CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

217512Orig1s000

OTHER REVIEW(S)

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	January 19, 2024
Requesting Office or Division:	Division of Gastroenterology (DG)
Application Type and Number:	NDA 217512
Product Name, Dosage Form, and Strength:	Pantoprazole Sodium in 0.9% Sodium Chloride Injection 40 mg/100 mL (0.4 mg/mL) 40 mg/50 mL (0.8 mg/mL) 80 mg/100 mL (0.8 mg/mL)
Applicant/Sponsor Name:	Baxter Healthcare Corporation (Baxter)
TTT ID #:	2023-6047-1
DMEPA 1 Safety Evaluator:	Sherly Abraham, R.Ph.
DMEPA 1 Team Leader(Acting):	Damon Birkemeier, PharmD, FISMP, NREMT

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels and carton labeling received on January 12, 2024 for Pantoprazole Sodium in 0.9% Sodium Chloride Injection. The Division of Gastroenterology (DG) requested that we review the revised container labels and carton labeling for Pantoprazole Sodium in 0.9% Sodium Chloride Injection (Appendix A) to determine if they are 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

We previously recommended to remove the bolding from the storage statement, "Protect from light when stored frozen or under refrigeration" from container labels and carton labeling; however, the Applicant stated that they believe this statement ".. *is a unique statement applicable to the proposed premixed product compared to other injectable pantoprazole products. Hence, Baxter left this highlighted in bold to gain attention for the safe use of the*

[a] Abraham, S. Label and Labeling Review for Pantoprazole Sodium in 0.9% Sodium Chloride Injection (NDA 217512). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 DEC 8. TTT ID No.: 2023-6047.

product." Given that the frozen or refrigerated product should be protected from light is important information to prevent the degradation of the product, we find the Applicant's proposal to retain the bolding in the storage statement "Protect from light when stored frozen or under refrigeration" reasonable.

We also recommended to relocate the linear bar code from the back of the container label to the front, if space allows; however, the Applicant stated that, "*Baxter has numerous products approved in the Galaxy container with 1D barcode on the back side of the container (bag). Baxter uses* (b) (4) *Barcode location is required by the filling equipment and relocation would cause the equipment to be incompatible*". We find the Applicant's rationale acceptable for keeping the barcode on the back of the container label.

The Applicant implemented all of our other recommendations and we have no additional recommendations at this time.

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/s/

SHERLY ABRAHAM
01/19/2024 11:02:35 AM

DAMON A BIRKEMEIER
01/19/2024 11:17:48 AM

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

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

Memorandum

Date: January 2, 2024

To: Kristina Luong, Project Manager, DG

From: Meeta Patel, Pharm.D., Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Adewale Adeleye, Pharm.D., Team Leader, OPDP

Subject: OPDP Labeling Comments for **PANTOPRAZOLE SODIUM IN SODIUM CHLORIDE injection, for intravenous use**

NDA: 217512

In response to DG's consult request dated December 15, 2023, OPDP has reviewed the proposed product labeling (PI) and carton/container labeling for Pantoprazole

Labeling: OPDP has no comments on the proposed labeling based on the draft labeling received by electronic mail from DG on December 19, 2023.

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling submitted by the Sponsor to the electronic document room, and we do not have any comments.

Thank you for your consult. If you have any questions, please Meeta Patel at (301) 796-4284 or meeta.patel@fda.hhs.gov.

