CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

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

Trade Name:	TEMODAR
Generic or Proper Name:	temozolomide
Sponsor:	Merck Sharp & Dohme LLC
Approval Date:	September 14, 2023
Indications:	• Newly diagnosed glioblastoma concomitantly with radiotherapy and then as maintenance treatment. • Anaplastic astrocytoma • Adjuvant treatment of adults with newly diagnosed anaplastic astrocytoma • Treatment of adults with refractory anaplastic astrocytoma

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

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APPLICATION NUMBER:

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APPROVAL LETTER

NDA 021029/S-036, S-037, S-038
NDA 022277/S-017, S-018, S-019

SUPPLEMENT APPROVAL

Merck Sharp & Dohme LLC, a subsidiary of Merck& Co., Inc.
Attention: Smaran Patel
Associate Principal Scientist, Regulatory Liaison, Global Regulatory Affairs
126 E. Lincoln Avenue, PO Box 2000
Rahway, NJ 07065

Dear Smaran Patel:

Please refer to your supplemental new drug applications (sNDAs) dated and received June 14, 2023, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Temodar (temozolomide) capsules and for injection.

In connection with Project Renewal, these Prior Approval sNDAs provide for the following updates:

- NDA 021029/S-038 and NDA 022277/S-017: Revisions to the Indication section to include a new indication for adjuvant treatment of adults with newly diagnosed anaplastic astrocytoma and its associated recommended dosage regimens;

- NDA 021029/S-037 and NDA 022277/S-018: Revisions to the Dosage and Administration section for the existing indication for newly diagnosed glioblastoma;

- NDA 021029/S-036 and NDA 022277/S-019: Revisions to the Indication section for the existing indication for refractory anaplastic astrocytoma to remove the stipulation that patients should have experienced disease progression while on a drug regimen containing procarbazine and nitrosourea, and its associated recommended dosage regimens;

- Revisions to the Warnings and Precautions, Adverse Reactions, and Patient Counseling Information sections to incorporate relevant safety information;

- Edits to other sections to conform to current labeling guidances, as applicable.

APPROVAL & LABELING

We have completed our review of this application. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Patient Package Insert), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.[2]

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the carton and container labeling submitted on August 9, 2023 and August 11, 2023 as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 021029/S-36-S-38 and NDA 022277/S-17-S-19**." Approval of this submission by FDA is not required before the labeling is used.

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[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for these applications because this product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients and is not likely to be used in a substantial number of pediatric patients.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety-related information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4).

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, contact Adriene King-Ducre, Health Scientist, at Adriene.King-Ducre@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Jennifer Gao, MD
Associate Director
Oncology Center of Excellence

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

JENNIFER J GAO
09/14/2023 09:47:09 AM