

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

213687Orig1s000

PRODUCT QUALITY REVIEW(S)

RECOMMENDATION

☒ Approval
☐ Approval with Post-Marketing Commitment
☐ Complete Response

NDA 213687 Assessment 1

Drug Product Name	Dojolvi (triheptanoin) oral liquid
Dosage Form	Liquid
Strength	100% w/w
Route of Administration	Oral
Rx/OTC Dispensed	Rx
Applicant	Ultragenyx Pharmaceutical Inc., Novato, CA
US agent, if applicable	N/A

Submission(s) Assessed	Document Date	Discipline(s) Affected
Original	7/31/2019	OPQ
Amendment	8/29/2019	ONDP
Amendment	9/20/2019	ONDP, OPMA
Amendment	11/27/2019	ONDP, OPMA
Amendment	12/4/2019	ONDP
Amendment – Labeling	2/14/2020	ONDP

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessment	Secondary Assessment
Drug Substance	Sukhmaya (Sam) Bain	Donna Christner
Drug Product	Caroline Strasinger	Moo-Jhong Rhee
Manufacturing / Facilities	Peter Krommenhoek	Aditi Thakur
Microbiology	Yan Zheng	Jesse Wells
Regulatory Business Process Manager	Oumou Barry	
Application Technical Lead	Hitesh Shroff	
Environmental	Caroline Strasinger	Moo-Jhong Rhee

EXECUTIVE SUMMARY

I. RECOMMENDATIONS AND CONCLUSION ON APPROVABILITY

The applicant has provided sufficient CMC information to assure the identity, strength, purity, and quality of the proposed Dojolvi (triheptanoin) oral liquid, 100% w/w.

The Office of Pharmaceutical Manufacturing Assessment (OPMA) has made a final overall “**Approval**” recommendation for the facilities involved in this application,

The claim for the Categorical Exclusion for the Environmental Assessment is granted.

The label/labeling issues have been satisfactorily resolved from the CMC perspective.

Therefore, from the OPQ perspective, this NDA is recommended for “**Approval**”.

II. SUMMARY OF QUALITY ASSESSMENTS

A. Product Overview

Dojolvi (triheptanoin) oral liquid is a synthetic medium odd-chain (7) triglyceride. It is a non-sterile colorless to light yellow liquid. It is supplied in 500 mL glass bottles.

Proposed Indication(s) including Intended Patient Population	Dojolvi is indicated as a source of calories and odd-chain fatty acids for the treatment of pediatric and adult patients with molecularly confirmed long-chain fatty acid oxidation disorders (LC-FAOD).
Duration of Treatment	As needed
Maximum Daily Dose	The recommended target daily dosage of DOJOLVI is up to 35% of the patient’s total prescribed DCI divided into at least four doses and administered at mealtimes or with snacks.
Alternative Methods of Administration	Dojolvi may be administered via silicone or polyurethane feeding tubes (oral or enteral).

B. Quality Assessment Overview

Drug Substances: Adequate



The drug substance reviewer determined that clinical batches of triheptanoin are pharmaceutical grade and comparable to the commercial batches because they were manufactured at the same manufacturing facility in similar scale and met the proposed commercial triheptanoin specification for identity, strength, purity and quality. As Dojolvi contains only triheptanoin the clinical batches of Dojolvi are comparable in overall quality to the commercial batches.

Based on long-term and accelerated stability testing of multiple batches of triheptanoin, a retest period of (b) (4) is granted when stored at (b) (4) in

The drug substance reviewer, Dr. Sukhamaya (Sam) Bain, concluded that the applicant has submitted adequate CMC information regarding the raw materials, manufacturing process as well as the specification for identity, purity and quality of the drug substance, Triheptanoin. (see the **Drug Substance** review).

Drug Product: Adequate

Dojolvi (triheptanoin) oral liquid is a synthetic medium odd-chain (C7) triglyceride colorless to light yellow liquid. It is supplied in 500 mL glass bottles.

