use the needle if the protective tab is damaged or missing, as the needle may not be sterile.



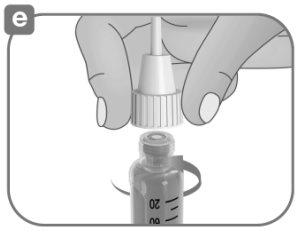
B While holding the pen body facing upwards, attach the outer cap straight on to the cartridge holder as shown. **Do not** attach the outer cap sideways as this may cause the needle to bend or become damaged (See Figure d).

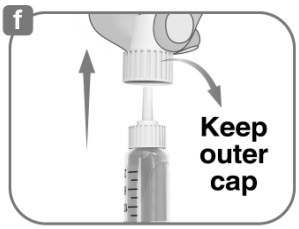
C Turn the outer cap in a clockwise (right) direction until it feels tightly fixed on the pen (See Figure e).



D Carefully pull off the outer cap and put it off to the side (See Figure f). **Do not** throw it away. You will need the outer cap later.

E Carefully pull off the inner cap and throw it away in the sharps container (See Figure g).



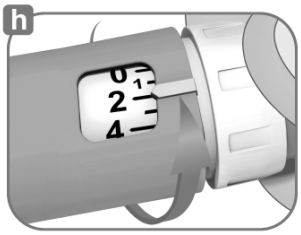


Step 3. Prime your pen needle

A Always prime a new pen needle before each injection.

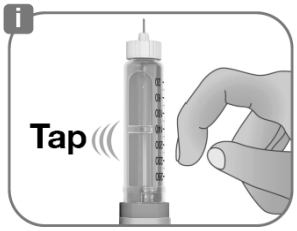
B Turn the white dose knob to 2 dose units (See Figure h). You will hear a “click” for each unit turned.

If you accidentally turn past 2 units, turn back the dose knob in the opposite direction to the correct number of units.



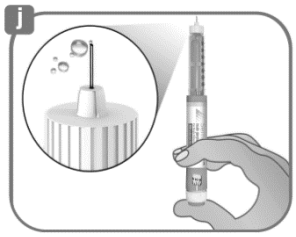
C Hold the pen body facing upwards with 1 hand.

D Tap the cartridge gently with your finger to help any large air bubbles to move to the top of the cartridge (See Figure i). Small bubbles may still be visible. This is normal.



E With the pen needle facing upwards, press the injection button until it stops moving and the dose window shows “0”.

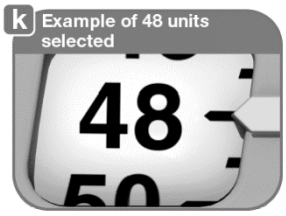
F Repeat steps 3B through 3E up to 4 times until you see drops of insulin at the tip of the needle. Priming is complete when you can see drops of insulin (See Figure j).



If you do not see any insulin at the needle tip after trying to prime the needle 4 times, the needle may be clogged. If this occurs:

- Go to Step 7 for instructions on safely removing the needle.
- Restart the process at step 2A to attach and prime a new needle.

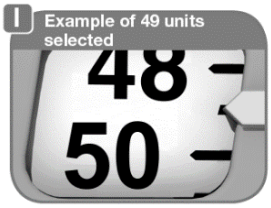
Step 4. Select your dose



A Check that the dose window shows “0”.

B Turn the white dose knob until the yellow dose pointer lines up with your required dose.

