CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

218643Orig1s000

PRODUCT QUALITY REVIEW(S)

NDA Executive Summary

1. Application/Product Information

NDA Number.	218643		
Applicant Name	American Genomics, LLC		
Drug Product Name	CYKLX (Articaine ophthalmic solution)		
Dosage Form.	Solution/drops		
Proposed Strength(s)	8%		
Route of Administration	Ophthalmic		
Maximum Daily Dose	(b) (4)		
Rx/OTC Dispensed	Rx		
Proposed Indication	Local anesthetic indicated for ocular surface anesthesia prior to ocular procedures and/or intraocular injections		
Drug Product Description	Articaine ophthalmic solution is a clear, colorless, sterile, preservative-free aqueous solution and packaged in single dose blow-fill-seal vias		
Co-packaged product information	NA		
Device information:	Single dose vials; CDRH consult was determined to be not necessary on 10/25/2024.		
Storage Temperature/ Conditions	20-25 °C		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Sa Wang	Sithamalli Chandramouli
	Drug Product/ Labeling	Milton Sloan	Chunchun Zhang
	Manufacturing	Chamara Gunawardana	Nathan Davis
	Biopharmaceutics	NA	NA

	Microbiology	Dustin Thomas	Yuansha Chen
	Other (specify):		
	RBPM	Shazma Aftab	
	ATL	Chunchun Zhang	
Consults	NA		

2. Final Overall Recommendation - Approval

3. Action Letter Information

a. Expiration Dating: An expiration-dating period of 36 months for the commercial product is granted for Articaine ophthalmic solution, 8% stored in a single dose vial at 20 °C to 25 °C (68 °F to 77 °F).

b. Additional Comments for Action: NA

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

Satisfactory information and responses have been submitted to support the drug substance, drug product, manufacturing process and quality microbiology aspects.

The product is regulated as a drug and device combination product per the Genus decision. CDRH confirmed that no CDRH consult was necessary on Oct 25, 2024.

OPMA issued an overall recommendation of "approval" on Jul 6, 2025. Therefore, NDA 218643 is recommended Approval from Product Quality perspective.

Labeling recommendations from the Product Quality perspective will be provided to the OND PM for consideration during final labeling discussion.

b. Is the overall recommendation in agreement with the individual discipline recommendations? Yes

Recommendation by Subdiscipline:

Drug Substance	**-**	**Adequate**
Drug Product	**-**	**Adequate**
Quality Labeling	**-**	**Adequate**
Manufacturing	**-**	**Adequate**
Biopharmaceutics	**-**	**N/A**
Microbiology	**-**	**Adequate**

Environmental Assessment: Categorical Exclusion - Adequate
QPA for EA(s): No

5. Life-Cycle Considerations

Established Conditions per ICH Q12: No
Comments: NA

Comparability Protocols (PACMP): No
Comments: NA

Additional Lifecycle Comments: NA

Application Technical Lead Name and Date: Chunchun Zhang, Ph. D., Jul 22, 2025

CHAPTER IV: LABELING

IQA NDA Assessment Guide Reference

1.0 PRESCRIBING INFORMATION

Assessment of Product Quality Related Aspects of the Prescribing Information:

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

(b) (4)

Item	Information Provided in the NDA	Assessor's Comments
Product Title in Highlights		
Proprietary name	Yes	"CYKLX" found acceptable
Established name(s)	Yes	Acceptable
Route(s) of administration	Yes	Acceptable
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system.	ophthalmic solution 8%	Acceptable
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	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	N/A

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)

The recommended dose of BRANDNAME is 2 drops applied 30 seconds apart to the ocular surface.

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)	N/A	

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

BRANDNAME (articaine ophthalmic solution 8% contains 80 mg per mL of articaine hydrochloride in single- dose vial.

Item	Information Provided in the NDA	Assessor's Comments
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)		
Strength(s) in metric system		
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance		USP monograph exception for historical established salt name inclusion
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, and imprinting	N/A	
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.	N/A	

1.2.3 Section 11 (DESCRIPTION)

(b) (4)

Item	Information Provided in the NDA	Assessor's Comments
DESCRIPTION section		
Proprietary and established name(s)	Yes	Proprietary pending separate review
Dosage form(s) and route(s) of administration	Yes	
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per FDA Guidance.	Yes	contains 90.2 mg articane hydrochloride as the active ingredient, equivalent to 80 mg of articane free base
List names of all inactive ingredients. Use USP/NF names. Avoid Brand names.	Yes	Inactive ingredients in the ophthalmic solution are: boric acid, mannitol, sodium acetate trihydrate, glacial acetic acid, edetate disodium dihydrate, water for injection.
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)	Yes	
Pharmacological/ therapeutic class	Yes	amide local anesthetic
Chemical name, structural formula, molecular weight		
If radioactive, statement of important nuclear characteristics.	N/A	
Other important chemical or physical properties (such as pKa or pH)	Yes	formulated at a pH range of 4.5- 5.0.

