ANDA 40-167

L. Perrigo Company
Attention: Elizabeth Pileggi
117 Water St.
Allegan, MI 49010

Dear Madam:

Reference is made to your abbreviated new drug application dated September 12, 1995, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act for Doxylamine Succinate Tablets USP, 25 mg.

Reference is also made to your amendment dated May 10, 1996.

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 over-the-counter (OTC) labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined that your Doxylamine Succinate Tablets USP, 25 mg, are bioequivalent to the listed drug (Unisom® Tablets 25 mg by Pfizer Laboratories, Division of Pfizer Inc.).

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.

Sincerely yours,

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

Final Printed Labeling
Doxylamine Succinate
ANDA 40-167
Carton

MYLAR#
661

Doxylamine Succinate Tablets, 25 mg
NIGHTTIME SLEEP AID

INDICATIONS: Helps to reduce difficulty in falling asleep.
DIRECTIONS: Take ONE tablet 30 minutes before going to bed. Take once daily or as directed by a physician.

WARNINGS: Do not take this product if you have asthma, glaucoma, or enlargement of the prostate gland except under the advice and supervision of a physician.

• If sleeplessness persists continuously for more than two weeks, consult your physician. Insomnia may be a symptom of serious underlying medical illness. • Do not take this product if presently taking any other drug, without consulting your physician or pharmacist. • Take this product with caution if alcohol is being consumed. • Do not take this product if pregnant or nursing a baby. • For adults only. Do not give to children under 12 years of age. • Keep this and all medications out of the reach of children. • CAUTION: This product contains an antihistamine and will cause drowsiness. It should be used only at bedtime.

ATTENTION: USE ONLY IF TABLET BLISTER SEALS ARE UNBROKEN

ACTIVE INGREDIENT: Doxylamine Succinate 25 mg.
OTHER INGREDIENTS: Dicalcium Phosphate, FD&C Blue #1 Aluminum Lake, Magnesium Stearate, Microcrystalline Cellulose, Sodium Starch Glycolate.
Store at room temperature 59°-86°F (15°-30°C). Retain in carton until time of use

Manufactured By Perrigo Co., Allegan, MI 49010, U.S.A

PRODUCTION QUALITY
SAMPLE
NOT FOR RESALE

Doxylamine Succinate Tablets, 25 mg
NIGHTTIME SLEEP AID

COMPARE TO UNISOM®'S
ACTIVE INGREDIENT

NDC 0113-0441-64

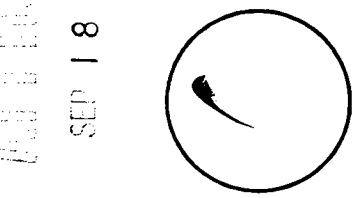
Doxylamine Succinate Tablets, 25 mg

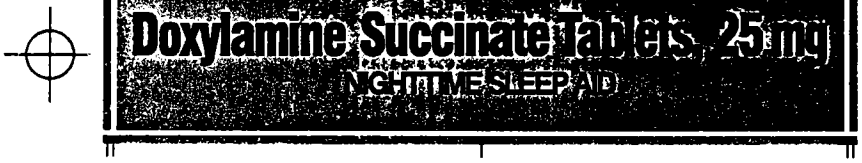
NIGHTTIME SLEEP AID

Get to sleep *fast*

DOSAGE:
1 TABLET

32 TABLETS





Doxylamine Succinate Tablets, 25 mg
NIGHTTIME SLEEP AID

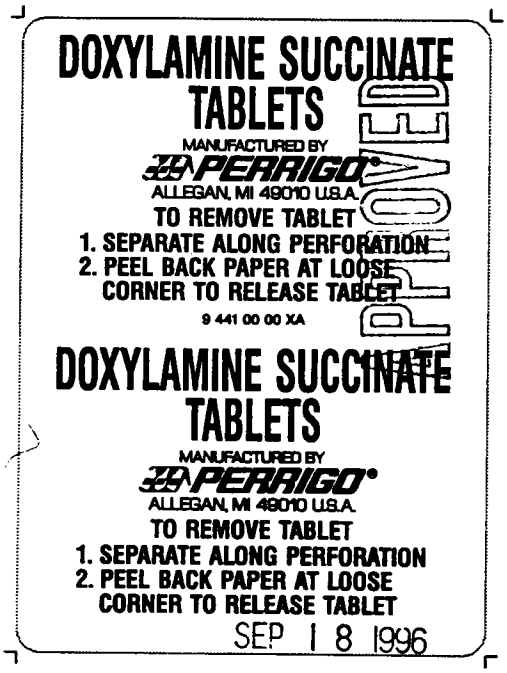
Doxylamine Succinate Tablets, 25 mg
NIGHTTIME SLEEP AID

3 441 64 PQ A

APPROVED
SEP 18 1996

87

Final Printed Labeling
Doxylamine Succinate
ANDA 40-167
Blister Pack



1. CHEMISTRY REVIEW NO. 2

2. ANDA # 40-167

3. NAME AND ADDRESS OF APPLICANT

L. Perrigo Company
117 Water Street
Allegan, MI 49010

4. LEGAL BASIS FOR SUBMISSION

The firm claims that there no patents claim the listed drug product and there is no market exclusivity.

