CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

40-434

TradeName:	Percocet 7.5mg/325 mg and 10mg/325mg
Generic Name:	Oxycodone Hydrochloride and Acetaminophen Tablets, USP
Sponsor:	Endo Pharmaceuticals, Inc.
Approval Date:	November 23, 2001

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
40-434

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40-434

APPROVAL LETTER

ANDA 40-434

NOV 23 2001

Endo Pharmaceuticals, Inc.
Attention: Carol Patterson
500 Endo Blvd.
Garden City, NY 11530

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated April 6, 2001, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for two additional strengths of Percocet® Tablets; e.g., Percocet Tablets 7.5 mg/325 mg and Percocet Tablets 10 mg/325 mg (Oxycodone Hydrochloride and Acetaminophen Tablets USP).

Submission of this ANDA is based upon a Suitability Petition submitted pursuant to 21 CFR 314.93 and approved by the agency on September 9, 2000 (Docket No. 00P-1270/CP1).

Reference is also made to your amendment dated September 14, 2001 and June 11, 2001.

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 drug products, Percocet® Tablets 7.5 mg/325 mg and Percocet Tablets 10 mg/325 mg (Oxycodone Hydrochloride and Acetaminophen Tablets USP), 7.5 mg/325 mg and 10 mg/325 mg, respectively, can be expected to have the same therapeutic effect as equivalent doses of the listed drug product upon which the Agency relied as the basis of safety and effectiveness. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under Section 506A of the Act, 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 and 314.98. 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 that 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-40). 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-40) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

/s/ for

11/23/2001

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40-434

Final Printed Labeling

Endo®

ENDO LABORATORIES

PERCOCET®

(Oxycodone and Acetaminophen Tablets, USP)

CII

R_x only

DESCRIPTION

Each tablet, for oral administration, contains oxycodone hydrochloride and acetaminophen in the following strengths:

Oxycodone Hydrochloride	7.5 mg*
Acetaminophen, USP	325 mg

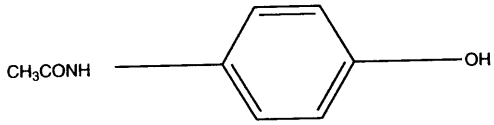
*7.5 mg oxycodone HCl is equivalent to 6.7228 mg of oxycodone.

Oxycodone Hydrochloride	10 mg*
Acetaminophen, USP	325 mg

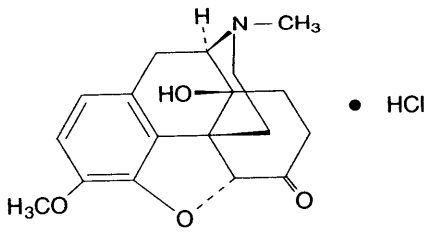
*10 mg oxycodone HCl is equivalent to 8.9637 mg of oxycodone.

Both strengths of PERCOCET also contain the following inactive ingredients: Colloidal silicon dioxide, croscarmellose sodium, crospovidone, microcrystalline cellulose, povidone, pregelatinized starch, and stearic acid. In addition, the 7.5 mg/325 mg strength contains FD&C Yellow No. 6 Aluminum Lake and the 10 mg/325 mg strength contains D&C Yellow No. 10 Aluminum Lake.

Acetaminophen, 4'-hydroxyacetanilide, is a non-opiate, non-salicylate analgesic and antipyretic which occurs as a white, odorless, crystalline powder, possessing a slightly bitter taste. The molecular formula for acetaminophen is $C_8H_9NO_2$ and the molecular weight is 151.17. It may be represented by the following structural formula:



Oxycodone, 14-hydroxydihydrocodeinone, is a semisynthetic opioid analgesic which occurs as a white, odorless, crystalline powder having a saline, bitter taste. The molecular formula for oxycodone hydrochloride is $C_{18}H_{21}NO_4 \cdot HCl$ and the molecular weight 351.83. It is derived from the opium alkaloid thebaine, and may be represented by the following structural formula:



CLINICAL PHARMACOLOGY

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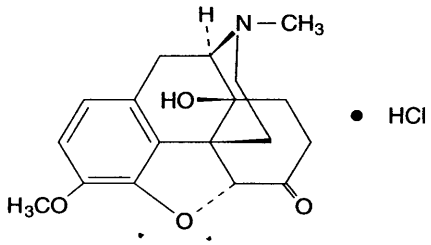

CLINICAL PHARMACOLOGY

The principal ingredient, oxycodone, is a semisynthetic opioid analgesic with multiple actions qualitatively similar to those of morphine; the most prominent involves the central nervous system and organs composed of smooth muscle. The principal actions of therapeutic value of the oxycodone in PERCOCET are analgesia and sedation.

Oxycodone is similar to codeine and methadone in that it retains at least one-half of its analgesic activity when administered orally.

Acetaminophen is a non-opiate, non-salicylate analgesic and antipyretic.

INDICATIONS AND USAGE

PERCOCET is indicated for the relief of moderate to moderately severe pain.

CONTRAINDICATIONS

PERCOCET should not be administered to patients who are hypersensitive to oxycodone, acetaminophen, or any other components of this product.

WARNINGS

Drug Dependence

Oxycodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of PERCOCET (Oxycodone and Acetaminophen Tablets, USP), and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral opioid-containing medications. Like other opioid-containing medications, PERCOCET is subject to the Federal Controlled Substances Act (Schedule II).

PRECAUTIONS

General

Head Injury and Increased Intracranial Pressure: The respiratory depressant effects of opioids and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, opioids produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute Abdominal Conditions: The administration of PERCOCET or other opioids may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Special Risk Patients: PERCOCET should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

Information for Patients

Oxycodone may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using PERCOCET should be cautioned accordingly.

Drug Interactions

Patients receiving other opioid analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with PERCOCET may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

The concurrent use of anticholinergics with opioids may produce paralytic ileus.

Usage in Pregnancy

Teratogenic Effects; Pregnancy Category C: Animal reproductive studies have not been conducted with PERCOCET. It is also not known whether PERCOCET can cause fetal harm

PERCOCET may exhibit an additive
combined therapy is contemplated, the dose of one or both agents should be reduced.

4

The concurrent use of anticholinergics with opioids may produce paralytic ileus.

Usage in Pregnancy

Teratogenic Effects; Pregnancy Category C: Animal reproductive studies have not been conducted with PERCOCET. It is also not known whether PERCOCET can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. PERCOCET should not be given to a pregnant woman unless in the judgment of the physician, the potential benefits outweigh the possible hazards.

Nonteratogenic Effects: Use of opioids during pregnancy may produce physical dependence in the neonate.

Labor and Delivery: As with all opioids, administration of PERCOCET to the mother shortly before delivery may result in some degree of respiratory depression in the newborn and the mother, especially if higher doses are used.

Nursing Mothers

It is not known whether PERCOCET is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when PERCOCET is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

The most frequently observed adverse reactions include lightheadedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation, skin rash and pruritus. At higher doses, oxycodone has most of the disadvantages of morphine including respiratory depression.

DRUG ABUSE AND DEPENDENCE

PERCOCET (Oxycodone and Acetaminophen Tablets, USP) is a Schedule II controlled substance.

Oxycodone can produce drug dependence and has the potential for being abused (See WARNINGS).

OVERDOSAGE

Acetaminophen

Signs and Symptoms: In acute acetaminophen overdosage, dose-dependent, potentially fatal hepatic necrosis is the most serious adverse effect. Renal tubular necrosis, hypoglycemic coma and thrombocytopenia may also occur.

In adults, hepatic toxicity has rarely been reported with acute overdoses of less than 10 grams and fatalities with less than 15 grams. Importantly, young children seem to be more resistant than adults to the hepatotoxic effect of an acetaminophen overdose. Despite this, the measures outlined below should be initiated in any adult or child suspected of having ingested an acetaminophen overdose.

Early symptoms following a potentially hepatotoxic overdose may include: nausea, vomiting, diaphoresis and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post-ingestion.

Treatment: The stomach should be emptied promptly by lavage or by induction of emesis with syrup of ipecac. Patient's estimates of the quantity of a drug ingested are notoriously unreliable. Therefore, if an acetaminophen overdose is suspected, a serum acetaminophen assay should be obtained as early as possible, but no sooner than four hours following ingestion. Liver function studies should be obtained initially and repeated at 24-hour intervals.

The antidote, N-acetylcysteine, should be administered as early as possible, preferably within 16 hours of the overdose ingestion for optimal results, but in any case, within 24 hours. Following recovery, there are no residual, structural, or functional hepatic abnormalities.

Oxycodone

Signs and Symptoms: Serious overdosage with oxycodone is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or

emesis with syrup of ipecac. Patient's estimates of the quantity of a drug ingested are notoriously unreliable. Therefore, if an acetaminophen overdose is suspected, a serum acetaminophen assay should be obtained as early as possible, but no sooner than four hours following ingestion. Liver function studies should be obtained initially and repeated at 24-hour intervals.

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Oxycodone

Signs and Symptoms: Serious overdosage with oxycodone is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. In severe overdosage, apnea, circulatory collapse, cardiac arrest and death may occur.

Treatment: Primary attention should be given to the reestablishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The opioid antagonist naloxone hydrochloride is a specific antidote against respiratory depression which may result from overdosage or unusual sensitivity to

opioids, including oxycodone. Therefore, an appropriate dose of naloxone hydrochloride (usual initial adult dose 0.4 mg to 2 mg) should be administered preferably by the intravenous route, and simultaneously with efforts at respiratory resuscitation (see package insert). Since the duration of action of oxycodone may exceed that of the antagonist, the patient should be kept under continued surveillance and repeated doses of the antagonist should be administered as needed to maintain adequate respiration.

An antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

Gastric emptying may be useful in removing unabsorbed drug.

DOSAGE AND ADMINISTRATION

Dosage should be adjusted according to the severity of the pain and the response of the patient. It may occasionally be necessary to exceed the usual dosage recommended below in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of opioids. PERCOCET (Oxycodone and Acetaminophen Tablets, USP) is given orally. The usual adult dosage is one tablet every 6 hours as needed for pain. The total daily dose of acetaminophen should not exceed 4 grams (maximal daily dose of PERCOCET 7.5 mg/325 mg and PERCOCET 10 mg/325 mg is 8 tablets and 6 tablets, respectively).

HOW SUPPLIED

PERCOCET (Oxycodone and Acetaminophen Tablets, USP) is supplied as follows:

7.5 mg/325 mg Peach oval-shaped tablet debossed with "PERCOCET" on one side and "7.5/325" on the other.	Bottles of 100 Bottles of 500 Unit dose package of 100 tablets	NDC 63481-628-70 NDC 63481-628-85 NDC 63481-628-75
10 mg/325 mg Yellow capsule-shaped tablet debossed with "PERCOCET" on one side and "10/325" on the other.	Bottles of 100 Bottles of 500 Unit dose package of 100 tablets	NDC 63481-629-70 NDC 63481-629-85 NDC 63481-629-75

Store at controlled room temperature, 15° to 30°C (59° to 86°F) [see USP].

Dispense in a tight, light-resistant container as defined in the USP, with a child-resistant closure (as required).

DEA Order Form Required.

Manufactured for:

10 mg/325 mg Yellow capsule-shaped tablet debossed with "PERCOCET" on one side and "10/325" on the other.	Bottles of 100 Bottles of 500 Unit dose package of 100 tablets	NDC 63481-629-70 NDC 63481-629-85 NDC 63481-629-75

8

Store at controlled room temperature, 15° to 30°C (59° to 86°F) [see USP].

Dispense in a tight, light-resistant container as defined in the USP, with a child-resistant closure (as required).

DEA Order Form Required.

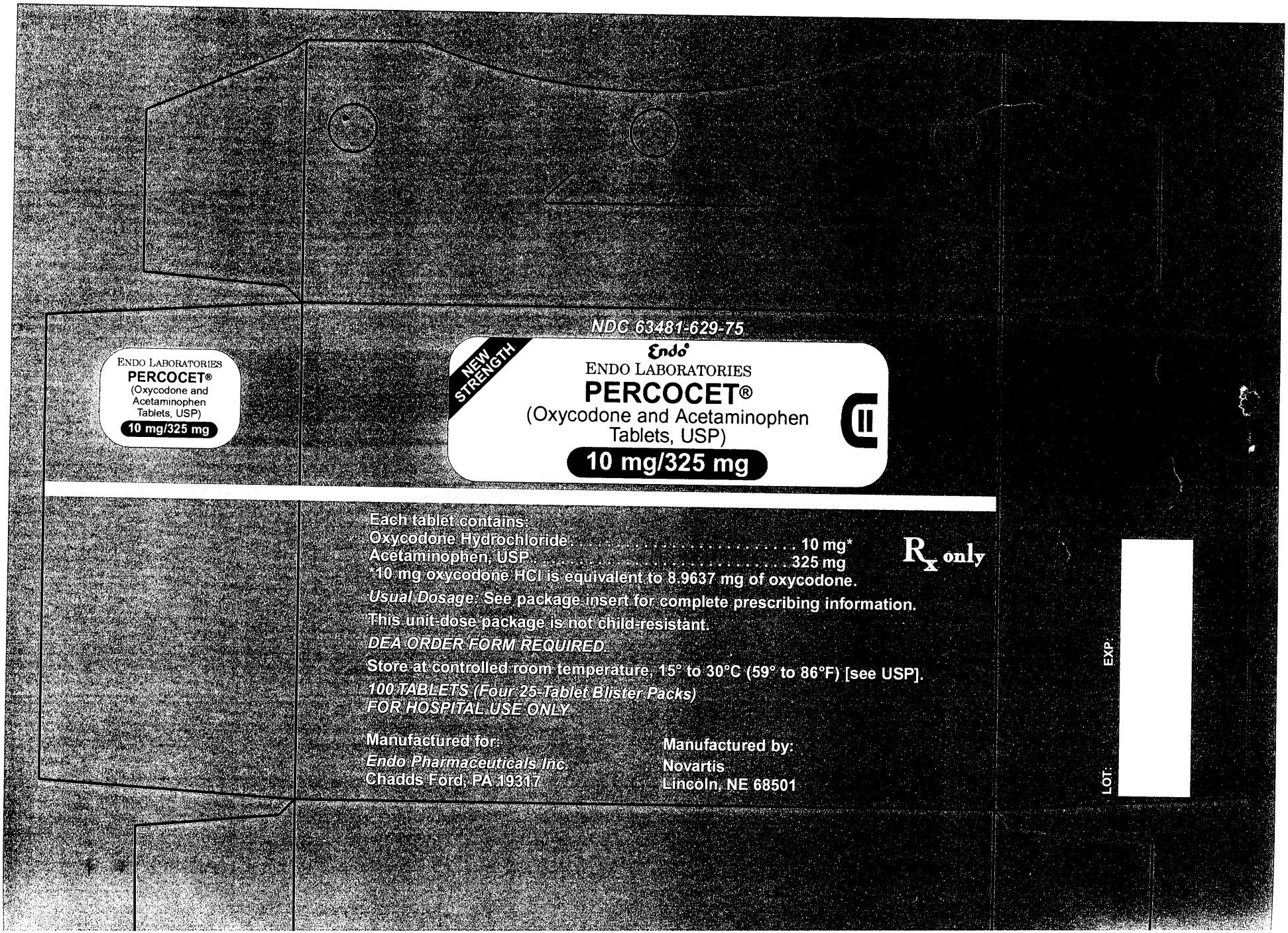
Manufactured for:
Endo Pharmaceuticals Inc.
Chadds Ford, Pennsylvania 19317