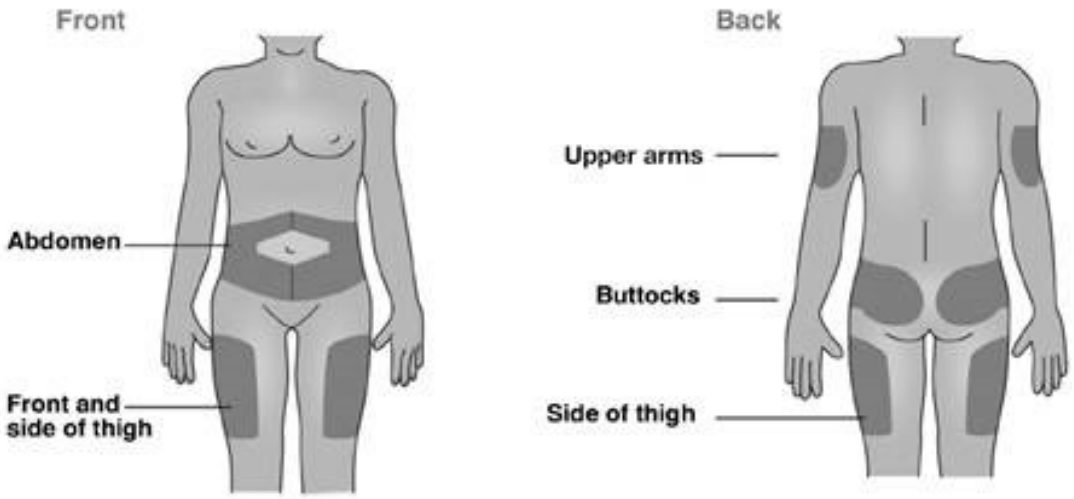
- The pen dials 1 unit at a time.
- The white dose knob clicks and becomes longer as you turn it.
- **Do not** push the purple injection button while you are turning the white dose knob.
- **Do not** dial your dose by counting the clicks because you may dial the wrong dose.
- The **even** numbers are printed on the dial (See Figure k).
  The **odd** numbers are shown as lines in between the even numbers (See Figure l).
- You can correct the dose by turning the dose knob in either direction until the correct dose lines up with the yellow dose pointer.
- **Do not** force the white dose knob to turn beyond 80 units. If you need a dose greater than 80 units you should give it as two or more injections.
- The pen will not let you dial a dose more than the number of units left in the pen. If your dose is more than the number of units left in the pen you can either:
  - Inject the amount left in your pen and use a new pen to give the rest of your dose
  or
  - Get a new pen and inject the full dose.



Do not push the purple injection button when turning the white dose knob.

Step 5. Select and clean the injection site

A Select the injection site as explained to you by your healthcare provider. SEMGLEE is injected under the skin (subcutaneously) of your stomach area (abdomen), thigh, buttocks or upper arms. You should change (rotate) your injection site for each injection. Clean with a new alcohol wipe and let your skin dry before you inject your dose.



Inject your insulin exactly as your healthcare provider has shown you.

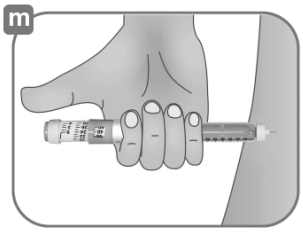
Change (rotate) your injection sites within the area you choose for each dose to reduce your risk of getting pits in the skin or thickened skin (lipodystrophy) and skin with lumps (localized cutaneous amyloidosis) at the injection sites.

Do not inject where the skin has pits, is thickened or has lumps.

Do not inject where the skin is tender, bruised, scaly or hard or into scars or damaged skin.

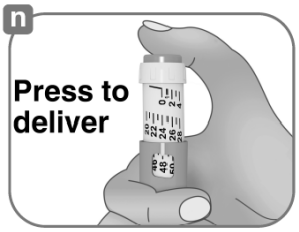
Step 6. Inject your dose

A Some injection sites may need to be pinched during your injection. Ask your healthcare provider if you are not sure if your skin needs to be pinched during the injection. If instructed by your healthcare provider you can pinch the cleaned skin between your fingers.

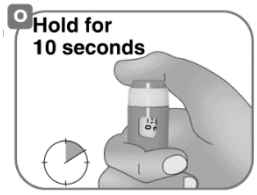


B Push the needle straight into the skin as shown by your healthcare provider (See Figure m).
Do not inject with the needle at an angle.

C Press the purple injection button all the way in (See Figure n). The white dose knob will turn and you will hear “clicks” as you press down.



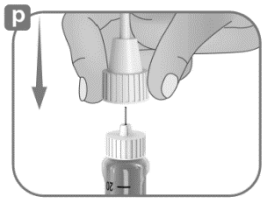
D After the dose window shows “0”, continue to hold the purple injection button down and slowly count to 10 to make sure that the full dose of insulin is injected. If you do not keep the injection button pressed down for 10 seconds after “0” is displayed you may get the wrong dose of medicine (See Figure o).



Do not push the injection button sideways or block the white dose knob with your fingers as this will stop you from injecting the medicine.

