

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 76-897

Name: Oxandrolone Tablets USP, 2.5 mg and 10 mg

Sponsor: Sandoz Inc.

Approval Date: December 1, 2006

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-897

CONTENTS

Reviews / Information Included in this Review

Approval Letter	X
Tentative Approval Letter(s)	
Approved Labeling	X
Labeling Review(s)	X
Medical Review(s)	
Chemistry Reviews	X
Bioequivalence Reviews	X
Statistical Review(s)	
Microbiology Review(s)	
Administrative Documents	X
Correspondence	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-897

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 76-897

Sandoz Inc.
Attention: Dietrich Bartel
4700 Eon Drive
Wilson, NC 27893

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated November 11, 2003, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Oxandrolone Tablets USP, 2.5 mg and 10 mg.

Reference is also made to your amendments dated August 19 and 25, September 2, and November 4, 2004; and February 11, March 31, May 4, July 11 and 21, and August 1, 2005; and November 6, 14, 15, and 29, 2006. We also refer to your correspondence dated April 26, 2005, addressing patent issues listed below.

We have completed the review of this ANDA and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is approved. The Division of Bioequivalence has determined your Oxandrolone Tablets, 2.5 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug, Oxandrin Tablets, 2.5 mg, of Savient Pharmaceuticals Inc. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA.

The reference listed drug (RLD) upon which you have based your ANDA, Oxandrin Tablets, 2.5 mg, of Savient Pharmaceuticals Inc., is subject to periods of patent protection. The following patents and expiration dates are currently listed in the Agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"):

<u>U.S. Patent No.</u>	<u>Expiration Date</u>
5,872,147 (the '147 patent)	December 5, 2017
6,090,799 (the '799 patent)	July 18, 2017
6,576,659 (the '659 patent)	December 5, 2017

6,670,351 (the '351 patent)
6,828,313 (the '313 patent)

October 20, 2012
December 5, 2017

FDA has determined that information on the '147, '799, '659, and '351 patents was submitted to FDA by the NDA holder after the date of the submission of your ANDA. FDA has also determined that information on the '147, '799, '659, and '351 patents was submitted by the NDA holder more than 30 days after the patent was issued by the U.S. Patent and Trademark Office (PTO). Therefore, under 21 CFR 314.94(a)(12)(vi), no person with an appropriate patent certification at the time of the submission of the patents was required to submit an amended patent certification to address the '147, '799, '659, and '351 patents. You elected not to submit an amended patent certification with respect to these patents.

With respect to the '313 patent, which was submitted to the agency within 30 days of issuance by the PTO, your ANDA contains a statement under section 505(j)(2)(A)(viii) of the Act indicating that the '313 patent is a method of use patent that does not claim any of the indications for which you are seeking approval.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Postmarketing reporting requirements for this ANDA 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.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert(s) directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,

{See appended electronic signature page}

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

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Robert L. West
12/1/2006 02:04:35 PM
for Gary Buehler

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-897

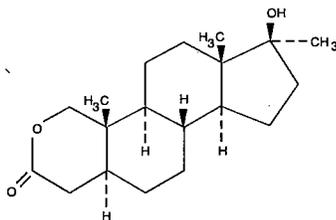
APPROVED LABELING

Oxandrolone Tablets USP

Rx only

**DESCRIPTION**

Oxandrolone oral tablets contain 2.5 mg or 10 mg of the anabolic steroid oxandrolone. Oxandrolone is 17 β -hydroxy-17 α -methyl-2-oxa-5 α -androstan-3-one with the following structural formula:

Molecular Formula: C₁₉H₃₀O₃

Molecular Weight: 306.44

Inactive ingredients include: hypromellose, lactose monohydrate, pregelatinized starch, and magnesium stearate.

CLINICAL PHARMACOLOGY

Anabolic steroids are synthetic derivatives of testosterone. Certain clinical effects and adverse reactions demonstrate the androgenic properties of this class of drugs. Complete dissociation of anabolic and androgenic effects has not been achieved. The actions of anabolic steroids are therefore similar to those of male sex hormones with the possibility of causing serious disturbances of growth and sexual development if given to young children. Anabolic steroids suppress the gonadotropic functions of the pituitary and may exert a direct effect upon the testes.

During exogenous administration of anabolic androgens, endogenous testosterone release is inhibited through inhibition of pituitary luteinizing hormone (LH). At large doses, spermatogenesis may be suppressed through feedback inhibition of pituitary follicle-stimulating hormone (FSH).

Anabolic steroids have been reported to increase low-density lipoproteins and decrease high-density lipoproteins. These levels revert to normal on discontinuation of treatment.

INDICATIONS AND USAGE

Oxandrolone is indicated as adjunctive therapy to offset the protein catabolism associated with prolonged administration of corticosteroids, and for the relief of the bone pain frequently accompanying osteoporosis (see **DOSAGE AND ADMINISTRATION**).

DRUG ABUSE AND DEPENDENCE

Oxandrolone is classified as a controlled substance under the Anabolic Steroids Control Act of 1990 and has been assigned to Schedule III (non-narcotic).

