CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

219840Orig1s000

OTHER REVIEW(S)

MEMORANDUM
REVIEW OF REVISED LABEL

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
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 10, 2025
Requesting Office or Division:	Division of Imaging and Radiation Medicine (DIRM)
Application Type and Number:	NDA 219840
Product Name, Dosage Form, and Strength:	E-Z-DISK (barium sulfate) Tablets, 700 mg
Applicant Name:	Bracco Diagnostics Inc. (Bracco)
FDA Received Date:	July 8, 2025
TTT ID #:	2024-11963-1 2025-15406
DMEPA 2 Safety Evaluator:	Devin Kane, PharmD
DMEPA 2 Team Leader:	Stephanie DeGraw, PharmD

Reference ID: 5622363

1 PURPOSE OF MEMORANDUM

Bracco Diagnostics Inc. (Bracco) submitted the revised container label received on July 8, 2025 for E-Z-DISK (barium sulfate). The Division of Imaging and Radiation Medicine (DIRM) requested that we review the revised container label for E-Z-DISK (Appendix A) to determine if it is 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

Bracco Diagnostics Inc. implemented all of our recommendations and we have no additional recommendations at this time.

[a] Kane, D. Label and Labeling Review for E-Z-DISK (NDA 219840). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2025 MAY 06. TTT ID: 2024-11963.

APPENDIX A. IMAGE OF LABEL RECEIVED ON JULY 8, 2025

- Container Label:

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/s/

DEVIN R KANE
07/10/2025 01:09:23 PM

STEPHANIE L DEGRAW
07/10/2025 01:21:30 PM

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

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

Memorandum

Date: June 17, 2025

To: Frank Lutterodt, Regulatory Project Manager,
Division of Imaging and Radiation Medicine (DIRM)

Younsook Kim, Associate Director for Labeling, DIRM

From: David Foss, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Jim Dvorsky, Team Leader, OPDP

Subject: OPDP Labeling Comments for E-Z-DISK (barium sulfate) tablets, for oral use

NDA: 219840

Background:

In response to DIRM's consult request dated January 29, 2025, OPDP has reviewed the proposed Prescribing Information (PI) and carton and container labeling for the original NDA submission for E-Z-DISK.

PI:

OPDP's review of the proposed PI is based on the draft labeling accessed from SharePoint on June 12, 2025, and our comments are provided below.

Container Labeling:

OPDP's review of the proposed container labeling is based on the draft labeling accessed from SharePoint on June 13, 2025, and we do not have any comments at this time.

Thank you for your consult. If you have any questions, please contact David Foss at (240) 402-7112 or david.foss@fda.hhs.gov.

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

Reference ID: 5610552

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/s/

DAVID F FOSS
06/17/2025 05:35:36 PM

LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	May 6, 2025
Requesting Office or Division:	Division of Imaging and Radiation Medicine (DIRM)
Application Type and Number:	NDA 219840
Product Name, Dosage Form, and Strength:	E-Z-DISK (barium sulfate) tablets, 700 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Bracco Diagnostics Inc. (Bracco)
FDA Received Date:	November 21, 2024 and April 9, 2025
TTT ID #:	2024-11963
DMEPA 2 Safety Evaluator:	Devin Kane, PharmD
DMEPA 2 Team Leader:	Stephanie DeGraw, PharmD

Reference ID: 5585988

1 REASON FOR REVIEW

As part of the approval process for E-Z-DISK (barium sulfate) tablets, the Division of Imaging and Radiation Medicine (DIRM) requested that we review the proposed E-Z-DISK prescribing information (PI) and container label for areas of vulnerability that may lead to medication errors.

1.1 BACKGROUND OR REGULATORY HISTORY

E-Z-DISK (barium sulfate) has been in marketed in the US since September 2009; however, this product has not been approved by the FDA. Therefore, on November 21, 2024, Bracco submitted NDA 219840 to seek FDA approval for E-Z-DISK.

E-Z-DISK is a proposed 505(b)(2) NDA that relies upon the reference listed drug (RLD), E-Z-HD (barium sulfate) tablets under NDA 208036. See Appendix A for a comparison of product information for E-Z-DISK and E-Z-HD.

