CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208157Orig1s000

OTHER REVIEW(S)

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

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

Memorandum

Date: May 28, 2019

Callie Cappel-Lynch, Regulatory Project Manager
Division of Metabolism and Endocrinology Products (DMEP)

Monika Houstoun, Associate Director for Labeling, (DMEP)

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

CC: Melinda McLawhorn, Team Leader, OPDP

Subject: OPDP Labeling Comments for MYXREDLIN™ (insulin human in sodium chloride injection), for intravenous use

NDA: 208157

In response to DMEP's consult request dated May 1, 2018, OPDP has reviewed the proposed product labeling (PI) and carton and container labeling for the original NDA submission for Myxredlin.

PI: OPDP's comments on the proposed labeling are based on the draft PI received by electronic mail from DMEP (Cappel-Lynch) on May 22, 2019, and are provided below.

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling obtained from SharePoint on May 22, 2019, 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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/s/

ANKUR S KALOLA
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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:	May 17, 2019
Requesting Office or Division:	Division of Metabolism and Endocrinology Products (DMEP)
Application Type and Number:	NDA 208157
Product Name and Strength:	Myxredlin (insulin human in 0.9% sodium chloride), injection, 100 units per 100 mL
Applicant/Sponsor Name:	Celerity Pharmaceuticals, LLC
FDA Received Date:	May 15, 2019
OSE RCM #:	2018-905-2
DMEPA Safety Evaluator:	Ariane O. Conrad, PharmD, BCACP, CDE
DMEPA Team Leader:	Hina Mehta, PharmD

1 PURPOSE OF MEMORANDUM

Division of Metabolism and Endocrinology Products (DMEP) requested that we review the revised carton and container labels for Myxredlin (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that were made during a previous label and labeling review.[a] We note the addition of the phrase "Insulin Human (REGULAR)" for identification of type of insulin as recommended per discussion with the Office of Biotechnology Products.

2 CONCLUSION

The revised carton and container labeling are acceptable from a medication error perspective. We have no further recommendations at this time.

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[a] Conrad A. Review of Revised Label and Labeling for Myxredlin (NDA 208157). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 Mar 15. RCM No.: 2018-905-1.

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/s/

ARIANE O CONRAD
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HINA S MEHTA
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M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: May 07, 2019

TO: Lisa Yanoff, M.D.
Director (Acting)
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Office of New Drugs

FROM: Sripal Reddy Mada, Ph.D.
Pharmacologist
Division of Generic Drug Bioequivalence Evaluation (DGDBE)
Office of Study Integrity and Surveillance (OSIS)

THROUGH: John A. Kadavil, Ph.D.
Deputy Director
Division of Generic Drug Bioequivalence Evaluation (DGDBE)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: Routine inspection of clinical site supporting clinical endpoint Study CEL-HI-200 (NDA 208157)

1. Inspection Summary

The Office of Study Integrity and Surveillance (OSIS) arranged an inspection of ProSciento, Inc., Chula Vista, CA.

No objectionable conditions were observed, and Form FDA 483 was not issued at the close-out of the inspection. The final inspection classification for the inspected site is No Action Indicated (NAI).

1.1. Recommendation

After reviewing the inspectional findings, I conclude the data from the audited study CEL-HI-200 (NDA 208157) are reliable to support a regulatory decision.

2. Inspected Study:

The following study was audited during the inspection:

NDA 208157

Study Number: CEL-HI-200
Study Title: "A Double-Blind, Randomized, Crossover, Euglycemic Glucose Clamp Study to Test for Bioequivalence between Celerity's Premixed Regular Human Insulin (rDNA origin) Injection 1 USP unit/mL in 0.9% Sodium Chloride and Novolin® R in Healthy Subjects"
Dates of conduct: 05/22/2017 – 10/21/2017

Site:
Site Name: ProSciento, Inc.
Street Address: 855 3rd Avenue, Suite 4400
City, State: Chula Vista, CA, 91911
Investigator Name: Rachel Peterson, MD

3. Inspectional Findings

ORA investigators Lakecha N. Lewis, CSO (Lead) and Marilyn S. Babu, CSO inspected ProSciento, Inc., Chula Vista, CA from April 08-12, 2019.

