CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

212640Orig1s000

OTHER REVIEW(S)

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:	October 31, 2019
Requesting Office or Division:	Division of Neurology Products (DNP)
Application Type and Number:	NDA 212640
Product Name and Strength:	Exservan (riluzole) oral film, 50 mg
Applicant/Sponsor Name:	Aquestive Therapeutics
OSE RCM #:	2019-339-3
DMEPA Safety Evaluator:	Chad Morris, PharmD, MPH
DMEPA Team Leader (Acting):	Briana Rider, PharmD, CPPS

1 PURPOSE OF MEMORANDUM

Aquestive Therapeutics submitted revised carton labeling on October 25, 2019 for Exservan in response to a recommendation developed upon internal discussion with The Office of Prescription Drug Promotion (OPDP). We concurred with OPDP to recommend Aquestive add the statement "Do not administer with liquids" after the statement "Keep in place until film dissolves" under the "How to Use" section on the carton labeling.[a] The Division of Neurology Products (DNP) requested that we review the revised carton labeling for Exservan (Appendix A).

2 CONCLUSION

Aquestive implemented the recommendation, and we have no additional recommendations at this time.

[a] Recommendation submitted to Aquestive Therapeutics via email on October 23, 2019. Email available at: \\cdsesub1\evsprod\nda212640\0011\m1\us\112-other-corr\request-for-information-additional-labeling-comments.pdf

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BRIANA B RIDER
10/31/2019 09:16:59 AM

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

PATIENT LABELING REVIEW

Date:	October 23, 2019
To:	William Dunn, MD Director **Division of Neurology Products (DNP)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Sharon W. Williams, MSN, BSN, RN Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Sapna Shah, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Instructions for Use
Drug Name (established name):	EXSERVAN (riluzole)
Dosage Form and Route:	oral film
Application Type/Number:	NDA 212640
Applicant:	Aquestive Therapeutics

1 INTRODUCTION

On January 31, 2019, Aquestive Therapeutics. submitted for the Agency's review an Orignal New Drug Application (NDA) for EXSERVAN (riluzole) oral film. The purpose of the submission is to seek approval for marketing EXSERVAN (riluzole) for the treatment of amyotrophic lateral sclerosis (ALS).

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 Neurology Products (DNP) on April 3, 2019 for DMPP and OPDP respectively to review the Applicant's proposed IFU for EXSERVAN.

2 MATERIAL REVIEWED

- Draft EXSERVAN (riluzole) IFU received on January 31, 2019, and received by DMPP and OPDP on October 17, 2019.
- Draft EXSERVAN (riluzole) use Prescribing Information (PI) received on January 31, 2019, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on October 17, 2019.

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.

Additonally, 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.

In our collaborative review of the IFU we:

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

4 CONCLUSIONS

The IFU is 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 IFU 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 IFU.

Please let us know if you have any questions.

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LASHAWN M GRIFFITHS
10/23/2019 02:43:49 PM

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

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

Memorandum

Date: October 21, 2019

To: Rainer Paine, M.D.
Division of Neurology Products (DNP)

Michelle Mathers, Regulatory Project Manager, (DNP)

Tracey Peters, Associate Director for Labeling, (DNP)

From: Sapna Shah, PharmD, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Aline Moukhtara, RN, MPH, Team Leader, OPDP

Subject: OPDP Labeling Comments for EXSERVAN™ (riluzole) oral film

NDA: 212640

In response to the DNP consult request dated April 3, 2019, OPDP has reviewed the proposed product labeling (PI), Instructions for Use (IFU), and carton and container labeling for the original NDA submission for EXSERVAN™ (riluzole) oral suspension (Exservan).

PI: OPDP's has reviewed the proposed labeling for the draft PI received by electronic mail from DNP (Michelle Mathers) on October 17, 2019, and we do not have any comments at this time.

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

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling submitted by the sponsor on September 25, 2019, and our comments are provided below.

Thank you for your consult. If you have any questions, please contact Sapna Shah (240) 402-6068 or Sapna.Shah@fda.hhs.gov.

