CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

214907Orig1s000

PRODUCT QUALITY REVIEW(S)

Office of Pharmaceutical Quality

New Drug Application (NDA) 214907

Integrated Quality Assessment Template

U.S. FOOD & DRUG ADMINISTRATION

Contents

U.S. FOOD & DRUG ADMINISTRATION

RECOMMENDATION

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

NDA 214907
Assessment 1

Drug Product Name	CYTALUX (pafolacianine) injection
Dosage Form	Injection
Strength	2 mg/mL (3.2 mg/1.6 mL)
Route of Administration	Intravenous
Rx/OTC Dispensed	Rx
Applicant	On Target Laboratories, Inc.
US agent, if applicable	N/A

Submission(s) Assessed	Document Date	Discipline(s) Affected
Original (0001)	29-Dec-2020	All
Amendment (0006)	10-Frb-2021	Microbiology
Amendment (0019)	02-Mar-2021	Microbiology
Amendment (0015)	07-May2021	Drug Product
Amendment (0018)	11-May-2021	Drug Product
Amendment (0019)	20-May-2021	Drug Product; Drug Substance
Amendment (0023)	04-Jun-2021	Drug Product
Amendment (0027)	17-Jun-2021	Drug Product; Drug Substance
Amendment (0028)	21-Jun-2021	Microbiology
Amendment (0029)	21-Jun-2021	Drug Product
Amendment (0033)	08-Jul-2021	Drug Product; Microbiology
Amendment (0041)	04-Aug-2021	Drug Product; Drug Substance
Amendment (0042)	10-Aug-2021	Drug Product
Amendment (0043)	11-Aug-2021	Drug Substance
Amendment (0044)	13-Aug-2021	Drug Product
Amendment (0045)	16-Aug-2021	Drug Product
Amendment (0046)	03-Sep-2021	Drug Product (labeling)
Amendment (0047)	14-Sep-2021	Drug Product (labeling)
Amendment (0048)	20-Sep-2021	Drug Product
Amendment(0049)	10-Oct-2021	Drug Product (labeling)

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessment	Secondary Assessment
Drug Substance	Monica Cooper	Suong Tran
Drug Product	Ravindra Kasliwal	Danae Christodoulou
Manufacturing	Sateesh Sathigari	Vidya Pai
Microbiology	David Bateman	Yeissa ChabrerRosello
Biopharmaceutics	N/A	N/A
Regulatory Business Process Manager	Anika Lalmansingh	
Application Technical Lead	Ravindra Kasliwal	
Laboratory (OTR)	N/A	N/A
Environmental	N/A	N/A

EXECUTIVE SUMMARY

I. RECOMMENDATIONS AND CONCLUSION ON APPROVABILITY

The applicant has provided sufficient information to assure the identity, strength, purity, quality, including sterility of the proposed drug product. The proposed drug product is a single use, sterile, liquid injectable solution provided in an amber glass vial. The drug is both temperature sensitive and photosensitive, so it is packaged in an amber glass vial with outer carton and is to be stored in freezer at -20°C (± 5°C). At the time of use, it is thawed and diluted with a 250 mL bag of 5% dextrose solution (D5W) for intravenous administration. All the issues around freezer storage, thaw period, dilution, storage and use of diluted infusion solution have been adequately resolved and are reflected in product labeling.

The company has evaluated saline as the diluent for the proposed drug product and found that this resulted in hypersensitive reactions in IND subjects. An investigation was conducted and concluded that the hypersensitivity was most likely due to the formation of aggregates. Hence following warning has been included in the section 5 of PI: Use of the incorrect diluent to prepare the CYTALUX™ infusion solution can cause the aggregation of pafolacianine (b) (4) Use only 5% Dextrose Injection USP to prepare the CYTALUX™ infusion solution. Do not use other diluents.

The key review issues (assurance of sterility, container closure integrity, assay, chiral purity, impurities, storage and use conditions, expiration and use periods and the cGMP status of a listed facilities) have been adequately resolved and were deemed to have minimal likely impact on patient efficacy or safety and do not preclude approval of this product. The labels and labeling include adequate quality information as required. All associated manufacturing, testing, packaging facilities were deemed acceptable. Based on the OPQ review team's evaluation of the information provided in the submission, CYTALUX (pafolacianine) injection possesses the necessary attributes to ensure indicated safety and efficacy.

