CLINICAL UPDATE

Brand Name	Semglee®
Generic Name	insulin glargine-yfgn
Drug Manufacturer	Mylan Pharmaceuticals Inc.

Clinical Update

TYPE OF CLINICAL UPDATE

New Formulation

FDA APPROVAL DATE

July 28, 2021

LAUNCH DATE

3rd Quarter of 2021

REVIEW DESIGNATION

N/A

TYPE OF REVIEW

Biologic License Application (BLA): 761201

DISPENSING RESTRICTIONS

N/A

Overview

INDICATION(S) FOR USE

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.

Limitations of Use: Not recommended for treating diabetic ketoacidosis.

MECHANISMS OF ACTION

The primary activity of insulin, including insulin glargine products, 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.

DOSAGE FORM(S) AND STRENGTH(S)

Injection: 100 units/mL (U-100) available as:

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

DOSE & ADMINISTRATION

- Individualize dosage based on metabolic needs, blood glucose monitoring, glycemic control, type of diabetes, prior insulin use.

- Administer subcutaneously into the abdominal area, thigh, or deltoid once daily at any time of day, but at the same time every day.
- Do not dilute or mix with any other insulin or solution.
- Rotate injection sites to reduce the risk of lipodystrophy and localized cutaneous amyloidosis.
- Closely monitor glucose when changing to Semglee® and during initial weeks thereafter.

EFFICACY

The safety and effectiveness of insulin glargine given once-daily at bedtime was compared to that of once-daily and twice-daily NPH insulin in open-label, randomized, active-controlled, parallel studies of 2,327 adult patients and 349 pediatric patients with type 1 diabetes mellitus and 1,563 adult patients with type 2 diabetes mellitus In general, the reduction in glycated hemoglobin (HbA1c) with insulin glargine was similar to that with NPH insulin.

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

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 insulin glargine or NPH insulin. Regular human insulin was administered before each meal. Insulin glargine 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 another clinical study (Study C), patients with type 1 diabetes (n = 619) were randomized to 16 weeks of basal-bolus treatment with insulin glargine or NPH insulin. Insulin lispro was used before each meal. Insulin glargine was administered once daily at bedtime and NPH insulin was administered once or twice daily.

In these 3 studies, insulin glargine and NPH insulin had similar effects on HbA1c with a similar overall rate of severe symptomatic hypoglycemia.

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**	
	Insulin Glargine	**NPH**	**Insulin Glargine**	**NPH**	**Insulin Glargine**	**NPH**
Number of subjects treated	292	293	264	270	310	309
HbA1c						
Baseline HbA1c	8.0	8.0	7.7	7.7	7.6	7.7
Adjusted mean change at trial end	+0.2	+0.1	-0.2	-0.2	-0.1	-0.1
Treatment Difference (95% CI)	+0.1 (0.0; +0.2)		+0.1 (-0.1; +0.2)		0.0 (-0.1; +0.1)	
Basal insulin dose						
Baseline mean	21	23	29	29	28	28
Mean change from baseline	-2	0	-4	+2	-5	+1
Total insulin dose						
Baseline mean	48	52	50	51	50	50

Mean change from baseline	-1	0	0	+4	-3	0
Fasting blood glucose (mg/dL)						
Baseline mean	167	166	166	175	175	173
Adj. mean change from baseline	-21	-16	-20	-17	-29	-12
Body weight (kg)						
Baseline mean	73.2	74.8	75.5	75.0	74.8	75.6
Mean change from baseline	0.1	-0.0	0.7	1.0	0.1	0.5

Type 1 Diabetes – Pediatric

Treatment duration **Treatment in combination with**	**Study D** **28 weeks** **Regular insulin**	
	Insulin Glargine + 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)	
Basal insulin dose		
Baseline mean	19	19
Mean change from baseline	-1	+2
Total insulin dose		
Baseline mean	43	43
Mean change from baseline	+2	+3
Fasting blood glucose (mg/dL)		
Baseline mean	194	191
Mean change from baseline	-23	-12
Body weight (kg)		
Baseline mean	45.5	44.6
Mean change from baseline	2.2	2.5

Clinical Studies in Adults with Type 2 Diabetes:

In a randomized, controlled clinical study (Study E) (n = 570), insulin glargine 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 with mean BMI was approximately 29.1. The rate of severe symptomatic hypoglycemia was similar in insulin glargine and NPH insulin treated patients. Insulin glargine had similar effectiveness as either once- or twice-daily NPH insulin in reducing HbA1c and fasting glucose with a similar incidence of hypoglycemia.

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**	
	Insulin Glargine	**NPH**	**Insulin Glargine**	**NPH**	**Insulin Glargine**	**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
Insulin Glargine – NPH	-0.1		+0.2		+0.2	
95% CI for Treatment difference	(-0.3; +0.1)		(0.0; +0.4)		(+0.1; +0.4)	
Basal insulin dose*						
Baseline mean	14	15	44.1	45.5	39	44
Mean change from baseline	+12	+9	-1	+7	+23	+30
Total insulin dose*						
Baseline mean	14	15	64	67	48	53
Mean change from baseline	+12	+9	+10	+13	+41	+40
Fasting blood glucose (mg/dL)						
Baseline mean	179	180	164	166	190	180
Adj. mean change from baseline	-49	-46	-24	-22	-45	-44
Body weight (kg)						
Baseline mean	83.5	82.1	89.6	90.7	100	99
Adj. mean change from baseline	2.0	1.9	0.4	1.4	3.7	4.8

* In Study G, the baseline dose of basal or total insulin was the first available on-treatment dose prescribed during the study (on visit month 1.5)

Insulin Glargine Timing of Daily Dosing

Treatment duration Treatment in Combination with:	Study H 24 weeks nsulin lispro			Study I 24 weeks ilimepiride		
	Insulin Glargine Breakfast	Insulin Glargine Dinner	Insulin Glargine Bedtime	Insulin Glargine Breakfast	Insulin Glargine 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
Basal insulin dose (U)						
Baseline mean	22	23	21	19	20	19
Mean change from baseline	5	2	2	11	18	18
Total insulin dose (U)						
Baseline mean	52	52	49	NA†	NA	NA
Mean change from baseline	2	3	2			
Body weight (kg)						
Baseline mean	77.1	77.8	74.5	80.7	82	81
Mean change from baseline	0.7	0.1	0.4	3.9	3.7	2.9

* Intent-to-treat
†Not applicable