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LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
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:	December 8, 2023
Requesting Office or Division:	Division of Gastroenterology (DG)
Application Type and Number:	NDA 217512
Product Name, Dosage Form, and Strength:	Pantoprazole Sodium in 0.9% Sodium Chloride Injection 40 mg/100 mL (0.4 mg/mL) 40 mg/50 mL (0.8 mg/mL) 80 mg/100 mL (0.8 mg/mL)
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Baxter Healthcare Corporation (Baxter)
FDA Received Date:	August 17, 2023
TTT ID #:	2023-6047
DMEPA 1 Safety Evaluator:	Sherly Abraham, R.Ph.
DMEPA 1 Team Leader (Acting):	Damon Birkemeier, PharmD, FISMP, NREMT

1 REASON FOR REVIEW

As part of the approval process for Pantoprazole Sodium in 0.9% Sodium Chloride Injection, the Division of Gastroenterology (DG) requested that we review the proposed Pantoprazole Sodium in 0.9% Sodium Chloride Injection prescribing information, container labels, and carton labeling for areas of vulnerability that may lead to medication errors.

1.1 BACKGROUND

NDA 217512 is a 505(b)(2) NDA and the listed drug product is Protonix I.V., NDA 020988. We note the proposed Pantoprazole Sodium in 0.9% Sodium Chloride Injection product has the same active ingredient, indication, route of administration (intravenous infusion), and dosing regimen as the reference listed drug, Protonix I.V. The proposed product will differ from the reference listed drug in terms of strength as it is being proposed for two additional strengths [40 mg/50 mL (0.8 mg/mL) and 80 mg/100 mL (0.8 mg/mL)] as ready-to-use single dose Galaxy plastic containers in 0.9% Sodium Chloride Injection.

2 MATERIALS REVIEWED

Table 1. Materials Considered for this Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B
ISMP Newsletters*	C – N/A
FDA Adverse Event Reporting System (FAERS)*	D – N/A
Other	E – N/A
Labels and Labeling	F

N/A=not applicable for this review
*We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 CONCLUSION AND RECOMMENDATIONS

The proposed prescribing information (PI), container labels, and carton labeling may be improved to promote the 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 in Section 4 for the Division and in Section 5 for Baxter Healthcare Corporation (Baxter).

4 RECOMMEDATIONS FOR DIVISION OF GASTROENTEROLOGY (DG)

A. Prescribing Information

1. Highlights (HL) of Prescribing Information

a. Recommendations to increase the readability of important product information for Highlights are noted in track changes below:

(b) (4)

[redacted]

2. Full Prescribing Information: Section 2 Dosage and Administration

a. Recommendations to increase the readability and prominence of important dosage and administration within Section 2 are noted in track changes below:

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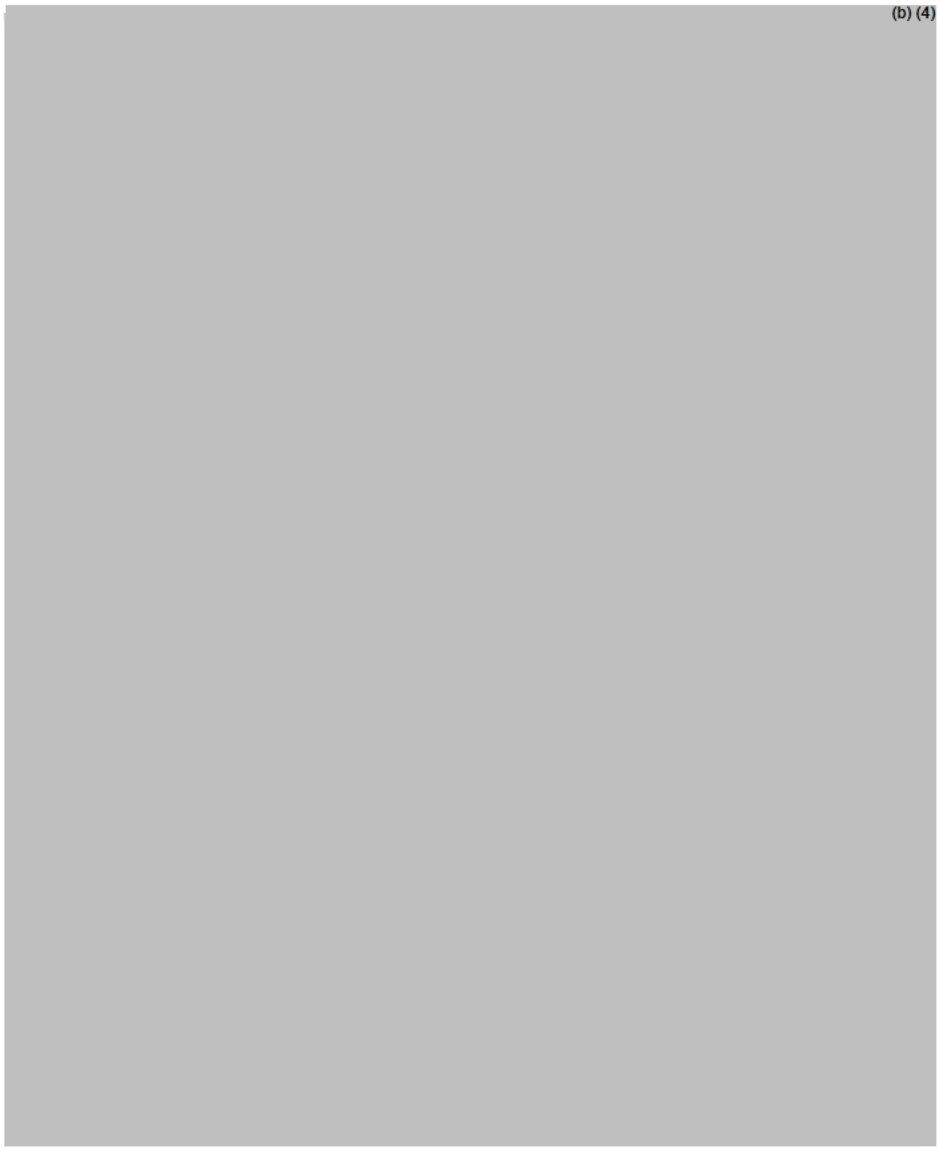