2 MATERIALS REVIEWED

This section lists the materials considered for our review of NDA 219840.

Table 1. Materials Considered for this Review	
Material(s) Reviewed	Appendix Section
Relevant Product Information	A
Labels and Labeling	B

3 CONCLUSION

The proposed E-Z-DISK Prescribing Information (PI) and container label may be improved to promote safe use of this product from a medication error perspective. We provide the identified medication error issues, our rationale for concern, and our proposed recommendations to minimize the risk for medication error for the Division of Imaging and Radiation Medicine (DIRM) in Section 4 and for Bracco Diagnostics Inc. in Section 5.

4 RECOMMENDATIONS FOR DIVISION OF IMAGING AND RADIATION MEDICINE (DIRM)

A. General Comments (Highlights of Prescribing Information and Full Prescribing Information)

1. There are numeric values presented throughout the prescribing information (PI) that are not immediately followed by the appropriate units. We recommend including the appropriate units after all numeric values presented in the highlights of PI and full PI to avoid confusion. For example, (b) (4)

Reference ID: 5585988

B. Highlights of Prescribing Information

1. Highlights of Dosage and Administration

   a. The Highlights of Dosage and Administration does not include the timeframe for administration (i.e. "during imaging") nor directions for swallowing the tablet whole. We recommend revising this statement to specify when the tablet should be administered, to include a "swallow whole" statement, and to remove the unnecessary sub-bullet. For example, revise to read: "The recommended adult dose is one tablet swallowed whole during imaging".

2. Highlights of Dosage Forms and Strengths

   a. The proposed Highlights of Dosage Forms and Strengths includes the package type "(b) (4)". We recommend removing the package type term as it is not needed for packages containing oral tablet formulations. Revise to read "Tablets: 700 mg barium sulfate.".

C. Prescribing Information

1. Section 2: Dosage and Administration

   a. The statement in Section (b) (4) can be revised to include the timeframe for administration, to remove the unnecessary (b) (4), and to improve readability. Revise to read: "The recommended adult dose is one tablet orally during imaging.".

   b. The (b) (4) under Section (b) (4) includes the directions "(b) (4)". We recommend revising this statement to remove the timeframe for administration as this will be added to the recommended dosing statement and to replace "(b) (4)" with the more accurate and more commonly used description "whole". For example, revise to read "Instruct the patient to swallow one tablet whole…". Additionally, we recommend adding a second statement as part of this (b) (4) to reiterate that the tablet must be swallowed whole. For example: "The tablet must not be cut, crushed, or chewed.".

   c. The last (b) (4) states that the tablet will (b) (4); however, there are reports of tablets not (b) (4) which then requires the HCP to manually remove the tablet. We recommend the division consider adding language to this bullet point that provides the HCP with instructions for tablet removal should the tablet not dissolve. For example, "(b) (4)".

2. Section 3: Dosage Forms and Strengths

a. As currently presented, Section 3: Dosage Forms and Strengths lacks a physical description of the E-Z-DISK tablets. We recommend revising Section 3 to include a physical description. Revise to read: "Tablets: 700 mg barium sulfate as a white to lightly colored, 12.7mm (½ inch) in diameter, flat-sided disk with EZEM inscribed on one side and 778 on the other side."

3. Section 16: How Supplied/Storage and Handling

   a. The proposed Section 16 currently includes [redacted] (b) (4) How Supplied and [redacted] (b) (4) Storage and Handling. We recommend removing the [redacted] (b) (4) and replacing them with section headers to separate out the important information.

   b. The How Supplied information includes the package type term "[redacted] (b) (4) ". We recommend removing the package type term as it is not needed for packages containing oral tablet formulations. Additionally, this Information can be improved for readability. We recommend revising to read "E-Z-DISK (barium sulfate) tablet 700 mg is supplied as a white to lightly colored, 12.7 mm (½ inch) in diameter, flat-sided disk with EZEM inscribed on one side and 778 on the other side. E-Z-DISK is supplied in glass bottles containing 100 tablets (NDC 10361-778-31).".

   c. The storage statement presented under Storage and Handling can be revised to improve readability of the important information. Additionally, to ensure the tablets are protected from moisture, we recommend including "store in original container" as part of the storage instructions. Revise to read "Store at room temperature 20°C to 25°C (68°F to 77° F) [see USP controlled room temperature]. Store in original container and protect from moisture.".