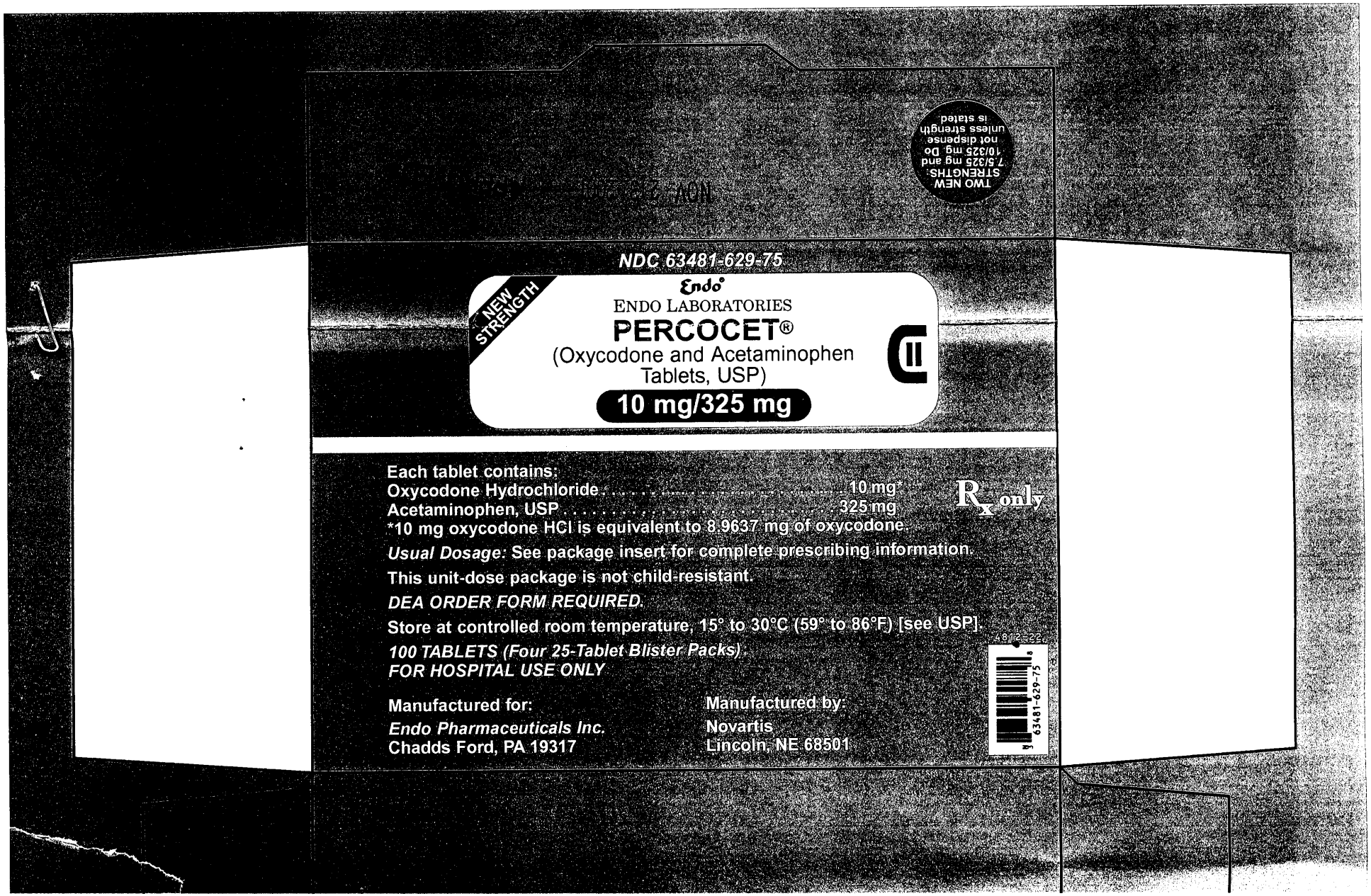
Endo®

PERCOCET® is a Registered Trademark of Endo Pharmaceuticals Inc.

Printed in U.S.A.

6556-00/August, 2001
4091-42


ENDO LABORATORIES
PERCOCET®
(Oxycodone and Acetaminophen Tablets, USP)
10 mg/325 mg
NDC 63481-629-75
NEW STRENGTH
Endo
ENDO LABORATORIES
PERCOCET®
(Oxycodone and Acetaminophen Tablets, USP)
10 mg/325 mg
CII
Each tablet contains:
Oxycodone Hydrochloride..... 10 mg*
Acetaminophen, USP..... 325 mg
*10 mg oxycodone HCl is equivalent to 8.9637 mg of oxycodone.
Usual Dosage: See package insert for complete prescribing information.
This unit-dose package is not child-resistant.
DEA ORDER FORM REQUIRED.
Store at controlled room temperature, 15° to 30°C (59° to 86°F) [see USP].
100 TABLETS (Four 25-Tablet Blister Packs)
FOR HOSPITAL USE ONLY
℞ only
Manufactured for:
Endo Pharmaceuticals Inc.
Chadds Ford, PA 19317
Manufactured by:
Novartis
Lincoln, NE 68501
LOT:
EXP:


TWO NEW STRENGTHS: 7.5/325 mg and 10/325 mg. Do not dispense unless strength is stated.
NDC 63481-629-75
NEW STRENGTH
Endo
ENDO LABORATORIES
PERCOCET®
(Oxycodone and Acetaminophen Tablets, USP)
CII
10 mg/325 mg
Each tablet contains:
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Acetaminophen, USP . . . . . 325 mg
*10 mg oxycodone HCl is equivalent to 8.9637 mg of oxycodone.
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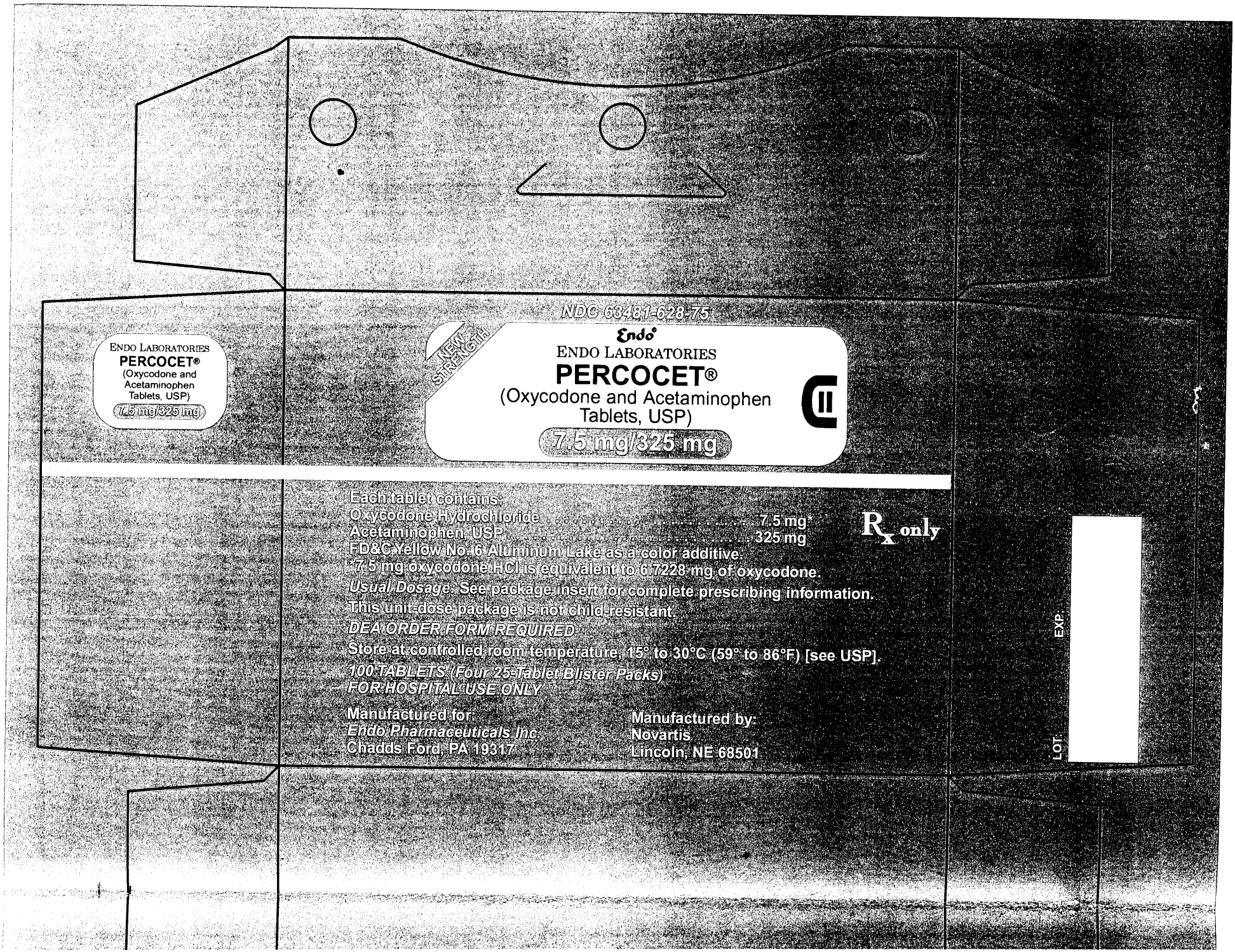
NDC 63481-628-75
ENDO LABORATORIES
PERCOCET®
(Oxycodone and Acetaminophen Tablets, USP)
7.5 mg/325 mg
NEW STRENGTH
Endo
ENDO LABORATORIES
PERCOCET®
(Oxycodone and Acetaminophen Tablets, USP)
7.5 mg/325 mg
II
Each tablet contains:
Oxycodone Hydrochloride ..... 7.5 mg*
Acetaminophen, USP ..... 325 mg
FD&C Yellow No. 6 Aluminum Lake as a color additive.
*7.5 mg oxycodone HCl is equivalent to 6.7228 mg of oxycodone.
Usual Dosage: See package insert for complete prescribing information.
This unit dose package is not child-resistant.
DEA ORDER FORM REQUIRED
Store at controlled room temperature, 15° to 30°C (59° to 86°F) [see USP].
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Rx only
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EXP:
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TWO NEW STRENGTHS: 7.5/325 mg and 10/325 mg. Do not dispense unless strength is stated.