The applicant has provided adequate data to support the proposed storage and shipping condition (b) (4) and the proposed shelf life of 36 months under the recommended storage condition.

Based on data, the drug product can tolerate three freeze thaw cycles. Further, the drug product has been shown to tolerate up to 24 hours of thawed time during processing and handling. For use, the drug is thawed, removed from the vial, and is diluted into D5W, protected from light, and can be stored for up to 24 hours at 2-8°C prior to administration to the patient.

II. SUMMARY OF QUALITY ASSESSMENTS

A. Product Overview

Cytalux contains pafolacianine active ingredient as a tetrasodium salt referred to as pafolacianine sodium. Pafolacianine sodium is a water soluble, amorphous, hygroscopic dark green to black solid that is light and heat sensitive and is stored frozen. Cytalux injection will be supplied as a single dose vial for IV administration. Cytalux is a (b) (4) single use, sterile, liquid solution provided in an amber glass (b) (4) vial with (b) (4) (b) (4) rubber closure and crimp seal. Each vial contains 3.2 mg of pafolacianine free acid in 1.6 mL volume (2.0 mg/mL concentration). The formulation excipients are (b) (4) with hydrochloric acid and/or sodium hydroxide, as necessary.

Through this new drug application (NDA) the Applicant seeks approval for the adjunctive use of 0.025 mg/kg intravenous (IV) dose of Cytalux during intraoperative fluorescence-guided surgery in patients with ovarian cancer. Cytalux, excited by near-infrared (NIR) light between the wavelengths of 760-(b) (4) nm (with maximum excitation at (b) (4)-776 nm), emits light at wavelengths in the NIR spectrum (maximum emission (b) (4)-796 nm). This fluorescence of malignant tissue can be used to guide surgical resection of tumor.

Cytalux administered at a dose of 0.025 mg/kg has been shown to be safe in achieving the primary efficacy endpoint (evaluable ovarian cancer lesion confirmed by central pathology (truth standard) that was detected with Cytalux and fluorescent light but not under normal light or palpation) with a favorable benefit-risk profile for its use as an adjunct for intraoperative guidance during debulking surgery in patients with ovarian cancer, a serious disease with largely unmet medical needs.

The Applicant submitted NDA 214907 as a 505 (b)(1) application on December 29, 2021. The drug is an NME and was granted priority review status. The drug was initially reviewed under IND 118215.

Proposed Indication(s) including Intended Patient Population	CYTALUX™ is an optical imaging agent indicated for adult women with ovarian cancer as an adjunct for intraoperative identification of malignant lesions.
Duration of Treatment	One time intravenous injection prior to intraoperative procedure.
Maximum Daily Dose	0.025 mg/kg (adult)
Alternative Methods of Administration	None.

B. Quality Assessment Overview

Drug Substance: *Adequate*

See drug substance assessment summary.

Drug Product: *Adequate*

See drug product assessment summary.

Labeling: *Adequate*

See labeling review assessment.

Manufacturing: *Adequate*

See manufacturing assessment summary.

Biopharmaceutics: *Adequate*

A biopharmaceutics review was not performed as the drug product is an injectable solution.

Microbiology : *Adequate*

The drug product is [redacted] (b) (4) filled into 3 mL vials. See microbiology assessment.

C. Risk Assessment

From Initial Risk Identification			Assessment		
Attribute/ CQA	**Factors that can impact the CQA**	**Initial Risk Ranking**	**Risk Mitigation Approach**	**Final Risk Evaluation**	**Lifecycle Considerations/ Comments**
Appearance	The solution is Dark Bluish Green in color. It is photosensitive and temperature sensitive. [redacted] (b) (4)	L	[redacted] (b) (4)	Acceptable	None
pH	It is an intravenously injected drug product, and a physiologically compatible pH is critical to patient comfort (avoid	L		Acceptable	None

	injection pain). In this case the pH of the injection will be largely determined by the diluent.		(b) (4)		
Osmolality	(b) (4)	L		Acceptable	None.
Chiral purity	(b) (4)	H		Acceptable	None

Impurities	(b) (4)	H	(b) (4)	Adequate	The drug substance and the drug product is (b) (4) The DP should be prepared (thawed, diluted with 250 mL 5% dextrose injection bag, stored (kept) in dark) and used as described in the product's PI.

