CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number : 040163

Trade Name : MEPERIDINE HYDROCHLORIDE INJECTION USP

Generic Name: Meperidine Hydrochloride Injection USP, 10mg/ml 60ml syringe

Sponsor : Mallinckrodt Chemical, Inc.

Approval Date: May 12, 1997

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION 040163

CONTENTS

	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
Tenative Approval Letter				
Approvable Letter				
Final Printed Labeling	X			
Medical Review(s)				
Chemistry Review(s)	X			
EA/FONSI				
Pharmacology Review(s)				
Statistical Review(s)				
Microbiology Review(s)				
Clinical Pharmacology Biopharmaceutics Review(s)				
Bioequivalence Review(s)	X			
Administrative Document(s)				
Correspondence				

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 040163

APPROVAL LETTER

ANDA 40-163

MAY 12 1997

Mallinckrodt Chemical, Inc.
Attention: Marianne Robb
16305 Swingley Ridge Drive
Chesterfield, MO 63017

Dear Madam:

This is in reference to your abbreviated new drug application dated August 31, 1995, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Meperidine Hydrochloride Injection USP, 10 mg/mL; 60 mL syringe. This application was submitted based upon your approved petition pursuant to Section 505(j)(2)(C)(i) of the Act.

Reference is also made to your amendments dated October 31, 1996; and January 24, and April 17, 1997.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Meperidine Hydrochloride Injection USP, 10 mg/mL to be bioequivalent and, therefore, therapeutically equivalent to that of the listed drug (Meperidine Hydrochloride Injection USP, 10 mg/mL, of Abbott Laboratories Hospital Products Division) upon which the Agency relied as the basis of safety and effectiveness.

Under 21 CFR 314.70, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-240). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-240) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

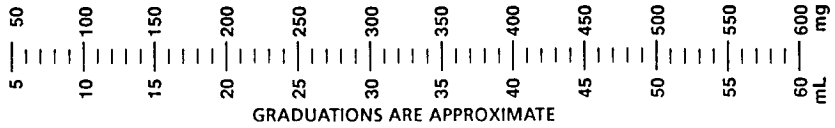
/S/ 5/12/97

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 040163

FINAL PRINTED LABELING



NDC 0406-8760-04

CII

Sterile Solution 60 mL

Meperidine Hydrochloride Injection, USP

WARNING: MAY BE HABIT FORMING

600 mg (10 mg/mL)

CAUTION: Federal (U.S.A.) law prohibits dispensing without prescription.

Mfg. For: **Mallinckrodt Chemical, Inc.** Chesterfield, MO 63017 USA

FOR SLOW INTRAVENOUS USE. ONLY for use with compatible PCA infusion pumps.
Single use syringe. Discard unused portion.
Usual Dosage: See Package Insert.
Protect from freezing.
Store at controlled room temperature 15°C-30°C (59°F-86°F).
332B96

Lot: Exp. Date:

MAY 12 1997

Meperidine Hydrochoride Injection, USP 60ml Handheld syringe plate

Meperidine Hydrochloride Injection, USP

WARNING: MAY BE HABIT FORMING

NDC 0406-8760-04

600 mg (10 mg/mL)

60 mL Prefilled Syringe

FOR SLOW INTRAVENOUS USE.

ONLY FOR USE WITH COMPATIBLE PCA INFUSION PUMPS.

10 single use syringes

SAMPLE

Caution: Federal (U.S.A.) law prohibits dispensing without prescription.

Protect from freezing. Store at controlled room temperature 15° to 30°C (59° to 86°F). Do not remove syringe from package until ready for use.

Each mL contains: meperidine hydrochloride 10 mg, with citric acid anhydrous 0.30 mg and 0.30 mg sodium citrate dihydrate added as buffers. Sodium hydroxide and/or hydrochloric acid may have been added for adjustment to pH 3.5 to 6.0.

Single use syringe • Discard unused portion and syringe.

