

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER: NDA 21029**

**CHEMISTRY REVIEW(S)**

Division of Oncologic Drug Products  
 Review of Chemistry, Manufacturing and Controls

NDA #: 21-029      CHEM. REVIEW#: 3      REVIEW DATE: July 29, 1999

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Original	Aug. 12, 1998	Aug. 14, 1998	Aug. 19, 1998
BC	Dec. 22, 1998	Dec. 23, 1998	Jan. 4, 1999
BL	April 23, 1999	April 26, 1999	April 28, 1999
NC	May 27, 1999	May 28, 1999	June 1, 1999
BL	May 19, 1999	May 20, 1999	May 20, 1999
BC	May 24, 1999	June 1, 1999	June 1, 1999

NAME AND ADDRESS OF APPLICANT:      Schering Corporation  
 2000 Galloping Hill Rd.  
 Kenilworth, NJ 07033

DRUG PRODUCT NAMES:

Proprietary:      Temodar  
 Nonproprietary/USAN:      Temozolomide  
 Code Name/#:      CAS 85622-93-1  
 Chem. Type/Ther. Class      1-P

PHARMACOL. CATEGORY/INDICATION:

DOSAGE FORM/STRENGTHS:      250 mg; 100 mg; 20mg; 5mg/capsules

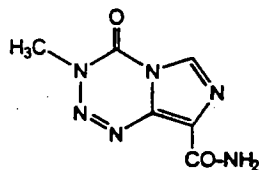
ROUTE OF ADMINISTRATION:      Oral

MANUFACTURER:

B. Drug Product  
 Schering Corp.  
 2000 Galloping Hill Rd.  
 Kenilworth, NJ 07033

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR WEIGHT:

3,4-Dihydro-3-methyl-4-oxoimidazo[5,1-d]-as-tetrazine-8-carboxamide  
 $C_6H_6N_6O_2$ , MW = 194.15



SUPPORTING DOCUMENTS:

DMF

Reviewed by  
 Dr. Riggleman (HFD-160)  
 dated 5/6/1992

DMF

Reviewed by: Dr. Berta  
(HFD-570) dated 5/8/96

DMF

Reviewed by Dr. E. Duffy  
(HFD-635) dated 8/12/93.

DMF

Reviewed by Dr. Shing Hou  
Liu, (HFD-625) dated 2/1/94

**CONSULTS:**

Consult	Status	
EER	Acceptable	1/25/1999
Trademark	Acceptable	
Biopharmaceuticals	Acceptable	1/11/1999
Microbiology	Acceptable	12/1/98
Environmental Assessment	Categorical	Acceptable
	Exclusion	

**REMARK/COMMENTS:**

The applicant has provided the updated information regarding the drug trade name, bottle/carton labels and minor modification in the description of DP capsule shell. The information is found to be adequate.

**CONCLUSIONS AND RECOMMENDATIONS:**

Approval of NDA 21-029 is recommended with respect to CMC issue. However, the Project Manager should communicate following issues to the applicant:

1. The circle beside the trade name should be deleted.
2. The "capsules" should be appeared following the established name temozolomide to read as: "Temodar (temozolomide) capsules" .

*ISI* *8/2/99*  
\_\_\_\_\_  
Chengyi Liang, Ph.D., Review Chemist

*ISI* *08/02/99*  
*100* \_\_\_\_\_  
Liang Zhou, Ph.D.  
Chemistry Team Leader

CC:

Orig. NDA 21-029  
HFD-150 Division File  
HFD-150/CLiang  
HFD-150/LZhou  
HFD-150/Pguinn  
HFD-810/Directors

Division of Oncologic Drug Products  
Review of Chemistry, Manufacturing and Controls

NDA #: 21-029      CHEM. REVIEW#: 2      REVIEW DATE: Jan. 19, 1999

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Original	Aug. 12, 1998	Aug. 14, 1998	Aug. 19, 1998
BC	Dec. 22, 1998	Dec. 23, 1998	Jan. 4, 1999

NAME AND ADDRESS OF APPLICANT:      Schering Corporation  
2000 Galloping Hill Rd.  
Kenilworth, NJ 07033

DRUG PRODUCT NAMES:

Proprietary:      Temodal  
Nonproprietary/USAN:      Temozolomide  
Code Name/#:      CAS 85622-93-1  
Chem. Type/Ther. Class      1-P

PHARMACOL. CATEGORY/INDICATION:

DOSAGE FORM/STRENGTHS:      250 mg; 100 mg; 20mg; 5mg/capsules

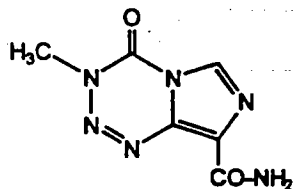
ROUTE OF ADMINISTRATION:      Oral

MANUFACTURER:

B. Drug Product  
Schering Corp.  
2000 Galloping Hill Rd.  
Kenilworth, NJ 07033

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR WEIGHT:

3,4-Dihydro-3-methyl-4-oxoimidazo[5,1-d]-as-tetrazine-8-carboxamide  
C<sub>6</sub>H<sub>6</sub>N<sub>6</sub>O<sub>2</sub>, MW = 194.15