NDC 63481-628-75

NEW STRENGTH

Endo

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(Oxycodone and Acetaminophen Tablets, USP)

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Chadds Ford, PA 19317

Manufactured by:
Novartis
Lincoln, NE 68501

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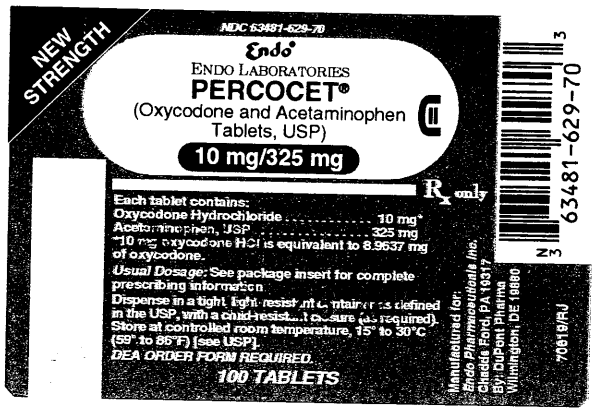
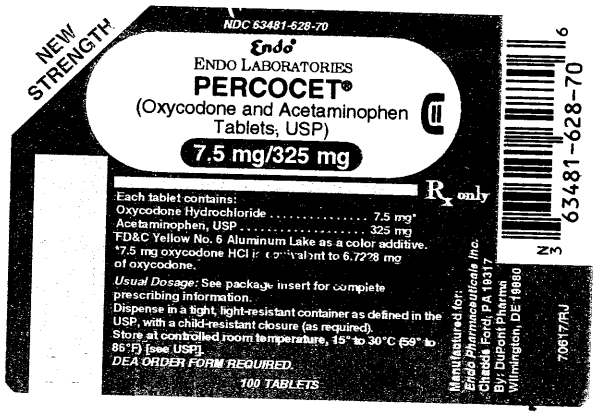
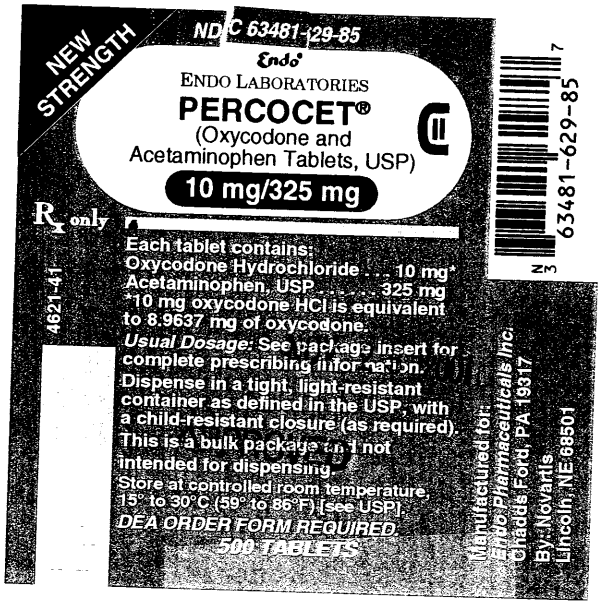
63481-628-75

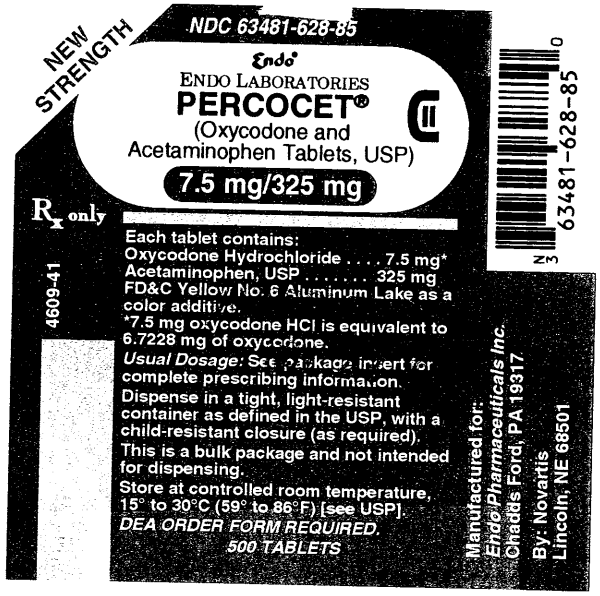
40-434

AP 11/25/02



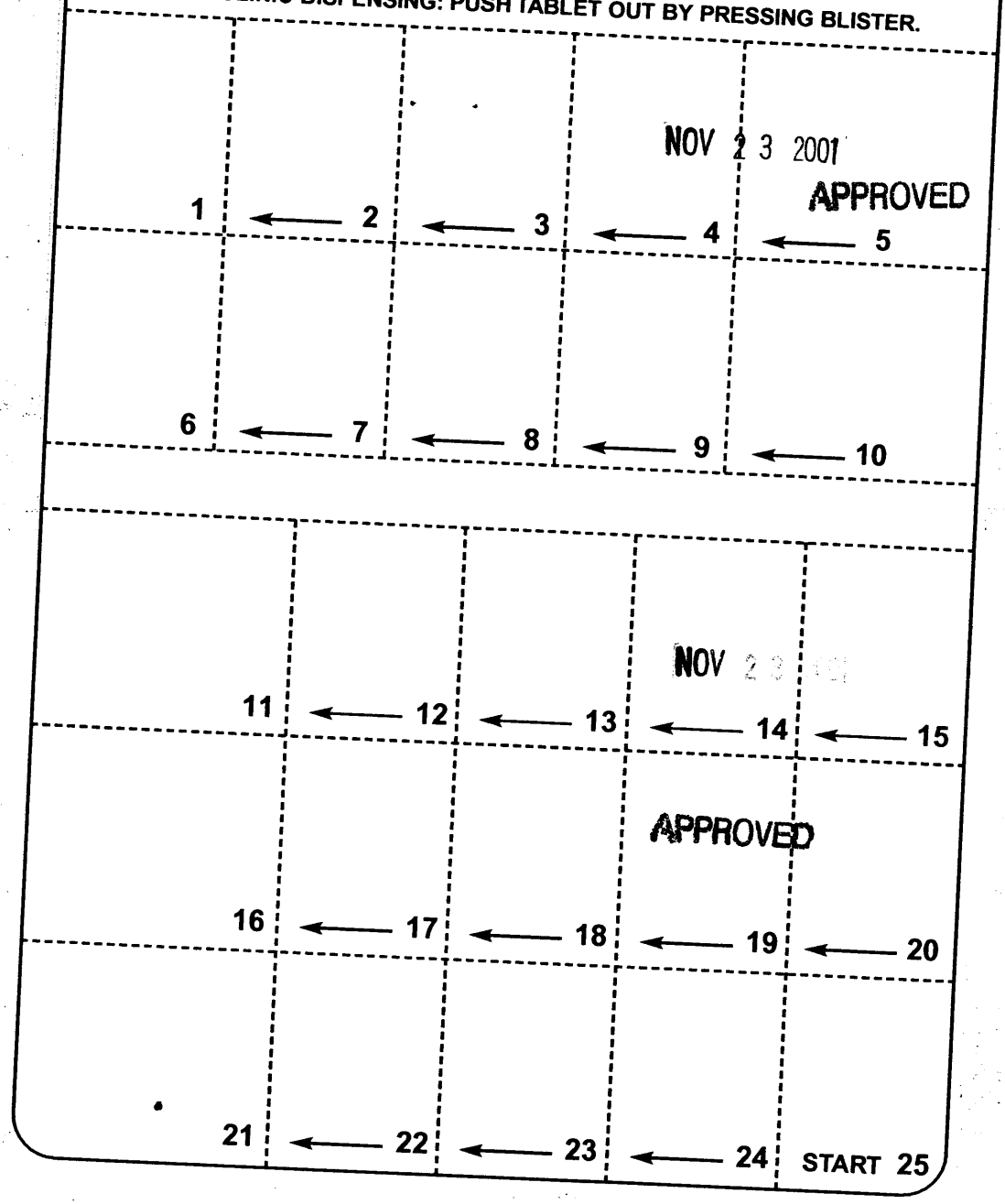






DIRECTIONS:

1. START WITH UNIT #25 (LOWER RIGHT CORNER) AND WORK SEQUENTIALLY BACKWARDS TO #1.
2. FOR BEDSIDE DISPENSING: TEAR OFF BLISTER ALONG PERFORATIONS.
3. FOR CLINIC DISPENSING: PUSH TABLET OUT BY PRESSING BLISTER.



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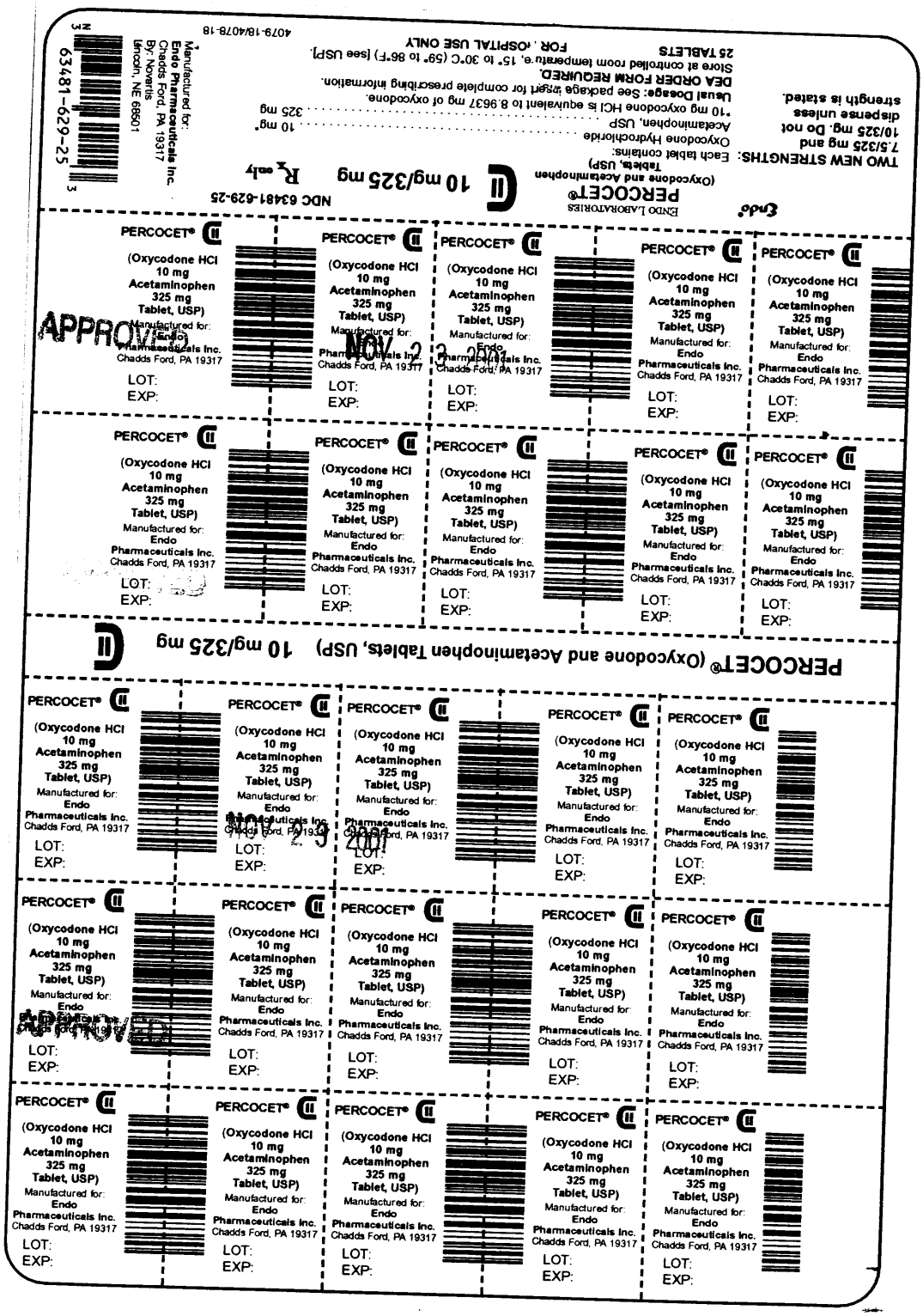

