CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

021029Orig1s036, s037, s038
022277Orig1s017, s018, s019

OTHER REVIEW(S)

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING

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)

Date of This Memorandum:	August 18, 2023
Requesting Office or Division:	Oncology Center of Excellence (OCE)
Application Type and Number:	NDA 022277 S-17, S-18, S-19 NDA 021029 S-36, S-37, S-38
Product Name and Strength:	Temodar (temozolamide) for injection, 100 mg and Temodar (temozolamide) capsules, 5 mg, 20 mg, 100 mg, 140 mg, 180 mg, and 250 mg
Applicant/Sponsor Name:	Merck
OSE RCM #:	2023-5367-1
DMEPA 2 Safety Evaluator:	Sali Mahmoud, PharmD, BCPS
DMEPA 2 Team Leader:	Ashleigh Lowery, PharmD

PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels and carton labeling received on August 9 and 11, 2023 for Temodar. The Oncology Center of Excellence (OCE) requested that we review the revised container labels and carton labeling for Temodar (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.[1]

CONCLUSION

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

[1] Mahmoud, S. Label and Labeling Review for Temodar (NDA 022277 S-17, S-18, S-19 NDA 021029 S-36, S-37, S-38). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2023 JUL 13. RCM No.: 2023-5367.

11 Pages of Draft Labeling have been Withheld in Full as B4 (CCI/TS) immediately following this page

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

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

Memorandum

Date: July 17, 2023

To: Adriene King-Ducre, PhD, Health Scientist, OCE

From: Mispa Ajua-Alemanji, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Rachael Conklin, Team Leader, OPDP

Subject: OPDP Labeling Comments for TEMODAR® (temozolamide) capsule, for oral use and TEMODAR® (temozolamide) injection, for intravenous use

NDA: 021029, S-36, S-37 and S-38
022277, S-17, S-18, and S-19

Background:

In response to OCE's consult request dated, June 29, 2023, OPDP has reviewed the proposed Prescribing Information (PI) and Patient Package Insert (PPI) for TEMODAR® (temozolomide) capsules, for oral use and injection, for intravenous use (Temodar). These supplements (S-36 through 38 and S-17 through 19) propose labeling revisions as part of OCE's Project Renewal.

PI/PPI:

OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on June 30, 2023, and our comments are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) review will be completed, and comments on the proposed PPI will be filed under separate cover.

Thank you for your consult. If you have any questions, please contact Mispa Ajua-Alemanji at Mispa.Ajua-Alemanji@fda.hhs.gov.

PI:

Section	Statement from Draft (if applicable)	OPDP Comment
2.2 Recommended Dosage and Dosage Modifications for Newly Diagnosed Glioblastoma	"Other administration schedules have been used."	OPDP is concerned that the vague language regarding the use of "other administration schedules" is promotional in tone and may create a confusing impression regarding the appropriate dosage and administration for Temodar. This may lead to the promotion of administration schedules that lack sufficient evidence for safety and/or efficacy; however, due to this vague language in the approved product labeling, OPDP would not be able to object to such presentations. We recommend revising to provide recommendations for *specific* administration schedules or to delete this statement.
2.4 Preparation and Administration	"Administer TEMODAR consistently with respect to food (fasting vs. nonfasting) *[see Clinical Pharmacology (12.3)]*. To reduce nausea and vomiting, take TEMODAR on an empty stomach or at bedtime and consider antiemetic therapy prior to and following TEMODAR administration."	The language regarding taking Temodar "consistently with respect to food," may be somewhat confusing, especially given the subsequent recommendation to take it on an empty stomach at bedtime to reduce nausea. Additionally, there is no timeframe include to qualify what is considered "fasting" or "on an empty stomach"—such vague recommendations may be difficult for providers to interpret into actionable instructions for patients. OPDP asks that the review division please consider the following revisions: • Direct language to describe that Temodar can be taken with or without food (if this is accurate). • A recommendation regarding the timing for taking Temodar (e.g., "at the same time each day"). A specific timeframe for what is considered to be "fasting" or an "empty stomach" (e.g., two hours before or after meals)
5.1 Myelosuppression	"In MK-7365-006, myelosuppression **usually occurred** during the first few cycles of therapy and **was generally not cumulative**." (emphasis added)	The phrasing "usually occurred" and "was generally not cumulative" is vague, promotional in tone, and may minimize the risk of myelosuppression associated with the drug. OPDP recommends revising this language to include the specific percentages of patients from MK-7365-006 with myelosuppression by cycle and the percentage of patients with cumulative myelosuppression.

