CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761201Orig1s000

OTHER REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Medical Policy Initiatives
Division of Medical Policy Programs

PATIENT LABELING REVIEW

Date:	June 30, 2021
To:	Michael G. White, PhD Senior Regulatory Project Manager **Division of Diabetes, Lipid Disorders, and Obesity (DDLO)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Nyedra W. Booker, PharmD, MPH Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Ankur Kalola, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Patient Package Insert (PPI) and Instructions for Use (IFU)
Drug Name (established name):	SEMGLEE (insulin glargine-yfgn)
Dosage Form and Route:	injection, for subcutaneous use
Application Type/Number:	BLA 761201
Applicant:	Mylan

1 INTRODUCTION

On July 29, 2020 Mylan submitted for the Agency's review a 351(k) Biologics License Application (BLA) for SEMGLEE (insulin glargine-yfgn) injection, for subcutaneous use (BLA 761201). The purpose of this submission is to request licensure of SEMGLEE (insulin glargine-yfgn) as a proposed interchangeable biosimilar with US-LANTUS® (insulin glargine injection) for subcutaneous injection (NDA and deemed BLA 021081). This proposed interchangeable biosimilar product is the same product as the currently licensed insulin glargine product SEMGLEE (insulin glargine injection), for subcutaneous use (BLA 210605).

The proposed indication for SEMGLEE (insulin glargine-yfgn) injection, for subcutaneous use is to improve glycemic control in adults and pediatric patients with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus. SEMGLEE (insulin glargine-yfgn) injection, for subcutaneous use is not recommended for treating diabetic ketoacidosis.

This collaborative review is written by the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) in response to a request by the Division of Diabetes, Lipid Disorders, and Obesity (DDLO) on August 22, 2020, for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) and Instructions for Use (IFU) for SEMGLEE (insulin glargine-yfgn) injection, for subcutaneous use.

2 MATERIAL REVIEWED

- Draft SEMGLEE (insulin glargine-yfgn) injection, for subcutaneous use PPIs and IFUs received on July 29, 2020, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on June 8, 2021 (PPIs) and June 29, 2021 (IFUs).
- Draft SEMGLEE (insulin glargine-yfgn) injection, for subcutaneous use Prescribing Information (PI) received on July 29, 2020, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on June 8, 2021.
- Approved labeling for LANTUS (insulin glargine injection) for subcutaneous use (BLA 021081) dated November 15, 2019.
- Approved labeling for SEMGLEE (insulin glargine injection), for subcutaneous use (BLA 210605) dated June 11, 2020.

3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level and have a reading ease score of at least 60%. A reading ease score of 60% corresponds to an 8th grade reading level.

Additionally, in 2008 the American Society of Consultant Pharmacists Foundation (ASCP) in collaboration with the American Foundation for the Blind (AFB)

published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. The ASCP and AFB recommended using fonts such as Verdana, Arial or APHont to make medical information more accessible for patients with vision loss. We reformatted the PPI and IFU documents using the Arial font, size 10 and 11 respectively.

In our collaborative review of the PPIs and IFUs we have:

- simplified wording and clarified concepts where possible
- ensured that the PPIs and IFUs are consistent with the Prescribing Information (PI)
- removed unnecessary or redundant information
- ensured that the PPIs and IFUs are free of promotional language or suggested revisions to ensure that it is free of promotional language
- ensured that the PPIs and IFUs meet the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)

4 CONCLUSIONS

The PPIs and IFUs are acceptable with our recommended changes.

5 RECOMMENDATIONS

- Please send these comments to the Applicant and copy DMPP and OPDP on the correspondence.
- Our collaborative review of the PPIs and IFUs is appended to this memorandum. Consult DMPP and OPDP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the PPIs and IFUs.

Please let us know if you have any questions.