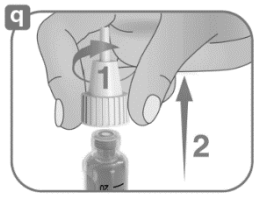
Pull the needle out of your skin.

A drop of insulin at the needle tip is normal. It will not affect your dose.



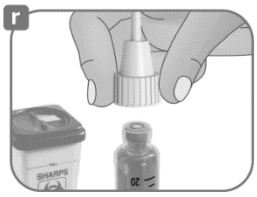
Step 7. After your injection

A Take the outer cap that you had saved in step 2D, hold it at the widest part and carefully cover the needle without touching it (See Figure p).

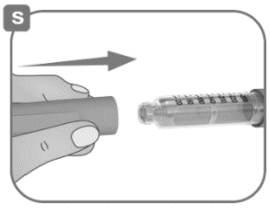


B Squeeze the wide part of the outer cap and unscrew the needle in a counter-clockwise (left) direction (See Figure q). Keep twisting the needle until it comes off the pen. It may take several twists to release the needle.

C Put the needle in a sharps disposal container (See Step 8 Needle disposal at the end of this Instructions for Use) (See Figure r).



D Replace the pen cap over the cartridge (See Figure s).



E If there is still medicine left in your pen, store the pen at room temperature (up to 86°F or 30°C).
Do not store the pen with a used needle attached.

Step 8. Needle disposal

Put your used needle in an FDA-cleared sharps disposal container right away after use. **Do not** throw away (dispose of) loose needles in your household trash.

If you do not have an FDA-cleared sharps container, you may use a household container that is:

- Made of heavy duty plastic,
- Can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- Upright and stable during use,
- Leak-resistant, and
- Properly labeled to warn of hazardous waste inside the container.

When your sharps disposable container is almost full you will need to follow your community guidelines for the right way to dispose of your sharps container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA website at: www.fda.gov/safesharpsdisposal

Do not dispose of a used sharps disposal container in your household trash unless guidelines permit this.
Do not recycle your used sharps disposal container.

Pen care

- Always carry an extra insulin pen in case your pen gets lost or damaged.
- Always use a new sterile disposable needle for each injection.
- Protect SEMGLEE from direct heat and light.
- The used pen may be discarded in your household trash after you have removed the needle.
- You can clean the outside of your pen by wiping it with a damp cloth.
- Avoid dropping your pen as this can cause the cartridge to break, or can damage the pen.
- **Do not** share your pen with other people, even if the needle has been changed. You may give other people serious infection or get a serious infection from them.

- **Do not** soak or wash your pen. **Do not** use alcohol, hydrogen peroxide, bleach, or any other liquids to clean your pen. **Do not** apply lubricants such as oil. This could damage the pen.

- **Do not** try to fix an unusable or damaged pen. Remove the needle as shown in Step 7, safely throw it away in a sharps container as shown in Step 8 and return the pen to the manufacturer letting them know of the problem. Use a new pen instead.

This Instructions for Use has been approved by the Food and Drug Administration.

BD Ultra-Fine™ is a trademark of Becton, Dickinson, and Company. SEMGLEE™ is a trademark of Mylan Pharmaceuticals, Inc.

Manufactured for:
Mylan Specialty L.P.
Morgantown, WV 26505 U.S.A.

Product of India

KR/DRUGS/KTK/28D/07/2006

Approved: 6/2020
IN:B:IFUP:INGLIJP:RX7

INSTRUCTIONS FOR USE

Semglee™ (Sehm-GLEE)

(insulin glargine injection)

For Single Patient Use Only

100 units/mL (U-100)

1 Prefilled pen with 3 mL cartridge

Read this Instructions for Use carefully before using SEMGLEE single-patient-use prefilled pen and each time you get another pen. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment. If you are unable to read or follow all of the instructions on your own, ask for help from someone trained to use this pen.

Your healthcare provider should show you or a caregiver how to use SEMGLEE the right way before you use it for the first time.

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 sugar level.