CONTRAINDICATIONS

1. Known or suspected carcinoma of the prostate or the male breast.
2. Carcinoma of the breast in females with hypercalcemia (androgenic anabolic steroids may stimulate osteolytic bone resorption).
3. Pregnancy, because of possible masculinization of the fetus. Oxandrolone has been shown to cause embryotoxicity, fetotoxicity, infertility, and masculinization of female animal offspring when given in doses 9 times the human dose.
4. Nephrosis, the nephrotic phase of nephritis.
5. Hypercalcemia.

WARNINGS

PELIOSIS HEPATIS, A CONDITION IN WHICH LIVER AND SOMETIMES SPLENIC TISSUE IS REPLACED WITH BLOOD-FILLED CYSTS, HAS BEEN REPORTED IN PATIENTS RECEIVING ANDROGENIC ANABOLIC STEROID THERAPY. THESE CYSTS ARE SOMETIMES PRESENT WITH MINIMAL HEPATIC DYSFUNCTION, BUT AT OTHER TIMES THEY HAVE BEEN ASSOCIATED WITH LIVER FAILURE. THEY ARE OFTEN NOT RECOGNIZED UNTIL LIFE-THREATENING LIVER FAILURE OR INTRA-ABDOMINAL HEMORRHAGE DEVELOPS. WITHDRAWAL OF DRUG USUALLY RESULTS IN COMPLETE DISAPPEARANCE OF LESIONS.

LIVER CELL TUMORS ARE ALSO REPORTED. MOST OFTEN THESE TUMORS ARE BENIGN AND ANDROGEN-DEPENDENT, BUT FATAL MALIGNANT TUMORS HAVE BEEN REPORTED. WITHDRAWAL OF DRUG OFTEN RESULTS IN REGRESSION OR CESSATION OF PROGRESSION OF THE TUMOR. HOWEVER, HEPATIC TUMORS ASSOCIATED WITH ANDROGENS OR ANABOLIC STEROIDS ARE MUCH MORE VASCULAR THAN OTHER HEPATIC TUMORS AND MAY BE SILENT UNTIL LIFE-THREATENING INTRA-ABDOMINAL HEMORRHAGE DEVELOPS. BLOOD LIPID CHANGES THAT ARE KNOWN TO BE ASSOCIATED WITH INCREASED RISK OF ATHEROSCLEROSIS ARE SEEN IN PATIENTS TREATED WITH ANDROGENS OR ANABOLIC STEROIDS. THESE CHANGES INCLUDE DECREASED HIGH-DENSITY LIPOPROTEINS AND SOMETIMES INCREASED LOW-DENSITY LIPOPROTEINS. THE CHANGES MAY BE VERY MARKED AND COULD HAVE A SERIOUS IMPACT ON THE RISK OF ATHEROSCLEROSIS AND CORONARY ARTERY DISEASE.

Cholestatic hepatitis and jaundice may occur with 17-alpha-alkylated androgens at a relatively low dose. If cholestatic hepatitis with jaundice appears or if liver function tests become abnormal, oxandrolone should be discontinued and the etiology should be determined. Drug-induced jaundice is reversible when the medication is discontinued.

In patients with breast cancer, anabolic steroid therapy may cause hypercalcemia by stimulating osteolysis. Oxandrolone therapy should be discontinued if hypercalcemia occurs.

Edema with or without congestive heart failure may be a serious complication in patients with pre-existing cardiac, renal, or hepatic disease. Concomitant administration of adrenal cortical steroid or ACTH may increase the edema.

In children, androgen therapy may accelerate bone maturation without producing compensatory gain in linear growth. This adverse effect results in compromised adult height. The younger the child, the greater the risk of compromising final mature height. The effect on bone maturation should be monitored by assessing bone age of the left wrist and hand every 6 months (see **PRECAUTIONS, Laboratory Tests**).

Geriatric patients treated with androgenic anabolic steroids may be at an increased risk for the development of prostatic hypertrophy and prostatic carcinoma.

ANABOLIC STEROIDS HAVE NOT BEEN SHOWN TO ENHANCE ATHLETIC ABILITY.

PRECAUTIONS

Concurrent dosing of oxandrolone and warfarin may result in unexpectedly large increases in the International Normalized Ratio (INR) or prothrombin time (PT). When oxandrolone is prescribed to patients being treated with warfarin, doses of warfarin may need to be decreased significantly to maintain the desirable INR level and diminish the risk of potentially serious bleeding (See **PRECAUTIONS, Drug Interactions).**

General

Women should be observed for signs of virilization (deepening of the voice, hirsutism, acne, clitoromegaly). Discontinuation of drug therapy at the time of evidence of mild virilism is necessary to prevent irreversible virilization. Some virilizing changes in women are irreversible even after prompt discontinuance of therapy and are not prevented by concomitant use of estrogens. Menstrual irregularities may also occur.

Anabolic steroids may cause suppression of clotting factors II, V, VII, and X, and an increase in prothrombin time.

Information for Patients

The physician should instruct patients to report immediately any use of warfarin and any bleeding.

The physician should instruct patients to report any of the following side effects of androgens:

Males: Too frequent or persistent erections of the penis, appearance or aggravation of acne.