The inspection included a thorough examination of study records, case report forms (CRFs), informed consent process, protocol deviations, institutional review board approvals, sponsor and monitor correspondence, test article accountability and storage, randomization, and adverse events.

At the conclusion of the inspection, investigators Lakecha Lewis and Marilyn Babu did not observe any objectionable conditions and did not issue Form FDA 483 to the clinical site.

4. Conclusion:

After reviewing the inspectional findings, I conclude the data from the audited study are reliable. (b) (4) [redacted]

Sripal Reddy Mada, Ph.D.
Pharmacologist

Final Classification:

NAI - ProSciento, Inc.
Chula Vista, CA 91911
FEI#: 3004445267

cc:
OTS/OSIS/Kassim/Mitchell/Fenty-Stewart
OTS/OSIS/DNDBE/Bonapace/Dasgupta/Ayala/Biswas
OTS/OSIS/DGDBE/Cho/Kadavil/Choi/Skelly/Au/Mada
ORA/OMPTO/OBIMO/ORABIMOW.Correspondence@fda.hhs.gov

Draft: SRM 05/02/2019
Edit: YMC 05/03/2019; JAK 05/07/2019

ECMS: Cabinets/CDER_OTS/Office of Study Integrity and Surveillance/INSPECTIONS/BE Program/CLINICAL/ProSciento, Inc., Chula Vista, CA, USA

OSIS File #: BE 8263 (NDA 208157)
(b) (4)

FACTS: 11888324

Attachment 1

(b) (4)

Site:
Site Name: ProSciento, Inc.
Street Address: 855 3rd Avenue
City, State: Chula Vista, CA, 91911
Investigator Name: (b) (4)

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/s/

SRIPAL R MADA
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JOHN A KADAVIL
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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:	March 15, 2019
Requesting Office or Division:	Division of Metabolism and Endocrinology Products (DMEP)
Application Type and Number:	NDA 208157
Product Name and Strength:	Myxredlin (regular human insulin in 0.9% sodium chloride), injection, 100 units per 100 mL
Applicant/Sponsor Name:	Celerity Pharmaceuticals, LLC
FDA Received Date:	February 28, 2019
OSE RCM #:	2018-905-1
DMEPA Safety Evaluator:	Ariane O. Conrad, PharmD, BCACP, CDE
DMEPA Team Leader:	Hina Mehta, PharmD

1 PURPOSE OF MEMORANDUM

Division of Metabolism and Endocrinology Products (DMEP) requested that we review the revised carton and container labels for Myxredlin (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] Of note, Celerity responded to each labeling recommendation, provided comparisons to the prior iteration of labeling, and clarified that each labeled carton contains a single container of Myxredlin which will be packed into a "shipping carton" containing 12 units.[b]

[a] Conrad A. Label and Labeling Review for Myxredlin (NDA 208157). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 Feb 6. RCM No.: 2018-905.

[b] Celerity Pharmaceuticals LLC. Cover Letter Re: Labeling Amendment for regular human insulin in sodium chloride injection (NDA 208157). Submitted to FDA February 28, 2019. Available via: \\cdsesub1\evsprod\nda208157\0010\m1\us\cover-letter-2019feb28.pdf.

Celerity Pharmaceuticals LLS. Annotated Draft Labeling Text for regular human insulin in sodium chloride injection (NDA 208157). Submitted to FDA February 28, 2019. Available via: \\cdsesub1\evsprod\nda208157\0010\m1\us\carton-container-annotated-comparison-novo-nordisk-novolin.pdf.

2 CONCLUSION

The revised carton and container labeling are unacceptable from a medication error perspective. We provide additional recommendations for the sponsor in Section 3.