6.1 Clinical Trials Experience	"Newly Diagnosed Glioblastoma" The most common adverse reactions (≥ (b) (4) %) in patients treated with TEMODAR were (b) (4) "	OPDP notes that according to table 3, in the maintenance use phase, patients experienced (b) (4) Should the statement regarding the most common ARs ≥ (b) (4) % be revised to include these ARs?
6.1 Clinical Trials Experience		OPDP notes that information regarding dose interruptions, dose adjustments, discontinuations due to ARs, and fatal ARs is not included in this section. We acknowledge that this information may not be available due to the nature of the data; however, if it *is* available, we recommend that it be included in order to provide a more comprehensive picture of the safety profile of the drug.
14.2 Refractory Anaplastic Astrocytoma	"The efficacy of TEMODAR was evaluated in Study MK-7365-006, a **single-arm**, multicenter trial" (emphasis added) "In this population, progression-free survival at 6 months was 45% (95% CI: 31%, 58%) and progression-free survival at 12 months was 29% (95% CI: 16%, 42%). Median progression-free survival was 4.4 months. Overall survival at 6 months was 74% (95% CI: 62%, 86%) and 12-month overall survival was 65% (95% CI: 52%, 78%). Median overall survival was 15.9 months."	OPDP is extremely concerned with the inclusion of time-to-event endpoint data from a single-arm trial in approved product labeling. As stated in the *Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics* Guidance for Industry, "Single-arm trials do not adequately characterize time-to event endpoints such as overall survival, DFS (and EFS), TTP, or PFS. Because of variability in the natural history of many forms of cancer, a randomized study is necessary to evaluate time-to-event endpoints." OPDP has consistently objected to the presentation of time-to-event endpoints such as OS and PFS in promotional materials for drugs approved based on single-arm trials and we have received consistent support for such objections in the form of consult responses to the review division. Inclusion of this data in the product labeling for a single-arm trial would preclude OPDP from being able to object to the presentation of such data in promotional materials. Additionally, it does not seem consistent with our current labeling practices for including such data in the PI. We acknowledge that this information has been in the label for a long time; however, OPDP has not been consulted on the labeling since 2008 and labeling practices have changed substantially since that time.

17 Patient Counseling Information **Hepatotoxicity**	"Advise patients of the increased risk of hepatotoxicity and to contact their healthcare provider immediately for signs or symptoms of hepatotoxicity."	OPDP recommends revising the patient counseling information for hepatotoxicity to include information regarding the need for monitoring during treatment. Specifically, we note that section 5.2 states: "Perform liver tests at baseline, midway through the first cycle, prior to each subsequent cycle, and approximately two to four weeks after the last dose of TEMODAR."
17 PATIENT COUNSELING INFORMATION (b) (4)		OPDP notes (b) (4) We recommend revising (b) (4)

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Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Medical Policy

PATIENT LABELING REVIEW

Date:	July 17, 2023
To:	Adriene King-Ducre; PhD Health Scientist **Oncology Center of Excellence (OCE)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Sharon R. Mills, BSN, RN, CCRP Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Mispa Ajua-Alemanji, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Patient Package Insert (PPI)
Drug Name (established name), Dosage Form and Route, Application Type/Number, Supplement Number:	TEMODAR (temozolomide) capsules for oral use, NDA 021029/S-036, S-037, and S-038 TEMODAR (temozolomide) for injection, NDA 022277/S-017, S-018, and S-019
Applicant:	Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc.