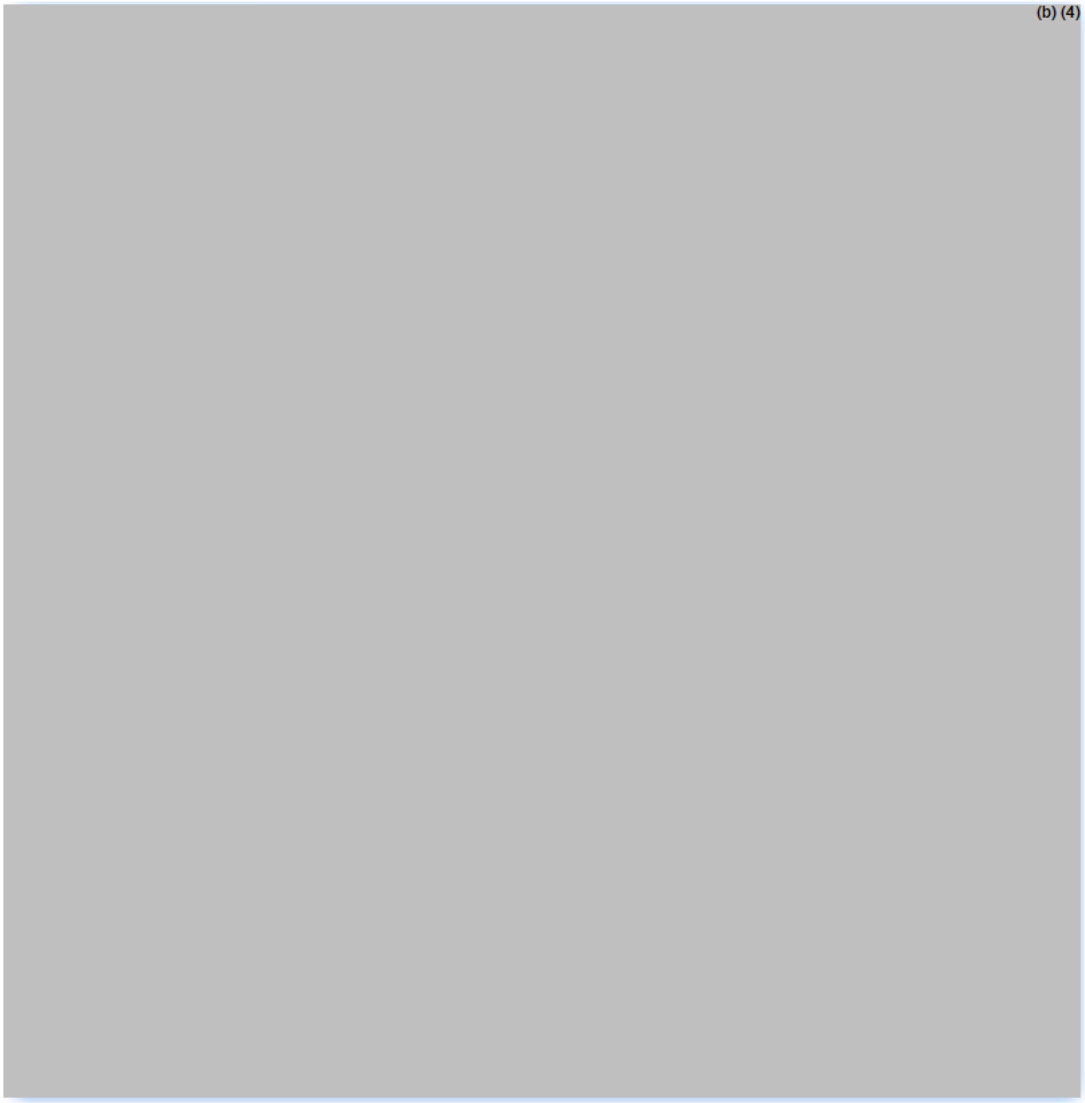
3. Full Prescribing Information: Section 3 Dosage forms and Strengths

    a. A description of the dosage form is not provided [e.g., colorless solution or other identifying characteristics such as clarity (e.g., clear to slightly cloudy)]. A description of identifying characteristics of the dosage form is required per 21 CFR 201.57(c)(4)(ii). Provide a description of the dosage form.

4. Section 16 Storage/How Supplied

    a. A description of the dosage form is not provided [e.g., colorless solution or other identifying characteristics such as clarity (e.g., clear to slightly cloudy)]. A description of identifying characteristics of the dosage form is required per 21 CFR 201.57(c)(17)(iii). Provide a description of the dosage form.

b. Recommendations to increase the readability and prominence of important information within Section 16 are noted in track changes below:



5 RECOMMENDATIONS FOR BAXTER HEALTHCARE CORPORATION (BAXTER)

Table. Identified Issues and Recommendations for Baxter Healthcare Corporation (Baxter) (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Label(s) and Carton Labeling			
1.	As currently presented, the terminology (b) (4) (b) (4) See prescribing information" is inconsistent with the terminology in the Prescribing Information (i.e., Recommended Dosage).	The recommended dosage statement terminology should be consistent across the labeling to mitigate risk of confusion.	To ensure consistency with the Prescribing Information, we recommend revising the recommended dosage statement, to read "Recommended Dosage: See prescribing information."
2.	The "Rx only statement" is bolded.	Overuse of bold font may diminish its effect on prominence for other important product information.	Reserve the use of bolded font only for the most important product information on the label and labeling; remove bold font from the "Rx only" statement.
3.	The usage of symbols ("/" and "-") are noted in the storage statements and the first temperature numerical for each temperature range are missing degree symbols and temperature units (C/F).	The presentation of the storage statement should be clearly stated to avoid storage errors.	Revise the storage statements to read, "Store frozen at or below -20°C (-4°F). Thaw at room temperature 20°C to 25°C (68°F to 77°F) or under refrigeration 2°C to 8°C (36°F to 46°F)."
Container Label(s)			
1.	The barcode is presented on the back of the container label.	When barcode is scanned, the product would need to be flipped over to check the name presentation and strength statement which would be an additional step in verification process.	If space allows, we recommend relocating the bar code from the back of the container label to the front. Additionally, ensure sufficient blank space is provided surrounding the barcode to allow the barcode to be scanned correctly in