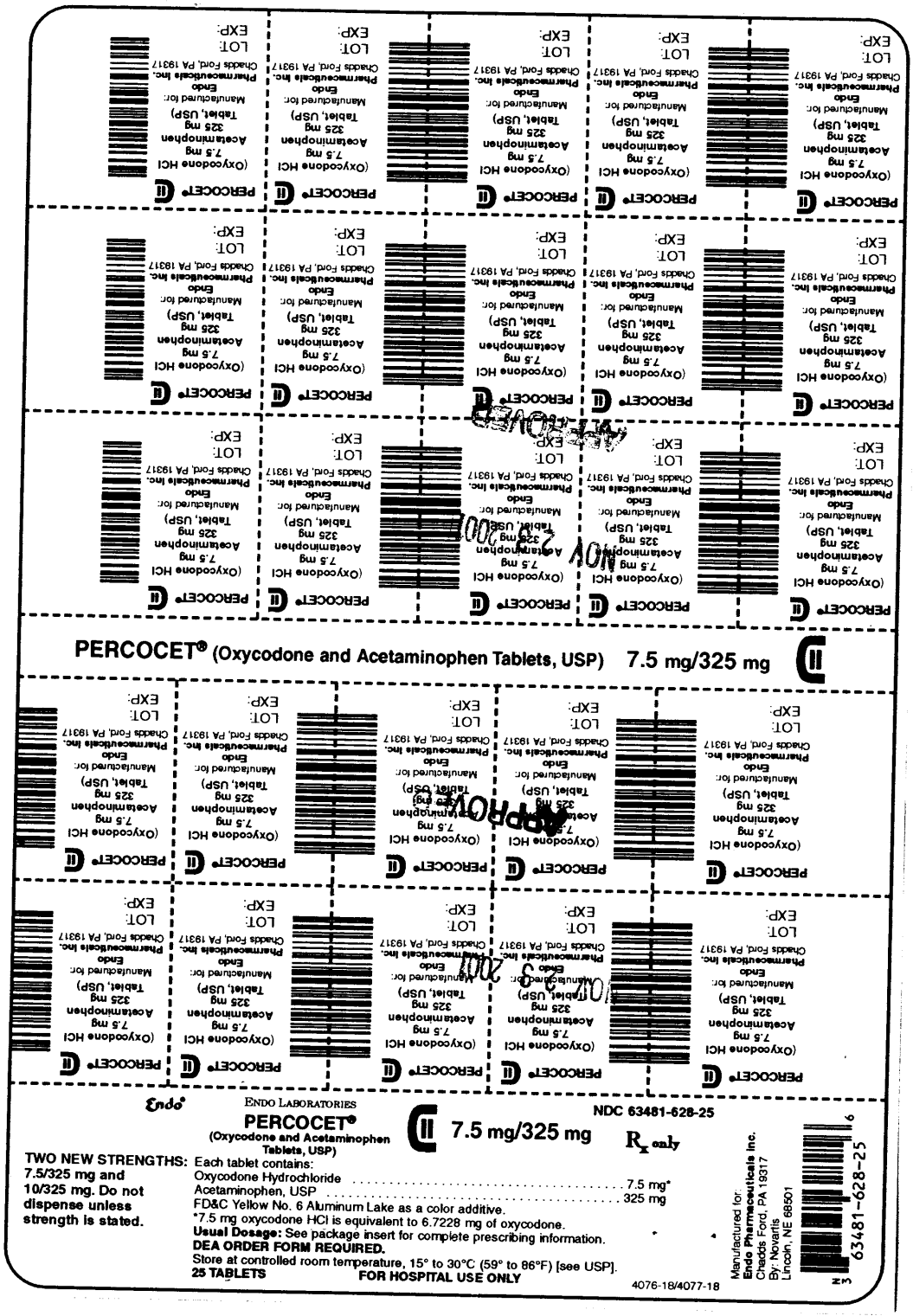

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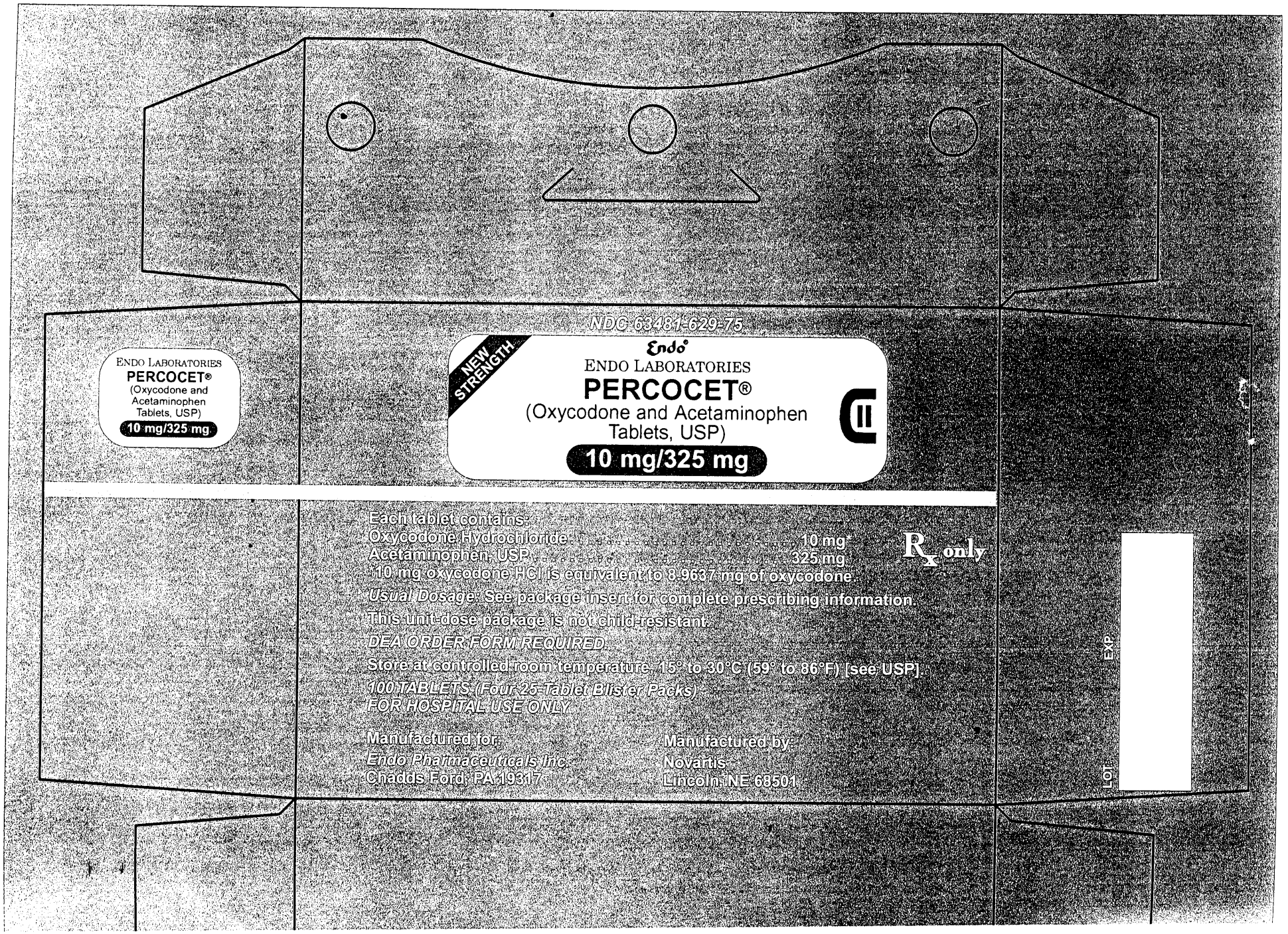
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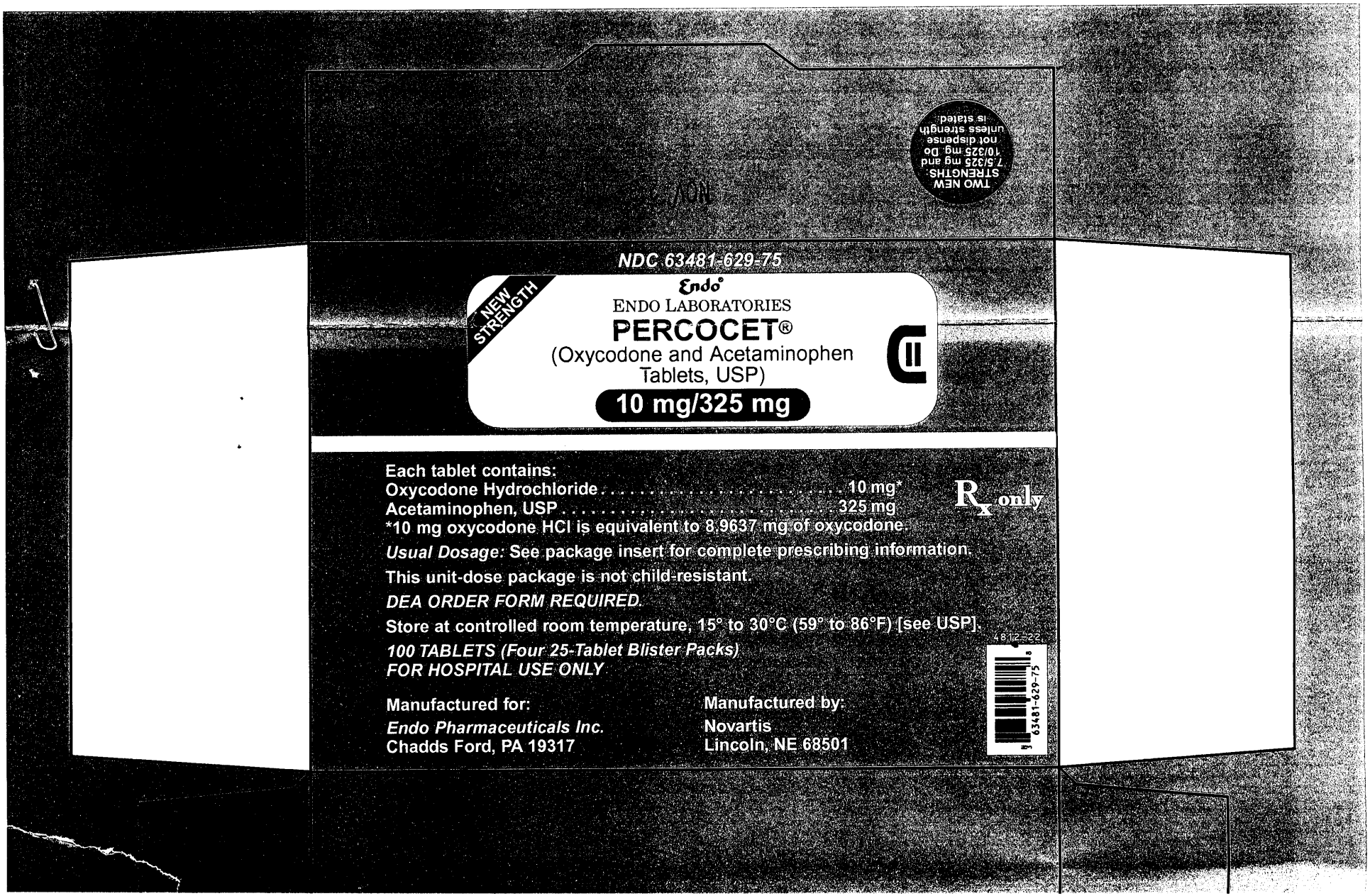
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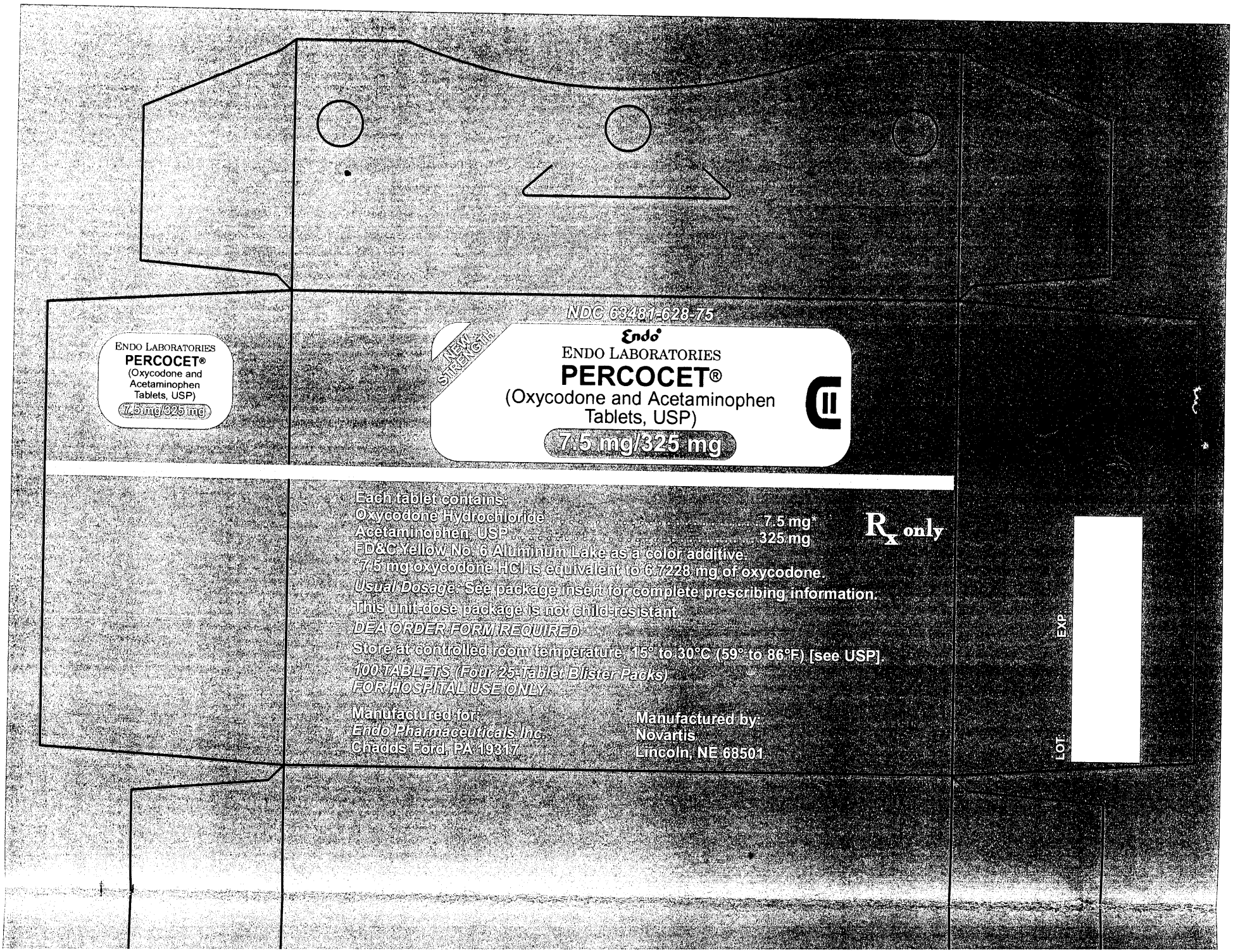
FOR HOSPITAL USE ONLY
Manufactured for:
Endo Pharmaceuticals Inc.
Chadds Ford, PA 19317
Manufactured by:
Novartis
Lincoln, NE 68501
4812-22
63481-629-75


ENDO LABORATORIES
PERCOCET®
(Oxycodone and
Acetaminophen
Tablets, USP)
7.5 mg/325 mg
NDC 63481-628-75
NEW STRENGTH
Endo
ENDO LABORATORIES
PERCOCET®
(Oxycodone and Acetaminophen
Tablets, USP)
7.5 mg/325 mg
CII
Each tablet contains:
Oxycodone Hydrochloride ..... 7.5 mg*
Acetaminophen, USP ..... 325 mg
FD&C Yellow No. 6 Aluminum Lake as a color additive.
*7.5 mg oxycodone HCl is equivalent to 6.7228 mg of oxycodone.
Usual Dosage: See package insert for complete prescribing information.
This unit-dose package is not child-resistant.
DEA ORDER FORM REQUIRED.
Store at controlled room temperature, 15° to 30°C (59° to 86°F) [see USP].
100 TABLETS (Four 25-Tablet Blister Packs)
FOR HOSPITAL USE ONLY
Rx only
Manufactured for:
Endo Pharmaceuticals Inc.
Chadds Ford, PA 19317
Manufactured by:
Novartis
Lincoln, NE 68501
EXP
LOT

TWO NEW STRENGTHS: 7.5/325 mg and 10/325 mg. Do not dispense unless strength is stated.

APPROVED NOV 2 3 2001

TWO NEW STRENGTHS: 7.5/325 mg and 10/325 mg. Do not dispense unless strength is stated.