(b) (4)

(b) (4)

The overall drug product control strategy is deemed adequate

(b) (4)

The compatibility study with various types of enteral feeding tubes was performed. Dojolvi may be administered via silicone or polyurethane feeding tubes (oral or enteral). However, PVC feeding tubes are not recommended for enteral feeding with Dojolvi. Polystyrene is immediately degraded by the drug product so Dojolvi should not be administered or stored in polystyrene containers. Due to the significant loss of drug product in feeding tubes it should not be administered as a neat liquid. Dojolvi is stable up to 4 hours at 25°C and up to 48 hours at 2°C – 8°C in apple sauce, skim milk and formula emulsion.

Based on satisfactory long-term and accelerated stability data of multiple batches of the drug product assuring the identity, strength, purity and quality, a 36-month of expiration dating period, when stored between 20°C to 25°C in the proposed glass bottles sealed with an induction seal and a cap, is granted (See the **Drug Product** review).

(b) (4)

Manufacturing: Adequate

(b) (4)



Microbiology: Adequate

Dojolvi is a non-sterile product. The drug product specification includes microbial enumeration test for total aerobic microbial count and total combined yeast/molds count per USP <61> and test for specified micro-organisms Escherichia Coli per USP <62>. The acceptance criteria will adhere to USP <1111> for non-sterile products. Microbial testing will be performed at release and stability.

The microbiology related information in the drug product manufacturing process, analytical methods, stability protocol, specification and labeling was rereviewed by Dr. Yan Zheng and deemed acceptable. (See the **Microbiology** review).

Labeling: Adequate

The proposed labels and labeling after revision are deemed adequate from the CMC perspective. (see the **Labeling** review).

Facilities Adequate

The Office of Process and Facilities (OPF) reviewer, Dr. Peter Krommenhoek has made an “Adequate” recommendation for the drug substance and drug product manufacturing and testing facilities. (see the **Manufacturing Integrated Assessment** review).

Environmental Assessment Adequate

The applicant has submitted a claim of categorical exclusion including a statement of no extraordinary circumstances. The categorical exclusion cited at 21 CFR 25.31(b or c) is appropriate for the estimated amount of drug to be produced for direct use. The claim of categorical exclusion is acceptable. (see the **Drug Product Review**).

C. Risk Assessment

Dojolvi (triheptanoin) oral liquid, 100% w/w

Product Attribute/CQA	Factors that can impact the CQA	Risk Ranking	Risk Mitigation Approach	Risk Evaluation	LifeCycle consideration/ Comments
Assay Impurities	- Raw materials - Starting materials - Manufacturing process - Process parameters	L	(b) (4)	No trends observed in assay during drug product stability testing period. The impurities and degradants remained within the proposed specification throughout the stability period. The drug product is expected to be safe for oral administration during the entire shelf life from the product quality perspective. Low to None	None

D. List of Deficiencies None

Application Technical Lead Name and Date:

Hitesh Shroff, Ph.D.
Application Technical Lead, Branch V
Division of New Drug Products II
March 16, 2020

Hitesh N. Shroff -S
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QUALITY ASSESSMENT DATA SHEET

IQA NDA Assessment Guide Reference

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
(b) (4)	Type III		(b) (4)	Active	N/A	LOA Oct 29, 2018

B. OTHER DOCUMENTS: *IND, RLD, RS, Approved NDA*

Document	Application Number	Description
IND	113386	Rely on all information and trial conducted under this IND.

2. CONSULTS

Discipline	Status	Recommendation	Date	Assessor
Biostatistics				
Pharmacology/Toxicology				
CDRH-ODE				
CDRH-OC				
Clinical				
Other				

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CHAPTER IV: LABELING

The below information and labeling deficiencies were agreed to by the Applicant on 18-FEB-2020. The deficiencies are presented below only for completeness of review. The Label and Labeling is now ADEQUATE from the ONDP perspective.