Table. Identified Issues and Recommendations for Baxter Healthcare Corporation (Baxter) (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
			accordance with 21 CFR 201.25(c)(1)(i).
2.	The Route of Administration (ROA) statement contains the word (b) (4)	We reserve the use of the word (b) (4) when there is a safety concern or data that supports the product must be given by a specific route.	We recommend revising the ROA statement so that it reads, "For intravenous infusion".
3.	The storage statements, "**Protect from light when stored frozen or under refrigeration"** and (b) (4) (b) (4) are bolded.	Overuse of bold font may diminish its effect on prominence for other important product information.	Remove the bolding from storage statements, "Protect from light when stored frozen or under refrigeration" and (b) (4) (b) (4)
Carton Labeling			
1.	As currently displayed, the (b) (4) below the strength statement competes for prominence with strength statement differentiating colors. It is unclear if the (b) (4) (b) (4) is intended to be included as a part of your final carton labels.	The use of (b) (4) on the PDP minimizes the difference between the different strength statements, which may lead to wrong strength selection errors.	Remove the (b) (4) below the strength presentation.
2.	The ROA statement is missing on the Principal Display Panel (PDP) of the carton labeling.	The ROA is considered to be "critical information." For more information see the Guidance for Industry, "*Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication*	Add the ROA statement "For Intravenous Infusion" to the PDP of the carton labeling.

Table. Identified Issues and Recommendations for Baxter Healthcare Corporation (Baxter) (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
		Errors."[a] To avoid medication errors involving wrong ROA, ROA statement should be prominently displayed on the PDP.	
3.	As currently presented, there are four sequences of numbers and letters (0's and X's) with unknown meaning on the PDP and the designated location for lot number and expiration date is not clearly marked.	Numbers or codes located in close proximity to the lot number and expiration date may be mistaken as the lot number and expiration date.	Ensure that all sequences of numbers and letters present on the label are necessary and that the lot number and expiration date have prominence.
4.	As currently presented, there are two placeholders for barcodes (on PDP and side/back panel) of the carton labeling.	Since the drug barcode is often used as an additional verification before drug administration in the inpatient setting, the presence of multiple barcodes is confusing to the healthcare providers.	Please clarify the intention of having two barcodes on the carton labeling, i.e., if one is a linear barcode and the other one is a quick response (QR) code or data matrix code required by DSCSA. We recommend you move the barcode that does not contain the NDC number to the side or the back panel of the carton labeling, away from the barcode containing the NDC number, and present it in a size that does not compete with, distract from the presentation of other required or recommended information on the label.

[a] Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors. May 2022. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/safety-considerations-container-labels-and-carton-labeling-design-minimize-medication-errors.

Table. Identified Issues and Recommendations for Baxter Healthcare Corporation (Baxter) (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
5.	As currently displayed, the manufacturer name ("Baxter") located on the PDP completes with the prominence of the critical information on the PDP.	The proprietary name and established or proper name along with the product strength, route of administration, and warnings or cautionary statements should be the most prominent information on the principal display panel (PDP).	Decrease the prominence of the manufacturer name "Baxter" relative to the prominence of the critical information on the PDP needed for proper identification and use of your proposed product in accordance with 21 CFR 201.15(a)(6). For example, this may be accomplished through increasing the prominence of the critical information and/or minimizing the manufacturer name itself or moving it to another panel.
6.	The storage statement, "Protect from light when stored frozen or under refrigeration" is bolded.	Overuse of bold font may diminish its effect on prominence for other important product information.	Remove the bolding from storage statement, "Protect from light when stored frozen or under refrigeration".
7.	As currently presented, the net quantity statements "Contains 6 units of Single-Dose bags. Each bag contains 100 mL." and "Contains 12 units of Single-Dose bags. Each bag contains 50 mL." lack clarity.	Lack of clarity regarding the net quantity statements may lead to confusion and increase the risk for medication errors.	We recommend revising the net quantity statement to read "6 x 50 mL Single-Dose bags." or "12 x 100 mL Single-dose bags."