Females: Hoarseness, acne, changes in menstrual periods, or more facial hair.

All patients: Nausea, vomiting, changes in skin color, or ankle swelling.

Geriatric Use: Certain geriatric use information is protected by marketing exclusivity.

Laboratory Tests

Women with disseminated breast carcinoma should have frequent determination of urine and serum calcium levels during the course of therapy (see **WARNINGS**).

Because of the hepatotoxicity associated with the use of 17-alpha-alkylated androgens, liver function tests should be obtained periodically.



Rev. 12/06

ZONDOX

Oxandrolone
Tablets USP

Periodic (every 6 months) x-ray examinations of bone age should be made during treatment of children to determine the rate of bone maturation and the effects of androgen therapy on the epiphyseal centers.

Androgenic anabolic steroids have been reported to increase low-density lipoproteins and decrease high-density lipoproteins. Therefore, caution is required when administering these agents to patients with a history of cardiovascular disease or who are at risk for cardiovascular disease. Serum determination of lipid levels should be performed periodically and therapy adjusted accordingly. Hemoglobin and hematocrit should be checked periodically for polycythemia in patients who are receiving high doses of anabolic steroids.

Drug Interactions

Anticoagulants: Anabolic steroids may increase sensitivity to oral anticoagulants. Dosage of the anticoagulant may have to be decreased in order to maintain desired prothrombin time. Patients receiving oral anticoagulant therapy require close monitoring, especially when anabolic steroids are started or stopped.

Warfarin: A multidose study of oxandrolone, given as 5 or 10 mg BID in 15 healthy subjects concurrently treated with warfarin, resulted in a mean increase in S-warfarin half-life from 26 to 48 hours and AUC from 4.55 to 12.08 ng-hr/mL; similar increases in R-warfarin half-life and AUC were also detected. Microscopic hematuria (9/15) and gingival bleeding (1/15) were also observed. A 5.5-fold decrease in the mean warfarin dose from 6.13 mg/day to 1.13 mg/day (approximately 80-85% reduction of warfarin dose), was necessary to maintain a target INR of 1.5. When oxandrolone therapy is initiated in a patient already receiving treatment with warfarin, the INR or prothrombin time (PT) should be monitored closely and the dose of warfarin adjusted as necessary until a stable target INR or PT has been achieved.

Furthermore, in patients receiving both drugs, careful monitoring of the INR or PT, and adjustment of the warfarin dosage if indicated are recommended when the oxandrolone dose is changed or discontinued. Patients should be closely monitored for signs and symptoms of occult bleeding.

Oral Hypoglycemic Agents: Oxandrolone may inhibit the metabolism of oral hypoglycemic agents.

Adrenal Steroids or ACTH: In patients with edema, concomitant administration with adrenal cortical steroids or ACTH may increase the edema.

Drug/Laboratory Test Interactions

Anabolic steroids may decrease levels of thyroxine-binding globulin, resulting in decreased total T₄ serum levels and increased resin uptake of T₃ and T₄. Free thyroid hormone levels remain unchanged. In addition, a decrease in PBI and radioactive iodine uptake may occur.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal Data: Oxandrolone has not been tested in laboratory animals for carcinogenic or mutagenic effects. In 2-year chronic oral rat studies, a dose-related reduction of spermatogenesis and decreased organ weights (testes, prostate, seminal vesicles, ovaries, uterus, adrenals, and pituitary) were shown.

Human Data: Liver cell tumors have been reported in patients receiving long-term therapy with androgenic anabolic steroids in high doses (see **WARNINGS**). Withdrawal of the drugs did not lead to regression of the tumors in all cases. Geriatric patients treated with androgenic anabolic steroids may be at an increased risk for the development of prostatic hypertrophy and prostatic carcinoma.

Pregnancy

Teratogenic effects—Pregnancy Category X (see **CONTRAINDICATIONS**).

Nursing Mothers

It is not known whether anabolic steroids are excreted in human milk. Because of the potential of serious adverse reactions in nursing infants from oxandrolone, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Anabolic agents may accelerate epiphyseal maturation more rapidly than linear growth in children and the effect may continue for 6 months after the drug has been stopped. Therefore, therapy should be monitored by x-ray studies at 6-month intervals in order to avoid the risk of compromising adult height. Androgenic anabolic steroid therapy should be used very cautiously in children and only by specialists who are aware of the effects on bone maturation (see **WARNINGS**).

ADVERSE REACTIONS

Patients with moderate to severe COPD or COPD patients who are unresponsive to bronchodilators should be monitored closely for COPD exacerbation and fluid retention.

The following adverse reactions have been associated with use of anabolic steroids:

Hepatic

Cholestatic jaundice with, rarely, hepatic necrosis and death. Hepatocellular neoplasms and peliosis hepatis with long-term therapy (see **WARNINGS**). Reversible changes in liver function tests also occur including increased bromsulphthalein (BSP) retention, changes in alkaline phosphatase and increases in serum bilirubin, aspartate aminotransferase (AST, SGOT) and alanine aminotransferase (ALT, SGPT).

In Males

Prepubertal: Phallic enlargement and increased frequency or persistence of erections.