3 RECOMMENDATIONS FOR CELERITY

We recommend the following be implemented prior to approval of this NDA:

A. The barcode is denoted by a placeholder on the labels and labeling. Therefore, we request you add the product's linear barcode to each Myxredlin carton and container label as required per 21CFR 201.25(c)(2). In addition, ensure that that the barcode is surrounded by sufficient white space to allow scanners to correctly read the barcode in accordance with 21 CFR 201.25(c)(i). Please resubmit for review.

B. Based on the clarification you provided regarding your packaging, we note that you plan to package cartons containing 1 Galaxy container within a larger carton containing 12 units. We note that the carton containing 12 units of Myxredlin, the labeled carton containing 1 unit of Myxredlin, and the container label each use different NDC package codes. However, the container label for one unit and the carton labeling for 1 unit should have the same NDC package code. Revise the NDC numbers so that the carton labeling for 1 unit and container labels use the same NDC package code and resubmit for review.

C. Revise the word "units" to appear with a lower case "U" in your product labeling to minimize the risk of readers misinterpreting the "U" as the number zero (0) in the product strength.

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M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: February 21, 2019

TO: Lisa Yanoff, M.D.
Director (Acting)
Division of Metabolism and Endocrinology Products (DMEP)
Office of Drug Evaluation II (ODEII)
Office of New Drugs (OND)

FROM: Li-Hong Yeh, Ph.D.
Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

Kara A. Scheibner, Ph.D.
Division of Generic Drug Bioequivalence Evaluation (DGDBE)
OSIS

THROUGH: Arindam Dasgupta, Ph.D.
Deputy Director
DNDBE, OSIS

SUBJECT: Surveillance inspection of (b) (4) (b) (4)

1. Inspection Summary

OSIS inspected the analytical portion (Studies CA19891-01 (Regular Human Insulin) and CA19891-02 (Human C-peptide)) of the clinical Study CEL-HI-200 (NDA 208157, Regular Human Insulin) conducted at (b) (4) .

We did not observe objectionable conditions and did not issue Form FDA 483 at the inspection close-out. The final inspection classification is No Action Indicated (NAI).

There were 3 corrective actions from the previous ((b) (4)) inspection of the site: (1) revised procedure for sample entry in the Watson system, (2) revised procedure for archiving the log books, and (3) revised procedure for labeling the condition of the sample when received. The site implemented these corrective actions.

1.1. Recommendation

Based on our review of the inspectional findings, we conclude the analytical data from the audited studies are reliable to support a regulatory decision. Analytical data from studies using similar methods conducted between the previous inspection ((b) (4)) and the end of the current surveillance interval should be considered reliable without an inspection.

2. Inspected Analytical Studies

Study CA19891-01 (NDA 208157)
"Determination of Human Insulin in Human Serum Samples from "A Double-Blind, Randomized, Crossover, Euglycemic Glucose Clamp Trial to Test for Bioequivalence between Celerity's Premixed Human Insulin (rDNA origin) Injection 1 USP unit/mL in 0.9% Sodium Chloride and Novolin® R in Healthy Subjects (CEL-HI-200)" by ELISA"

Sample Analysis Period: 10/31/2017 – 11/15/2017

Study CA19891-02 (NDA 208157)
"Determination of C-peptide in Human Serum Samples from "A Double-Blind, Randomized, Crossover, Euglycemic Glucose Clamp Trial to Test for Bioequivalence between Celerity's Premixed Human Insulin (rDNA origin) Injection 1 USP unit/mL in 0.9% Sodium Chloride and Novolin® R in Healthy Subjects (CEL-HI-200)" by ELISA"

Sample Analysis Period: 11/17/2017 – 01/11/2018

3. Scope of Inspection

Analytical Site: (b) (4)

OSIS scientists Li-Hong Yeh, Ph.D. and Kara A. Scheibner, Ph.D. audited the analytical studies **CA19891-01 and CA19891-02** at (b) (4) from (b) (4) – (b) (4) .