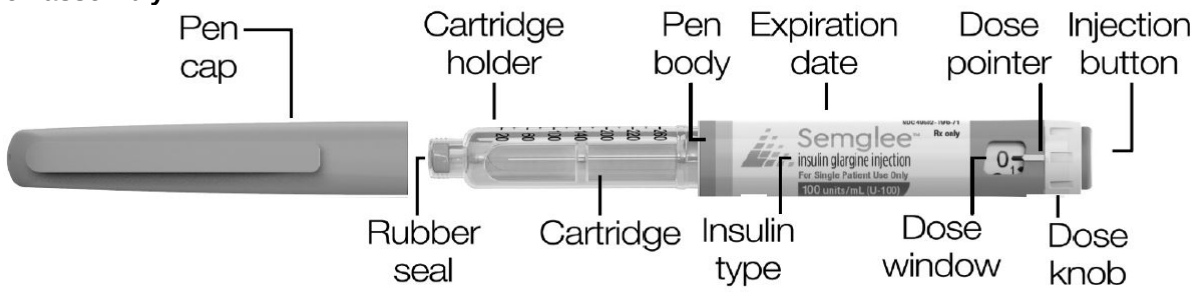
SEMGLEE is a disposable single-patient-use prefilled pen injector that contains a total of 300 units of insulin glargine. Each pen contains more than one dose of medicine. You can select doses from 1 to 80 units in steps of 1 unit. If your prescribed dose is more than 80 units, you will need to give yourself more than 1 injection.

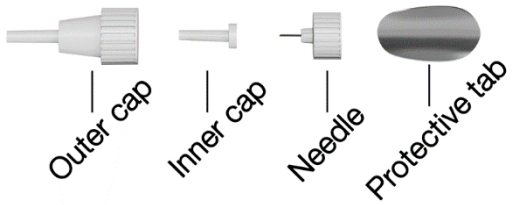
Do not share your SEMGLEE prefilled pen with other people, even if the needle has been changed. You may give other people a serious infection or get a serious infection from them.

People who are blind or have vision problems should not use SEMGLEE prefilled pen without help from a person trained to use SEMGLEE prefilled pen.

Before you use the pen for the first time check that the SEMGLEE disposable prefilled pen injector carton is sealed and that the sticker sealing the carton is not broken. After opening the carton look at the pen to make sure that it looks new and is not broken.

Pen assembly





BD Ultra-Fine needles are compatible with SEMGLEE.

Needles are sold separately.

Required Supplies

- SEMGLEE single-patient-use prefilled pen
- Needle compatible with this pen
- Alcohol wipes
- A sharps container to throw away used needles. See “Step 8 Needle disposal” at the end of this Instructions for Use.

Storage

Unused Pens

- Before using the pen, store the cartons containing the pen in the refrigerator between 36°F to 46°F (2°C to 8°C) until the expiration date. If your unused pen is stored at room temperature up to 86°F (30°C), it should be thrown away after 28 days.
- **Do not** freeze the pen.

In-use Pen

- When using a new pen that has been stored in the refrigerator, take the pen out of the refrigerator. Rest it on a flat surface and wait for it to reach room temperature.
- While using the pen, store it at room temperature up to 86°F (30°C). **Do not** put the pen back in the refrigerator after using it.
- Always store the pen with the pen cap on to prevent contamination. **Do not** leave the needle attached to the pen during storage or re-use needles. You should safely throw away any used needles. See “Step 8 Needle disposal” at the end of this Instructions for Use.
- The pen that you are using should be thrown away 28 days after removing it from the refrigerator, even if the pen has insulin left in it.

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

Always use a new sterile needle for each injection as this helps stop blocked needles and prevents infections.

Each time you use the pen

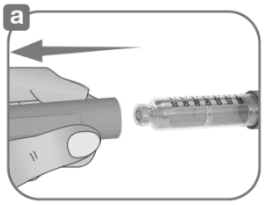
- Wash your hands with soap and water before using your pen.
- Check the pen label to make sure that it is the correct type of insulin. The pen has a purple and white label and a purple injection button.

- Check the expiration date on the pen label. **Do not** use the pen after the expiration date.
- Check that the medicine in the pen cartridge looks clear and colorless. **Do not** use the pen if the medicine in the cartridge looks cloudy, colored or if you can see particles.
- Always use a new sterile disposable needle for each injection.
- Use an injection site that your healthcare provider has shown you.

Step 1. Prepare your pen

A Inspect the pen. Check the purple and white label on the pen to make sure:
- It is the correct insulin type.
- The expiration date has not passed.

B Hold the pen body with 1 hand. With the other hand pull off the pen cap. Put the pen cap off to the side to be used later (See Figure a).