5 RECOMMENDATIONS FOR BRACCO DIAGNOSTICS INC.

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

A. Container Label

1. The proposed container label includes the statement [redacted] (b) (4) " on the right-hand side of the container label. We recommend revising this statement to read "Recommended Dosage: see Prescribing Information" to ensure consistency with the terminology in the prescribing information.

2. As currently presented, the top of the right-hand side of the container label includes the statement "[redacted] (b) (4) ". We recommend removing this statement as the package type term, "[redacted] (b) (4)

[redacted]", is not required for oral tablet bulk bottle container labels, and "For Oral Use Only" is already included on the principal display panel (PDP).

3. The proposed container label includes the product strength as "700 mg" on the PDP and as "0.7 g" in the product description on the right-hand side of the container label. We recommend revising the product description to align with the units used for the product strength on the PDP. Revise "0.7 g" in the product description to read "700 mg".

4. We recommend revising the storage information statement on the proposed container label to align with the storage information statement presented in the E-Z-DISK Prescribing Information. Revise to read "Store at room temperature 20°C to 25°C (68°F to 77° F) [see USP controlled room temperature]. Store in original container and protect from moisture.".

5. The proposed container label contains a placeholder for the expiration date as "YYYYMM". To minimize confusion and reduce the risk for deteriorated drug medication errors, FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. We recommend that the expiration date appears in YYYY-MM-DD format if only numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a hyphen or forward slash to separate the portions of the expiration date. See Guidance for Industry: *Product Identifiers under the Drug Supply Chain Security Act - Questions and Answers* (June 2021).

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for E-Z-DISK received on April 9, 2025 from Bracco Diagnostics Inc., and the listed drug (LD).

Table 2. Relevant Product Information for E-Z-DISK and Listed Drug		
Product Name	E-Z-DISK (NDA 219840)	E-Z-HD[a] (NDA 208036)
Initial Approval Date	N/A	January 11, 2016
Active Ingredient	barium sulfate	
Indication	E-Z-DISK is a (b) (4) contrast agent indicated for (b) (4)	E-Z-HD, a radiographic contrast agent, is indicated for use in double-contrast radiographic examinations of the esophagus, stomach and duodenum to visualize the gastrointestinal (GI) tract in patients 12 years and older.
Route of Administration	oral	
Dosage Form	tablets	for oral suspension
Strength	700 mg	334 grams of barium sulfate (98% w/w)
Dose and Frequency	(b) (4)	Recommended reconstituted oral dose for adults and pediatric patients 12 years and older is between 65 mL to 135 mL (155 grams to 321 grams of barium sulfate, respectively)
How Supplied	E-Z-DISK is supplied as a white to lightly colored tablet, ½ inch in diameter, with EZEM inscribed on one side and 778 on the other side, in a (b) (4) glass bottle containing 100 tablets of barium sulfate (700 mg). 1 bottle (NDC 10361-778-31)	E-Z-HD (barium sulfate) for suspension, is supplied as a fine, white to lightly colored powder (98 % w/w) in a single-dose HDPE plastic bottle containing 334 grams of barium sulfate. 24 bottles per pack (NDC 32909-764-01)

[a] E-Z-HD [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2017 FEB 08. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208036s006lbl.pdf

Storage	Store at USP controlled room temperature 20°C to 25°C (68°F to 77°F). Protect from moisture.	Store at USP controlled room temperature, 20°C to 25°C (68°F to 77°F).

APPENDIX B. LABELS AND LABELING

B.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[b] along with postmarket medication error data, we reviewed the following E-Z-DISK labels and labeling submitted by Bracco Diagnostics Inc.

- Prescribing Information received on April 9, 2025, available from \\CDSESUB1\EVSPROD\nda219840\0005\m1\us\m1-14-1-3-draft-labeling-text-word-redline.docx
- Container Label received on November 21, 2024

B.2 Container Label(s) and Carton Labeling Images

- Container Label

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

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/s/

DEVIN R KANE
05/06/2025 02:46:31 PM

STEPHANIE L DEGRAW
05/06/2025 03:01:54 PM