Medication and Fluid Pathway are sterile and nonpyrogenic. Outside of syringe is not sterile.

Discard contents if either syringe seal is broken or if leaking is observed.

Usual Dosage: See Package Insert.

Manufactured for:
Mallinckrodt Chemical, Inc.
Chesterfield, MO 63017 U.S.A.

Manufactured by:
Mallinckrodt Medical, Inc.
Raleigh, NC 27616 U.S.A.

Printed in U.S.A.

MALLINCKRODT CHEMICAL

MAY 12 1997

334B96

Meperidine Hydrochloride Injection, USP

WARNING: MAY BE HABIT FORMING

NDC 0406-8760-04

600 mg (10 mg/mL)

60 mL Prefilled Syringe

FOR SLOW INTRAVENOUS USE.

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Printed in U.S.A.

MALLINCKRODT CHEMICAL

MAY 12 1997

334B96

Peel Here

Meperidine Hydrochloride Injection, USP

WARNING: MAY BE HABIT FORMING

NDC 0406-8760-04

600 mg (10 mg/mL)

60 mL Prefilled Syringe

FOR SLOW INTRAVENOUS USE

ONLY FOR USE WITH COMPATIBLE PCA INFUSION PUMPS.

1 single use syringe

SAMPLE

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Manufactured for:
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Chesterfield, MO 63017 U.S.A.

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Raleigh, NC 27616 U.S.A.

Printed in U.S.A.

333B96

MALLINCKRODT CHEMICAL

MAY 12 1997

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 040163

CHEMISTRY REVIEW(S)

OFFICE OF GENERIC DRUGS

DIVISION OF CHEMISTRY II

ANDA REVIEW

1. CHEMIST'S REVIEW NO. 2

2. ANDA # 40-163

3. NAME AND ADDRESS OF APPLICANT

   Mallinckrodt Chemical, Inc.
   Attention: Marianne Robb
   16305 Swingley Ridge Drive
   Chesterfield, MO 63017

4. LEGAL BASIS for ANDA SUBMISSION page 8

   Innovator: Abbott Laboratories/N-88432
   Patent & Exclusivity: page 13, No patent or exclusivity remaining.

5. SUPPLEMENT(s) None

6. PROPRIETARY NAME

   None

7. NONPROPRIETARY NAME

   Meperidine Hydrochloride Inj. USP

8. SUPPLEMENT(s) PROVIDE(s) FOR: None

9. AMENDMENTS AND OTHER DATES:

   Firm:
   - 08.31.95 - Original
   - 03.15.96 - Amendment
   - 04.15.96 - Amendment
   - 10.31.96 - Minor Amendment **Subject of this review**
   - 01.24.97 - Telephone amendment **Subject of this review**

   FDA:
   - 10.6 95 - Refuse to file
   - 3.28.96 - Acceptable for filing
   - 08.27.96 - NA letter #1

10. PHARMACOLOGICAL CATEGORY

    Narcotic Analgesic

11. Rx or OTC

    Rx

12. RELATED IND/NDA/DMF(s) see attached list

13. DOSAGE FORM

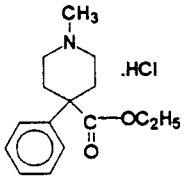
    Injection

14. POTENCY

    10 mg/mL

15. CHEMICAL NAME AND STRUCTURE

Meperidine Hydrochloride USP



4-Piperidinecarboxylic acid, 1-methyl-4-phenyl-, ethyl ester, hydrochlori

$C_{15}H_{21}NO_2.HCl$ 283.80

16. RECORDS AND REPORTS None

17. COMMENTS

a. Bio-waiver request acceptable - M. Kochar, 6.25.96
b. Microbiology review acceptable - A. High, 12.3.96
c. EER - acceptable, 5.3.96
d. Professional Labeling review - not satisfactory, C. Hoppes, 11.12.96;??
e. MV not required - compendial articles
f. DMF 11636 is satisfactory.
g. CMC is satisfactory.