1.0 PRESCRIBING INFORMATION

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

TRADENAME (triheptanoin) ~~liquid for oral use~~, oral liquid

Initial U.S. Approval: YYYY

-----DOSAGE FORMS AND STRENGTHS-----

Oral Liquid: 100% w/w (3)

Item	Information Provided in the NDA	Assessor's Comments
Product Title in Highlights		
Proprietary name	TRADENAME	ADEQUATE (tradenname has a location)
Established name(s)	(triheptanoin) liquid for oral use	INADEQUATE It needs to be revised to “(triheptanoin) oral liquid” This was satisfactorily resolved on 2/18/20
Route(s) of administration	oral	ADEQUATE
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system.	Liquid, 100% w/w	INADEQUATE It needs to be revised to “Oral Liquid” This was satisfactorily resolved on 2/18/20

Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state “functionally scored”	N/A	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.	N/A	

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)

Item	Information Provided in the NDA	Assessor’s Comments
DOSAGE AND ADMINISTRATION section		
Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents, storage conditions needed to maintain the stability of the reconstituted or diluted product)		<i>CMC defers to OND/Patient Labeling for the appropriateness of these updated instructions. From a chemistry standpoint they are true statements.</i>

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

3 DOSAGE FORMS AND STRENGTHS

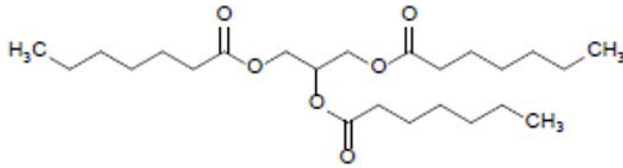
Oral liquid: (b) (4) clear, colorless to light yellow (b) (4) liquid (b) (4)
 (b) (4) supplied in 500 mL bottles containing 100% w/w of triheptanoin

Item	Information Provided in the NDA	Assessor's Comments
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Liquid for oral use	INADEQUATE This needs to be revised to "Oral Liquid" This was satisfactorily resolved on 2/18/20
Strength(s) in metric system	100%	ADEQUATE
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance	N/A	
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, and imprinting	Colorless to light yellow clear liquid	INADEQUATE This needs to be revised to "Clear, colorless to light yellow liquid" This was satisfactorily resolved on 2/18/20
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	
For injectable drug products for parental administration, use appropriate labeling term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package.	Supplied in 500 mL bottles containing 100w/w% of triheptanoin	ADEQUATE (not an injectable but the 500 mL bottle is suitable to aid in identifying characteristics)

1.2.3 Section 11 (DESCRIPTION)

11 DESCRIPTION

TRADENAME (triheptanoin) is a synthetic medium odd-chain (C7) triglyceride supplied as a clear, colorless to light yellow clear-oral liquid. (b) (4) The chemical name of triheptanoin is heptanoic acid, 1,1',1''-(1,2,3-propanetriyl) ester. The empirical formula is $C_{24}H_{44}O_6$ and its molecular weight is 428.6 g/mol. The chemical structure is:



The caloric value of triheptanoin is 8.3 kcal/mL.

Item	Information Provided in the NDA	Assessor's Comments
DESCRIPTION section		
Proprietary and established name(s)	TRADENAME (triheptanoin) liquid for oral use	INADEQUATE It needs to be revised to "TRADENAME (triheptanoin) oral Liquid" This was satisfactorily resolved on 2/18/20
Dosage form(s) and route(s) of administration	Liquid for oral use	INADEQUATE This needs to be revised to "Oral Liquid" This was satisfactorily resolved on 2/18/20
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per FDA Guidance.	N/A	
List names of all inactive ingredients. Use USP/NF names. Avoid Brand names.	N/A	ADEQUATE (The formulation is 100% active)
For parenteral injectable dosage forms, include the name and quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect.	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Statement of being sterile (if applicable)	N/A	
Pharmacological/therapeutic class	Synthetic medium chained triglyceride	ADEQUATE
Chemical name, structural formula, molecular weight	Chemical names and structures provided	ADEQUATE

If radioactive, statement of important nuclear characteristics.	N/A	
Other important chemical or physical properties (such as pKa or pH)	Colorless to light yellow clear liquid (b) (4)	INADEQUATE Request rewording of drug product description. See edits above. This was satisfactorily resolved on 2/18/20

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)

16 HOW SUPPLIED/STORAGE AND HANDLING

TRADENAME (triheptanoin) oral (b) (4) liquid, (b) (4)
(b) (4) is supplied in (b) (4) glass bottles as follows:

500 mL bottle	NDC 69794-050-50

Store at 20° - 25°C (68° - 77°F); excursions permitted to 15° - 30°C (59° - 86°F) (see USP Controlled Room Temperature). Do not freeze. Opened bottles of TRADENAME can be used for up to 90 days after opening, but not beyond the expiration date on the bottle.