Postpubertal: Inhibition of testicular function, testicular atrophy and oligospermia, impotence, chronic priapism, epididymitis, and bladder irritability.

In Females

Clitoral enlargement, menstrual irregularities.

CNS

Habituation, excitation, insomnia, depression, and changes in libido.

Hematologic

Bleeding in patients on concomitant anticoagulant therapy.

Breast

Gynecomastia.

Larynx

Deepening of the voice in females.

Hair

Hirsutism and male pattern baldness in females.

Skin

Acne (especially in females and prepubertal males).

Skeletal

Premature closure of epiphyses in children (see **PRECAUTIONS, Pediatric Use**).

Fluid and Electrolytes

Edema, retention of serum electrolytes (sodium chloride, potassium, phosphate, calcium).

Metabolic/Endocrine

Decreased glucose tolerance (see **PRECAUTIONS, Laboratory Tests**), increased creatinine excretion, increased serum levels of creatinine phosphokinase (CPK). Masculinization of the fetus. Inhibition of gonadotropin secretion.

OVERDOSAGE

No symptoms or signs associated with overdosage have been reported. It is possible that sodium and water retention may occur.

The oral LD₅₀ of oxandrolone in mice and dogs is greater than 5,000 mg/kg. No specific antidote is known, but gastric lavage may be used.

DOSE AND ADMINISTRATION

Therapy with anabolic steroids is adjunctive to and not a replacement for conventional therapy. The duration of therapy with oxandrolone will depend on the response of the patient and the possible appearance of adverse reactions. Therapy should be intermittent.

Adults

The response of individuals to anabolic steroids varies. The daily adult dosage is 2.5 mg to 20 mg given in 2 to 4 divided doses. The desired response may be achieved with as little as 2.5 mg or as much as 20 mg daily. A course of therapy of 2 to 4 weeks is usually adequate. This may be repeated intermittently as indicated.

Children

For children the total daily dosage of oxandrolone is ≤ 0.1 mg per kilogram body weight or ≤ 0.045 mg per pound of body weight. This may be repeated intermittently as indicated.

HOW SUPPLIED

Oxandrolone Tablets USP are supplied as follows:

2.5 mg Tablets: white, modified oval-shaped, debossed "E 271" on one side and bisected on the reverse side.

Bottles of 100

Bottles of 1000

10 mg Tablets: white, capsule-shaped, debossed "E 272" on one side and plain on the reverse side.

Bottles of 100

Bottles of 1000

Store at 20° - 25°C (68° - 77°F) [see USP Controlled Room Temperature].

Sandoz Inc.
Princeton, NJ 08540

Rev. 12/06
MF0271REV12/06
OS8072

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-897

LABELING REVIEW(S)

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

ANDA Number: 76-897 Date of Submission: November 11, 2003

Applicant's Name: Eon Labs, Inc.

Established Name: Oxandrolone Tablets, USP 2.5 mg and 10 mg

Labeling Deficiencies:

1. GENERAL COMMENT

Revise the "Manufactured by." address on all labeling to read:

Eon Labs, Inc.
Wilson, NC 27893

2. CONTAINER LABELS

See GENERAL COMMENT

3. INSERT

a. Revise the chemical name of oxandrolone in the DESCRIPTION section to read:

17 β -hydroxy-17 α -methyl-2-oxa-5 α -androstan-3-one

b. Using bold print, insert the following information as the first paragraph of the PRECAUTIONS section:

Concurrent dosing of oxandrolone and warfarin may result in unexpectedly large increases in the INR or prothrombin time (PT). When oxandrolone is prescribed to patients being treated with warfarin, doses of warfarin may need to be decreased significantly to maintain the desirable INR level and diminish the risk of potentially serious bleeding. (See PRECAUTIONS: Drug Interactions).

c. Insert the following information as the first paragraph of the "Information for patients" subsection of the PRECAUTIONS section:

The physician should instruct patients to report immediately any use of warfarin and any bleeding.

d. Insert the following information as the second subsection of the PRECAUTIONS: Drug Interactions section:

Warfarin:

A multidose study of oxandrolone, given as 5 or 10 mg BID in 15 healthy subjects concurrently treated with warfarin, resulted in a mean increase in S-warfarin half-life from 26 to 48 hours and similar increases in R-warfarin half-life and AUC were also detected. A 5.5-fold decrease in the mean warfarin dose from 6.13 mg/day to 1.13 mg/day (approximately 80-85% reduction of warfarin dose); was necessary to maintain a target INR of 1.5. INR or prothrombin time (PT) should be monitored closely for up to 4 weeks or until a stable INR or PT has been achieved. Monitoring of INR is recommended when the oxandrolone dose is changed or when oxandrolone is discontinued during concomitant therapy. Patients should be closely monitored for signs and symptoms of occult

bleeding.

Please revise your labels and labeling, as instructed above, and submit 4 draft copies for a tentative approval or 12 final printed copies for a full approval of this application. If draft labeling is provided, please be advised that you will be required to submit 12 final printed copies of all labels and labeling at least 60 days prior to full approval of this application. In addition, you should be aware that color and other factors (print size, prominence, etc.) in final printed labeling could be found unacceptable and that further changes might be requested prior to approval.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -

<http://www.fda.gov/cder/cdernew/listserv.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.