Section 11 (DESCRIPTION) Continued

Item	Information Provided in the NDA	Assessor's Comments
For oral prescription drug products, include gluten statement if applicable	N/A	
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity"	N/A	

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)

(b) (4)

Item	Information Provided in the NDA	Assessor's Comments
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s)	Yes	Topical ophthalmic
Strength(s) in metric system	Yes	8% (80mg/mL)
Available units (e.g., bottles of 100 tablets)	Yes	
Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number	N/A	
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.)	YES	Not intended for patient self-administration
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.		
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."		
Include information about child-resistant packaging		

1.2.5 Other Sections of Labeling

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 parenterals, 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	Yes	

2.0 PATIENT LABELING

Assessment of Product Quality Related Aspects of Patient Labeling (e.g., Medication Guide, Patient Information, Instructions for Use):

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

3.0 CARTON AND CONTAINER LABELING

3.1 Container Label

(Copy/paste or refer to a representative example of a proposed container)

(b) (4)

[redacted]

3.2 Carton Labeling

(Copy/paste or refer to a representative example of a proposed carton labeling)

1 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

Item	Information Provided in the NDA	Assessor's Comments about Carton Labeling
Proprietary name, established name, and dosage form (font size and prominence	Yes	Remove (b) (4) from established name on carton
Dosage strength	Yes	Remove (b) (4) from PDP of carton.
Route of administration	Yes	
If the active ingredient is a salt, include the equivalency statement per FDA Guidance	Yes	Acceptable
Net contents (e.g. tablet count)	Yes	
"Rx only" displayed on the principal display	Yes	
NDC number	Yes	
Lot number and expiration date	Yes	
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new BUD.	Yes	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use)	N/A	
Other package terms include pharmacy bulk package and imaging bulk package which require "Not for direct infusion" statement.	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Bar code	Yes	

Item	Information Provided in the NDA	Assessor's Comments about Carton Labeling
Name of manufacturer/distributor	Yes	
Medication Guide (if applicable)		
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	N/A	

Assessment of Carton and Container Labeling: ***Adequate***

Reviewer concurs with the labeling recommendations of DMEPA for carton and pouch in review dated Mar 24, 2025.
Labeling comments have been proposed in shared draft.

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

ITEMS FOR ADDITIONAL ASSESSMENT

Items are included in above table as comments and recommendations

Overall Assessment and Recommendation:

Adequate with recommendations.

Primary Labeling Assessor Name and Date:

Milton. J. Sloan, PhD,
Sr. Chemistry Reviewer
OPQ/OPQA II/DPQA IX

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

Chunchun Zhang, Ph.D.,
Quality Assessment Lead,
OPQ/OPQA II/DPQA IX

Milton Sloan

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Chunchun Zhang

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CHAPTER VII: MICROBIOLOGY

IQA NDA Assessment Guide Reference

Product Information	
NDA Number	218643
Assessment Cycle Number	MR01
Drug Product Name/ Strength	(b) (4) (Articaine Sterile Topical Ophthalmic Solution, 8%)
Route of Administration	Topical Ocular
Applicant Name	American Genomics, LLC
Therapeutic Classification/ OND Division	
Manufacturing Site	Woodstock Sterile Solutions, LLC 210 Lake Shore Drive Woodstock, IL 60098
Method of Sterilization	(b) (4) followed by aseptic filling

Assessment Recommendation: **Adequate**

Assessment Summary:

List Submissions being assessed (table):

Document(s) Assessed	Date Received
0001 (1) Original	**10/16/2024**
0008 (8) IR response	**04/09/2025**
0011 (11) IR Response	**06/05/2025**
0012 (12) IR Response	**07/03/2025**
0013 (13) IR Response	**07/16/2025**

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

Remarks: The submission is in the eCTD format; some figures and tables have been copied from the original application. The submission dated 04/09/2025 is in response to an IR sent on 03/12/2025. The submission dated 06/05/2025 is in response to an IR sent on 05/29/2025. The submission dated

07/03/2025 is in response to an IR sent on 06/12/2025, which replaces the proposed commercial production line from room 9 to room 8. All equipment in room 8 is identical to room 9, therefore SIP validation and media fill will be reviewed. The process, specifications, drug product composition, BFS Filling manifold and environmental monitoring procedures are all the same. The submission dated 07/16/2025 contains the validation information for Room 8.

Concise Description of Outstanding Issues

(List bullet points with key information and update as needed):

Supporting Documents: N/A

S Drug Substance

Drug substance is non-sterile and not reviewed – N/A

P.1 Description of the Composition of the Drug Product

Description of drug product – The Articaine Sterile Topical Ophthalmic Solution Drug Product (DP) is a non-preserved aqueous solution contained within a 0.5 mL single-dose low-density polyethylene (LDPE) blow-fill-seal (BFS) vial. The fill volume for this product is 0.40 ± (b) (4) mL.

Drug product composition –

Component	Function	Target Concentration (% w/v)	Amount per Vial (0.4 mL)
Articaine Hydrochloride (USP)	Active Ingredient	9.02[1]	(b) (4)
Boric Acid (NF)	(b) (4)		
D-Mannitol (USP)			
Sodium Acetate Trihydrate (USP)			
Glacial Acetic Acid (USP)			
Edetate Disodium Dihydrate (USP)			
Water for Injection (USP)			
(b) (4)			

[1] Equivalent to 8.0% of Articaine, as free base

(b) (4)

Component	Composition
BFS Vials	(b) (4)

(b) (4)

Assessment: ***Adequate***

P.2 Pharmaceutical Development

(b) (4)

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Nathan Davis

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