NDC 63481-628-75

NEW STRENGTH

Endo

ENDO LABORATORIES

PERCOCET®

(Oxycodone and Acetaminophen Tablets, USP)

CII

7.5 mg/325 mg

Each tablet contains:
Oxycodone Hydrochloride ..... 7.5 mg
Acetaminophen, USP ..... 325 mg
FD&C Yellow No. 6 Aluminum Lake as a color additive.
*7.5 mg oxycodone HCl is equivalent to 6.7228 mg of oxycodone.

Usual Dosage: See package insert for complete prescribing information.

This unit-dose package is not child-resistant.

DEA ORDER FORM REQUIRED.

Store at controlled room temperature, 15° to 30°C (59° to 86°F) [see USP].

100 TABLETS (Four 25-Tablet Blister Packs)
FOR HOSPITAL USE ONLY

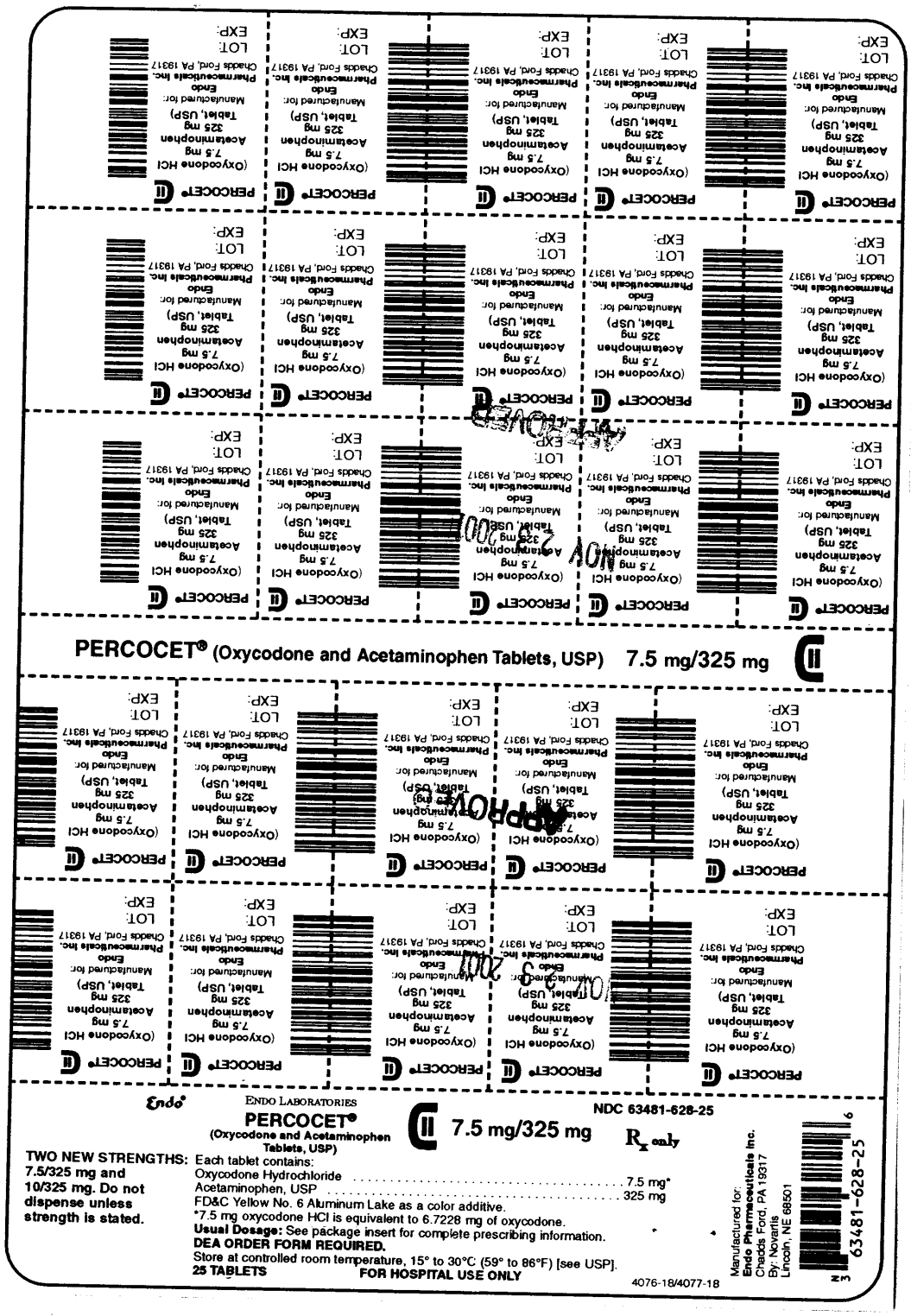
Rx only

4811-22

63481-628-75

Manufactured for:
Endo Pharmaceuticals Inc.
Chadds Ford, PA 19317

Manufactured by:
Novartis
Lincoln, NE 68501

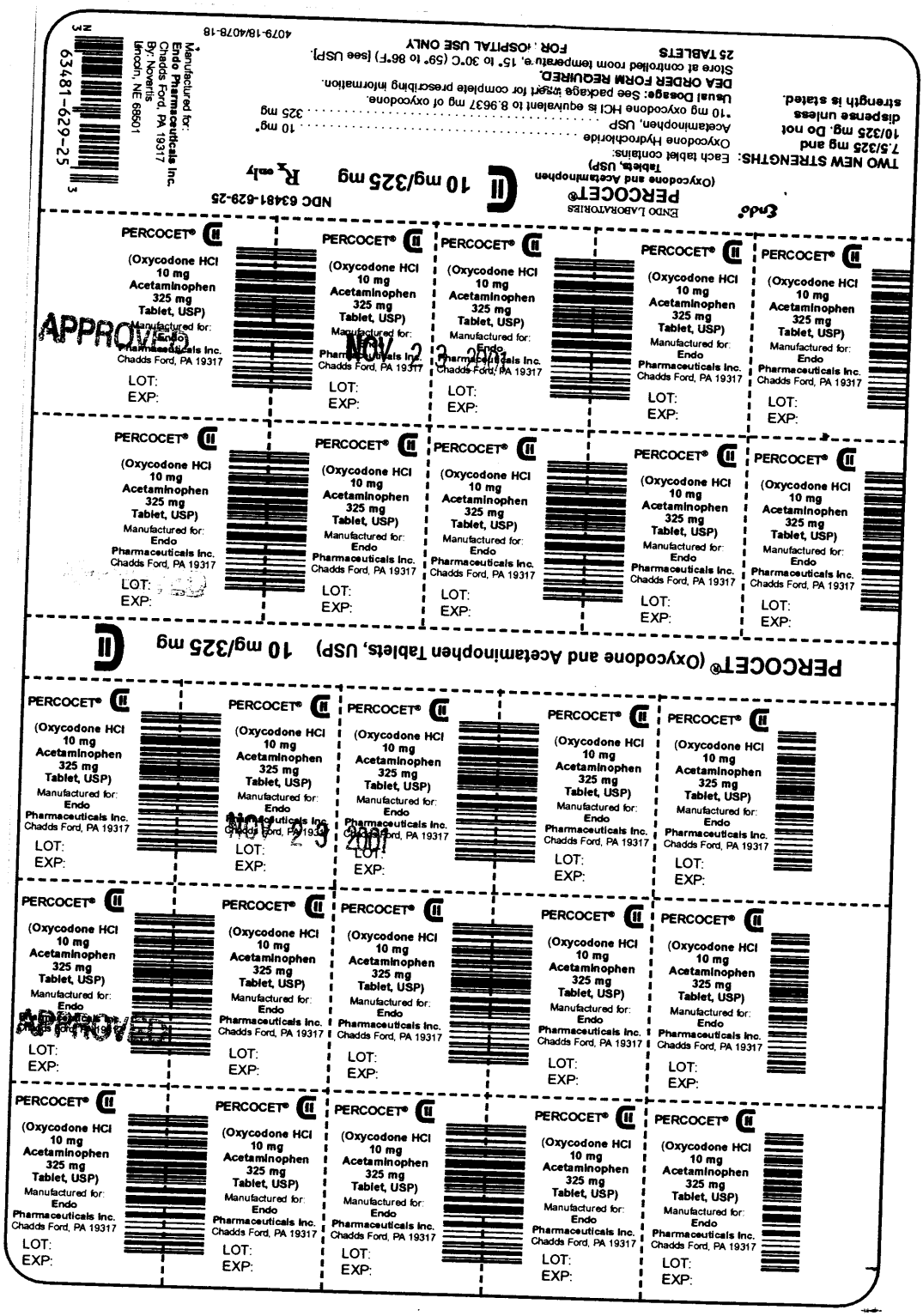


40-434

AP 11/23/01

40-434

AP 11/25/01



TWO NEW STRENGTHS: 7.5/325 mg and 10/325 mg. Do not dispense unless strength is stated.

NDC 63481-629-75

NEW STRENGTH

Endo

ENDO LABORATORIES

PERCOCET®

(Oxycodone and Acetaminophen Tablets, USP)

CII

10 mg/325 mg

Each tablet contains:
Oxycodone Hydrochloride . . . . . 10 mg*
Acetaminophen, USP . . . . . 325 mg
*10 mg oxycodone HCl is equivalent to 8.9637 mg of oxycodone.

R_x only

Usual Dosage: See package insert for complete prescribing information.

This unit-dose package is not child-resistant.

DEA ORDER FORM REQUIRED.

Store at controlled room temperature, 15° to 30°C (59° to 86°F) [see USP].

100 TABLETS (Four 25-Tablet Blister Packs)
FOR HOSPITAL USE ONLY

4812-22

63481-629-75

Manufactured for:
Endo Pharmaceuticals Inc.
Chadds Ford, PA 19317

Manufactured by:
Novartis
Lincoln, NE 68501

Manufactured for:
Endo Pharmaceuticals Inc.
Chadds Ford, PA 19317

Manufactured by:
Novartis
Lincoln, NE 68501

Lot:

NDC 63481-628-75

NEW STRENGTH

Endo

ENDO LABORATORIES

PERCOCET®

(Oxycodone and Acetaminophen Tablets, USP)

7.5 mg/325 mg

C II

Each tablet contains:
Oxycodone Hydrochloride . . . . . 7.5 mg*
Acetaminophen, USP . . . . . 325 mg
FD&C Yellow No. 6 Aluminum Lake as a color additive.
*7.5 mg oxycodone HCl is equivalent to 6.7228 mg of oxycodone.

R_x only

Usual Dosage: See package insert for complete prescribing information.

This unit-dose package is not child-resistant.

DEA ORDER FORM REQUIRED.

Store at controlled room temperature, 15° to 30°C (59° to 86°F) [see USP].

4811-22

100 TABLETS (Four 25-Tablet Blister Packs)
FOR HOSPITAL USE ONLY

Manufactured for:
Endo Pharmaceuticals Inc.
Chadds Ford, PA 19317

Manufactured by:
Novartis
Lincoln, NE 68501

63481-628-75

TWO NEW STRENGTHS: 7.5/325 mg and 10/325 mg. Do not dispense unless strength is stated.

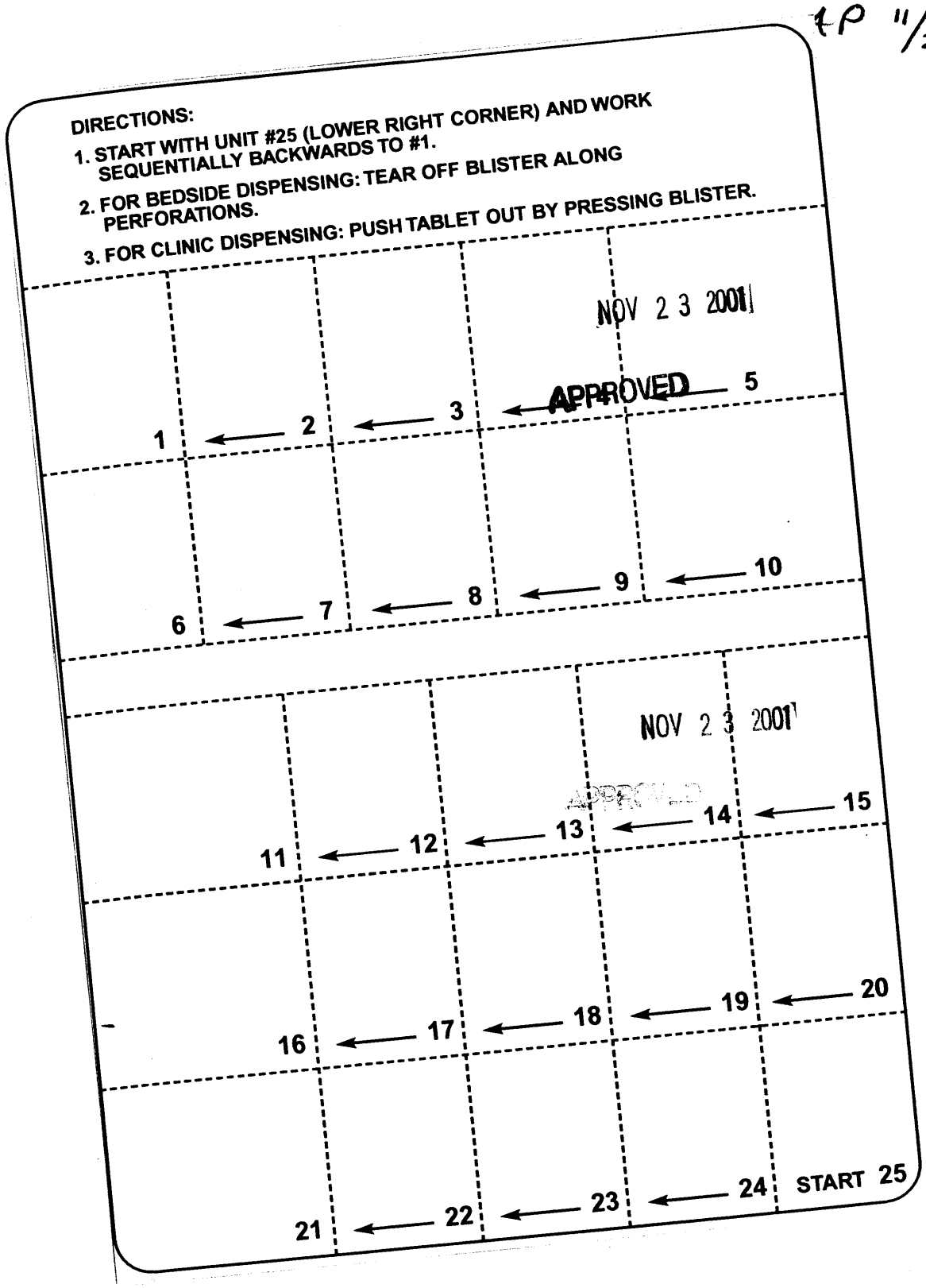
LOT:

40-434

tP 11/23/01

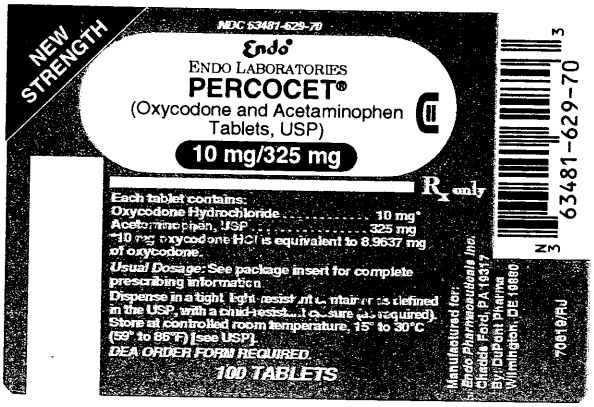
DIRECTIONS:

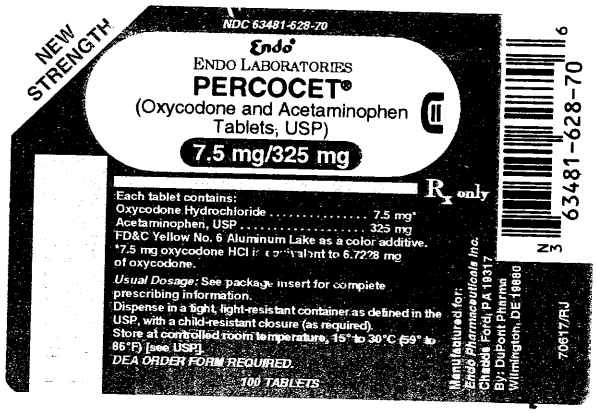
1. START WITH UNIT #25 (LOWER RIGHT CORNER) AND WORK SEQUENTIALLY BACKWARDS TO #1.
2. FOR BEDSIDE DISPENSING: TEAR OFF BLISTER ALONG PERFORATIONS.
3. FOR CLINIC DISPENSING: PUSH TABLET OUT BY PRESSING BLISTER.

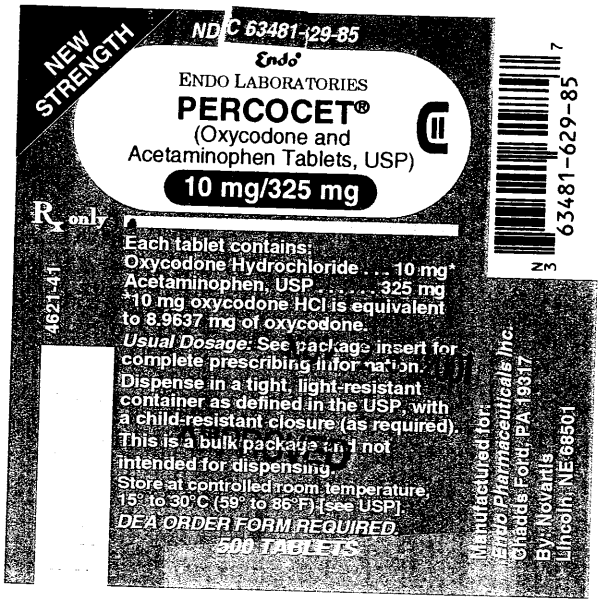


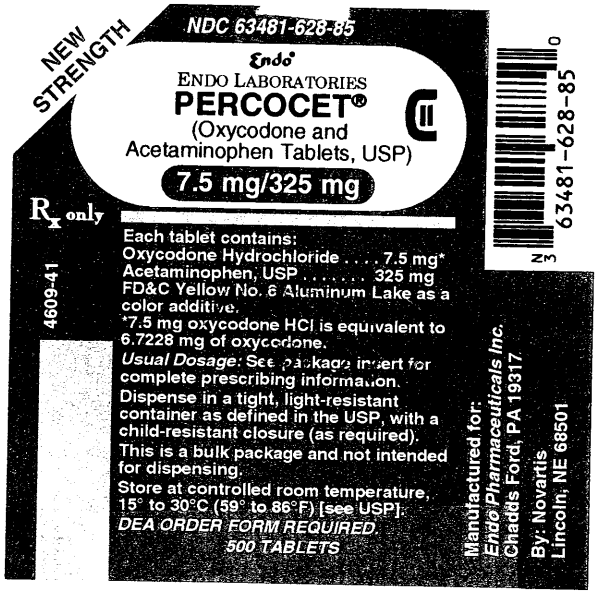
40-434

AP 11/25/04









CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40-434

CHEMISTRY REVIEW(S)

1. CHEMISTRY REVIEW NO. 1

2. ANDA # 40-434

3. NAME AND ADDRESS OF APPLICANT
Endo pharmaceuticals Inc.
500 Endo Blvd.
Garden City NY 11530

4. LEGAL BASIS FOR SUBMISSION
Percocet® is the reference listed drug. Endo is the holder of the approved application. There are no patents or exclusivities for Percocet tablets.

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME
Percocet

7. NONPROPRIETARY NAME
Oxycodone HCl and Acetaminophen

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:

Original Submission	April 6, 2001
Ack Ltr	April 9, 2001

10. PHARMACOLOGICAL CATEGORY
Analgesic

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM
Tablet

14. POTENCIES
7.5mg/325mg
10mg/325mg

15. CHEMICAL NAME AND STRUCTURE

16. RECORDS AND REPORTS
None

17. COMMENTS
This ANDA has been submitted in order to provide for new tablet strengths for Percocet. The already approved strengths are 7.5mg/500mg and 10mg/650mg.

18. CONCLUSIONS AND RECOMMENDATIONS
Not approvable; Minor.

19. REVIEWER: A.Langowski

DATE COMPLETED: 07/09/01

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pages of trade secret and/or confidential commercial information

1. CHEMISTRY REVIEW NO. 2

2. ANDA # 40-434

3. NAME AND ADDRESS OF APPLICANT
Endo pharmaceuticals Inc.
Attention: Carol Patterson
500 Endo Blvd.
Garden City NY 11530

4. LEGAL BASIS FOR SUBMISSION
Percocet® is the reference listed drug. Endo is the holder of the approved application. There are no patents or exclusivities for Percocet tablets.

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME
Percocet

7. NONPROPRIETARY NAME
Oxycodone HCl and
Acetaminophen

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:

Original Submission	April 6, 2001
Ack Ltr	April 9, 2001
NC	April 4, 2001
DEF Ltr	Aug 23, 2001
Amendment	Sep 14, 2001

10. PHARMACOLOGICAL CATEGORY
Analgesic

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM
Tablet

14. POTENCIES
7.5mg/325mg
10mg/325mg

15. CHEMICAL NAME AND STRUCTURE

16. RECORDS AND REPORTS
None

17. COMMENTS
This ANDA has been submitted in order to provide for new tablet strengths for Percocet. The already approved strengths are 7.5mg/500mg and 10mg/650mg.

18. CONCLUSIONS AND RECOMMENDATIONS
Approve

19. REVIEWER: A.Langowski

DATE COMPLETED: 10/31/01

APPEARS THIS WAY
ON ORIGINAL

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pages of trade secret and/or confidential commercial information

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40-434

BIOEQUIVALENCE REVIEW

BIOEQUIVALENCY COMMENTS

ANDA: 40-434 APPLICANT: Endo Pharmceuticals

DRUG PRODUCT: Oxycodone and Acetaminophen Tablets USP, 7.5 mg/325 mg and 10 mg/325 mg

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

In future applications, please include the address of the laboratories conducting the dissolution testing in the bioequivalence section of the ANDA.

We acknowledge that the dissolution testing has been incorporated into your stability and quality control programs as specified in USP 24.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

/S/

for Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

#9

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA # : 40-434 SPONSOR : Endo Pharmaceuticals
DRUG AND DOSAGE FORM : Oxycodone and Acetaminophen Tablets USP
STRENGTH(S) : 7.5 mg/325 mg and 10 mg/325 mg
TYPES OF STUDIES : N/A
CINICAL STUDY SITE(S) : N/A
ANALYTICAL SITE(S) : N/A

STUDY SUMMARY : N/A
DISSOLUTION : Acceptable
WAIVER: Acceptable

DSI INSPECTION STATUS

Inspection needed: NO	Inspection status:	Inspection results:
First Generic _____	Inspection requested: (date)	
New facility _____	Inspection completed: (date)	
For cause _____		
Other _____		

PRIMARY REVIEWER : Hoainhon Nguyen BRANCH : I
INITIAL : __ /S/ _____ DATE : 6/5/01

TEAM LEADER : Yih-Chain Huang BRANCH : I
INITIAL : ___ /S/ DATE : 6/5/2001

DIRECTOR, DIVISION OF BIOEQUIVALENCE : DALE P. CONNER, Pharm. D.
fw
INITIAL : __ /S/ DATE : 6/19/2001

OXYCODONE AND ACETAMINOPHEN TABLETS USP
7.5 mg/325 mg & 10 mg/325 mg
ANDA 40-434
Reviewer: Hoainhon Nguyen
W #40434dw.401

Endo Pharmaceuticals Inc.
Garden City, NY

Submission Date: 04/06/01

Review of Dissolution Data and Waiver Requests (Electronic Submission)

Introduction

Indication: For the relief of moderate to moderately severe pain
Contents of Submission: Dissolution data and waiver requests
RLD: Percocet, 7.5 mg/500 mg and 10 mg/650 mg oxycodone and acetaminophen tablets, by Endo Pharmaceuticals. Other available strengths of the reference product are 5.0 mg/325 mg and 2.5 mg/325 mg oxycodone and acetaminophen tablets.
Recommended Dose: The usual adult dosage is one tablet every 6 hours as needed for pain. The total daily dose of acetaminophen should not exceed 4 grams.

Background

The firm has requested a biowaiver for the proposed new strengths, 7.5 mg/325 mg and 10 mg/325 mg oxycodone and acetaminophen. The two new strengths were found suitable for submission as an ANDA via approval of the firm's Suitability Petition (Petition Docket No. 00P-1270/CP1). A copy of the suitability petition approval letter is enclosed in Section II – "Basis for ANDA Submission" of the current submission.

The drug product is rated **AA** in the Orange Book.

Formulation(Not to be released under FOI): **Proposed Strengths**

Ingredient	Strength 10;325 mg	Strength 7.5;325 mg
COLLOIDAL SILICON DIOXIDE, NF	—	—
D&C YELLOW #10 ALUMINUM LAKE	—	
(ACETAMINOPHEN USP)	— (325.0)	— (325.0)
CROSCARMELLOSE SODIUM, NF	—	—
MICROCRYSTALLINE CELLULOSE, NF	—	—
OXYCODONE HYDROCHLORIDE, USP	10.00	7.500
STEARIC ACID, NF	—	—
FD&C YELLOW #6 ALUMINUM LAKE		—

Formulation(Not to be released under FOI): **RLD Product: Endo's Percocet (ANDA #40-341)**

Ingredient	Strength 10;650 mg	Strength 7.5;500 mg
COLLOIDAL SILICON DIOXIDE, NF	—	—
—, D&C YELLOW #10 ALUMINUM LAKE	—	
ACETAMINOPHEN USP	650	500
CROSCARMELLOSE SODIUM, NF	—	—
MICROCRYSTALLINE CELLULOSE, NF	—	—
OXYCODONE HYDROCHLORIDE, USP	10.00	7.500
STEARIC ACID, NF	—	—
—, FD&C YELLOW #6 ALUMINUM LAKE		—

Formulation Comments: T

[redacted]

The excipients as proposed are within the limits of the IIG (1996).