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MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	June 16, 2021
Requesting Office or Division:	Division of Diabetes, Lipid Disorders, and Obesity (DDLO)
Application Type and Number:	BLA 761201
Product Name and Strength:	Semglee (insulin glargine-yfgn) injection, 100 units per mL
Applicant/Sponsor Name:	Mylan Pharmaceuticals Inc. (Mylan)
OSE RCM #:	2020-1674-1
DMEPA Safety Evaluator:	Ariane O. Conrad, PharmD, BCACP, CDCES
DMEPA Team Leader (Acting):	Ebony Whaley, PharmD, BCPPS

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels and carton labeling for Semglee on June 16, 2021. The Division of Diabetes, Lipid Disorders, and Obesity (DDLO) requested that we review the revised container labels and carton labeling for Semglee (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

2 CONCLUSION

The Applicant implemented all of our recommendations and we have no additional recommendations at this time.

[a] Conrad, A. Comparative Threshold Analysis and Label and Labeling Review for Semglee (BLA 761201). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 Apr 14. RCM No.: 2020-1673 and 2020-1674.

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FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: June 14, 2021

To: Ann Miller, M.D.
Division of Diabetes, Lipid Disorders, and Obesity Products (DDLO)

Julie Van der Waag, Regulatory Project Manager, (DDLO)

Monika Houstoun, Associate Director for Labeling, (DDLO)

From: Ankur Kalola, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Melinda McLawhorn, Team Leader, OPDP

Subject: OPDP Labeling Comments for SEMGLEE® (insulin glargine-yfgn) injection, for subcutaneous use

BLA: 761201

In response to DDLO's consult request dated August 22, 2020, OPDP has reviewed the proposed product labeling (PI), patient package insert (PPI), Instructions for Use (IFU), and carton and container labeling for the original BLA submission for SEMGLEE® (insulin glargine-yfgn) injection, for subcutaneous use.

Labeling: OPDP's review of the proposed labeling is based on the draft labeling received by electronic mail from DDLO (Julie Van der Waag) on June 8, 2021, and we have no comments at this time.

A combined OPDP and Division of Medical Policy Programs (DMPP) review will be completed, and comments on the proposed PPI and IFU will be sent under separate cover.

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling submitted by the Sponsor to the electronic document room on May 19, 2021, and we do not have any comments.

Thank you for your consult. If you have any questions, please contact Ankur Kalola at (301) 796-4530 or Ankur.Kalola@fda.hhs.gov.

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COMPARATIVE THRESHOLD ANALYSIS AND LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)
*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	April 14, 2021
Requesting Office or Division:	Division of Diabetes, Lipid Disorders, and Obesity (DDLO)
Application Type and Number:	BLA 761201
Product Name, Dosage Form, and Strength:	Semglee[a] (insulin glargine-yfgn[b]) Injection, 100 units per mL
Total Product Content:	1,000 units per 10 mL vial 300 units per 3 mL prefilled pen
Product Type:	Single Component Product; Combination Product (Biologic-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Mylan Pharmaceuticals Inc.(Mylan)
FDA Received Date:	July 29, 2020; December 1, 2020; February 5, 2021
OSE RCM #:	2020-1673 and 2020-1674
DMEPA Safety Evaluator:	Ariane O. Conrad, PharmD, BCACP, CDCES
DMEPA Team Leader:	Ebony Whaley, PharmD, BCPPS
DMEPA Associate Director for Human Factors (Acting):	Lolita White, PharmD
DMEPA Associate Director for Nomenclature and Labeling:	Mishale Mistry, PharmD, MPH

[a] The proposed proprietary name Semglee was found conditionally acceptable by DMEPA on October 21, 2020. Of note, Mylan refers to Semglee as MYL-1501D throughout their submission.

[b] Mena-Grillasca, C. Suffix Review for Nonproprietary Name for Semglee (insulin glargine-yfgn, BLA 761201). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 Jan 15. RCM No.: 2020-2570.