The inspection included a thorough examination of study records,

facilities, laboratory equipment, method validation, sample analyses, and interviews with the site's management and staff.

4. Inspectional Findings

At the conclusion of the inspection, we did not observe objectionable conditions. We did not issue Form FDA 483 to (b) (4)

5. Conclusion

After reviewing the inspectional findings, we conclude that the analytical data from Studies CA19891-01 and CA19891-02 of the clinical Study CEL-HI-200 are reliable to support a regulatory decision.

Analytical data from studies using similar analytical methods conducted between the previous inspection ((b) (4) and the end of the current surveillance interval should be considered reliable without an inspection.

Li-Hong Yeh, Ph.D.
Chemist
Kara A. Scheibner, Ph.D.
Pharmacologist

Final Classification:
Analytical site
NAI - (b) (4)

cc: OTS/OSIS/Kassim/Mitchell/Fenty-Stewart
OTS/OSIS/DNDBE/Bonapace/Dasgupta/Ayala/Biswas/Yeh
OTS/OSIS/DGDBE/Cho/Kadavil/Choi/Skelly/Au/Scheibner
ORA/OMPTO/OBIMO/FDAInternational BIMO@fda.hhs.gov

Draft: PY 02/16/2019; 02/21/2019
Edit: KAS 02/20/2019; RCA 2/20/2019, 2/21/2019; AD 2/20/2019,2/21/2019

ECMS:
http://ecmsweb.fda.gov:8080/webtop/drl/objectId/0b0026f881a0949a

OSIS File #:
Direct inspections
BE #: (b) (4)

FACTS: (b) (4)

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/s/

LI-HONG P YEH
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02/22/2019 10:14:41 AM

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02/22/2019 01:54:05 PM

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:	February 6, 2019
Requesting Office or Division:	Division of Metabolism and Endocrinology Products (DMEP)
Application Type and Number:	NDA 208157
Product Name and Strength:	Myxredlin (regular human insulin in 0.9% sodium chloride), injection, 100 units per 100 mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription
Applicant/Sponsor Name:	Celerity Pharmaceuticals, LLC
FDA Received Date:	April 26, 2018, October 26, 2018, and November 21, 2018
OSE RCM #:	2018-905
DMEPA Safety Evaluator:	Ariane O. Conrad, PharmD, BCACP, CDE
DMEPA Team Leader:	Hina Mehta, PharmD

1 REASON FOR REVIEW

This review evaluates the proposed labels and labeling for Myxredlin (regular human insulin in 0.9% sodium chloride), originally submitted under NDA 208157 on April 26, 2018, to identify areas of vulnerability that may lead to medication errors. The listed drug product (Novolin R, NDA 019938) was approved June 25, 1991.

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.

Table 1. Materials Considered for this Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B
Human Factors Study	n/a
ISMP Newsletters	n/a
FDA Adverse Event Reporting System (FAERS)*	n/a
Comparison of labeling for the listed drug	C
Labels and Labeling	D

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

3 FINDINGS & RECOMMENDATIONS

Tables 2 and 3 below include the identified medication error issues with the submitted packaging, label and labeling, DMEPA's rationale for concern, and the proposed recommendation to minimize the risk for medication error.

Table 2: Identified Issues and Recommendations for Division of Metabolism and Endocrinology Products (DMEP)

Prescribing Information (PI)			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
Highlights of Prescribing Information			
Dosage and Administration			
1.	The dosing information currently states, (b) (4)	The product is only available in one concentration (as compared to the RLD, which can be	Revise the statement as follows: "Intravenous use: Administer by intravenous