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SAPNA P SHAH
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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: October 4, 2019

TO: Billy Dunn, MD
Director
Division of Neurology Products (DNP)
Office of New Drugs

Bing Li, Ph.D.
Acting Director
Office of Bioequivalence
Office of Generic Drugs

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

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

SUBJECT: Routine inspection of Syneos Health, Inc. (fka inVentiv Health Clinical Research Services), Miami, FL.

1 Inspection Summary

The Office of Study Integrity and Surveillance (OSIS) arranged an inspection of study 162020 (NDA 212640) conducted at Syneos Health, Inc. (fka inVentiv Health Clinical Research Services), Miami, FL.

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

1.1. Recommendation

After reviewing the inspectional findings, I conclude the data from the audited study is reliable to support a regulatory decision.

2 Inspected Study:

NDA 212640

Study Number: 162020
Study Title: "A Pivotal, Open-Label, Randomized, Single Dose, Five-period, Replicate Crossover, Comparative Bioavailability Study of Riluzole 50 mg Oral Soluble Films and RILUTEK® 50 mg Tablets in Healthy Male and Female Volunteers under Fasting Conditions with Evaluation of Food Effect"
Dates of conduct: 02/16/2017 – 04/07/2017

Clinical site: Syneos Health, Inc. (fka inVentiv Health Clinical Research Services)
1951 Northwest 7th Avenue, Suite 450
Miami, FL 33136

ORA investigator Ladislav Kermet inspected Syneos Health, Inc. (fka inVentiv Health Clinical Research Services), Miami, FL, on September 09-11, 2019.

The inspection included a thorough examination of case report forms, medical records and worksheets, inclusion and exclusion criteria, randomization schedules, correspondence between the IRB and clinical investigator, correspondence between the sponsor and the clinical investigator, informed consent forms for all subjects screened, collection, processing, and storage of study samples, monitoring visits and electronic records, and test article records and reserve samples.

3 Inspectional Findings

At the conclusion of the inspection, investigator Ladislav Kermet 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 study 162020 (NDA 212640) is reliable. In addition, the data from studies of similar design that were not audited but submitted to pending applications (**Attachment 1**) are reliable for Agency review.

Based on the inspectional findings, studies of similar design conducted between the previous inspection (December 2016) and

the end of the current surveillance interval should be considered reliable without an inspection.

Sripal Reddy Mada, Ph.D.
Pharmacologist

Final Classification:

NAI - Syneos Health, Inc. (fka inVentiv Health Clinical Research Services)
Miami, FL
FEI#: 3011234940

cc:
OTS/OSIS/Kassim/Dasgupta/Mitchell/Fenty-Stewart/Taylor/Haidar/Mirza
OTS/OSIS/DNDSI/Bonapace/Au/Ayala/Biswas
OTS/OSIS/DGDSI/Cho/Kadavil/Choi/Skelly/Lewin/Mada
ORA/OMPTO/OBIMO/ORABIMOE.Correspondence@fda.hhs.gov

Draft: SRM 09/25/2019
Edit: YMC 09/26/2019; JAC 10/3/2019

ECMS: Cabinets/CDER_OTS/Study Integrity and Surveillance/INSPECTIONS/BE Program/CLINICAL/Syneos Health, Inc. (fka inVentiv Health Clinical Research Services), Miami, FL, USA

OSIS File #: BE 8472 (NDA 212640)

Non-Responsive

FACTS: 11924239

Attachment 1

Studies not audited but submitted to pending applications

Application #	Study #	Study Type	Drug Name	Dates of conduct
Non-Responsive				

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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:	October 2, 2019
Requesting Office or Division:	Division of Neurology Products (DNP)
Application Type and Number:	NDA 212640
Product Name and Strength:	Exservan (riluzole) oral film, 50 mg
Applicant/Sponsor Name:	Aquestive Therapeutics
FDA Received Date:	September 25, 2019
OSE RCM #:	2019-339-2
DMEPA Safety Evaluator:	Chad Morris, PharmD, MPH
DMEPA Team Leader (Acting):	Briana Rider, PharmD, CPPS

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container label and carton labeling received on September 25, 2019 for Exservan. The Division of Neurology Products (DNP) requested that we review the revised container label and carton labeling for Exservan (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] Morris, C. Label and Labeling Review MEMO for Exservan (riluzole) NDA 212640. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 SEP 06. RCM No.: 2019-339-1.