Do not dose or store in polystyrene containers.

Pharmacist: Dispense only in Glass or HDPE bottles.

Item	Information Provided in the NDA	Assessor's Comments
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s)	Liquid for oral use	INADEQUATE "for oral use" should be changed to "oral liquid" This was satisfactorily resolved on 2/17/20
Strength(s) in metric system	Not present	INADEQUATE It needs to be expressed as 100%. This was satisfactorily resolved on 2/18/20
Available units (e.g., bottles of 100 tablets)	500 mL bottle	ADEQUATE
Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number	present	ADEQUATE
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.	N/A	

Section 16 (HOW SUPPLIED/STORAGE AND HANDLING) (Continued)

Item	Information Provided in the NDA	Assessor's Comments

Special handling about the supplied product (e.g., protect from light, refrigerate). If there is a statement to “Dispense in original container,” provide reason why (e.g. to protect from light or moisture, to maintain stability, etc.)	Do not freeze. Open bottles of TRADENAME can be used for up to 90 days after opening but not beyond the expiration date on the bottle. Do not dose or store in polystyrene containers. Pharmacist: Dispense only in Glass or HDPE bottles.	ADEQUATE
If the product contains a desiccant, ensure the size and shape differ from the dosage form and desiccant has a warning such as “Do not eat.”	N/A	
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	Store at 20°C to 25°C (68°F to 77°F) excursions permitted 15°C to 30°C (59 to 86°F) [see USP Controlled Room Temperature].	ADEQUATE
Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of natural rubber latex, state: “Not made with natural rubber latex. Avoid statements such as “latex-free.”	N/A	ADEQUATE
Include information about child-resistant packaging	N/A	ADEQUATE

1.2.5 Manufacturing Information After Section 17 (for drug products)

Item	Information Provided in the NDA	Assessor’s Comments
Manufacturing Information After Section 17		
Name and location of business (street address, city, state and zip code) of the manufacturer, distributor, and/or packer	Manufactured for: Ultragenyx Pharmaceutical Inc. 60 Leveroni Court Novato, CA 94949	ADEQUATE

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Item	Information Provided in the NDA	Assessor's Comments about Carton Labeling
Proprietary name, established name, and dosage form (font size and prominence)	TRADE NAME Triheptanoin Oral liquid	ADEQUATE
Dosage strength	100% w/w	ADEQUATE
Route of administration	Oral use or by gastronomy tube	ADEQUATE
If the active ingredient is a salt, include the equivalency statement per FDA Guidance	N/A	
Net contents (e.g. tablet count)	500 mL	ADEQUATE
"Rx only" displayed on the principal display	Present	ADEQUATE
NDC number	Present	ADEQUATE
Lot number and expiration date	Present	ADEQUATE
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new BUD.	Store upright at 20°C to 25°C (68°F to 77°F) excursions permitted 15°C to 30°C (59 to 86°F) [see USP Controlled Room Temperature].	ADEQUATE
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use)	Do not freeze. Open bottles of TRADENAME can be used for up to 90 days after opening but not beyond the expiration date on the bottle. Do not dose or store in polystyrene containers. Pharmacist: Dispense only in Glass or HDPE bottles.	ADEQUATE
Other package terms include pharmacy bulk package and imaging bulk package which require "Not for direct infusion" statement.		
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Bar code	Present	ADEQUATE

Item	Information Provided in the NDA	Assessor's Comments about Carton Labeling
Name of manufacturer/distributor	Mfd. For: Ultragenyx Pharmaceutical Inc. 60 Leveroni Court Novato, CA 94949	ADEQUATE
Medication Guide (if applicable)	N/A	Revise the statement "See patient instructions" to "Recommended Dosage: See prescribing information".
No text on Ferrule and Cap overseal	N/A	
When a drug product differs from the relevant USP standard of strength, quality, or purity, as determined by the application of the tests, procedures, and acceptance criteria set forth in the relevant compendium, its difference shall be plainly stated on its label.	N/A	
And others, if space is available	ADEQUATE	

Assessment of Carton and Container Labeling: ADEQUATE

ITEMS FOR ADDITIONAL ASSESSMENT

None

Overall Assessment and Recommendation:

On January 27, 2020, the above deficiencies were communicated to the Applicant. The Applicant agreed to all OPQ related deficiencies on February 18, 2020. The Label and Labeling of NDA 213687 is ADEQUATE.