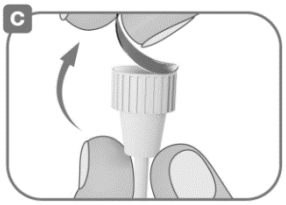


C Check the insulin through the cartridge holder to make sure:
- The insulin looks clear and colorless.
- There are no cracks, breaks or leaks around the cartridge holder.

D Wipe the rubber seal (at the front of the cartridge) with a new alcohol wipe (See Figure b).

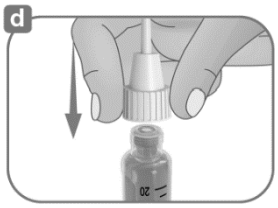
Step 2. Attach a new needle

A Take a new sterile disposable needle and peel off the protective tab (See Figure c). **Do not** use the needle if the protective tab is damaged or missing, as the needle may not be sterile.



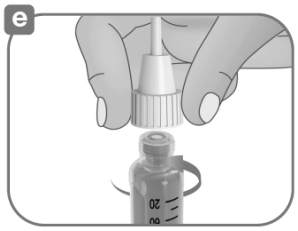
B While holding the pen body facing upwards, attach the outer cap straight on to the cartridge holder as shown. **Do not** attach the outer cap sideways as this may cause the needle to bend or become damaged (See Figure d).

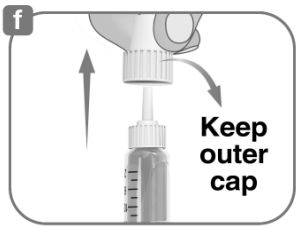
C Turn the outer cap in a clockwise (right) direction until it feels tightly fixed on the pen (See Figure e).



D Carefully pull off the outer cap and put it off to the side (See Figure f). **Do not** throw it away. You will need the outer cap later.

E Carefully pull off the inner cap and throw it away in the sharps container (See Figure g).



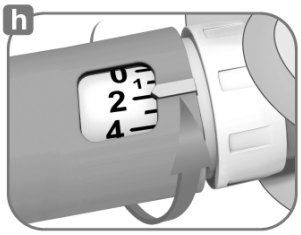


Step 3. Prime your pen needle

A Always prime a new pen needle before each injection.

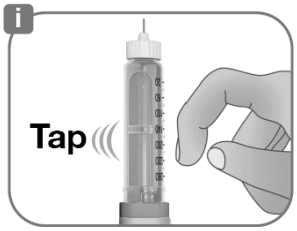
B Turn the white dose knob to 2 dose units (See Figure h). You will hear a “click” for each unit turned.

If you accidentally turn past 2 units, turn back the dose knob in the opposite direction to the correct number of units.



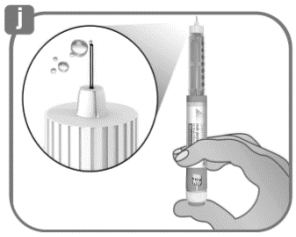
C Hold the pen body facing upwards with 1 hand.

D Tap the cartridge gently with your finger to help any large air bubbles to move to the top of the cartridge (See Figure i). Small bubbles may still be visible. This is normal.



E With the pen needle facing upwards, press the injection button until it stops moving and the dose window shows “0”.

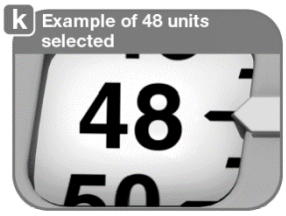
F Repeat steps 3B through 3E up to 4 times until you see drops of insulin at the tip of the needle. Priming is complete when you can see drops of insulin (See Figure j).



If you do not see any insulin at the needle tip after trying to prime the needle 4 times, the needle may be clogged. If this occurs:

- Go to Step 7 for instructions on safely removing the needle.
- Restart the process at step 2A to attach and prime a new needle.

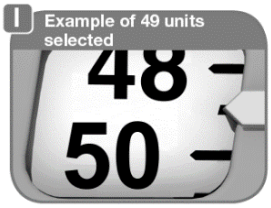
Step 4. Select your dose



A Check that the dose window shows “0”.

B Turn the white dose knob until the yellow dose pointer lines up with your required dose.