5. SUPPLEMENT(s)

N/A

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME

Doxylamine Succinate

8. SUPPLEMENT(s) PROVIDE(s) FOR:

N/A

9. AMENDMENTS AND OTHER DATES:

Original 9/12/95
Amendment 12/4/95
Amendment 12/12/95
Amendment 5/10/96

10. PHARMACOLOGICAL CATEGORY

Reduce difficulty in falling asleep

11. Rx or OTC

OTC

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM

Tablet

14. POTENCY

25mg

15. CHEMICAL NAME AND STRUCTURE

2-[α[2-(Dimethylamino)ethoxy]-α-methylbenzyl]pyridine succinate (1:1)

16. RECORDS AND REPORTS

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS

The application is approvable.

19. REVIEWER:	DATE COMPLETED:
Nashed E. Nashed, Ph.D.	5/23/96
Supervisor: Paul Schwartz, Ph.D.	5/24/96

DIV

ANDA 40-167

L. Perrigo Company
Attention: Elizabeth M. Pileggi
117 Water Street
Allegan MI 49010

FEB - 8 1996

Dear Madam:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505 (j) of the Federal Food, Drug and Cosmetic Act for Doxylamine Succinate Tablets USP, 25 mg.

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

2. The following dissolution testing will need to be incorporated into your stability and quality control programs:

   The dissolution testing should be conducted in 900 mL of 0.1N HCl, at 37 °C using USP 23 apparatus 2 (paddle) at 50 rpm. The test product should meet the following specifications:

   Not less than of the labeled amount of the drug in the dosage form is dissolved in 30 minutes.

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,

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

FEB 2 1996

Doxylamine Succinate
25 mg Tablets
ANDA #40-167
Reviewer: Moheb H. Makary
WP 40167DW.995

Perrigo Company
Allegan, Michigan
Submission Date:
September 12, 1995

Review of a Dissolution Data and Waiver Request

I. Introduction:

Doxylamine Succinate is an ethanolamine antihistamine which characteristically shows a high incidence of sedation. It produces a reduced latency to end of wakefulness and early onset of sleep.

Doxylamine Succinate 25 mg (Unisom^R) is marketed by Pfizer as an OTC drug product.

II. Objective:

The firm has requested a waiver of *in vivo* bioequivalence requirements for its Doxylamine Succinate Tablets, 25 mg. The firm conducted dissolution testing on its test product comparing it to Pfizer's Unisom^R 25 mg Tablets.

Doxylamine Succinate Tablet is a DESI effective drug and is not on the published or current list of drugs having known or potential bioequivalence problems.

III. Dissolution Testing:

The following USP 23 conditions were used:

Apparatus:	2 (paddle) at 50 rpm
Medium:	900 mL of 0.1N HCl
Specifications:	NLT in 30 minutes
Test product:	Perrigo's Doxylamine Succinate 25 mg Tablets, lot #5N0554

Reference product: Pfizer's Unisom^R 25 mg Tablets, lot #94014

The dissolution testing results are shown in Table I.

IV. Formulation:

The formulation of the test product is shown below:

Component	25 mg mg/Tablet
Blue #1 FD&C Aluminum Lake	
Dicalcium Phosphate Anhydrous, USP	
Dicalcium Phosphate Dihydrate,	
Doxylamine Succinate, USP	25.00
Magnesium Stearate NF	
Microcrystalline Cellulose, NF	
Sodium Starch Glycolate, NF	
	=======
	156.00

V. Comments:

The dissolution testing results for the test product met the USP specifications.

VI. Recommendations:

1. The dissolution testing conducted by Perrigo Company on its Doxylamine Succinate, 25 mg Tablets, lot #5N0554 is acceptable. Waiver of the *in vivo* bioequivalence study requirements is granted for the test product Doxylamine Succinate 25 mg Tablets based on 21 CFR 320.22 (c) of the Bioequivalence/Bioavailability regulations. The 25 mg tablets of the test product is therefore deemed bioequivalence to the 25 mg tablets of Unisom[R] manufactured by Pfizer.

2. The dissolution testing should be incorporated into the firm's manufacturing controls and stability program. The dissolution testing should be conducted in 900 mL of 0.1N HCl, at 37 ^{o}C using USP 23 apparatus 2 (paddle) at 50 rpm.
The test product should meet the following specifications:

Not less than of the labeled amount of the drug in the dosage form is dissolved in 30 minutes.

The firm should be informed of the above recommendations.

Moheb H. Makary, Ph.D.
Division of Bioequivalence
Review Branch III

RD INITIALLED RMHATRE
FT INITIALLED RMHATRF

Concur _____ Date: 2/2/96

Keith Chan, Ph.D.
Director
Division of Bioequivalence

MMakary/1-31-96 wp 40167DW.995
cc: ANDA #40-167, (original, HFD-600 (Hare), HFD-630, HFD-658 (Mhatre, Makary), Drug File.

Table I. In Vitro Dissolution Testing

Drug (Generic Name): Doxylamine Succinate Tablets
Dose Strength: 25 mg
ANDA No.: 40-167
Firm: Perrigo Company
Submission Date: September 12, 1995
File Name: 40167DW.995

I. Conditions for Dissolution Testing:

USP 23 Basket: Paddle: X RPM: 50
No. Units Tested: 12
Medium: 900 mL of 0.1N HCl
Specifications: NLT in 30 minutes
Reference Drug: Unisom
Assay Methodology:

II. Results of In Vitro Dissolution Testing

Sampling Times (Minutes)	Test Product Lot # 5N0554 Strength(mg) 25			Reference Product Lot # 94014 Strength(mg) 25		
	Mean %	Range	%CV	Mean %	Range	%CV
10	91		7.8	80		13
20	97		5.8	102		3.1
30	98		6.5	102		2.5
40	97		5.8	103		2.7