1 REASON FOR REVIEW

This review evaluates the comparative (threshold) analysis and proposed product labeling submitted under BLA 761201 for Semglee (insulin glargine- yfgn) on July 29, 2020 to determine whether Mylan needs to submit the results of a comparative use human factors (CUHF) study to support their 351(k) application seeking licensure as an interchangeable biosimilar with US-licensed Lantus (BLA 021081).

Semglee is a combination product with a prefilled pen (PFP) device constituent part. Mylan is also seeking licensure for a multiple dose vial formulation. The proposed indication is to improve glycemic control in adults and children with diabetes mellitus.

1.1 PRODUCT INFORMATION

Mylan is seeking licensure of Semglee with the same indications and dosage and administration claims as US-licensed Lantus. These products are administered via subcutaneous injection and the presentations include a 10 mL multiple-dose vial and 3 mL single patient use, multi-dose prefilled pen injector. The proposed Semglee PFP (insulin glargine-yfgn) uses the (b) (6) Disposable Pen Device platform, which is the same device platform that Mylan uses for their US-licensed Semglee pen (insulin glargine).[c] Mylan claims that the proposed Semglee PFP, which is the subject of this review, was developed with the same user requirements, technical operating principles, dosing increments, sequence of operation and labeling as US-licensed Lantus® Solostar®.

This review focuses on the proposed Semglee PFP presentation. The graphic below depicts US-licensed Lantus SoloStar (top) and the Semglee PFP (bottom).[d]

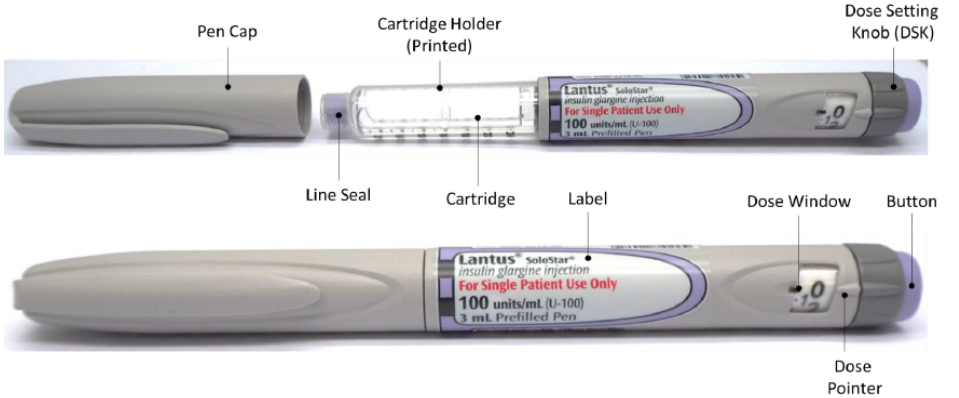

Figure 2 - Illustration of the physical characteristics of Lantus Solostar

[c] NDA 210605 for Semglee (insulin glargine) was approved on June 11, 2020. Upon approval, the marketing application ceased to exist as a new drug application and was deemed to be an approved BLA under section 351(a) of the PHS Act.

[d] As noted above, the proposed Semglee PFP is physically identical to the US-licensed Semglee PFP.