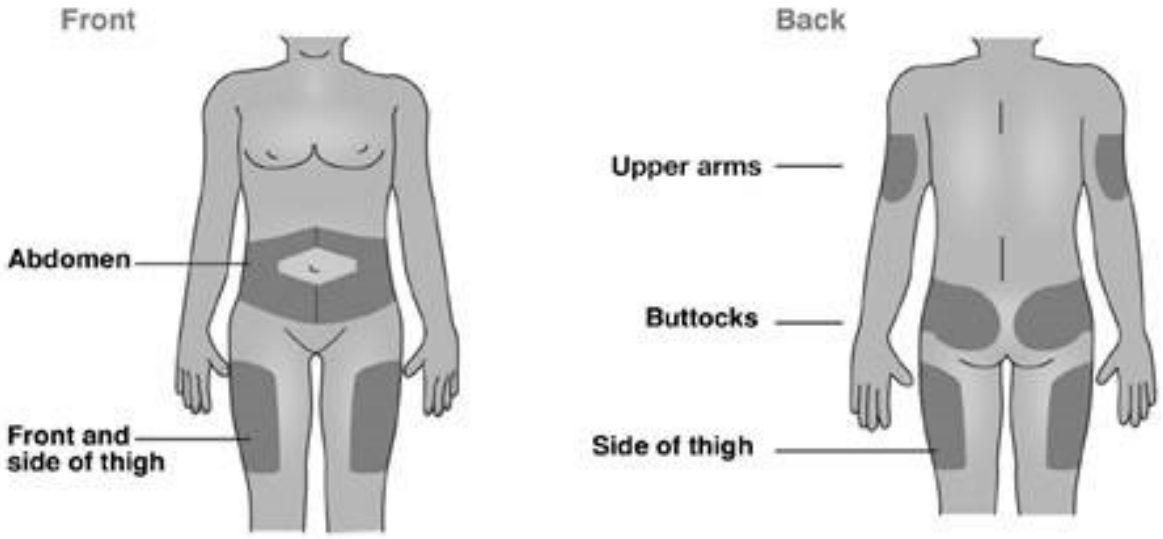
- The pen dials 1 unit at a time.
- The white dose knob clicks and becomes longer as you turn it.
- **Do not** push the purple injection button while you are turning the white dose knob.
- **Do not** dial your dose by counting the clicks because you may dial the wrong dose.
- The **even** numbers are printed on the dial (See Figure k).
  The **odd** numbers are shown as lines in between the even numbers (See Figure l).
- You can correct the dose by turning the dose knob in either direction until the correct dose lines up with the yellow dose pointer.
- **Do not** force the white dose knob to turn beyond 80 units. If you need a dose greater than 80 units you should give it as two or more injections.
- The pen will not let you dial a dose more than the number of units left in the pen. If your dose is more than the number of units left in the pen you can either:
  - Inject the amount left in your pen and use a new pen to give the rest of your dose
  or
  - Get a new pen and inject the full dose.



Do not push the purple injection button when turning the white dose knob.

Step 5. Select and clean the injection site

A Select the injection site as explained to you by your healthcare provider. SEMGLEE is injected under the skin (subcutaneously) of your stomach area (abdomen), thigh, buttocks or upper arms. You should change (rotate) your injection site for each injection. Clean with a new alcohol wipe and let your skin dry before you inject your dose.



Inject your insulin exactly as your healthcare provider has shown you.

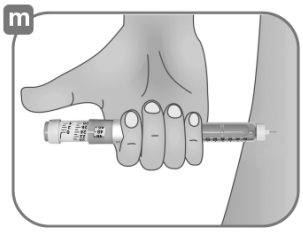
Change (rotate) your injection sites within the area you choose for each dose to reduce your risk of getting pits in the skin or thickened skin (lipodystrophy) and skin with lumps (localized cutaneous amyloidosis) at the injection sites.

Do not inject where the skin has pits, is thickened or has lumps.

Do not inject where the skin is tender, bruised, scaly or hard or into scars or damaged skin.

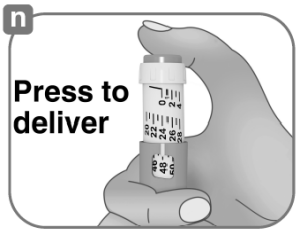
Step 6. Inject your dose

A Some injection sites may need to be pinched during your injection. Ask your healthcare provider if you are not sure if your skin needs to be pinched during the injection. If instructed by your healthcare provider you can pinch the cleaned skin between your fingers.