Assay	[redacted]	H	[redacted]	Acceptable	The drug substance and the drug product is [redacted] The DP should be prepared (thawed, diluted with 250 mL 5% dextrose injection bag, stored (kept) in dark) and used as described in the product's PI.
Particulate Matter	The particulate matter could come from [redacted] The particle could also form during storage.	M		Acceptable	Only 5% Dextrose Injection, USP [redacted] should be used for dilution of the supplied drug product for infusion. Use of the other / incorrect diluent to prepare the CYTALUX™ infusion solution can cause the aggregation of pafolacianine and can induce hypersensitivity reactions.

			(b) (4)		
Compatibility with diluent	Incompatibility may change the drug product attribute. It is important that the drug product safety and performance does not change upon dilution.	H		Acceptable	Only 5% Dextrose Injection, USP (b) (4) should be used for dilution of the supplied drug product for infusion. Use of the other / incorrect diluent to prepare the CYTALUX™ infusion solution can cause the aggregation of pafolacianine and can induce hypersensitivity reactions.
Bacterial Endotoxins	Contamination of materials, manufacturing equipment or from personal may lead to excessive bacterial endotoxins.	H		Adequate	None

			(b) (4)		
Sterility	Contamination from materials, manufacturing equipment or from personal may lead to a non-sterile product. (b) (4)	H		Acceptable.	The container closure integrity was not tested during the stability studies. The applicant provided an acceptable stability program for microbial testing and will be adding container closure integrity testing to the stability program as an additional test with Sterility and Bacterial Endotoxins.

D. List of Deficiencies for Complete Response None

1. Overall Quality Deficiencies (Deficiencies that affect multiple sub-disciplines)

None

2. Drug Substance Deficiencies

None. There are some post marketing agreements. These are documented in the drug product review.

3. Drug Product Deficiencies

None

4. Labeling Deficiencies

All issues have been resolved. None

5. Manufacturing Deficiencies

None

6. Biopharmaceutics Deficiencies

NA

7. Microbiology Deficiencies

None

8. Other Deficiencies (Specify discipline, such as Environmental)

NA

Application Technical Lead Name and Date:

Ravindra K. Kasliwal, PhD., CMC reviewer, Branch 6, Division of New Drug Products-III, Office of New Drug Products, Office of Pharmaceutical Quality (OPQ)

19-Oct-2021

U.S. FOOD & DRUG ADMINISTRATION

QUALITY ASSESSMENT DATA SHEET

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
(b) (4)	III		(b) (4)	Adequate	28-Nov-2016 by Valerie R Amspacher.	(b) (4)
	III			Adequate	14-Jul-2021	
	III			Adequate	NA	
	I			NA	14-Jul-2021	

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

Document	Application Number	Description
IND	118215	Investigational studies IND

2. CONSULTS - *None*

CHAPTER IV: LABELING

1.0 PRESCRIBING INFORMATION

Assessment of Product Quality Related Aspects of the Prescribing Information: Submission 10-Aug-2021 (Sequence# 0042); 14-Sep-2021 (Sequence 0049); 08-Oct-2021 (Sequence# 0029)

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

Item	Information Provided in the NDA	Assessor's Comments
Product Title in Highlights		
Proprietary name	CYTALUX™	Acceptable as per DMEPA
Established name(s)	Pafolacianine	This is the USAN Name. Acceptable.
Route(s) of administration	Intravenous	Highlight section indicates for intravenous use.
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system.	Injection: 3.2 mg/1.6 mL (2 mg/mL) of pafolacianine in a single-dose vial.	The description is correct and supported by CMC information in submission.
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	NA	NA
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.	Indicates single-dose vial	The prescribed dose is 0.025 mg/kg body weight. So each patient will receive a different total amount of the drug product. The formulation provides sufficient drug (3.2 mg/1.6 mL) to dose a patient up to 115 kg (assuming 90% of vial content is withdrawn from the vial). For any patients that weighs less than 115 kg, a single vial will include some overage of drug. This is acceptable.
Warning and Precautions	Indicates to only use 5% Dextrose Injection, USP for dilution. Do not use other diluents.	Use of the incorrect diluent to prepare the CYTALUX™ infusion solution can cause the aggregation of pafolacianine and can induce hypersensitivity reactions. Hence following warning statement was requested: Use only 5% Dextrose Injection USP to prepare the CYTALUX™

		infusion solution. Do not use other diluents. Adequate.