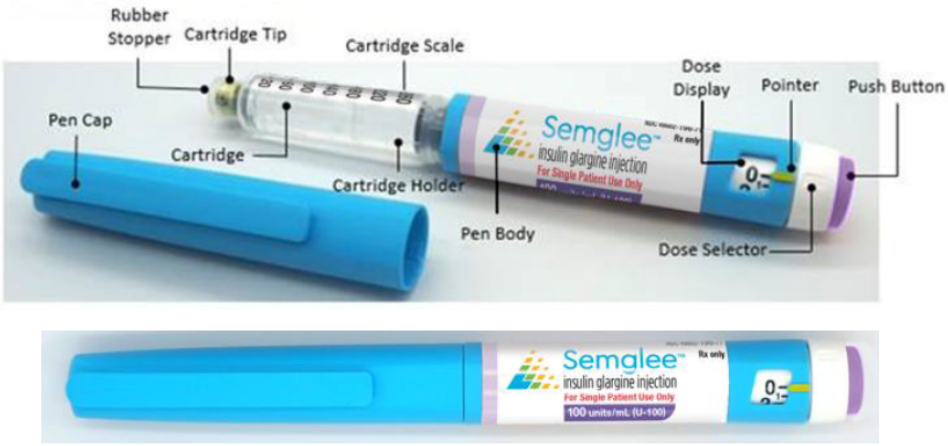

Figure 1 Illustration of the physical characteristics of Semglee PFP

1.2 REGULATORY HISTORY RELATED TO THE HUMAN FACTORS DEVELOPMENT PROGRAM

We evaluated Mylan's HF validation studies for the US-licensed Semglee (insulin glargine) pen, submitted under NDA 210605 on April 27, 2017 and February 28, 2019, in prior reviews[e,f]. The NDA received a complete response letter (CRL) on May 17, 2018 and Mylan's response to the Complete Response (CR) received a subsequent CR on August 28, 2019. Mylan submitted their response to the CRL on December 16, 2019 and NDA 210605 was subsequently approved on June 11, 2020.[g]

In a July 3, 2020 written response to their May 8, 2020 BPD type 2 meeting request (submitted to IND 140431), we advised Mylan to submit a comparative task analysis, labeling comparison, and physical comparison between the US-licensed Lantus SoloStar to their proposed interchangeable biosimilar product to support a demonstration of interchangeability.

On July 29, 2020, Mylan submitted a 351(k) application under BLA 761201 for Semglee as a proposed interchangeable biosimilar with US-licensed Lantus (U-100, BLA 021081).

2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

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[e] Conrad A. Label and Labeling and Human Factors Results Review for Semglee (NDA 210605). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 Apr 4. RCM No. 2017-842 and 2017-1868.

[f] Flint J. Label and Labeling and Human Factors Results Review for Semglee (NDA 210605). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 Aug 15. RCM No.: 2017-842-1 and 2017-1868-1.

[g] NDA 210605 for Semglee (insulin glargine) was approved on June 11, 2020. Upon approval, the marketing application ceased to exist as a new drug application and was deemed to be an approved BLA under section 351(a) of the PHS Act.

Table 1. Materials Considered for this Review	
Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B
Threshold Analysis	C
ISMP Newsletters*	N/A
FDA Adverse Event Reporting System (FAERS)*	N/A
Currently Approved Labels for US-Licensed Semglee	D
Labels and Labeling	E

N/A=not applicable for this review
*We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

To support a demonstration of interchangeability, Mylan submitted a physical comparison, comparative task analysis, and labeling comparison of the proposed insulin glargine-yfgn PFP to US-licensed Lantus SoloStar (insulin glargine U-100, BLA 021081), to identify any differences which may affect the safe and effective use of their product as interchangeable with US-licensed Lantus.

3.1 REVIEW OF COMPARATIVE THRESHOLD ANALYSIS

We provide our evaluation of the physical comparison, comparative task analysis, and labeling comparison in the sections below.

3.1.1 PHYSICAL COMPARISON

Mylan identified five physical differences between the proposed Semglee PFP and the US-licensed Lantus SoloStar that are minor differences:

1. pen length (Semglee PFP is 7 mm shorter in length)
2. injection button (color and diameter of Semglee's PFP button is 0.7 mm larger)
3. size of the dose window (Semglee PFP dose window is 1.6 mm shorter and 0.4 mm wider)
4. dose marking indicator (US-licensed Lantus SoloStar has dose indicators on the right and left of the number while the proposed pen has both indicators to the right of the number)
5. dose selector texture (US-licensed Lantus SoloStar has raised ridges while the proposed pen has recessed ridges)

Mylan concluded that the risk of these user interface design differences are acceptable and that the design differences would not impact the safe and effective use of the proposed product by the intended users. We reviewed the identified physical differences and based upon our independent heuristic review, we determined that they are unlikely to impact users' ability to complete the critical tasks needed to dial and administer the dose in a clinically meaningful way. Therefore, we determine that these differences do not warrant data from a comparative use human factors study at this time.