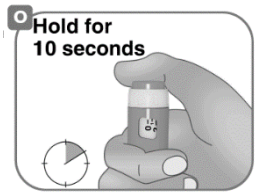


B Push the needle straight into the skin as shown by your healthcare provider (See Figure m).
Do not inject with the needle at an angle.

C Press the purple injection button all the way in (See Figure n). The white dose knob will turn and you will hear “clicks” as you press down.



D After the dose window shows “0”, continue to hold the purple injection button down and slowly count to 10 to make sure that the full dose of insulin is injected. If you do not keep the injection button pressed down for 10 seconds after “0” is displayed you may get the wrong dose of medicine (See Figure o).



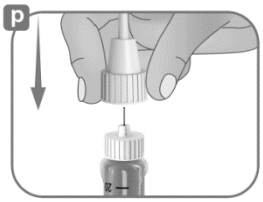
Do not push the injection button sideways or block the white dose knob with your fingers as this will stop you from injecting the medicine.

Pull the needle out of your skin.

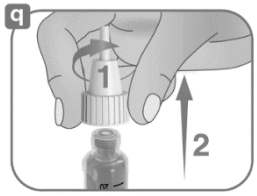
A drop of insulin at the needle tip is normal. It will not affect your dose.

Step 7. After your injection

A Take the outer cap that you had saved in step 2D, hold it at the widest part and carefully cover the needle without touching it (See Figure p).

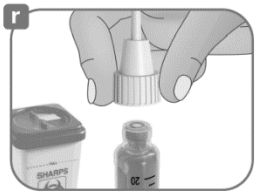


B Squeeze the wide part of the outer cap and unscrew the needle in a counter-clockwise (left) direction (See Figure q). Keep twisting the needle until it comes off the pen. It may take



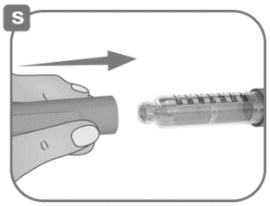
several twists to release the needle.

C Put the needle in a sharps disposal container (See Step 8 Needle disposal at the end of this Instructions for Use) (See Figure r).



D Replace the pen cap over the cartridge (See Figure s).

E If there is still medicine left in your pen, store the pen at room temperature (up to 86°F or 30°C).
Do not store the pen with a used needle attached.



Step 8. Needle disposal

Put your used needle in an FDA-cleared sharps disposal container right away after use. **Do not** throw away (dispose of) loose needles in your household trash.

If you do not have an FDA-cleared sharps container, you may use a household container that is:

- Made of heavy duty plastic,
- Can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- Upright and stable during use,
- Leak-resistant, and
- Properly labeled to warn of hazardous waste inside the container.

When your sharps disposable container is almost full you will need to follow your community guidelines for the right way to dispose of your sharps container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA website at: www.fda.gov/safesharpsdisposal

Do not dispose of a used sharps disposal container in your household trash unless guidelines permit this.
Do not recycle your used sharps disposal container.

Pen care

- Always carry an extra insulin pen in case your pen gets lost or damaged.
- Always use a new sterile disposable needle for each injection.
- Protect SEMGLEE from direct heat and light.
- The used pen may be discarded in your household trash after you have removed the needle.
- You can clean the outside of your pen by wiping it with a damp cloth.
- Avoid dropping your pen as this can cause the cartridge to break, or can damage the pen.

- **Do not** share your pen with other people, even if the needle has been changed. You may give other people serious infection or get a serious infection from them.

- **Do not** soak or wash your pen. **Do not** use alcohol, hydrogen peroxide, bleach, or any other liquids to clean your pen. **Do not** apply lubricants such as oil. This could damage the pen.

- **Do not** try to fix an unusable or damaged pen. Remove the needle as shown in Step 7, safely throw it away in a sharps container as shown in Step 8 and return the pen to the manufacturer letting them know of the problem. Use a new pen instead.

This Instructions for Use has been approved by the Food and Drug Administration.

BD Ultra-Fine™ is a trademark of Becton, Dickinson, and Company. SEMGLEE™ is a trademark of Mylan Pharmaceuticals, Inc.

Manufactured for:
Mylan Specialty L.P.
Morgantown, WV 26505 U.S.A.

Manufactured by: **Biocon Sdn.** Bhd., Malaysia

Approved: 6/2020
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