Wm. Peter Rickman

Director

Division of Labeling and Program Support

Office of Generic Drugs

Center for Drug Evaluation and Research

BASIS OF APPROVAL:**APPROVAL SUMMARY** (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? Yes No If no, list why:

Container Labels:

Professional Package Insert Labeling:

Revisions needed post-approval:

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Oxandrin® tablets

NDA Number: NDA 13-718

NDA Drug Name: Oxandrin® tablets

NDA Firm: BTG Pharmaceuticals

Date of Approval of NDA Insert and supplement #: April 21, 2003

Has this been verified by the MIS system for the NDA? Yes

Was this approval based upon an OGD labeling guidance?

Basis of Approval for the Container Labels:

Basis of Approval for the Carton Labeling:

Other Comments

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured, USP 26	x		
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			x
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		x	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			x
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?			x
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?		x	
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)	x		

Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		x	
Is the "Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by..." statement needed?	x		
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?		x	
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		x	
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?		x	
Has the firm failed to describe the scoring in the HOW SUPPLIED section?		x	
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		x	
Do any of the inactives differ in concentration for this route of administration?		x	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		x	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		x	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?		x	
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)		x	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	
Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		x	
Does USP have labeling recommendations? If any, does ANDA meet them?		x	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		x	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.		x	
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			x
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.			x
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.		x	

NOTES/QUESTIONS TO THE CHEMIST:

FOR THE RECORD:

1. Review based on the labeling of Oxandrin® tablets (NDA 13-718) approved April 21, 2003.

2. PATENT/ EXCLUSIVITIES

Patent Data -

No	Expiration	Use Code	Use	File
None				III

Exclusivity Data -

Code/sup	Expiration	Use Code	Description	Labeling Impact
None			There is no unexpired exclusivity for this product	

3. MANUFACTURING FACILITY

Eon Labs, Inc.
4700 Eon Drive
Wilson, NC 27893

4. SCORING:

NDA - 2.5 mg scored, 10 mg unscored
ANDA - 2.5 mg bisected, 10 mg unscored

5. STORAGE CONDITIONS:

NDA - Store at Room Temperature (59-77°F)
ANDA - Store at 20-25° (68-77°F) excursions permitted to 15°-30°C (59-86°F) [see USP Controlled Room Temperature]
USP- Preserve in tight, light-resistant containers

6. DISPENSING RECOMMENDATIONS:
NDA - Dispense in a tight, light-resistant, child-resistant container.
ANDA - Dispense in a tight, light-resistant containers as defined in the USP, with a child-resistant closure, as required.
7. INACTIVE INGREDIENTS:
The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 82 of Volume A1.1.
8. PACKAGING CONFIGURATIONS:
NDA- 2.5 mg and 10 mg bottles of 100
ANDA- 2.5 mg and 10 mg bottles of 100 and 1000
9. CONTAINER/CLOSURE SYSTEM:
2.5 mg Bottles of 100 60 cc white, round, opaque HDPE, 38 mm white PP CRC, innerseal/liner () and white pulp liner, 16 gram cotton
2.5 mg Bottles of 1000 250 cc white opaque HDPE, 45 mm white PP screw caps, innerseal/liner () and white pulp liner, 16 gram cotton
10 mg Bottles of 100 100 cc white, round, opaque HDPE, 38 mm white PP CRC, innerseal/liner () and white pulp liner, 16 gram cotton
10 mg Bottles of 1000 950 cc white, round, opaque HDPE, 53 mm white PP screw caps, innerseal/liner () and white pulp liner, 16 gram cotton
(Vol. A1.3, p. 422)
10. The tablet have been accurately described in the HOW SUPPLIED section as required by 21 CFR 206, et al. (Imprinting of Solid Oral Dosage Form Products for Human Use; Final Rule, effective 9/13/95).
2.5 mg white, modified oval, debossed "E 271" on one side and bisected on the reverse side
10 mg white, capsule-shaped, debossed "E 272" on one side and plain on the reverse side

Date of Review: April 20, 2004
Date of Submission: November 11, 2003
Primary Reviewer: Postelle Birch *MB* Date: April 22, 2004
Team Leader: John Grace Date:

cc: ANDA: 76-897
DUP/DIVISION FILE
HFD-613/PBirch /JGrace (no cc)
V:\FIRMSAME\ONLTRS&REV\76-897na1.label.DOC
Review

John Grace for JGrace
4/26/04

Superseded by Labeling Approval Summary dated 12/11/05
(review of 5/11/05 amendments)

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

ANDA Number: 76-897 Dates of Submission: August 19, 2004 and September 2, 2004
Applicant's Name: Eon Labs, Inc.
Established Name: Oxandrolone Tablets, USP 2.5 mg and 10 mg

BASIS OF APPROVAL:

APPROVAL SUMMARY

Do you Final Printed Labels and Labeling? Yes

Container Labels

Bottles of 100 tablets

2.5 mg-Satisfactory as of September 2, 2004 submission.