	(b) (4) [redacted]	diluted to a concentration of 0.5 unit/mL or 1 unit/mL before intravenous infusion); thus, we determined that use of the concentration statement here may imply that this is a concentration that is achieved by modifying the product instead of the commercially available concentration of the product. In addition, we determined that the route of administration statement could be improved for clarity.	infusion ONLY under medical supervision."
Dosage Forms and Strengths			
1.	(b) (4) [redacted] which we determined could be revised for improved clarity.	We recommend revising the statement to remove language that is not needed in this section (and should be in Section 16 of the PI instead) for improved readability of this information.	Revise the language in this section to read as follows: "MYXREDLIN: 100 units Regular Human Insulin in 100 mL of 0.9% Sodium Chloride Injection (1 unit/mL) infusion bag"
Full Prescribing Information			
Section 3 Dosage Forms and Strengths			
1.	The current statement reads (b) (4) [redacted]	We recommend revising the statement to remove language that is not needed in this section (and should be in Section 16 of the PI instead) for improved readability of this information.	Revise the language in this section to read as follows: "MYXREDLIN Injection, 100 units Regular Human Insulin in 100 mL 0.9% Sodium Chloride Injection (1 unit/mL) as a clear, colorless solution."

	(b) (4) which we determined could be revised for improved clarity.		
Section 16 How Supplied/Storage and Handling			
1.	The current statement reads (b) (4) which we determined could be revised for improved clarity.	We recommend revising the statement to remove language that is not needed in this section for improved readability of this information.	Revise the language in this section to read as follows: "MYXREDLIN (Regular Human Insulin in 0.9% Sodium Chloride Injection) is a clear and colorless solution containing 100 units per 100 mL (1 unit/mL) available as: 100 mL PL 2501 GALAXY plastic container, package of 12 • NDC 67798-3322-1"
2.	The current statement reads (b) (4)	We recommend revising the statement to remove language that is not needed in this section for improved readability of this information.	Revise the language in this section to read as follows: "MYXREDLIN should be stored in the refrigerator (36° - 46°F [2° - 8°C]). Do not use after the expiration date printed on the carton and container label. MYXREDLIN can be kept at room temperature if refrigeration is not available. Store in a cool temperature (not above 77°F [25°C]) [see USP Controlled Room Temperature]. Discard MYXREDLIN after 30 days if kept at room temperature. Do not freeze and do not use MYXREDLIN if it has been frozen. Keep MYXREDLIN in

	(b) (4) 		the carton to protect from light. Do not expose to heat or light."

Table 3: Identified Issues and Recommendations for Celerity (entire table to be conveyed to Applicant)

General Comments: Container Labels and Carton Labeling			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
1.	The established name is not at least half the size of the proprietary name.	The proprietary name and established name appear to be the same size and, thus, are not clearly differentiated.	Revise the established name to at least half the size of the proprietary name to be in accordance with 21 CFR 201.10(g)(2).
2.	The statement (b) (4) 	Inconsistent information can contribute to improper storage of the product.	Revise the statement as follows for consistency with the prescribing information: "Refrigerate at 36° - 46°F [2° - 8°C]. May store at room temperature (not above 77°F [25°C]) [see USP Controlled Room Temperature]. for up to 30 days. Discard after 30 days if stored at room temperature."

3.	As currently presented, the format for the expiration date is not defined.	The expiration date should be clear to the end user to minimize confusion and reduce the risk for deteriorated drug medication errors.	Identify the format you intend to use for the expiration date. FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a hyphen or a space be used to separate the portions of the expiration date.
Carton Labeling			
1.	The proposed carton contains the statement (b) (4)	The route of administration statement should be clearer to communicate that the product can only be administered via intravenous infusion.	Revise the statement to read "For intravenous infusion only". In addition, consider increasing the font size and using bold font to increase the prominence of the statement.
2.	The proposed carton contains the statement (b) (4) GALAXY Single Dose Container" on the PDP, which is not consistent	Section 16 of the PI states that the product is available in cartons containing 12 units but the statement on the carton communicates that it contains 1 container.	Revise the statement to read "12 GALAXY containers".

	with the language in the PI.		
3.	There is no statement regarding product identifiers in the submission.	In September 2018, FDA released draft guidance on product identifiers required under the Drug Supply Chain Security Act.[1] The Act requires manufacturers and repackagers, respectively, to affix or imprint a product identifier to each package and homogenous case of a product intended to be introduced in a transaction in(to) commerce beginning November 27, 2017, and November 27, 2018, respectively. [1]The draft guidance is available from: https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm621044.pdf	Review the draft guidance to determine if the product identifier requirements apply to your product's labeling.
4.	The "Rx Only" statement appears prominently in large bold font on the PDP.	The "Rx Only" statement appears more prominent than the route of administration statement on the label.	Decrease the prominence of the statement "Rx Only" by removing the bold font and decreasing the font size as this information appears more prominent than other important information on the PDP.