This application is deemed ready for APPROVAL from the OPQ/ONDP label/labeling perspective.

Primary Labeling Assessor Name and Date:

Caroline Strasinger, Ph.D. 27-FEB-2020
OPQ, ONDP, DNDP II, B4

Secondary Reviewer Name and Date (and Secondary Summary, as needed):

I agree with Dr. Strasinger's assessment of the labeling and labels and concur with her recommendation that this application is ready for APPROVAL.

Moo-Jhong Rhee, Ph.D. 27-FEB-2020
Chief, Branch 4
DNDP II/ONDP



Caroline
Strasinger

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Moo Jhong
Rhee

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CHAPTER VII: MICROBIOLOGY

[IQA NDA Assessment Guide Reference](#)

Product Information	
NDA Number	213687
Assessment Cycle Number	MR01
Drug Product Name/ Strength	UX007 (triheptamoin), 100% w/w
Route of Administration	Oral liquid
Applicant Name	Ultragenyx Pharmaceutical Inc.
Therapeutic Classification/ OND Division	OND/ODEIII/DGIEP
Manufacturing Site	(b) (4)
Method of Sterilization	N/A for non-sterile products

Assessment Recommendation: Adequate

Assessment Summary:

Document(s) Assessed	Date Received
Original submission	07/31/2019
Quality information	08/29/2019

List Submissions being assessed (table):

Highlight Key Issues from Last Cycle and Their Resolution: N/A

Remarks: None

Concise Description of Outstanding Issues

(List bullet points with key information and update as needed): None

Supporting Documents: N/A

P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT

Product description

The subject drug product is a non-sterile, non-aqueous, multi-dose liquid for oral administration. It is packaged as 500mL colorless to light yellow liquid in a

500mL glass bottle that is closed with a (b) (4) closure and a leak-proof seal.

Product composition: 100% w/w Triheptanoin (API).

Container closure system:

Component	Description	Supplier
Bottle	500 mL (b) (4) Glass	(b) (4)

Assessment: Adequate

The product description is acceptable.

P.2 PHARMACEUTICAL DEVELOPMENT

P.2.5 MICROBIOLOGICAL ATTRIBUTES

Container/Closure and Package Integrity—N/A for non-sterile products.

Antimicrobial Effectiveness Testing—N/A for non-sterile, non-aqueous products.

P.3 MANUFACTURE

P.3.1 MANUFACTURERS

Manufacturer of the product:

(b) (4)

Product testing sites are:

(b) (4)

Assessment: Adequate

The manufacturer information is acceptable.

P.3.3 DESCRIPTION OF THE MANUFACTURING PROCESS AND PROCESS CONTROLS

Overall Manufacturing Operation

Assessment: Adequate

The overall manufacturing process is acceptable.

P.5 CONTROL OF DRUG PRODUCT**P.5.1 SPECIFICATION**

Test	Test method	Acceptance criteria
TAMC	USP<61>	(b) (4)
TYMC	USP<61>	
<i>E.coli</i>	USP<62>	
Water content	USP<921>	

The acceptance criteria for microbial enumeration test are in accordance with USP<1111> recommendation for non-sterile, non-aqueous oral products.

Assessment: Adequate

The proposed product specification is acceptable.