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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:	September 6, 2019
Requesting Office or Division:	Division of Neurology Products (DNP)
Application Type and Number:	NDA 212640
Product Name and Strength:	Exservan (riluzole) oral film, 50 mg
Applicant/Sponsor Name:	Aquestive Therapeutics
FDA Received Date:	August 28, 2019
OSE RCM #:	2019-339-1
DMEPA Safety Evaluator:	Chad Morris, PharmD, MPH
DMEPA Team Leader (Acting):	Briana Rider, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container label and carton labeling received on August 28, 2019 for Exservan. The Division of Neurology Products (DNP) requested that we review the revised container label and carton labeling for Exservan (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 revised container label and carton labeling are unacceptable from a medication error perspective. We provide recommendations for Aquestive Therapeutics in Section 3.

3 RECOMMENDATIONS FOR AQUESTIVE THERAPEUTICS

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

[a] Morris, C. Label and Labeling Review for Exservan (riluzole) NDA 212640. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 JUL 24. RCM No.: 2019-339.

Table 1. Identified Issues and Recommendations for Aquestive Therapeutics (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Label(s) and Carton Labeling			
1.	The affirmative statement "(b) (4) " was added to the principal display panel. However, the statement does not clearly instruct what should be dissolved.	Lacks clarity.	Consider revising the statement to read "Place film on top of tongue until film dissolves" for clarity and consistency with the instructions on the back panel.
2.	The phrase "(b) (4) " is included on the label and labeling.	The product does not have a (b) (4).	Remove all references to "(b) (4) ."
Container Label			
1.	The warning "Keep product in foil pouch until ready to use" is located on the back panel.	Prominence can be improved to reduce the risk for improper storage medication errors.	Consider relocating the warning "Keep product in foil pouch until ready to use" to the principal display panel.
2.	The usual dose statement is not located in the "How to Use" section.	Prominence can be improved.	We recommend you relocate the usual dose statement to the "How to Use" section, similar to how it appears on the carton labeling.
Carton Labeling			
1.	The human-readable portion of the product identifier and the 2D data matrix barcode, required under the Drug Supply Chain Act (DSCSA), are not located near each other.	Not in alignment with recommendations found within the FDA draft guidance on product identifiers [b].	The human-readable product identifier contains the NDC, serial number, lot, and expiration date. The DSCSA guidance on product identifiers recommends the format below for the human-readable portion of the product identifier. The guidance also recommends that the human-readable portion be located near

[b] Guidance for Industry: Product Identifiers Under the Drug Supply Chain Security Act Questions and Answers. 2018. Available from https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM621044.pdf

Table 1. Identified Issues and Recommendations for Aquestive Therapeutics (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			the 2D data matrix barcode. NDC: [insert product's NDC] SERIAL: [insert product's serial number] LOT: [insert product's lot number] EXP: [insert product's expiration date]
2.	The usual dosage statement clutters the side panel.	Readability can be improved.	We note, you added the usual dosage statement to the side and back panels. Since the statement is now on the back panel, it can be removed from the side panel.

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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:	July 24, 2019
Requesting Office or Division:	Division of Neurology Products (DNP)
Application Type and Number:	NDA 212640
Product Name and Strength:	Exservan (riluzole) oral film, 50 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Aquestive Therapeutics
FDA Received Date:	January 31, 2019
OSE RCM #:	2019-339
DMEPA Safety Evaluator:	Chad Morris, PharmD, MPH
DMEPA Team Leader (Acting):	Briana Rider, PharmD

1 REASON FOR REVIEW

As part of the approval process for Exservan (riluzole) oral film, the Division of Neurology Products (DNP) requested that we review the proposed Exservan Prescribing Information (PI), Instructions for Use (IFU), Container label, and Carton labeling for areas of vulnerability that may lead to medication errors.

2 REGULATORY HISTORY

NDA 212640 is a 505(b)(2), developed under IND 130939. The listed drug product is Rilutek, NDA 020599.