4 CONCLUSION

Our evaluation of the proposed label and labeling identified areas of vulnerability that may lead to medication errors. Above, we have provided recommendations in Table 2 for the Division and Table 3 for Celerity. We ask that the Division convey Table 3 in its entirety to Celerity so that recommendations are implemented prior to approval of this NDA.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Myxredlin received on November 21, 2018 from Celerity, and the listed drug (LD).

Table 2. Relevant Product Information for Myxredlin and the Listed Drug

Product Name	**Myxredlin**	**Novolin R (NDA 019938)**
Initial Approval Date	n/a	June 25, 1991
Active Ingredient	Regular human insulin	Insulin human
Indication	short-acting human insulin indicated to improve glycemic control in adults and pediatric patients with diabetes mellitus	short-acting human insulin indicated to improve glycemic control in adults and pediatric patients with diabetes mellitus
Route of Administration	Intravenous infusion	Subcutaneous injection or intravenous infusion
Dosage Form	solution	Solution
Strength	100 units per 100 mL (1 unit/mL)	100 units/mL
Dose and Frequency	Administer intravenously ONLY under medical supervision at a concentration of 1 unit/mL	Subcutaneous injection: inject 30 minutes before a meal Intravenous infusion: administer under medical supervision at concentrations from 0.05 unit/mL to 1 unit/mL
How Supplied	100 units per 100 mL of 0.9% sodium chloride solution in 100 mL containers	10 mL vial 3 mL Novolin R FlexPen
Storage	Refrigerate (36° -46°F [2° - 8°C]). If refrigeration is not possible, can store at room temperature (not above 77°F [25°C]) [see USP Controlled Room Temperature]. Discard after 30 days if kept at room temperature.	Unopened pen or vial: refrigerate until expiration date Unopened vial: room temperature for 42 days Unopened pen: room temperature for 28 days In-use vial: room temperature or (b) (4) for 42 days In-use pen: room temperature for 28 days

APPENDIX B. PREVIOUS DMEPA REVIEWS

On January 14, 2019, we searched DMEPA's previous reviews using the terms, IND 124943 or NDA 208157. Our search identified 0 previous reviews.

APPENDIX C. COMPARISON OF LABELING FOR THE LISTED DRUG

Celerity submitted the following documents comparing their proposed labeling to the approved labeling for Novolin R on April 26, 2018:

Prescribing Information Side by Side Comparison:
\\cdsesub1\evsprod\nda208157\0000\m1\us\annotated-comparison-pi-novo-nordisk-novolin-r.pdf

4-26-18 comparison to RLD labeling.pdf

Carton and Container Side by Side Comparisons:
\\cdsesub1\evsprod\nda208157\0000\m1\us\carton-container-annotated-comparison-novo-nordisk-novolin.pdf

4-26-18 Carton and Container labels.pdf

APPENDIX D. LABELS AND LABELING

D.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[a] along with postmarket medication error data, we reviewed the following Myxredlin labels and labeling submitted by Celerity.

- Container label received on April 26, 2018
- Carton labeling received on April 26, 2018
- Prescribing Information received on November 21, 2018
    - \\cdsesub1\evsprod\nda208157\0008\m1\us\pi-draft-labeling-text-original-draft-v3.pdf

D.2 Label and Labeling Images

2 Page(s) of Draft Labeling have been Withheld in Full as B4 (CCI/TS) immediately following this page

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

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