P.5.2 ANALYTICAL PROCEDURES—see P5.1 and P5.3.**P.5.3 VALIDATION OF ANALYTICAL PROCEDURES**

Microbial enumeration test is performed according to USP<61> and USP<62>. Method suitability testing was performed at the product commercial testing laboratories, (b) (4)

At both testing sites, the recovery of microorganisms from the product challenge is 50-200% of that from the positive dilution control. TAMC testing method suitability was performed using *A. brasiliensis*, *B. subtilis*, *C. albicans*, *P. aeruginosa*, and *S. aureus*. TYMC method suitability testing was performed using *A. brasiliensis* and *C. albicans*. *E. coli* was able to be re-isolated via

enrichment from a 1:10 sample preparation and the negative controls were free of microbial growth (3.2.P.5.3, validation of analytical procedures, pp. 2-4).

Assessment: Adequate

The microbial enumeration test method and method suitability data are acceptable.

P.7 CONTAINER CLOSURE—See P.1

P.8 STABILITY

P.8.1 STABILITY SUMMARY AND CONCLUSION

The proposed shelf life is 36 months when stored at 20-25°C.

Assessment: Adequate

The stability summary is acceptable.

P.8.2 POST-APPROVAL STABILITY PROTOCOL AND STABILITY COMMITMENT

The applicant commits to continue the on-going stability study for the primary batches.

The applicant also commits to place one commercial drug product batch to the annual stability program each year. The post-approval stability samples are placed under long term (25°C/60% RH) condition.

Microbial enumeration test	0, 12, 24, 36 months
Water content	0, 3, 6, 9, 12, 18, 24, 36 months

The testing method and acceptance criteria are reviewed in P 5.1.

Assessment: Adequate

Post-approval stability commitment is acceptable.

P.8.3 STABILITY DATA

Registration batches are placed under long term and accelerated conditions.

Condition		Microbial enumeration testing frequency	Water content testing frequency
Long term	25°C/60% RH	0, 12, 24, 36 months	0, 1, 3, 6, 9, 12, 18, 24, 36 months
Accelerated	40°C/75% RH	0, 6 months	0, 1, 3, 6 months

The testing method and specifications are reviewed in Section P5.1.

Long term stability data up to 36 months is available for registration batches (A590, DD0521, DD0566). Accelerate stability data up to 6 months is available

for batch DD0521 and DD0566. The acceptance criteria are satisfied at all testing time points.

Developmental batches (AX41, AX42, and AX43) in the proposed 500mL glass bottles are also placed in the stability study. Long term stability data is available up to 3 months and accelerate stability data is available for up to 1 month. The acceptance criteria are satisfied at all testing time points.

Assessment: Adequate

The stability data is acceptable.

APPENDICES-N/A

R REGIONAL INFORMATION

Executed Batch Records

Executed batch record is available for product batch AX43.

Comparability Protocols—N/A

2. ASSESSMENT OF COMMON TECHNICAL DOCUMENT – QUALITY (CTD-Q) MODULE 1

2.A. Prescribing Information

The liquid product is intended for oral use or by gastrostomy tube. The storage condition is 20-25°C; excursions permitted between 15-30°C. Once opened, the product should be used within 90 days.

The target daily dose is ^{(b) (4)} % of the patient's total prescribed daily caloric intake (DCI), converted to mL. The product should be mixed thoroughly with food or drink and take by mouth or administer via a gastrostomy tube divided four times per day including at mealtimes or snacks.

- In-use study is performed where samples (batch AN84 and AN85) are taken out of opened bottles at specific days and tested for microbial limits and water content. Microbial limits testing samples are taken on day 21 and day 36. Water content samples are taken on day 1, 8, 16, 21, 24, 28, 31, and 36. The acceptance criteria are satisfied at all testing time points.
- In-use study is also performed where half content of the bottle is removed, and the half-full bottle is stored under long-term or accelerated condition. Batch AN83 and AN85 are used in the in-use study. Data up to 3 months is available and the acceptance criteria are satisfied.

Condition		Half-full bottle in-use testing frequency for microbial enumeration test and water content test
Long term	25°C/60% RH	0, 2, 3, 6, 9 months
Accelerated	40°C/75% RH	0, 2, 3, 6 months

Assessment: Adequate

The package insert is acceptable.

Primary Microbiology Assessor Name and Date: Yan Zheng, Ph.D. 09/04/2019

*Secondary Assessor Name and Date (and Secondary Summary, as needed):
Jesse Wells, Ph.D.*



Jesse
Wells

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Zheng

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