1 INTRODUCTION

On June 14, 2023, Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc. submitted for the Agency's review a total of six Prior Approval Supplements (PAS)-Efficacy to their approved New Drug Applications (NDA) 021029/S-036, S-037, and S-038 for TEMODAR (temozolomide) capsules and NDA 022277/S-017, S-018, S-019 for TEMODAR (temozolomide) for injection. These supplements were submitted in response to the Agency's Correspondence to the Applicant dated January 25, 2021 requesting their participation in Project Renewal, and a Prior Approval Supplement Request Letter dated March 1, 2023 related to Project Renewal, proposing the following labeling revisions to the Prescribing Information (PI):

- Updates to the current indications for Temodar (temozolomide) and their current recommended dosage regimens to contain additional relevant information and to enhance the safe use of this drug;
- Revisions to the Indication section to include one proposed new indication, and its associated recommended dosage regimens;
- Addition of a new subsection and revisions to the Warnings and Precautions section to reflect the relative clinical significance of these adverse reactions;
- Revisions to the Adverse Reactions section to incorporate relevant safety information for the proposed indications;
- Revisions ot the Clinical Studies section to include summaries of the clinical studies that facilitate an understanding of how to use the drug safely and effectively for the proposed indications, consistent with 21 CRR 201.57(c) (15);
- Edits to other sections to conform to current labeling guidandance, as applicable.

This collaborative review is written by the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) in response to a request by the Oncology Center of Excellence (OCE) on June 29, 2023, for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) for TEMODAR (temozolomide) capsules and TEMODAR (temozolomide) for injection.

2 MATERIAL REVIEWED

- Draft TEMODAR (temozolomide) capsules and TEMODAR (temozolomide) for injection PPI received on June 14, 2023.
- Draft TEMODAR (temozolomide) capsules and TEMODAR (temozolomide) for injection Prescribing Information (PI) received on June 14, 2023, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on June 30, 2023.
- Approved TEMODAR (temozolomide) capsules and TEMODAR (temozolomide) for injection labeling dated November 22, 2020.

3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level, and have a reading ease score of at least 60%. A reading ease score of 60% corresponds to an 8th grade reading level.

Additionally, in 2008 the American Society of Consultant Pharmacists Foundation (ASCP) in collaboration with the American Foundation for the Blind (AFB) published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. The ASCP and AFB recommended using fonts such as Verdana, Arial or APHont to make medical information more accessible for patients with vision loss. We reformatted the PPI document using the Arial font, size 10.

In our collaborative review of the PPI we:

- simplified wording and clarified concepts where possible
- ensured that the PPI is consistent with the Prescribing Information (PI)
- removed unnecessary or redundant information
- ensured that the PPI is free of promotional language or suggested revisions to ensure that it is free of promotional language
- ensured that the PPI meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)

4 CONCLUSIONS

The PPI is acceptable with our recommended changes.

5 RECOMMENDATIONS

- Please send these comments to the Applicant and copy DMPP and OPDP on the correspondence.
- Our collaborative review of the PPI is appended to this memorandum. Consult DMPP and OPDP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the PPI.

Please let us know if you have any questions.

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/s/

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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)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	July 13, 2023
Requesting Office or Division:	Oncology Center of Excellence (OCE)
Application Type and Number:	NDA 022277 S-17, S-18, S-19 NDA 021029 S-36, S-37, S-38
Product Name, Dosage Form, and Strength:	Temodar (temozolamide) for injection, 100 mg and Temodar (temozolamide) capsules, 5 mg, 20 mg, 100 mg, 140 mg, 180 mg, and 250 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Merck
FDA Received Date:	June 14, 2023; April 24, 2023; September 16, 2011
TTT ID #:	2023-5367
DMEPA 2 Safety Evaluator:	Sali Mahmoud, PharmD, BCPS
DMEPA 2 Team Leader:	Ashleigh Lowery, PharmD

1 REASON FOR REVIEW

As part of Project Renewal[a], FDA issued a Supplement Request letter to Merck on March 1, 2023 for Temodar[b]. In response, Merck submitted 3 Efficacy Supplements for Temodar (temozolamide) for injection NDA 022277 and 3 Efficacy supplements for Temodar (temozolamide) capsules NDA 021029 (one for each new indication requested to support the use of Temodar in patients with newly diagnosed anaplastic astrocytoma, refractory anaplastic astrocytoma, and newly diagnosed glioblastoma). X Subsequently, the Oncology Center of Excellence (OCE) requested that we review the proposed Temodar prescribing information (PI), Patient information, and carton labeling for areas of vulnerability that may lead to medication errors. Of note, there Merck did not propose edits to the container labels.