(\\Cdsesubogd1\n76897\N_000\2004-09-02\Oxandrolone 2'5 C.pdf)

10 mg-Satisfactory as of September 2, 2004 submission.

(\\Cdsesubogd1\n76897\N_000\2004-09-02\Oxandrolone 10 C.pdf)

Bottles of 1000 tablets

2.5 mg-Satisfactory as of September 2, 2004 submission.

(\\Cdsesubogd1\n76897\N_000\2004-09-02\Oxandrolone 2'5 M.pdf)

10 mg-Satisfactory as of September 2, 2004 submission.

(\\Cdsesubogd1\n76897\N_000\2004-09-02\Oxandrolone 10 M.pdf)

Professional Package Insert Labeling (Iss 05/04):

Satisfactory as of September 2, 2004 submission.

(\\Cdsesubogd1\n76897\N_000\2004-09-02\PI Content 05-04.pdf)

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Oxandrin® tablets

NDA Number: NDA 13-718

NDA Drug Name: Oxandrin® tablets

NDA Firm: BTG Pharmaceuticals

Date of Approval of NDA Insert and supplement #: April 21, 2003

Has this been verified by the MIS system for the NDA? Yes

Was this approval based upon an OGD labeling guidance?

Basis of Approval for the Container Labels:

Basis of Approval for the Carton Labeling:

Other Comments

PATENT/ EXCLUSIVITIES

Patent Data -

No.	Expiration	Use Code	Use	File
None				III

Exclusivity Data -

Code/sup	Expiration	Use Code	Description	Labeling Impact
None			There is no unexpired exclusivity for this product	

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 26	x		
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			x
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		x	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			x
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?			x
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?		x	
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)	x		
Labeling(continued)			
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA).		x	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by..." statement needed?	x		
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?		x	
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		x	
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?		x	
Has the firm failed to describe the scoring in the HOW SUPPLIED section?		x	
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		x	
Do any of the inactives differ in concentration for this route of administration?		x	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		x	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		x	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?		x	
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)		x	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	
Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		x	
Does USP have labeling recommendations? If any, does ANDA meet them?		x	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		x	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.		x	
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			

Insert labeling references a food effect or a no-effect? If so, was a food study done?			x
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.			x
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.		x	

NOTES/QUESTIONS TO THE CHEMIST:

FOR THE RECORD:

1. Review based on the labeling of Oxandrin® tablets (NDA 13-718) approved April 21, 2003.

2. **PATENT/ EXCLUSIVITIES**

Patent Data -

No	Expiration	Use Code	Use	File
None				III

Exclusivity Data -

Code/sup	Expiration	Use Code	Description	Labeling Impact
None			There is no unexpired exclusivity for this product	

3. **MANUFACTURING FACILITY**

Eon Labs, Inc.
4700 Eon Drive
Wilson, NC 27893

4. **SCORING:**

NDA - 2.5 mg scored, 10 mg unscored
ANDA - 2.5 mg bisected, 10 mg unscored

5. **STORAGE CONDITIONS:**

NDA - Store at Room Temperature (59-77°F)
ANDA - Store at 20-25° (68-77°F) excursions permitted to 15°-30°C (59-86°F) [see USP Controlled Room Temperature]
USP- Preserve in tight, light-resistant containers

6. **DISPENSING RECOMMENDATIONS:**

NDA - Dispense in a tight, light-resistant, child-resistant container.
ANDA - Dispense in a tight, light-resistant containers as defined in the USP, with a child-resistant closure, as required.

7. **INACTIVE INGREDIENTS:**

The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 82 of Volume A1.1.

8. **PACKAGING CONFIGURATIONS:**

NDA- 2.5 mg and 10 mg bottles of 100
ANDA- 2.5 mg and 10 mg bottles of 100 and 1000

9. **CONTAINER/CLOSURE SYSTEM:**

2.5 mg Bottles of 100 60 cc white, round, opaque HDPE, 38 mm white PP CRC, innerseal/liner and white pulp liner, 16 gram cotton

2.5 mg Bottles of 1000 250 cc white opaque HDPE, 45 mm white PP screw caps, innerseal/liner and white pulp liner, 16 gram cotton

10 mg Bottles of 100 100 cc white, round, opaque HDPE, 38 mm white PP CRC, innerseal/liner and white pulp liner, 16 gram cotton

10 mg Bottles of 1000 950 cc white, round, opaque HDPE, 53 mm white PP screw caps innerseal/liner and white pulp liner, 16 gram cotton

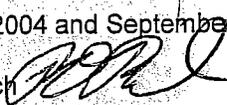
(Vol. A1.3, p. 422)

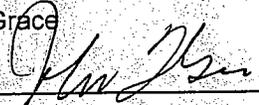
10. The tablet have been accurately described in the HOW SUPPLIED section as required by 21 CFR 206, et al. (Imprinting of Solid Oral Dosage Form Products for Human Use; Final Rule, effective 9/13/95).