Dissolution(Not to be released under FOI)

Test Procedure: USP Method

Dissolution Parameters:

Apparatus:	Apparatus 2: 50 rpm
Medium:	900 mL of 0.1N HCl at 37°C (± 0.5°C)
Sampling time points:	15, 30, 45, and 60 minutes (for unit sample)
Specifications: Oxycodone Hydrochloride, USP	Q = — at 45 minutes
Acetaminophen, USP	Q = — at 45 minutes

Results:

Dissolution Profile of PERCOCET® Tablets, 7.5/500 mg: Reference product
(Oxycodone Hydrochloride/Acetaminophen Tablets, 7.5/500 mg) Lot # NC190

% Oxycodone Hydrochloride Dissolved					% Acetaminophen Dissolved				
Time (min)	15	30	45	60	Time (min)	15	30	45	60
Mean	97.6	97.7	97.8	97.3	Mean	96.9	98.1	98.8	98.9
Range					Range				
%RSD	2.9	1.3	1.3	1.3	%RSD	3.2	1.6	1.4	1.2

Dissolution Profile of PERCOCET® Tablets, 10/650 mg: Reference product
(Oxycodone Hydrochloride/Acetaminophen Tablets, 10/650 mg) Lot # NC192

% Oxycodone Hydrochloride Dissolved					% Acetaminophen Dissolved				
Time (min)	15	30	45	60	Time (min)	15	30	45	60
Mean	98.4	98.9	98.5	97.9	Mean	97.7	98.5	98.9	98.9
Range					Range				
%RSD	4.4	1.6	1.3	1.3	%RSD	3.4	1.6	1.3	1.1

Dissolution Profile of EN3225 tablets, 7.5/325 mg: Test product
Oxycodone Hydrochloride/Acetaminophen Tablets, 7.5/325 mg Lot # 311160

% Oxycodone Hydrochloride Dissolved					% Acetaminophen Dissolved				
Time (min)	15 (min)	30 (min)	45 (min)	60 (min)	Time (min)	15 (min)	30 (min)	45 (min)	60 (min)
Mean	97.7	97.3	96.6	96.4	Mean	98.8	98.9	98.7	98.7
Range					Range				
%RSD	1.3	1.3	1.2	1.6	%RSD	1.0	1.1	1.1	1.3

Dissolution Profile of EN3225 tablets, 7.5/325 mg: Test product
Oxycodone Hydrochloride/Acetaminophen Tablets, 7.5/325 mg Lot # RO049

% Oxycodone Hydrochloride Dissolved					% Acetaminophen Dissolved				
Time (min)	15 (min)	30 (min)	45 (min)	60 (min)	Time (min)	15 (min)	30 (min)	45 (min)	60 (min)
Mean	98.4	98.6	98.5	98.5	Mean	98.1	98.2	98.1	98.4
Range					Range				
%RSD	1.0	0.8	0.7	1.0	%RSD	0.8	0.8	0.7	0.9

Dissolution Profile of EN3225 tablets, 10/325 mg: Test product Oxycodone Hydrochloride/Acetaminophen Tablets, 10/325 mg Lot # 311159									
% Oxycodone Hydrochloride Dissolved					% Acetaminophen Dissolved				
Time (min)	15 (min)	30 (min)	45 (min)	60 (min)	Time (min)	15 (min)	30 (min)	45 (min)	60 (min)
Mean	95.8	95.9	96.2	96.9	Mean	96.7	97.0	97.3	97.7
Range	—	—	—	—	Range	—	—	—	—
%RSD	1.1	1.4	1.5	1.3	%RSD	1.2	1.2	1.0	1.0

Dissolution Profile of EN3225 tablets, 10/325 mg: Test product Oxycodone Hydrochloride/Acetaminophen Tablets, 10/325 mg Lot # RO050									
% Oxycodone Hydrochloride Dissolved					% Acetaminophen Dissolved				
Time (min)	15 (min)	30 (min)	45 (min)	60 (min)	Time (min)	15 (min)	30 (min)	45 (min)	60 (min)
Mean	97.1	98.5	98.0	98.2	Mean	95.4	96.7	96.3	96.8
Range	—	—	—	—	Range	—	—	—	—
%RSD	2.4	1.2	1.0	0.9	%RSD	1.9	0.8	0.8	0.8

Dissolution Comments: The dissolution data for the test and reference products are acceptable. The test and reference products meet the USP specifications and are fast dissolving.

Recommendations: The Division of Bioequivalence agrees that the information submitted by Endo Pharmaceuticals demonstrates that the proposed strengths of its Percocet Tablets, 7.5 mg/325 mg and 10 mg/325 mg oxycodone and acetaminophen, fall under 21 CFR 320.22 (c) of the Bioavailability/Bioequivalence Regulations. The waiver of *in vivo* bioequivalence study requirements for the proposed strengths of the test product is granted.

/S/

Hoaithon Nguyen
Division of Bioequivalence
Review Branch I

RD INITIALED YHUANG
FT INITIALED YHUANG /S/ 6/5/2001

Concur: /S/ Date: 6/19/2001

for Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence

cc: ANDA # 40-434 (original, duplicate), HFD-652(Huang, Nguyen), Drug File, Division File
Hnguyen/05-18-01/W#40434dw.401

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40-434

ADMINISTRATIVE DOCUMENTS

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-434 **Date of Submission: April 6, 2001**

Applicant's Name: Endo Pharmaceuticals, Inc.

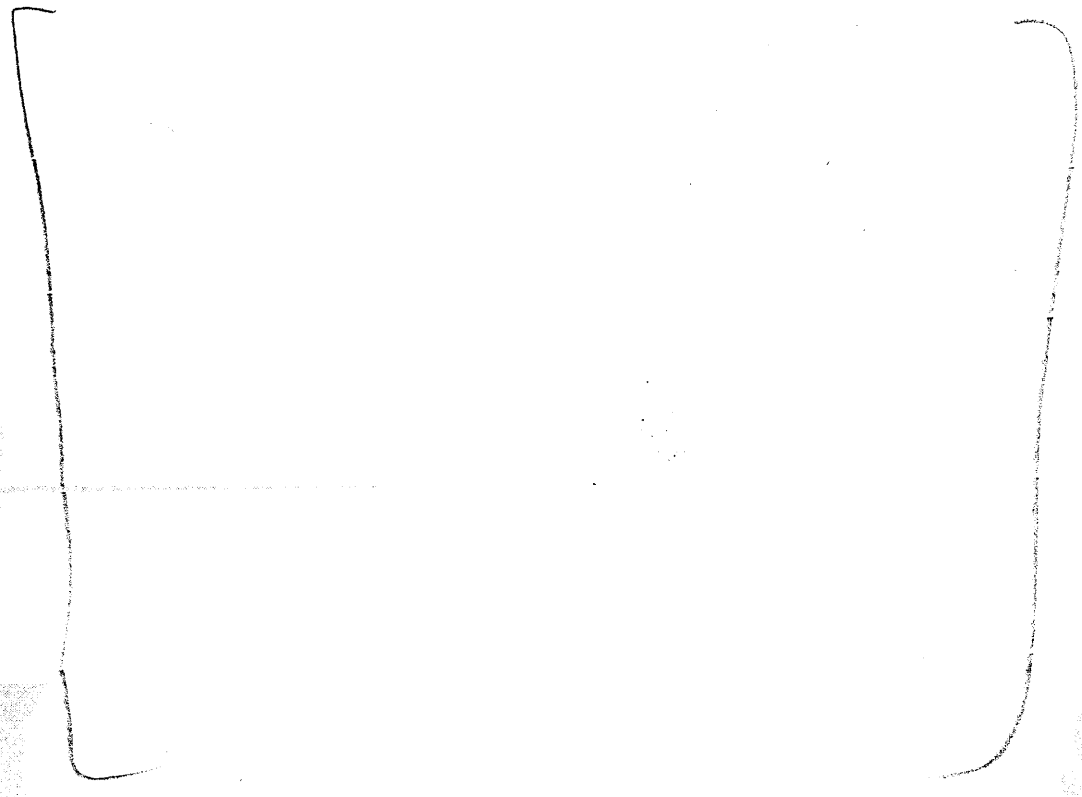
Established Name: Oxycodone and Acetaminophen Tablets USP, 7.5 mg/325 mg and 10 mg/325 mg

Proposed Proprietary name: ———

Labeling Deficiencies:

1. GENERAL COMMENTS:

   a. We acknowledge your new correspondence date May 24, 2001, in which you have proposed a proprietary name for these two new strengths of your drug product. Your proposed proprietary name ' ——— has been forwarded to the Office of Post-marketing Drug Risk Assessment (OPDRA) for their review and comment. OPDRA objects to using any modifier for this product, hence they do not recommend the use of ' ——— s the proprietary name. We have received the following comments:



[redacted]

over prescribe this new product and lead to acetaminophen poisoning. The acetaminophen should not be ingested more than 4 g daily.

We acknowledge the plans to provide sufficient education prior to availability of this product to familiarize health care practitioners with this new product, as confusion may occur between the existing products and a new product. Previous experience with medication errors has demonstrated that a lack of familiarity with a product added to an existing product line such as this can result in confusion when a prescription for the new product is received and possibly dispensed.

b. [redacted]

explain this discrepancy.

c. Revise the storage temperature statement to read "Store at controlled room temperature, 15° to 30° C (59° to 86°F) [see USP]"

2. CONTAINER – 100s & 500s

a. See comments above.

b. Please assure that the expression of the strength is clearly distinguished from other strengths.

3. UNIT DOSE BLISTER

Satisfactory in draft

4. BLISTER CARD

Increase the prominence of the text "Two new...stated.".

5. BLISTER PACK CARTON

a. See comments under CONTAINER.

b. Please assure that the text on the printed sticker regarding two new strengths appears sufficiently prominent. We note that the black lettering of the — background does not render a sufficient contrast. Please revise and/or comment.

6. BLISTER STICKER FOR THE BOTTLE

See comment 5(b) above.

7. INSERT

a. GENERAL

See general comments above.

b. DESCRIPTION

i. Include the pharmacological or therapeutic class for oxycodone hydrochloride. We refer you to 21 CFR 201.57(a)(v).

ii. Add an asterisk (*) to read as follows:

Oxycodone Hydrochloride 7.5 mg*
*7.5 mg oxycodone HCl...

Oxycodone Hydrochloride 10 mg*
*10 mg oxycodone HCl...

iii. Revise the molecular weight of oxycodone to read "351.83".

c. DOSAGE AND ADMINISTRATION

Please note that your proposed drug product must have the same therapeutic effect as the drug that you are referencing in order to comply with 21 CFR 314.93(d)(2). We believe it is possible that your drug product with the proposed dosing recommendations may have a different therapeutic effect than the reference listed drug.

Please revise the last sentence to read "...exceed 4 grams (maximal daily dose of _____, is 8 tablets and 6 tablets, respectively) or comment.

d. HOW SUPPLIED

We note that your drug products are debossed with "PERCOCET" on one side. Are you planning to change this debossing to read "_____" if the proposed proprietary name is found acceptable? Please comment.

Please revise your labels and labeling, as instructed above, and submit in draft. We will not request final print pending the findings of the OPDRA regarding your proposed proprietary name.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes-
http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

/S/

William Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

DIVISION REVIEW SUMMARY

ANDA: 40-434

FIRM: Endo pharmaceuticals Inc.
500 Endo Blvd.
Garden City NY 11530

DOSAGE FORM: Tablet STRENGTH: 7.5 mg/325 mg; 10 mg/325 mg

DRUG: Oxycodone Hydrochloride and Acetaminophen

CGMP STATEMENT/EIR UPDATE STATUS: AC 10/25/01

BIO STUDY INFORMATION: The Division of Bioequivalence agrees that the information submitted by Endo Pharmaceuticals demonstrates that the proposed strengths of its Percocet Tablets, 7.5 mg/325 mg and 10 mg/325 mg oxycodone and acetaminophen, fall under 21 CFR 320.22 (c) of the Bioavailability/Bioequivalence Regulations. The waiver of *in vivo* bioequivalence study requirements for the proposed strengths of the test product is granted.

Dissolution waiver acceptable per review by Nguyen dated 05/18/01.

METHODS VALIDATION: N/A

STABILITY:

The containers used in the stability study are of the same size and material as those described in the container section. The firm submitted accelerated stability data for the product packaged in all container sizes.

The stability tests and specifications are indicated in the following table:

TEST	SPECIFICATION	METHOD
Description	7.5/325 mg tablets: Peach oval-shaped, debossed with PERCOCET on one side and 7.5/325 on the other 10/325 mg tablets: Yellow, capsule-shaped tablet, debossed with PEWRCOCET on one side and 10/325 on the other	Visual
Dissolution: Oxycodone Hydrochloride Acetaminophen	 Q= [redacted] at 45 minutes Q = [redacted] in 45 minutes	[redacted]
Assay	Oxycodone HCl [redacted] Acetaminophen [redacted]	[redacted]
Oxycodone HCl Degradation Products: [redacted] Individual unknown Total knowns+unknowns Acetaminophen Degradation Products: [redacted] Individual unknown Total knowns+unknowns	 NMT [redacted] NMT [redacted] NMT [redacted] NMT [redacted] NMT [redacted] NMT [redacted] NMT [redacted]	[redacted]

Note: The applicant indicates that the proposed degradant limits are the same as those already approved in Percocet ANDAs 40-330 and 40-341; 2.5/325mg, 5/525 mg, 7.5/500 mg and 10/650 mg strengths.

A total of [redacted] batches were placed in stability. [redacted] batches manufactured at each site representing both tablet strengths. A list of the batch numbers, tablet strengths and storage conditions can be found on p. 1856.

The proposed expiration dating is 24 months based on the data submitted. Accelerated and room temperature stability data are provided on pp. 1853-1895. All data are with the stated specifications.

LABELING: Satisfactory 09/25/01.

STERILIZATION VALIDATION: N/A

SIZE OF BIO BATCH: Waiver was granted based on information submitted for the executed batches. See below.

SIZE OF STABILITY BATCHES:

The batch record for lot #RO049 (7.5mg/325 mg) manufactured by DuPont begins on p. 483. The [redacted] yield was [redacted]

The actual tableting yield was [redacted] The overall yield reflected a [redacted] The packaging accountability yield can be found on p. 524. [redacted] tablets were packaged into bottles of 100's and [redacted] tablets were packaged into bottles of 500 tablets. The packaging yield reflected a [redacted] which is within the stated specification. [redacted] was within stated limits for each package size.

The executed batch record for lot #311160 (7.5mg/325 mg) manufactured by Novartis begins on p. 603. The [redacted] yield is [redacted] The actual tableting yield was [redacted] The overall accountable yield reflected a [redacted] Data from [redacted] sampling begins on p. 643. The packaging reconciliation summary begins on p. 655. [redacted] tablets were packaged into bottles of 100's and [redacted] tablets were packaged into bottles of 500 tablets. [redacted] tablets were packaged into blister packs. The packaging yield reflected a [redacted] which is within the stated specification. [redacted] was within stated limits for each package size.

