

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-278**

**CHEMISTRY REVIEW(S)**

**NDA #: 21-278****DATE REVIEWED: 11/8/01****REVIEW #: 2****REVIEWER: Donald N. Klein, Ph.D.**

<b><u>SUBMISSION TYPE</u></b>	<b><u>DOCUMENT DATE</u></b>	<b><u>CDER DATE</u></b>	<b><u>ASSIGNED DATE</u></b>
Desk Copy: CMC	9/4/01	9/5/01	9/5/01
Information Request	9/14/01	9/14/01	not applicable
Fax from Celgene	9/25/01	not applicable	9/26/01
Complete Response	9/14/01	9/14/01	9/26/01
Acknowledgement Letter	10/11/01	10/11/01	not applicable
Fax from Celgene	10/24/01	not applicable	10/26/01
Fax from Celgene	10/29/01	not applicable	10/29/01
Amendment	10/30/01	10/30/01	11/6/01
Celgene E-mail attachment	11/6/01	not applicable	11/6/01

**NAME & ADDRESS OF APPLICANT:**

CELGENE CORPORATION  
7 Powder Horn Drive  
Warren, NJ 07059

**DRUG PRODUCT NAME:**

Proprietary:  
Established(USAN):  
Code Name(USAN):  
Chem. Type/Ther. Class:

TRADENAME  
dexmethylphenidate hydrochloride  
d-MPH  
3S

**PHARMACOL. CATEGORY/INDICATION:**

Attention Deficit Hyperactivity Disorder

**DOSAGE FORM:**

Tablet

**STRENGTHS:**

2.5mg(blue), 5.0mg(yellow), and 10.0mg(white)

**ROUTE OF ADMINISTRATION:**

Oral

**Rx/OTC:**

Rx

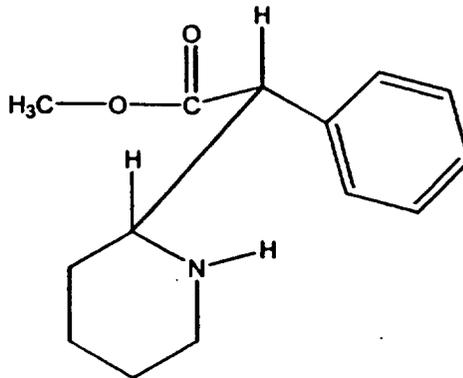
**SPECIAL PRODUCTS:**

Yes  No

**CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:**

The trivial name is *d-threo*-methylphenidate hydrochloride. The chemical names are  $\alpha$ -phenyl-2-piperidineacetic acid, methyl ester, hydrochloride, (R,R')-(+), or, methyl  $\alpha$ -phenyl-2-piperidineacetate hydrochloride, (R,R')-(+), or, methyl  $\alpha$ -phenyl-2R-piperidineacetate hydrochloride.

Molecular formula:  $C_{14}H_{20}ClNO_2$   
MW: 269.77



**COMMENTS:**

1. The following Drug Substance CMC sections of this complete response submission are acceptable: Synthesis/Method of Manufacture and Process Control; Regulatory Specifications/Analytical Methods; Description & Characterization; Manufacturer; Reference Standard; Container Closure System; and Stability.
2. The drug substance retest date is 15 months. The retest date can be extended based on the submission of real time stability data.
3. The following Drug Product CMC sections of this complete response are acceptable: Components/Composition; Specification & Methods for Inactive Components; Manufacturer; Container Closure System; Methods of Manufacturing and Packaging; Regulatory Specifications/Analytical Methods; and Stability.
4. The following package insert and labeling are acceptable: a. "Description" section of the package insert; b. "How Supplied" section of the package insert; c. container closure labels; d. secondary packaging and label.
5. Establishment Inspection: On 9/18/01 the Overall Compliance recommendation was acceptable.
6. The expiration date is 24 months for the 2.5mg, 5.0mg, and 10.0mg tablets.
7. Method Validation: The following analytical methods will be submitted to the FDA for validation:

Drug Substances:

Drug Products:

**CONCLUSIONS:** Recommend Approval of the CMC section of NDA 21-278.

[Redacted]

[Redacted]

1   page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

**NDA 21-278**

**DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS**  
Review of Chemistry, Manufacturing, and Controls

**NDA #: 21-278**

**DATE REVIEWED: 8/2/01**

**REVIEW #: 1**

**REVIEWER: Donald N. Klein, Ph.D.**

<b><u>SUBMISSION TYPE</u></b>	<b><u>DOCUMENT DATE</u></b>	<b><u>CDER DATE</u></b>	<b><u>ASSIGNED DATE</u></b>
ORIGINAL	10/25/00	10/25/00	11/7/00
Electronic Submission	not applicable	not applicable	11/15/00
Information Request	11/8/00	11/8/00	not applicable
Information Request	11/15/00	11/15/00	not applicable
Information Request	11/15/00	11/15/00	not applicable
(NC) Amendment	11/22/00	11/22/00	11/28/00
(NC) Amendment	12/4/00	12/4/00	12/12/00
(BC) Amendment	12/28/00	12/28/00	1/2/01
Information Request	2/1/01	2/1/01	not applicable
Information Request	2/2/01	2/2/01	not applicable
Information Request	2/2/01	2/2/01	not applicable
(BC) Amendment	2/13/01	2/13/01	2/20/01
(BL) Amendment	2/20/01	2/20/01	2/22/01
Fax from Celgene	2/28/01	not applicable	2/28/01
(BC) Amendment	3/8/01	3/8/01	3/16/01
Desk Copy	3/16/01	not applicable	3/16/01
(BC) Amendment	3/15/01	3/16/01	3/19/01
Fed-Ex from Celgene	not dated	not applicable	4/4/01
(BC) Amendment	4/9/01	4/9/01	4/12/01
Desk Copy	5/7/01	not applicable	5/11/01
(NC) Amendment	5/7/01	5/7/01	5/14/01
Desk Copy	5/21/01	not applicable	5/23/01
(BC) Amendment	5/21/01	5/22/01	5/29/01
Information Request	5/29/01	5/29/01	not applicable
Information Request	5/29/01	5/29/01	not applicable
Fax from Celgene	6/18/01	not applicable	6/18/01
Desk Copy	6/19/01	not applicable	6/20/01
Desk Copy	6/21/01	not applicable	6/25/01
(BC) Amendment	6/19/01	6/20/01	6/25/01
(BC) Amendment	6/21/01	6/21/01	7/2/01
Desk Copy	6/25/01	not applicable	7/2/01
(BC) Amendment	6/25/01	6/25/01	7/2/01
Information Request	7/2/01	7/2/01	not applicable
Fax from Celgene	7/6/01	not applicable	7/8/01
Fax from Celgene	7/10/01	not applicable	7/10/01
Desk Copy	7/12/01	not applicable	7/13/01
(BC) Amendment	7/12/01	7/12/01	7/18/01

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