2.5 mg white, modified oval, debossed "E 271" on one side and bisected on the reverse side
10 mg white, capsule-shaped, debossed "E 272" on one side and plain on the reverse side

Date of Review: September 16, 2004

Dates of Submission: August 19, 2004 and September 2, 2004

Primary Reviewer: Postelle Birch  Date: September 16, 2004

Team Leader: John Grace  Date: 9/21/04

cc: ANDA: 76-897
DUP/DIVISION FILE
HFD-613/PBirch /JGrace (no cc)
V:\FIRMSAM\EON\LTRS&REV\76-897ap.label.DOC
Review

This Labeling Approval Summary supersedes the Labeling Approval Summary dated May 4, 2005.

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

ANDA Number: 76-897 Dates of Submission: July 11, 2005 and August 1, 2005

Applicant's Name: Eon Labs, Inc.

Established Name: Oxandrolone Tablets, USP 2.5 mg and 10 mg

BASIS OF APPROVAL:

APPROVAL SUMMARY

Do you Final Printed Labels and Labeling? Yes

Container Labels

Bottles of 100 tablets

2.5 mg-Satisfactory as of September 2, 2004 submission.

Network Path: \\Cdsesubogd1\76897\N 000\2004-09-02\Oxandrolone 2'5 C.pdf

10 mg-Satisfactory as of September 2, 2004 submission.

Network Path: \\Cdsesubogd1\76897\N 000\2004-09-02\Oxandrolone 10 C.pdf

Bottles of 1000 tablets

2.5 mg-Satisfactory as of September 2, 2004 submission.

Network Path: \\Cdsesubogd1\76897\N 000\2004-09-02\Oxandrolone 2'5 M.pdf

10 mg-Satisfactory as of September 2, 2004 submission.

Network Path: \\Cdsesubogd1\76897\N 000\2004-09-02\Oxandrolone 10 M.pdf

Professional Package Insert Labeling (Iss 05/04):

Satisfactory as of May 5, 2005 submission.

Network Path: \\Cdsesub1\76897\N 000\2005-08-01\OS8072 Rev 08-05 Final.pdf

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Oxandrin® tablets

NDA Number: NDA 13-718

NDA Drug Name: Oxandrin® tablets

NDA Firm: BTG Pharmaceuticals

Date of Approval of NDA Insert and supplement #: June 20, 2005/S-023

Has this been verified by the MIS system for the NDA? Yes

Was this approval based upon an OGD labeling guidance?

Basis of Approval for the Container Labels:

Basis of Approval for the Carton Labeling:

Other Comments

PATENT/ EXCLUSIVITIES

Patent Data – NDA 13-718

No.	Expiration	Use Code	Use	File	Labeling Impact
5872147	12/05/2017	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6090799	07/18/2017	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6576659	12/05/2017	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6670351	10/20/2012	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6828313	12/05/2017	U-585	To promote weight gain after weight loss in certain types of patients	MOU	Carve-out

Exclusivity Data -

Code/sup	Expiration	Use Code	Description	Labeling Impact
M-42	6/20/2008		Addition of a geriatric use subsection to the precautions section of the package insert and geriatric dosing information	Carve-Out

REVIEW OF PROFESSIONAL LABELING CHECK LIST

	Yes	No	N.A.
Established Name			
Different name than on acceptance to file letter?		x	
Is this product a USP Item? If so, USP supplement in which verification was assured. USP 26	x		
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			x
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		x	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			x
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?			x
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?		x	
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)	x		
Labeling(continued)			
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		x	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by..." statement needed?	x		
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?		x	
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		x	
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?		x	
Has the firm failed to describe the scoring in the HOW SUPPLIED section?		x	
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		x	
Do any of the inactives differ in concentration for this route of administration?		x	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		x	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		x	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?		x	
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)		x	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	

Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		x	
Does USP have labeling recommendations? If any, does ANDA meet them?		x	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		x	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.		x	
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			x
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.			x
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.		x	

NOTES/QUESTIONS TO THE CHEMIST:

FOR THE RECORD:

1. Review based on the labeling of Oxandrin® tablets (NDA 13-718) approved April 21, 2003.
2. **PATENT/ EXCLUSIVITIES**
See Page 1 and #11 of FTR.
3. **MANUFACTURING FACILITY**
Eon Labs, Inc.
4700 Eon Drive
Wilson, NC 27893
4. **SCORING:**
NDA - 2.5 mg scored, 10 mg unscored
ANDA - 2.5 mg bisected, 10 mg unscored
5. **STORAGE CONDITIONS:**
NDA - Store at Room Temperature (59-77°F)
ANDA - Store at 20-25° (68-77°F) excursions permitted to 15°-30°C (59-86°F) [see USP Controlled Room Temperature]
USP- Preserve in tight, light-resistant containers
6. **DISPENSING RECOMMENDATIONS:**
NDA - Dispense in a tight, light-resistant, child-resistant container.
ANDA - Dispense in a tight, light-resistant containers as defined in the USP, with a child-resistant closure, as required.
7. **INACTIVE INGREDIENTS:**
The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 82 of Volume A1.1.
8. **PACKAGING CONFIGURATIONS:**
NDA- 2.5 mg and 10 mg bottles of 100
ANDA- 2.5 mg and 10 mg bottles of 100 and 1000
9. **CONTAINER/CLOSURE SYSTEM:**
2.5 mg Bottles of 100 60 cc white, round, opaque HDPE, 38 mm white PP CRC innerseal/liner and white pulp liner, 16 gram cotton
2.5 mg Bottles of 1000 250 cc white opaque HDPE, 45 mm white PP screw caps, innerseal/liner and white pulp liner, 16 gram cotton
10 mg Bottles of 100 100 cc white, round, opaque HDPE, 38 mm white PP CRC innerseal/liner and white pulp liner, 16 gram cotton
10 mg Bottles of 1000 950 cc white, round opaque HDPE, 53 mm white PP screw caps innerseal/liner and white pulp liner, 16 gram cotton