2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

Table 1. Materials Considered for this 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 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

We reviewed the proposed revisions to Section 2 (Dosage and administration), Section 3 (Dosage forms and strengths), Section 16 (How supplied/Storage and handling) and Section 17 (Patient counseling) of the Temodar PI and Patient Information and found Section 2 can be

[a] Lee, C. General Advice for NDA 021029 Temodar. Silver Spring (MD): FDA, CDER, OCE (US); 2021 JAN 25.

[b] King-Ducre, A. Prior Approval Supplement Request for Temodar NDA 22277; NDA 021029. Silver Spring (MD): FDA, CDER, OCE (US); 2023 MAR 01.

improved and the revisions to sections 3, 16 and 17 are acceptable from a medication error perspective. The Patient Information is acceptable. We also reviewed the carton labeling and the current container labels and determined that can also be improved for clarity and consistency.

4 CONCLUSION & RECOMMENDATIONS

DMEPA identified areas in the labels that can be improved to promote the safe use of the product. We provide recommendations in Section 4.1 for OCE and 4.2 for the Applicant to address these deficiencies.

4.1 RECOMMENDATIONS FOR ONCOLOGY CENTER OF EXCELLENCE (OCE)

A. Prescribing Information

1. Dosage and Administration Section (full PI)

a. We recommend titling section 2.1 more clearly to indicate that it contains monitoring parameters which decide treatment. Consider "Important Monitoring to Inform Dosage and Administration."

i. We recommend moving all monitoring information into this section and naming the indications that would require these schedules to facilitate retrieval of information.

b. Consider starting the title of each subsection with the indication to improve readability. For example, revise "Recommended Dosage and Dosage Modifications for Newly Diagnosed Glioblastoma" to "Newly Diagnosed Glioblastoma - Recommended Dosage"

c. We recommend a separate subsection "Dosage modifications due to adverse reactions" to improve retrieval of information since Table 2 is shared between multiple indications. Include the pertinent indications in the titling of each table for clarity.

d. To clarify treatment days within a cycle we recommend adding "on day 1 to 5" following the dosage to emphasize the time interval.

Example "Cycle 1: 150 mg/m^2 per day on days 1 to 5

Cycles 2 to 12: 200 mg/m^2 per day on days 1 to 5"

4.2 RECOMMENDATIONS FOR MERCK

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

A. General Comments (Container labels and Carton Labeling)

1. Temodar is hazardous; however, the principal display panel of the carton labeling does not convey this information. Hazardous products require special handling procedures. We recommend adding the statement, "WARNING: Hazardous Drug" in bold font on the principal display panel of the container label and carton labeling or side panel. Update the term (b) (4) on side panel to "Hazardous drug."

B. Carton Labeling

1. For the intravenous product-

    a. As currently presented, the statement (b) (4) does not specify how to administer the product intravenously (e.g., intravenous infusion or bolus). Additionally, there are no instructions on the PDP to indicate that the product must be reconstituted. This may lead to wrong technique drug administration errors. We recommend revising the statement (b) (4) to "For Intravenous Infusion after Reconstitution" to indicate that the product must be reconstituted and to minimize the risk of the product being administered as an intravenous bolus.

2. For capsules-

    a. A product identifier is not present on the carton. In June 2021, FDA finalized the Guidance for Industry on product identifiers required under the Drug Supply Chain Security Act (DSCSA). The Act requires manufacturers and re-packagers to affix or imprint a product identifier to each package and homogenous case of a product intended to be introduced in a transaction in(to) commerce. The product identifier includes the NDC, serial number, lot number, and expiration date in both a human-readable form and machine-readable (2D data matrix barcode) format. We recommend that you review the guidance to determine if the product identifier requirements apply to your product's labeling. See Guidance for Industry: Product Identifiers under the Drug Supply Chain Security Act - Questions and Answers (June 2021). If you determine that the product identifier requirements apply to your product's labeling, we request you add a place holder to the carton labeling.[d]

    b. The placeholder for the expiration date is missing. The expiration date is required on the immediate container and carton labeling per 21 CFR 211.137. We recommend you ensure that there are no other numbers located in close proximity to the expiration date. To minimize confusion and reduce the risk for deteriorated drug medication errors, we recommend identifying the expiration date format you intend to use. FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear 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.

c. The placeholder for the lot number is missing. Lot number statement is required on the immediate container AND carton labeling when there is sufficient space per 21 CFR 201.10(i)(1). Add the placeholder for the lot number in accordance 21 CFR 201.10(i)(1).

d. Replace (b) (4) with "Recommended Dosage: See Prescribing Information." Delete the remainder of the statement (b) (4)

e. To minimize confusion, we recommend deleting the (b) (4) (b) (4) statement (b) (4) (b) (4)

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Temodar received on June 14, 2023 from Merck.