3.1.2 COMPARATIVE TASK ANALYSIS

Mylan identified three minor differences in tasks that they state may have a minor impact on user perception between the proposed Semglee PFP and the US-licensed Lantus SoloStar:

1. the sequence of steps to prepare the pens for priming (the tasks required are the same but are presented in a different order)
2. the pen needles compatible with the prefilled pen (both pens are compatible with BD Ultra-Fine® pen needles which screw on to the pens; however, the Semglee label recommends screwing on the pen needle while the US-licensed Lantus label recommends screwing on or pushing on the pen needle depending on the type of needle used)
3. the number of times that the needle should be primed before discarding a needle that may be blocked (can repeat up to 4 times for the proposed Semglee pen and up to 2 more times for US-licensed Lantus SoloStar).

Our review of the identified task differences find that the performance of the priming of the PFP tasks are the same, though we note that there are minor differences based on task sequence in the IFU. Specifically, the US-licensed Lantus Solostar IFU states to remove the needle cap in the priming tasks outlined in Step 3 whereas the Semglee PFP IFU states to remove the needle cap in the prior tasks of attaching a new needle in Step 2. We find this minor difference does not pose risk of use error because both IFUs instruct users to remove the needle cap and it is unlikely that the timing of this task will impact usability. We also note that cap removal is not a critical task. We also find that the differences in compatible pen needles do not pose risk of use error because the physical design of the Semglee PFP will allow for the attachment of the needles that can be screwed on like the BD Ultra-Fine® pen needles and we don't anticipate that users who may initially try to screw on the needle would be unable to attach the needle for delivery of the product. With respect to the number of times to prime the pen until a drop of insulin appears at the tip of the needle, we note that if a US-licensed Lantus Solostar user primes the Semglee PFP up to two more times due to negative transfer, they would discard a pen needle "earlier" than intended as they believe it may be blocked. However, this would not impact their ability to use the pen as intended to administer their dose. Moreover, the number of times a user primes the pen does not change how the product works or the user's ability to ultimately deliver the dose.

Based on our review of the identified task differences, we determined that they are unlikely to impact users' ability to complete the critical tasks in a clinically meaningful way. Therefore, we

determine that these differences do not warrant data from a comparative use human factors study at this time.

3.1.3 LABELING COMPARISON

Mylan provided side by side comparisons of the Instructions for Use (IFU) for the proposed Semglee PFP and US-licensed Lantus SoloStar and identified multiple differences in labeling that correspond to the physical and task differences described in Sections 3.1.1 and 3.1.2 (product specific differences), which they classify as minor. As noted above, we note that the performance of the tasks is the same and we agree with Mylan's categorization of the minor IFU differences, as these differences do not impact performance of critical tasks for this specific product in a clinically meaningful way.

In addition, Mylan submitted side by side comparisons of the container and carton labels. They note the presence of what Mylan refers to as product specific identifiers required for regulatory approval, which are also included for product differentiation, such as the product name, strength, and trade dress; therefore, we do not have any concerns with the identified differences in the container labels and carton labeling. The graphics below depicts the carton and container labels for the U.S.-licensed Semglee pen[h] and the US-licensed Lantus SoloStar, as noted in Mylan's submission.

[h] As noted above, the proposed Semglee PFP is physically identical to the US-licensed Semglee pen. Although Mylan conducted its analysis by comparing the U.S.-licensed Semglee container labels and carton labeling to U.S.-licensed Lantus, it was determined that this approach was acceptable. This is because the differences between the container labels and carton labeling of the U.S.-licensed Semglee pen and the proposed Semglee PFP (*e.g.*, the nonproprietary name) would not impact the evaluation of the differences identified above from a medication error perspective.