The batch record for lot #RO050 (10mg/325 mg) manufactured by DuPont begins on p. 683. The [redacted] yield was [redacted] The actual tableting yield was [redacted]. The overall yield reflected a [redacted] loss. The packaging summary begins on p. 751. The packaging accountability summary can be found on p. 751. [redacted] tablets were packaged into bottles of 100's and [redacted] tablets were packaged into bottles of 500 tablets. The packaging yield reflected a [redacted] which is within the stated specification. [redacted] was within stated limits for each package size.

The executed batch record for lot #311159 (10mg/325 mg) [redacted] tablets) Novartis begins on p. 830. The [redacted] yield is [redacted]

The actual tableting yield was ——— The overall accountable yield reflected a ——— Data from ——— begins on p. 643. The packaging reconciliation summary begins on p. 881. ——— tablets were packaged into bottles of 100's and ——— tablets were packaged into bottles of 500 tablets. ——— tablets were packaged into blister packs. The packaging yield reflected a ——— which is within the stated specification. ——— was within stated limits for each package size.

Reprocessing statement can be found on p.478. The applicant will submit a prior-approval supplement in accordance with PPG 23-90.

PROPOSED PRODUCTION BATCH:

Copies of the blank batch records for each facility begin on p. 337.

Strength	Manufacturer	Batch Size
7.5mg/325mg	Dupont Pharmaceuticals	——— tablets ——— kg)
7.5mg/325mg	Novartis Consumer Health	——— tablets ——— kg
10mg/325mg	DuPont Pharmaceuticals	——— tablets ——— kg)
10mg/325mg	Novartis Consumer Health	——— tablets ——— kg

RECOMMENDATION: Approve.

SIGNATURE: /S/

/S/

DATE: 11/14/01

11/15/01

COMPONENTS AND COMPOSITION

7.5/325 mg

Ingredient	Tablet Composition (mg/tablet)	NCH[2] Exhibit Batch [redacted] tablets	DPC[3] Exhibit and Proposed commercial; batches [redacted] Tablets	NCH[2] Proposed Commercial Batch [redacted]
Oxycodone HCl USP	7.5			
[redacted] (Acetaminophen)	(325.00)			
Microcrystalline Cellulose NF				
[redacted] FD&C Y6 Lake				
Croscarmellose Sodium NF				
Colloidal Silicon Dioxide NF				
Stearic Acid NF				
Total				

[redacted] value based on [redacted] Acetaminophen USP. The other components in the composition are pregelatinized starch NF, Povidone USP, Crospovidone NF and Stearic Acid NF.

[2]NCH=Novartis Consumer health

[3]DPC=DuPont Pharmaceutical Company

10mg/325mg

Ingredient	Tablet Composition (mg/tablet)	NCH[2] Exhibit Batch [redacted] tablets	DPC[3] Exhibit and Proposed commercial; batches [redacted] Tablets	NCH[2] Proposed Commercial Batch [redacted]
Oxycodone HCl USP	10.00			
[redacted] (Acetaminophen)	(325.00)			
Microcrystalline				

Cellulose NF				
FD&C Y6 Lake				
Croscarmellose Sodium NF				
Colloidal Silicon Dioxide NF				
Stearic Acid NF				
Total				

value based on Acetaminophen USP. The other components in the composition are pregelatinized starch NF, Povidone USP, Crospovidone NF and Stearic Acid NF.

[2]NCH=Novartis Consumer health

[3]DPC=DuPont Pharmaceutical Company

LABORATORY CONTROLS (IN-PROCESS AND FINISHED DOSAGE FORM)

TEST	SPECIFICATION	METHOD
Description	7.5/325 mg tablets: Peach oval-shaped, debossed with PERCOCET on one side and 7.5/325 on the other 10/325 mg tablets: Yellow, capsule-shaped tablet, debossed with PERCOCET on one side and 10/325 on the other	Visual
Identification: A:	A: The Rf values obtained form the	

B:	B: The retention times of the major peaks in the sample correspond to those in the standard from assay preparation	
Dissolution: Oxycodone Hydrochloride Acetaminophen	 Q= at 45 minutes Q = in 45 minutes	
Uniformity of Dosage Units	Meets the USP requirements for content uniformity and respect to Oxycodone Hydrochloride	
Assay	Oxycodone HCl Acetaminophen	
    Individual unknown Total knowns+unknowns <u>Acetaminophen Degradation Products</u>: Individual unknown Total knowns+unknowns	 NMT NMT NMT NMT NMT NMT NMT	

The COAs along with for the executed batches can be found on pp. 1182-1226.

Note: The applicant indicates that the proposed degradant limits are the same as those already approved in Percocet ANDAs 40-330 and 40-341; 2.5/325mg, 5/525 mg, 7.5/500 mg and 10/650 mg strengths.

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40-434

CORRESPONDENCE

ANDA 40-434

Endo Pharmaceuticals Inc.

November 6, 2001

Gary Buehler
Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

NEW CORRESP
Nc

Re: General Correspondence - Manufacturing Site Company Name Change

Dear Mr. Buehler:

Reference is made to the attached list of all approved generic products owned by Endo Pharmaceuticals Inc. These products are manufactured by DuPont Pharmaceuticals Company in Garden City, New York and/or Manati, Puerto Rico.

Recently, DuPont Pharmaceuticals Company was purchased by Bristol-Myers Squibb Pharma Company (BMS). We are therefore, submitting this correspondence to inform the Agency of a change in the manufacturer's name from DuPont Pharmaceuticals Company to Bristol-Myers Squibb Pharma Company.

All manufacturing and control documents which reference DuPont Pharmaceuticals Company will eventually be revised to reflect the new name and the appropriate submission will be made to each application.

Field Certification

A "true copy" of this correspondence has been forward to the New York District Office, Jamaica, New York.

If there are any questions, please contact me at (516) 522-3305.

Sincerely,

Carol Patterson, MS
Director, Regulatory Affairs

attachments

CENTER FOR DRUG EVALUATION AND RESEARCH
NOV 0 8 2001
OGD

500 ENDO BOULEVARD • GARDEN CITY, NEW YORK 11530 • Tel: 516.522.3300 • Fax: 516.832.2148

Endo Pharmaceuticals Inc.

Minor Amendment

September 14, 2001

Gary Buehler
Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

Re: ANDA 40-434; Oxycodone Hydrochloride and Acetaminophen Tablets, USP (Percocet®) 7.5 mg/325 mg and 10 mg/325 mg
Response to Minor Deficiency Letter of August 23, 2001

Dear Mr. Buehler:

Reference is made to the original ANDA dated April 6, 2001 for the subject drug product. Reference is also made to the enclosed minor deficiency letter for Chemistry, Manufacturing, Controls and Labeling dated August 23, 2001.

Enclosed in this amendment are the following:

1) **CMC**: responses and corresponding attachments for the seven (7) comments

2) **Labeling:** copies of final printed labeling

3) **Bioequivalence:** acknowledgement statements and future commitment as specified by the Division of Bioequivalence

These responses complete all the documentation as requested by the Agency. Also enclosed is a completed FDA 356h Form.

If there are any further questions with regards to this application, please contact me at (516) 522-3305 or fax (516) 832-2291.

Sincerely,

Carol A. Patterson
Director, Regulatory Affairs

Endo Pharmaceuticals Inc.

April 20, 2001

Gary Buehler
Acting Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

NEW CORRESP
NC

Re: ANDA 40-434; Oxycodone Hydrochloride and Acetaminophen Tablets, USP (Percocet®) 7.5 mg/325 mg and 10 mg/325 mg
Gratuitous Amendment

Dear Mr. Buehler:

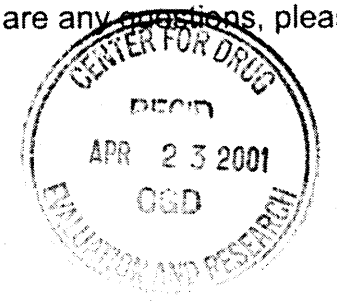
Reference is made to the original ANDA dated April 6, 2001 for the above-referenced product.

We are amending this ANDA with the following information:
- revised Field Certification
- USP moisture permeation test report for the blister package

Please note that a true copy of the ANDA was submitted to both the Kansas District and the New York District field offices, since manufacturing was done at both sites; however, the Field Copy Certification which was included in the original ANDA only referenced the New York District. We are, therefore, amending this application with a new certification which references both the New York and the Kansas District offices.

A copy of the cover letter from the original application is enclosed as reference.

If there are any questions, please contact me at (516) 522-3305.



Sincerely,

Carol Patterson, MS
Director, Regulatory Affairs

attachments

ANDA 40-434

Endo Pharmaceuticals Inc.
Attention: Carol Patterson
500 Endo Blvd.
Garden City, NY 11530

MAY 11 2001

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Acetaminophen and Oxycodone Tablets USP, 325 mg/7.5 mg and 325 mg/10 mg

DATE OF APPLICATION: April 6, 2001

DATE (RECEIVED) ACCEPTABLE FOR FILING: April 9, 2001

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Jeen Min
Project Manager
(301) 827-5849

Sincerely yours,

/S/

Wm Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Endo Pharmaceuticals Inc.

505(b)(2)(1) OK
/S/ 10-MAY-2001
/S/
N-000

April 6, 2001

Gary Buehler
Acting Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

Re: Original Abbreviated New Drug Application
Oxycodone Hydrochloride and Acetaminophen Tablets, USP
(Percocet®) 7.5 mg/325 mg and 10 mg/325 mg

Dear Mr. Buehler:

Pursuant to 21 CFR 314.94 and Section 505(j) of the Federal Food, Drug and Cosmetic Act, Endo Pharmaceuticals Inc. (Endo) hereby submits this original Abbreviated New Drug Application (ANDA) for the above-referenced drug product, Oxycodone and Acetaminophen Tablets, USP, 7.5 mg/325 mg and 10 mg/325mg.

These are two new strengths of Oxycodone and Acetaminophen Tablets which were found suitable for submission as an ANDA via approval of our Suitability Petition (Petition Docket No. 00P-1270/CP1). A copy of the suitability petition approval letter is enclosed in Section II – "Basis for ANDA Submission".

Reference Listed Product

The reference listed drug product for this ANDA is Endo's Percocet® (Oxycodone and Acetaminophen Tablets), 7.5 mg/500 mg and 10 mg/650 mg. These products are AA rated in the "Orange Book" (Approved Drug Products with Therapeutic Equivalence Evaluation), and have no patent or exclusivity associated with them.

Bioequivalence Study

Based on the AA rating for the reference listed drug products, Percocet® (Oxycodone and Acetaminophen Tablets), 7.5 mg/500 mg and 10 mg/650 mg, we are requesting a bioequivalence waiver for the proposed new strengths, oxycodone and acetaminophen, 7.5 mg/325 mg and 10 mg/325 mg. To support this waiver, we have enclosed in Volume 1.5, analytical results for the proposed new strengths and comparative analytical and dissolution data between these and the reference listed drug, in conformance with OGD requirements.

Manufacturing

Included in this ANDA are two contract manufacturing facilities, DuPont Pharmaceuticals, Garden City, New York and Novartis Consumer Health, Inc., Lincoln, Nebraska. One exhibit batch of each strength was manufactured at both sites and analytical data is provided for all batches. The manufacturing process and testing procedures are similar at both sites and a comparison is included throughout the submission.

Organization of the ANDA

This ANDA was compiled in accordance with the February 1999 Guidance. The ANDA consists of five volumes submitted in duplicate as archival and review copies as indicated in the table on the following page. The archival copies consist of 5 volumes in blue jackets designated as Volumes 1.1 to 1.5. The review copies consist of Volumes 1.1 to 1.4 in red jackets (CMC) and Volumes 1.5 in orange jackets (Bioequivalence – Product Information). In addition, the Methods Validation Package (Section XV) has been submitted, in duplicate, in separate black binders.

Technical Information	Volume
Chemistry, Manufacturing and Controls, and Labeling	1.1 - 1.4
Bioequivalence - Product Information	1.5

Please note that throughout this application the development name, EN3225, for this product has been used in several places. To assist in your review, preceding each volume is the cover letter, table of contents and a signed Form FDA 356h.

Electronic Submission Document (ESD)

An electronic submission of the information contained in this ANDA will be filed within 30 days of the filing of the paper ANDA in accordance with the guidelines issued by the Office of Generic Drugs. Endo Pharmaceuticals Inc. hereby declares to the best of our knowledge, the data contained in the electronic submission will be the same as in this paper submission unless otherwise noted.

Field Copy Certification

We have included a field copy certification in Section XXI which indicates that a copy of the chemistry, manufacturing and controls section of the ANDA (Volumes 1.1 to 1.4) have concurrently been sent to the New York District Office.

Please be advised that the materials and data contained in this submission are confidential. The legal protection of such confidential material is hereby claimed under the application provision 18U.S.C. Section 331(j).

Any questions regarding this application may be directed to me at (516) 522-3305. Any written communications may be faxed to me at (516) 832-2291.

Sincerely,

Carol Patterson, MS
Director, Regulatory Affairs

attachments

Endo Pharmaceuticals Inc.

April 20, 2001

Gary Buehler
Acting Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

NEW CORRESP
NC

Re: ANDA 40-434; Oxycodone Hydrochloride and Acetaminophen Tablets, USP (Percocet®) 7.5 mg/325 mg and 10 mg/325 mg
Gratuitous Amendment

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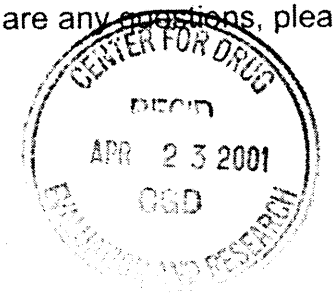

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Carol Patterson, MS
Director, Regulatory Affairs

attachments

Endo Pharmaceuticals Inc.

505(b)(2) OK
10-MAY-2001
/S/
/S/
N-000

April 6, 2001

Gary Buehler
Acting Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

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Sincerely,

Carol Patterson, MS
Director, Regulatory Affairs

attachments