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)	2.5 Preparation and Storage (b) (4) (b) (4) – Use aseptic technique for the preparation of CYTALUX infusion solution. – Do not use diluents (b) (4) due to incompatibility. – Thaw frozen CYTALUX vial in original carton at controlled room temperature between 20° to 25°C (68° to 77°F) for at least 90 minutes. – (b) (4) the thawed CYTALUX vial for 60 seconds. – Withdraw the calculated volume of CYTALUX for a dose of 0.025 mg/kg. Discard any unused portion in the vial. – Add into a 250 mL of 5% Dextrose Injection, USP. – Gently swirl the bag by hand for 1 minute to mix the solution. – (b) (4) in color and should not contain any visible particulate matter. – Protect the infusion bag from light (b) (4) – If not immediately used, store the diluted CYTALUX solution in a refrigerator at 2°C - 8°C (36°C-46°F) for not more than 24 hours. – Once the bag is removed from refrigeration, infusion must be completed within 3 hours. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.	The instructions submitted in the original submission have been revised. And the revised instructions, as indicated in the column, are acceptable and the use period, preparation diluent and storage temperature and time duration are supported by CMC data.

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

Item	Information Provided in the NDA	Assessor's Comments
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Injection	The product is intravenously administered.

Strength(s) in metric system	3.2 mg/1.6 mL (2 mg/mL) of pafolacianine in a single-dose vial	Adequate
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance	3.2 mg/1.6 mL (2 mg/mL) pafolacianine (equivalent to 3.4 mg/1.6 mL) pafolacianine sodium)	The active ingredient is a tetrasodium salt. Since the dose is administered on the basis of pafolacianine (free acid) the equivalent amount of salt is indicated in the statement.
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, and imprinting	Supplied as a dark bluish green, clear aqueous solution	Supported by CMC data and is adequate.
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	NA	NA
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.	single-dose vial.	Adequate.

1.2.3 Section 11 (DESCRIPTION)

(b) (4)

[redacted]

Item	Information Provided in the NDA	Assessor's Comments
DESCRIPTION section		
Proprietary and established name(s)	CYTALUX contains pafolacianine	Adequate.
Dosage form(s) and route(s) of administration	CYTALUX (pafolacianine) injection is a sterile, non-pyrogenic, dark bluish green, clear aqueous solution for intravenous use.	Both are included. Adequate.

If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per FDA Guidance.	Each vial contains 3.2 mg (2 mg/mL) pafolacianine (equivalent to 3.4 mg pafolacianine sodium)	Equivalent amount of the salt form is included. Adequate.
List names of all inactive ingredients. Use USP/NF names. Avoid Brand names.	14.4 mg sodium chloride, 0.23 mg potassium phosphate monobasic, 1.27 mg sodium phosphate dibasic heptahydrate	Amounts and generic names are included. Adequate.
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.	Each vial contains 3.2 mg (2 mg/mL) pafolacianine (equivalent to 3.4 mg pafolacianine sodium),14.4 mg sodium chloride, 0.23 mg potassium phosphate monobasic, 1.27 mg sodium phosphate dibasic heptahydrate in 1.6 mL volume. The pH is adjusted with sodium hydroxide and/or hydrochloric acid and is between 7.1 to 7.8.	Quantitative information of all the ingredients, the pH range of the solution and ingredients used for pH adjustments are included. Adequate.
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	NA	NA
Statement of being sterile (if applicable)	CYTALUX (pafolacianine) injection is a sterile, non-pyrogenic, dark bluish green, clear aqueous solution for intravenous use.	The word sterile is included. Adequate.
Pharmacological/ therapeutic class	CYTALUX contains pafolacianine, an optical imaging agent.	The pharmacological class is included. Adequate.
Chemical name, structural formula, molecular weight	See above.	Chemical name, structural formula, molecular weight are included. Adequate.
If radioactive, statement of important nuclear characteristics.	NA	NA
Other important chemical or physical properties (such as pKa or pH)	pH range (7.1-7.8) is included.	Adequate
For oral prescription drug products, include gluten statement if applicable	NA	NA
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity"	No such statements are in the description section.	NA