3.2 REVIEW OF PROPOSED LABELS AND LABELING

We performed a review of the proposed prescribing information (PI), IFU, container labels, and carton labeling submitted for the proposed Semglee pen and vial (submitted under BLA 761201) to identify areas of vulnerability that may lead to medication errors and other areas of improvement. We note that the IFU for proposed Semglee PFP is essentially the same as the previously validated IFU for the US licensed Semglee PFP approved under BLA 210605 with minor differences (*e.g.*, the difference in nonproprietary name). Additionally, given Mylan's communication of its plans to request revocation of the 351(a) license for BLA 210605 if the 351(k) for BLA 761201 is approved and they exhaust the supply of their existing 351(a) product[i], Mylan's proposal to use essentially the same design strategy is acceptable. Our review of the PI and IFUs determined that they are acceptable from a medication error perspective. Our review of the proposed carton labeling and container labels identified one area of concern and we provide our recommendation below in Section 4.1.

4 CONCLUSION & RECOMMENDATIONS

Our review of the comparative analyses and product user interface identified minor design differences between the proposed Semglee (insulin glargine-yfgn) prefilled pen and US-licensed Lantus SoloStar that do not impact the performance of critical tasks in a clinically meaningful way. Therefore, we conclude that no further information or data (e.g., data from a comparative use human factors study) is needed in this particular case. However, we provide a labeling recommendation below based on best labeling practices.

4.1 RECOMMENDATIONS FOR MYLAN PHARMACEUTICALS INC.

We refer to your intention to seek licensure of your proposed insulin aspart-yfgn prefilled pen

[i] Thomas, T. Teleconference Meeting Minutes for MYL-1501D (insulin glargine-xxxx), 100 units/mL (BLA 761201). Silver Spring (MD): FDA, CDER, OSE (US); 2020 Oct 15.

injector product as interchangeable with US-licensed Lantus Solostar and to the associated human factors (HF) considerations. Based on our review of your comparative analyses and justification, we have determined that you do not need to submit the results of a comparative use human factors study to support your 351(k) application for a proposed interchangeable biosimilar with US-licensed Lantus. Please note that if you modify the product user interface, additional human factors consideration may apply.

In addition, we recommend the following change to your proposed container labels and carton labeling prior to approval of this BLA:

A. As presented, important product information may be overlooked. To improve the readability of the net quantity and package type statements on the vial container label ("10 mL multiple-dose vial"), vial carton ("One 10 mL multiple-dose vial"), and pen cartons ("one 3 mL prefilled pen", "three 3 mL prefilled pens", "five 3 mL prefilled pens"), we recommend that you consider using (b) (4) text in the colored boxes instead of (b) (4) text.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Semglee received on December 1, 2020 from Mylan Pharmaceuticals Inc., and US-licensed Lantus.

Table 2. Relevant Product Information for Semglee and the Listed Drug		
Product Name	Semglee (MYL-1501D)	US-licensed Lantus[j]
Initial Approval Date	N/A	04/20/2000
Proper Name	insulin glargine-yfgn	Insulin glargine
Indication	to improve glycemic control in adults and pediatric patients with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus	
Route of Administration	subcutaneous	
Dosage Form	Injection	
Strength	100 units per mL	
Dose and Frequency	once daily at any time of day, but at the same time every day	
How Supplied	• Carton containing one 10 mL multiple dose vial • Carton containing one, three, or five 3 mL single patient use prefilled pens	• Carton containing one 10 mL multiple dose vial • Carton containing five 3 mL single patient use SoloStar prefilled pens
Storage	• Unopened: refrigerate (2° to 8°C [36° to 46°F]) until expiration date • Unopened: room temperature (up to 30°C [86°F]) for up to 28 days • Opened vial: refrigerated or at room temperature for up to 28 days • Opened pen: room temperature for up to 28 days (do not refrigerate)	
Intended Users	Patients with type 1 or type 2 diabetes mellitus, their caregivers and healthcare providers	
Intended Use Environment	Home, clinical	

[j] Lantus [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2021 Feb 10. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021081s073s074lbl.pdf.