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 3 presents relevant product information for Pantoprazole Sodium in 0.9% Sodium Chloride Injection that Baxter Healthcare Corporation (Baxter) submitted on August 17, 2023, and the Protonix IV.

Table 3. Relevant Product Information for Protonix I.V. and Pantoprazole Sodium in 0.9% Sodium Chloride Injection		
Product Name	Protonix IV (NDA 020988)	Pantoprazole Sodium in 0.9% Sodium Chloride injection
Initial Approval Date	March 22, 2001	N/A
Active Ingredient	pantoprazole sodium	pantoprazole sodium and sodium chloride
Indication	Pantoprazole sodium is indicated in adults for the following: Short-term treatment (7 to 10 days) of gastroesophageal reflux disease (GERD) associated with a history of Erosive Esophagitis (EE). Pathological hypersecretion conditions including Zollinger-Ellison (ZE) Syndrome.	
Route of Administration	intravenous	
Dosage Form	injection	
Strength	40 mg	40 mg/100 mL (0.4 mg/mL) 40 mg/50 mL (0.8 mg/mL) 80 mg/100 mL (0.8 mg/mL)
Dose and Frequency	GERD Associated with EE: The recommended adult dosage is 40 mg given once daily by intravenous infusion for 7 to 10 days. Pathological Hypersecretion Conditions, Including ZE Syndrome: The recommended adult dosage is 80 mg administered every 12 hours by intravenous infusion.	
How Supplied	Carton containing 1 vial, 10 vials, or 25 vials.	12 count of 40 mg/100 mL (0.4 mg/mL) GALAXY containers 24 count of 40 mg/50 mL (0.8 mg/mL) GALAXY containers 12 count of 80 mg/100 mL (0.8 mg/mL) GALAXY containers

Table 3. Relevant Product Information for Protonix I.V. and Pantoprazole Sodium in 0.9% Sodium Chloride Injection		
Product Name	Protonix IV (NDA 020988)	Pantoprazole Sodium in 0.9% Sodium Chloride injection
Storage	Store PROTONIX I.V. at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Protect from light.	Store frozen at or below -20°C /-4°F.

APPENDIX B. PREVIOUS DMEPA REVIEWS

On November 22, 2023, we searched for previous DMEPA reviews relevant to this current review using the terms, pantoprazole. Our search identified one previous review since the date of our last search on November 4, 2017[b], and we considered our previous recommendations to see if they are applicable for this current review.

APPENDIX F. LABELS AND LABELING

F.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[c] along with postmarket medication error experiences with similar products, we reviewed the following Pantoprazole Sodium in 0.9% Sodium Chloride Injection labels and labeling submitted by Baxter Healthcare Corporation (Baxter).

- Container label(s) received on August 17, 2023
- Carton labeling received on August 17, 2023
- Prescribing Information (Image not shown) received on August 17, 2023, available from \\CDSESUB1\EVSPROD\nda217512\0001\m1\us\pi-draft-labeling-text-original-draft-v1-c-ms-word.docx

[b] Barlow, M. Label and Labeling Review for Protonix and Protonix IV (NDA 22020/S-014; NDA 20988/S-058; NDA 20987/S-052). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 DEC 4. RCM No.: 2017-2304.

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

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