3 MATERIALS 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
ISMP Newsletters*	C (N/A)
FDA Adverse Event Reporting System (FAERS)*	D (N/A)
Other	E (N/A)
Labels and Labeling	F

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

4 FINDINGS AND RECOMMENDATIONS

We note, clinical manifestations of amyotrophic lateral sclerosis (ALS) may affect the ability of patients to successfully open the pouch containing the oral film. We discussed this risk with DNP, and find the benefit of adding this dosage form to the current treatment options in its current packaging outweighs the risk that patients may experience difficulty opening the pouch for the following reasons. First, the oral film dosage form may offer advantage over other forms of riluzole because patients with ALS may have difficulties swallowing the currently marketed dosage forms (tablet or oral solution). Next, we anticipate patients with ALS will have a caregiver to assist with medication administration, which will help to mitigate the risk associated with a patient's difficulty opening the pouch. Lastly, if prescribers determine the patient's disease state limitations preclude them from using the proposed product, then the tablets and oral solution may be safe and effective alternatives.

Tables 2 and 3 below include the identified medication error issues with the submitted Prescribing Information (PI), Instructions for Use (IFU), Container label, and Carton labeling, our

rationale for concern, and the proposed recommendation to minimize the risk for medication error.

Table 2. Identified Issues and Recommendations for Division of Neurology Products (DNP)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Instructions for Use			
1.	The orientation and format of the expiration date as presented in Step 1 are inconsistent with the proposed pouch label.	Can be improved for clarity.	We recommend all images of the packaging/labeling in the IFU are consistent with the commercial presentation.
2.	The images are not labeled.	Inconsistent with current practice.	We recommend you label each image as Figure 1, 2, etc. and refer to that image with a statement such as "see Figure" in the respective sentence.

Table 3. Identified Issues and Recommendations for Aquestive Therapeutics (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Label(s) and Carton Labeling			
1.	There is a warning containing a negative statement (that is, (b) (4)) on the principal display panel (PDP) of the carton labeling.	Post-marketing reports suggest negative statements may be misinterpreted as an affirmative action.	We recommend you revise the negative statement "(b) (4) " to an affirmative statement. We recommend the revised statement should also be placed on the PDP of the container label.
2.	The usual dose statement is not present.	Not in alignment with 21 CFR 201.55.	We recommend you add the statement "Recommended Dosage: See prescribing information" to the side panel of the carton labeling and the back panel of the foil pouch.
3.	There may not be sufficient white space surrounding the linear barcodes. Specifically, the proprietary and established names are close to the linear barcode	The barcode should be surrounded by sufficient white space to allow scanners to correctly read the barcode in accordance with 21 CFR 201.25(c)(i).	Ensure the linear barcodes are surrounded by sufficient white space.

Table 3. Identified Issues and Recommendations for Aquestive Therapeutics (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	on the carton labeling. Similarly, the black area for the lot/exp date is close to the linear barcode on the container label.		
Container Label(s)			
1.	The "Rx only" and net quantity statements are more prominent than the established name.	Not in alignment with our draft guidance[a].	Ensure the proprietary name, established name, and strength are the most prominent information on the container label. Consider decreasing the prominence of the "Rx only" and net quantity statements as this information appears more prominent than the established name.
2.	It is unclear if the barcode contains the required information to correctly identify the product in settings where individual pouches may be dispensed (for example, hospitals).	The drug barcode is often used as an additional verification before drug administration in the hospital setting; therefore, it is an important safety feature that should be part of the label whenever possible.	Ensure the barcode on the pouch contains the required information per 21CFR 201.25(c)(2).
3.	The numbers in the “TO OPEN:” statement do not make it immediately clear that the pouch is to be torn open with the pouch folded.	Can be improved for clarity.	We recommend revising the statement to read: “Fold along the solid line and tear down at the slit along the arrow.”
Carton Labeling			
1.	The net quantity statement	Not in alignment with our	Revise the net quantity

[a] Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors. Food and Drug Administration. 2013. Available from http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM349009.pdf

Table 3. Identified Issues and Recommendations for Aquestive Therapeutics (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	does not contain the package type.	draft guidance[b]. It is important to include the package type on the carton labeling in situations where it is unclear how the medication should be safely handled and used simply by viewing the container.	statement to include the package type. Consider revising to read: "60 pouches each containing 1 oral film", or a similar statement.
2.	It is unclear if the serial number (SN) is represented by the number "(b) (4)" positioned below the 2D data matrix barcode.	The SN is required on the smallest saleable unit in accordance with the Drug Supply Chain Security Act (DSCSA)[c].	Please clarify what the number "(b) (4)" represents. If it is not a placeholder for the SN, then we recommend you identify a placeholder for the SN in accordance with the DSCSA.