Table 2. Relevant Product Information for Temodar	
Initial Approval Date	August 11, 1999 (NDA 21029) February 27, 2009 (NDA 22277)
Active Ingredient	temozolamide
Indication	TEMODAR is an alkylating drug indicated for the treatment of adult patients with: • Newly diagnosed glioblastoma concomitantly with radiotherapy and then as maintenance treatment. • Anaplastic astrocytoma- adjuvant treatment of newly diagnosed and refractory anaplastic astrocytoma
Route of Administration	Oral; Intravenous
Dosage Form	Capsule; for injection
Strength	Capsules: 5 mg, 20 mg, 100 mg, 140 mg, 180 mg, and 250 mg For injection: 100 mg per vial
Dose and Frequency	Newly Diagnosed Glioblastoma: • 75 mg/m^2 once daily for 42 to 49 days concomitant with focal radiotherapy followed by initial maintenance dose of 150 mg/m^2 once daily for Days 1 to 5 of each 28-day cycle for 6 cycles. May increase maintenance dose to 200 mg/ m^2 for cycles 2 – 6 based on toxicity. • Provide Pneumocystis pneumonia (PCP) prophylaxis during concomitant phase and continue in patients who develop lymphopenia until resolution to grade 1 or less. • Anaplastic astrocytoma- adjuvant treatment of adults newly diagnosed: 150 mg/m^2 once daily for Days 1 to 5 of each 28-day cycle for 12 cycles. May increase to 200 mg/m^2 per day on day 1 to 5 if patient experienced no or minimal toxicity in Cycle 1. If the dose was not escalated at the onset of Cycle 2, do not increase the dose during Cycles 3 to 6. • Refractory Anaplastic Astrocytoma: Initial dose of 150 mg/m^2 once daily on Days 1 to 5 of each 28-day cycle. May increase to 200 mg/m^2 for some patients.
How Supplied	TEMODAR capsules are supplied in child-resistant sachets containing the following capsule strengths: 5 mg, 20 mg, 100 mg, 140 mg, 180 mg, and 250 mg.

	TEMODAR for injection is supplied in single-dose glass vials containing 100 mg temozolomide.
Storage	Store TEMODAR Capsules at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Store TEMODAR for injection refrigerated at 2°C to 8°C (36°F to 46°F).
Container Closure	Capsules: Two-piece, (b) (4) white, (b) (4) child resistant closure, with liner and innerseal. For injection: 100 mL-20 mm (b) (4) glass vials sealed with 20 mm (b) (4) rubber stopper and capped with aluminium 20 mm (b) (4) seals

APPENDIX B. PREVIOUS DMEPA REVIEWS

On July 7, 2023, we searched for previous DMEPA reviews relevant to this current review using the terms, temodar. Our search identified 2 previous reviews[c,d] since our last search on Feb 20, 2020, and we considered our previous recommendations to see if they are applicable for this current review.

[c] Thomas, S. Label and Labeling Review for Temodar (NDA 22277; NDA 021029). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 APR 24. OSE RCM No.: 2020-293.

[d] Thomas, S. Label and Labeling Review for Temodar (NDA 22277; NDA 021029). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 AUG 27. OSE RCM No.: 2020-293-1.

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,[e] along with postmarket medication error data, we reviewed the following Temodar labels and labeling submitted by Merck.

- Container label received on April 24, 2023; September 16, 2011
- Carton labeling received on June 14, 2023
- Prescribing Information (Image not shown) received on June 14, 2023, available from \\CDSESUB1\EVSPROD\nda022277\0135\m1\us\01-crt-uspi-mk7365-mtl-fda-project-renewal.doc
    - Patient information \\CDSESUB1\EVSPROD\nda022277\0135\m1\us\01-wrm-usppi-mk7365-mtl-fda-project-renewal.doc

F.2 Label and Labeling Images

Container labels

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

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