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)

Item	Information Provided in the NDA	Assessor's Comments
HOW SUPPLIED/STORAGE AND HANDLING section CYTALUX (pafolacianine) injection, 3.2 mg/1.6 mL (2 mg/mL), is a dark bluish green, clear aqueous solution packaged in a sealed amber glass single-dose vial and supplied in a box of 10 vials is individually packaged (b) (4) (b) (4) (NDC 81052-138-10). Storage and Handling Store frozen between -25° and -15°C (-13° and 5°F). Store in original carton to protect from light.		
Available dosage form(s)	Injection is included.	Adequate.
Strength(s) in metric system	3.2 mg/1.6 mL (2 mg/mL)	Adequate
Available units (e.g., bottles of 100 tablets)	box of 10 vials is individually packaged (b) (4) (b) (4)	Adequate.
Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number	dark bluish green, clear aqueous solution in a sealed amber glass single dose vial	Adequate
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	NA	NA
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.	Single-Dose Vial	Adequate

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.)	Store in original carton to protect from light.	The product is photosensitive. Statement to protect from light is included. 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."	NA	NA
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	Store frozen between -25° and -15°C (-13° and 5°F).	Adequate.
Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic	NA	NA

derivatives of natural rubber latex, state: "Not made with natural rubber latex. Avoid statements such as "latex-free."		
Include information about child-resistant packaging	NA	NA

1.2.5 Other Sections of Labeling - NA

There may be other sections of labeling that contain product-quality related information. For example, there are specific required/recommended warnings for certain inactive ingredients [e.g., aspartame, aluminum in large and small volume parenteral, sulfites, FD&C Yellow Number 5 (tartrazine), and benzyl alcohol]. Please notify the prescription drug division if the product contains any of these inactive ingredients.

Please include your comments about other sections of labeling if they contain product quality information.

1.2.6 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 by: Grand River Aseptic Manufacturing 140 Front Ave SW Grand Rapids, MI 49506 Distributed by: ThermoFisher Allentown Packaging Facility Or Patheon Logistics 100 Berkeley Dr. Swedesboro, NJ 08085 Packaged by: Fisher Clinical Services Inc. 7554 Schantz Rd. Allentown, PA 18100-9032	Adequate.

2.0 PATIENT LABELING - NA

Assessment of Product Quality Related Aspects of Patient Labeling (e.g., Medication Guide, Patient Information, Instructions for Use): NA. The product is to be administered at bedside before the surgical procedure. It is not directly dispensed to the patient.

Any deficiencies should be listed at the end in the "ITEMS FOR ADDITIONAL ASSESSMENT." NA

3.0 CARTON AND CONTAINER LABELING

3.1 Container Label

(b) (4)

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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	(b) (4)	Proprietary name, established name, font size and prominence seem to be appropriate.
Dosage strength		Correctly displayed. Adequate.
Route of administration	For intravenous use after Dilution	Adequate
If the active ingredient is a salt, include the equivalency statement per FDA Guidance	The content statement on carton labels indicates the salt equivalency: 3.2 mg pafolacianine (equivalent to 3.4 mg pafolacianine sodium)	Adequate
Net contents (e.g. tablet count)	The 10 vial carton label indicates 10 X 1.6 mL Single Dose Vials The one vial carton indicates 1 Single Dose Vial.	Adequate
"Rx only" displayed on the principal display	All labels include "Rx Only" statement.	Adequate
NDC number	All labels include NDA number.	Adequate
Lot number and expiration date	All labels include lot number and expiry date.	Adequate
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new BUD.	All labels include the following storage statement: **Store in freezer at -25° to -15°C (-13° to 5°F).** Store in original carton to protect from light.	Adequate
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use)	All labels include "Single -Dose Vial"	Adequate.
Other package terms include pharmacy bulk package and imaging bulk package which require "Not for direct infusion" statement.	The labels include: **For Intravenous Infusion After Dilution** Thaw at room temperature at (b) (4) to 25°C ((b) (4) to 77°F) for 90 minutes in the carton prior to (b) (4) preparation. Must dilute with **5% dextrose injection, USP only** before use. Store diluted solution in dark in refrigerator and use within 24 hrs. of preparation.	Adequate
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	NA	NA
Bar code	All labels include Bar Codes.	Adequate

