CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

212640Orig1s000

PRODUCT QUALITY REVIEW(S)

RECOMMENDATION: Approval

NDA 212640
Review 1

Drug Product Name	Exservan™ (riluzole)
Dosage Form	Oral film
Strength	50 mg
Route of Administration	Oral
Rx/OTC Dispensed	Rx
Applicant	Aquestive Therapeutics
US agent, if applicable	

QUALITY TEAM

Discipline	Primary Assessment	Secondary Assessment
Drug Substance	Gaetan Ladouceur	Suong (Su) Tran
Drug Product/Labeling	Mariappan Chelliah	Wendy Wilson-Lee
Manufacturing	Tianhong Tim Zhou	Nallaperumal Chidambaram
Microbiology	N/A	N/A
Biopharmaceutics	Kaushalkumar Dave	Ta-Chen Wu
Regulatory Business Process Manager	Dahlia Walters	
Application Technical Lead	Martha Heimann	
Laboratory (OTR)	N/A	N/A
Environmental	N/A	N/A

Submission(s) Reviewed	Document Date	Discipline(s) Affected
SD-001, Original NDA	1/31/2019	All
SD-003, Response to 74-Day Letter comments	5/13/2019	All
SD-005, Response to IR	7/26/2019	Manufacturing
SD-006, Labeling/Container	8/28/2019	Labeling
SD-007, Response to IR	9/5/2019	Drug Product, Biopharmaceutics
SD-008/Labeling/Container	9/25/2019	Labeling
SD-009, Response to IR	10/1/2019	Biopharmaceutics
SD-009, Response to IR	10/1/2019	Biopharmaceutics

QUALITY ASSESSMENT DATA SHEET

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessed	Comments
(b) (4)	II		(b) (4)	Adequate	3/6//2019	Reviewed by G. Ladouceur
	IV			Adequate [1]		
	III			N/A [2]		
	IV			N/A [2]		
	IV			N/A [2]		

[1] No updates to DMF since previous adequate review dated 9/22/2017.
[2] Adequate information provided in NDA.

B. Other Documents: *IND, RLD, or sister applications*

Document	Application Number	Description
NDA	20599	Rilutek® (riluzole) tablets, Covis Pharma NDA referenced under 505(b)(2) to support safety and efficacy of riluzole.
IND	130939	Aquestive Therapeutics, development of riluzole oral film
NDA	209080	Italfarmaco S.p.A. NDA for Tiglutik™ (riluzole) oral suspension (competitor product). Approved 9/5/2018.
		(b) (4)

2. CONSULTS

None

EXECUTIVE SUMMARY

I. RECOMMENDATIONS AND CONCLUSION ON APPROVABILITY

The OPQ review team recommends **Approval** of NDA 212640 for Exservan™ (riluzole) oral film. The application, as amended in response to Agency information requests (IRs), provides adequate information to ensure that the applicant can consistently manufacture a product that is suitable for use by the intended patients.

II. SUMMARY OF QUALITY ASSESSMENTS

A. Product Overview

Aquestive Therapeutics developed Exservan (riluzole) oral film 50 mg as an alternative to Rilutek (riluzole) tablets for treatment of amyotrophic lateral sclerosis (ALS) in patients who have difficulty swallowing tablets.[1] The applicant requests approval of the product under a 505(b)(2) NDA that relies on the prior approval of Rilutek (NDA 20599). FDA granted Orphan designation for this product.

Riluzole oral film is designed to disintegrate rapidly when placed on the tongue and release the active ingredient as a solid suspended in saliva. Gastrointestinal absorption occurs through natural salivary drainage and intentional swallowing of saliva, followed by dissolution of riluzole in the stomach. The applicant identified (b) (4) as Subjective Attributes, not critical to quality or performance, but desirable for the finished drug product. Identity, appearance, assay, content uniformity, degradation, microbiological limits, (b) (4) elemental impurities, (b) (4), dissolution, and disintegration are identified as Quality Attributes that ensure performance of the drug product. The initial risk assessment identified palatability as a moderate risk attribute for the product.

Proposed indication(s) including intended patient population	Treatment of patients with amyotrophic lateral sclerosis (ALS).
Duration of treatment	Chronic
Maximum daily dose	100 mg
Alternative methods of administration	None

[1] Prior to the September 5, 2018 approval of Tiglutik™ (riluzole) oral suspension (NDA 209080, Italfarmaco S.p.A.), the only approved dosage form for riluzole was a conventional tablet.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.