**SUPPORTING DOCUMENTS:**

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Reviewed by  
Dr. Riggleman (HFD-160)  
dated 5/6/1992

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DMF

Reviewed by Dr. E. Duffy  
(HFD-635) dated 8/12/93

DMF

Reviewed by Dr. Shing Hou  
Liu, (HFD-625) dated 2/1/94

**CONSULTS:**

<b>Consult</b>	<b>Status</b>	<b>Comments</b>
EER	Pending	Submitted on 8/20/98
Trademark	Pending	Submitted on 11/13/96
Biopharmaceuticals	Acceptable	1/11/1999
Microbiology	Acceptable	12/1/98
Environmental Assessment	Categorical Exclusion	Acceptable

**REMARK/COMMENTS:**

The applicant has provided the more detailed CMC information to address the deficiencies found in the original NDA review. These information is found to be adequate.

**CONCLUSIONS AND RECOMMENDATIONS:**

The NDA could be approval with respect to CMC issue pending EER.

*IS/*  
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Chengyi Liang, Ph.D. *1/22/99* Review Chemist

*IS/*  
\_\_\_\_\_  
Liang/Zhou, Ph.D. *1/21/99*  
Chemistry Team Leader

**CC:**

Orig. NDA 21029  
HFD-150 Division File  
HFD-150/CLiang  
HFD-150/Lzhou  
HFD-150/Pguinn  
HFD-810/Directors

## ADDENDUM

NDA 21-029

February 5, 1999

### Comments

1. EES inspection for this NDA is found to be acceptable. Please refer to the EER status report.
2. Fax amendment dated Feb. 4, 1999 was received. The applicant's justification for the Trade Mark seems to be acceptable from a CMC point of view. However, trademark's acceptability/occurrence regarding safety issues should be determined by the medical reviewers.

### Conclusions and Recommendations

This NDA is recommended for approval.

LSI 2/5/99

Liang Zhou, Ph.D.,  
Chemistry Team Leader

CC:  
Orig. NDA 21-029  
HFD-150 Division File  
HFD-150/CLiang  
HFD-150/LZhou  
HFD-150/PGuinn

NDA 21-029, Temodal (temozolomide capsules)

DEC 1 1998

Division of Oncologic Drug Products  
Review of Chemistry, Manufacturing and Controls

NDA #: 21-029      CHEM. REVIEW#: 1      REVIEW DATE: Nov. 31, 1998

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Original	Aug. 12, 1998	Aug. 14, 1998	Aug. 19, 1998

NAME AND ADDRESS OF APPLICANT: Schering Corporation  
2000 Galloping Hill Rd.  
Kenilworth, NJ 07033

DRUG PRODUCT NAMES:

Proprietary:	Temodal
Nonproprietary/USAN:	Temozolomide
Code Name/#:	CAS 85622-93-1
Chem. Type/Ther. Class	1-P

PHARMACOL. CATEGORY/INDICATION:

DOSAGE FORM/STRENGTHS: 250 mg; 100 mg; 20mg; 5mg/capsules

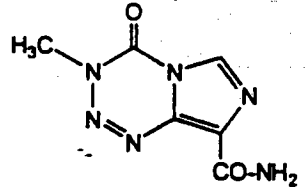
ROUTE OF ADMINISTRATION: Oral

MANUFACTURER:

B. Drug Product  
Schering Corp.  
2000 Galloping Hill Rd.  
Kenilworth, NJ 07033

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR WEIGHT:

3,4-Dihydro-3-methyl-4-oxoimidazo[5,1-d]-as-tetrazine-8-carboxamide  
C<sub>6</sub>H<sub>6</sub>N<sub>6</sub>O<sub>2</sub>, MW = 194.15



SUPPORTING DOCUMENTS:  
DMF

Reviewed by  
Dr. Riggleman (HFD-160)  
dated 5/6/1992

NDA 21-029, Temodal (temozolomide capsules)

DMF

Reviewed by Dr. Berta  
(HFD-570) dated 5/8/96

DMF

Dr. E. Duffy (HFD-635)  
dated 8/12/93

**CONSULTS:**

Consult	Status	Comments
Consult	Status	Comments
EER	Pending	Submitted on 8/20/98
Trademark	Pending	Submitted on 11/13/96
Statistics	Pending	Submitted on 9/21/98
Biopharmaceuticals	Pending	Submitted on 9/21/98
Microbiology	Pending	Submitted on 9/21/98
Environmental Assessment	Categorical	Acceptable
	Exclusion	

**REMARK/COMMENTS:**

The applicant has provided the more detailed CMC information regarding the drug substance and drug product. Although the several deficiencies found during the review are not the major problems, they still need to be addressed by the applicant.

**CONCLUSIONS AND RECOMMENDATIONS:**

The NDA could be approval with respect to CMC issue if the deficiencies are addressed satisfactorily and the consults/EER are satisfactory.

*ISI*  
\_\_\_\_\_  
Chengyi Liang, Ph.D., Review Chemis *11/30/98*

*ISI* *12/1/98*  
\_\_\_\_\_  
Liang Zhou, Ph.D.  
Chemistry Team Leader

**CC:**

Orig. NDA 21029  
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HFD-150/CLiang  
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