Item	Information Provided in the NDA	Assessor's Comments about Carton Labeling
Name of manufacturer/distributor	Carton Labels include: **Manufactured for:** On Target Laboratories West Lafayette, IN 47906	Adequate
Medication Guide (if applicable)	NA	NA
No text on Ferrule and Cap Overseal	NA	NA
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.	There is no USP monograph for the drug product.	NA
And others -if space is available		

Assessment of Carton and Container Labeling: ***Adequate***
Any deficiencies should be listed at the end in the "ITEMS FOR ADDITIONAL ASSESSMENT." None

ITEMS FOR ADDITIONAL ASSESSMENT

None

Overall Assessment and Recommendation:

The revised labeling as acceptable from a CMC perspective.

Primary Drug Product Assessor Name and Date:

Ravindra K. Kasliwal, PhD., CMC reviewer, Branch 6, Division of New Drug Products-III, Office of New Drug Products, Office of Pharmaceutical Quality (OPQ)

21-Sep-2021

Secondary Assessor Name and Date:

Danae D. Christodoulou, Ph.D., Branch Chief, Branch 6, Division of New Drug Products-III, Office of New Drug Products, Office of Pharmaceutical Quality (OPQ)

12-Oct-2021

Ravindra Kasliwal

Digitally signed by Ravindra Kasliwal
Date: 10/18/2021 07:38:27AM
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Danae Christodoulou

Digitally signed by Danae Christodoulou
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CHAPTER VII: MICROBIOLOGY

IQA NDA Assessment Guide Reference

Product Information	
NDA Number	214907
Assessment Cycle Number	MR01
Drug Product Name/ Strength	Pafolacianine Sodium Injection (Cytalux) 3.2 mg/ 3 mL vial, single -dose
Route of Administration	Intravenous injection
Applicant Name	On Target Laboratories, Inc.
Therapeutic Classification/ OND Division	Division of Medical Imaging Products
Manufacturing Site	Grand River Aseptic Manufacturing 140 Front Avenue SW Grand Rapids, MI 49504
Method of Sterilization	(b) (4)

Assessment Recommendation: **Adequate**

Assessment Summary:
The drug product is (b) (4) filled into 3 mL vials.

List Submissions being assessed (table):

Document(s) Assessed	Date Received
eCTD Seq #0001 Original	December 29, 2020
eCTD Seq #0006 Response to CMC	February 10, 2021
eCTD Seq #0010 Response to Micro IR	March 2, 2021
eCTD Seq #0019 Response to CMC	May 20, 2021
eCTD Seq #0028 Response to Micro	June 21, 2021
eCTD Seq #0033 Response to Micro	July 8, 2021

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

Remarks: Priority review has been granted for this application. The drug product is supplied as a solution in 3 mL vials.

Concise Description of Outstanding Issues
(List bullet points with key information and update as needed):
None.

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(b) (4)

Adequate

Reviewer's Assessment:
The applicant provided acceptable instructions and provided reconstitution hold time study to support the label conditions.

MICROBIOLOGY LIST OF DEFICIENCIES

None.

Primary Microbiology Assessor Name and Date:
David Bateman, Ph.D. (July 13, 2021)

Secondary Assessor Name and Date
Yeissa ChabrierRosello, Ph.D. (July 14, 2021)

David Bateman

Digitally signed by David Bateman
Date: 7/14/2021 11:56:52AM
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Yeissa Chabrier Rosello

Digitally signed by Yeissa Chabrier Rosello
Date: 7/14/2021 12:32:06PM
GUID: 5317ea990000ce969cecabfa83284493

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/s/

RAVINDRA K KASLIWAL
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