APPENDIX B. PREVIOUS DMEPA REVIEWS

On February 16, 2021, we searched for previous DMEPA reviews relevant to this current review using the terms, NDA/BLA 210605, BLA 761201, and IND 140431. Our search identified 5 previous reviews[k], and we considered our previous recommendations to see if they are applicable for this current review.

[k] Conrad, A. Review of Revised Label and Labeling for Semglee (NDA 210605). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 Mar 13. RCM No. 2017-842-4.

Conrad, A. Review of Revised Label and Labeling for Semglee (NDA 210605). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 Mar 5. RCM No. 2017-842-3.

Conrad, A. Review of Revised Label and Labeling for Semglee (NDA 210605). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 Aug 21. RCM No. 2017-842-2.

Flint, J. Label and Labeling and Human Factors Results Review for Semglee (NDA 210605). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 Aug 15. RCM No. 2017-842-1 and 2017-1868-1.

Conrad, A. Label and Labeling and Human Factors Results Review for Semglee (NDA 210605). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 Apr 4. RCM No. 2017-842 and 2017-1868.

APPENDIX C. THRESHOLD ANALYSIS

The threshold analysis, submitted July 29, 2020, can be assessed in the EDR via: \\CDSESUB1\evsprod\bla761201\0001\m3\32-body-data\32p-drug-prod\insulin-bioc-bnglr\32p2-pharm-dev\comparative-analysis-of-semglee-pre-filled-pen.pdf

APPENDIX D. CURRENTLY APPROVED LABELS FOR US-LICENSED SEMGLEE (UNDER BLA 210605)[l]

Prescribing Information, Patient Package Insert, Instructions for Use[m]

- https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/210605s000lbl.pdf

[l] Semglee [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2021 Feb 10. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/210605s000lbl.pdf.

[m] This information was reviewed, but we note that these are not the proposed labeling for this 351(k) BLA.

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APPENDIX E. LABELS AND LABELING

E.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[n] along with postmarket medication error data, we reviewed the following Semglee labels and labeling submitted by Mylan Pharmaceuticals Inc.

- Container Label and Carton Labeling received on February 5, 2021
    - \\CDSESUB1\evsprod\bla761201\0016\m1\us\114-labeling\draft\carton-and-container\draft-carton-andor-container-labels.pdf
- Professional Sample Container Label and Carton Labeling received on February 5, 2021
    - Pen: \\CDSESUB1\evsprod\bla761201\0016\m1\us\114-labeling\draft\carton-and-container\draft-carton-andor-container-labels-professional-sample.pdf
- Instructions for Use received on February 5, 2021
    - Pen: \\CDSESUB1\evsprod\bla761201\0016\m1\us\114-labeling\draft\labeling\draft-instructions-for-use-text-pen-clean-pdf-malaysia.pdf
    - Vial: \\CDSESUB1\evsprod\bla761201\0016\m1\us\114-labeling\draft\labeling\draft-instructions-for-use-text-vial-clean-pdf-malaysia.pdf
- Patient Package Insert (PPI) received on February 5, 2021
    - Pen: \\CDSESUB1\evsprod\bla761201\0016\m1\us\114-labeling\draft\labeling\draft-patient-information-text-pen-clean-pdf-malaysia.pdf
    - Vial: \\CDSESUB1\evsprod\bla761201\0016\m1\us\114-labeling\draft\labeling\draft-patient-information-text-vial-clean-pdf-malaysia.pdf
- Prescribing Information received on December 1, 2020
    - \\CDSESUB1\evsprod\bla761201\0011\m1\us\114-labeling\draft\labeling\draft-labeling-text-clean-pdf.pdf

E.2 Label and Labeling Images

[n] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

8 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

ARIANE O CONRAD
04/14/2021 11:38:00 AM

EBONY A WHALEY
04/14/2021 02:31:59 PM

LOLITA G WHITE
04/14/2021 03:30:45 PM

MISHALE P MISTRY
04/15/2021 09:54:30 AM