5 CONCLUSION

Our evaluation of the proposed Exservan Prescribing Information (PI), Instructions for Use (IFU), Container label, and Carton 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 the Applicant. We ask that the Division convey Table 3 in its entirety to Aquestive Therapeutics so that recommendations are implemented prior to approval of this NDA.

[b] Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors. Food and Drug Administration. 2013. Available from http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM349009.pdf

[c] Guidance for Industry: Product Identifiers Under the Drug Supply Chain Security Act Questions and Answers. 2018. Available from https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM621044.pdf

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 4 presents relevant product information for Exservan that Aquestive Therapeutics submitted on January 31, 2019, and the listed drug (LD).

Table 4. Relevant Product Information for Listed Drug and Exservan

Product Name	Rilutek	Exservan
Initial Approval Date	12/12/95	N/A
Active Ingredient	Riluzole	riluzole
Indication	Treatment of amyotrophic lateral sclerosis (ALS)	Treatment of amyotrophic lateral sclerosis (ALS)
Route of Administration	Oral	Oral
Dosage Form	Tablet	Oral film
Strength	50 mg	50 mg
Dose and Frequency	50 mg twice daily	50 mg twice daily
How Supplied	Bottles of 60 tablets	Carton of 60 pouches (each pouch contains 1 oral film)
Storage	20°C to 25°C (68°F to77°F), and protect from bright light	20°C to 25°C (68°F to77°F); excursions permitted to 59°F to 86°F (15°C to 30°C) and protect from bright light
Container Closure	HDPE bottle with (b) (4) closure and aluminum seal	(b) (4) foil pouch

APPENDIX B. PREVIOUS DMEPA REVIEWS

On June 27, 2019, we searched for previous DMEPA reviews relevant to this current review using the terms, Exservan and riluzole. Our search identified two previous reviews and 6 memos for other oral riluzole dosage forms.

Table 5. Summary of Previous DMEPA Reviews for Exservan

OSE RCM #	Review Date	Summary of Recommendations
2017-2447	03/21/18	We reviewed the URRA and L&L for Tiglutik (riluzole oral suspension). We identified areas in the labels and labeling that are vulnerable to medication error. We provided recommendations to DNP for the PI and the C&C to the Sponsor. We recommended the Sponsor increase the prominence of critical information and to ensure safe use and handling of the proposed product. Revisions assessed in review #2017-2447-1.
2017-2447-1	07/12/2018	We reviewed the revised C&C for Tiglutik. We identified areas in the labels and labeling that are vulnerable to medication error. We recommended the Sponsor increase the prominence of the strength statement on the container label and carton labeling in accordance with 21 CFR 201.15(a)(6). Revisions assessed in review #2017-2447-2.
2014-2447-2	07/20/18	We reviewed the revised C&C for Tiglutik. We confirmed our recommendations were implemented. No further recommendations.
2017-2447-3	09/26/18	We reviewed the final printed C&C for Tiglutek. No recommendations.

(b) (4), (b) (5)

[redacted]

Table 5. Summary of Previous DMEPA Reviews for Exservan		
OSE RCM #	Review Date	Summary of Recommendations
		(b) (4), (b) (5)

APPENDIX F. LABELS AND LABELING

F.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[d] along with postmarket medication error data, we reviewed the following Exservan labels and labeling submitted by Aquestive Therapeutics on January 31, 2019.

- Container label
- Carton labeling
- Instructions for Use (excerpt from submission)
- Prescribing Information (Image not shown)

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

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/s/

JOHN C MORRIS
07/24/2019 11:11:01 AM

BRIANA B RIDER
07/24/2019 11:53:06 AM