18. CONCLUSIONS AND RECOMMENDATIONS

The ANDA can be approval upon satisfactory label review.

19. REVIEWER: DATE COMPLETED:

U. V. Venkataram 12.2.96 (start); 01-24-97

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 040163

BIOEQUIVALENCE REVIEW(S)

Dw

ANDA 40-163

JUN 27 1996

Mallinckrodt Chemical, Inc.
Attention: Charles H. Smith
16305 Swingley Ridge Drive
Chesterfield, MO 63017-1777

Dear Mr Smith:

This is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Meperidine Hydrochloride Injection USP, 10 mg/mL, 60 mL syringe.

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments expressed in this letter are preliminary. The above bioequivalency comments may be revised after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling or other scientific or regulatory issues. A revised determination may require additional information and/or studies, or may conclude that the proposed formulation is not approvable.

Sincerely yours,

/S/

Keith K. Chan, Ph.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

JUN 20 1996

Meperidine HCl Injection
10mg/mL, 60 mL Syringe
ANDA # 40-163
Reviewer: Man M. Kochhar
40163W.895

Mallinckrodt Chemical
Chesterfield, Missouri.
Submission Date:
August 31, 1995

Review of a Waiver Request

The Firm has requested a waiver of *in vivo* bioequivalence study for its meperidine hydrochloride injections 10 mg/mL, 60 mL syringe based upon 21 CFR 320.22 (b) (1).

Comparative Formulation

Ingredients	Mallinckrodt Amount	Abbott Amount
Meperidine HCl, USP	10.0 mg/mL	10.0 mg/mL
Sodium Acetate, Anhydrous	(b)4 - Confidential Business	
Sodium Citrate, dihydrate		
Glacial Acetic Acid		
Citric Acid, hydrous		
Water for injection, USP		
USP(q.s. ad)		
pH		

Deficiency: None

Comments:

1. The formulation of the test product and the innovator product meperidine hydrochloride (Abbott) is similar in concentration of active ingredients. The test product uses sodium citrate and citric acid and reference product uses sodium acetate and glacial acetic acid. These ingredients are used as buffer and should not effect the bioavailability of the meperidine.

2. The dosage form, route of administration (intravenous), strength (10 mg/mL) and labeling of the test drug product are identical to those of the innovator product, meperidine. The reference product is in 30 mL syringe where as test product is in 60 mL syringe. The dosages of the test and reference products are same.

3. From the bioequivalence point of view, the waiver of *in vivo* bioequivalence study requirement should be granted based on 21 CFR 320.22 (b)(1). The batch size is 630 liters.

Recommendation:

The Division of Bioequivalence agrees that the information submitted by Mallinckrodt Chemical on its Meperidine Hydrochloride 10 mg/mL, in 60 mL Syringe injection falls under 21

CFR 320.22 (b)(1) of the Bioavailability/Bioequivalence Regulations. The waiver of in vivo bioequivalence study for 10 mg/mL, 60 mL Syringe injection of the test product is granted.

From the bioequivalence point of view, the Division of Bioequivalence deems the test injection of Meperidine 10 mg/mL to be bioequivalent to Meperidine Hydrochloride 10.0 mg/mL injection manufactured by Abbott Laboratories.

The firm should be informed of the recommendation.

/S/

Man M. Kochhar, Ph.D.
Review Branch III
Division of Bioequivalence

RD INITIALLED RMHATRE /S/
FT INITIALLED RMHATRE 6/18/96

/S/

Concu Date: 6/20/96
Keith K. Chan, Ph.D.
Director
Division of Bioequivalence

MMKochhar/mmk/5-29-96/ 6-18-96; 40-163

cc: ANDA # 40-163 original, HFD-600 (Hare), HFD-630, HFD-658 (Mhatre, Kochhar), Drug File, Division File.