(Vol. A1.3, p. 422)
10. The tablet have been accurately described in the HOW SUPPLIED section as required by 21 CFR 206,et al. (Imprinting of Solid Oral Dosage Form Products for Human Use; Final Rule, effective 9/13/95).

2.5 mg white, modified oval, debossed "E 271" on one side and bisected on the reverse side
10 mg white, capsule-shaped, debossed "E 272" on one side and plain on the reverse side

11. The following Email was sent to Debbie Catterson from Martin Shimer:

From: Shimer, Martin
Sent: Wednesday, May 04, 2005 12:51 PM
To: Catterson, Debra M
Cc: Park, Sarah Soojung
Subject: ANDA 76-897, Eon's Oxandrolone

Debbie,

Eon submitted a patent amendment on April 27, 2005 addressing the patents covering NDA 13-718 Oxandrin Tablets. Eon states that the '147, '799, '699 and '351 patents were late listed for Eon and therefore Eon declines to address these patents. They have provided a MOU statement to the '313 patent as this patent was timely filed. So this is just a heads up that they should be making some changes to their labeling to correspond to the MOU statement provided in the patent amendment.

Thanks,

Marty

Date of Review: September 6, 2005

Dates of Submission: July 11, 2005 and August 1, 2005

Primary Reviewer: Postelle Birch

Date: 9/6/05

Team Leader: John Grace

Date: 9/13/05

cc: ANDA: 76-897

DUP/DIVISION FILE

HFD-613/PBirch /JGrace (no cc)

V:\FIRMSAMEON\LTRS&REV\76-897apsupersede.label2.DOC

Review

This Labeling Approval Summary supersedes the Labeling Approval Summary dated August 19, 2004 and September 2, 2004.

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

ANDA Number: 76-897 Dates of Submission: May 4, 2005

Applicant's Name: Eon Labs, Inc.

Established Name: Oxandrolone Tablets, USP 2.5 mg and 10 mg

BASIS OF APPROVAL:

APPROVAL SUMMARY

Do you Final Printed Labels and Labeling? Yes

Container Labels

Bottles of 100 tablets

2.5 mg-Satisfactory as of September 2, 2004 submission.

Network Path: \\Cdsubogd1\76897W_000\2004-09-02\Oxandrolone 2'5 C.pdf

10 mg-Satisfactory as of September 2, 2004 submission.

Network Path: \\Cdsubogd1\76897W_000\2004-09-02\Oxandrolone 10 C.pdf

Bottles of 1000 tablets

2.5 mg-Satisfactory as of September 2, 2004 submission.

Network Path: \\Cdsubogd1\76897W_000\2004-09-02\Oxandrolone 2'5 M.pdf

10 mg-Satisfactory as of September 2, 2004 submission.

Network Path: \\Cdsubogd1\76897W_000\2004-09-02\Oxandrolone 10 M.pdf

Professional Package Insert Labeling (Iss 05/04):

Satisfactory as of September 2, 2004 submission.

Network Path: \\Cdsubogd1\76897W_000\2005-05-04\Oxandrolone Rev 05-05.pdf

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Oxandrin® tablets

NDA Number: NDA 13-718

NDA Drug Name: Oxandrin® tablets

NDA Firm: BTG Pharmaceuticals

Date of Approval of NDA Insert and supplement #: April 21, 2003/S-022

Has this been verified by the MIS system for the NDA? Yes

Was this approval based upon an OGD labeling guidance?

Basis of Approval for the Container Labels:

Basis of Approval for the Carton Labeling:

Other Comments

PATENT/ EXCLUSIVITIES

Patent Data – NDA 13-718

No	Expiration	Use Code	Use	File	Labeling Impact
5872147	12/05/2017	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6090799	07/18/2017	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6576659	12/05/2017	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6670351	10/20/2012	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6828313	12/05/2017	U-585	To promote weight gain after weight loss in certain types of patients	MOU	Carve-out

Exclusivity Data -

Code/sup	Expiration	Use Code	Description	Labeling Impact
None			There is no unexpired exclusivity for this product	None

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 26	x		
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			x
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		x	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a GRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			x
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?			x
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?		x	
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)	x		
Labeling(continued)			
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		x	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?	x		
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?		x	
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		x	
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?		x	
Has the firm failed to describe the scoring in the HOW SUPPLIED section?		x	
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		x	
Do any of the inactives differ in concentration for this route of administration?		x	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		x	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		x	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?		x	
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)		x	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	
Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		x	

Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.		X	
Bioequivalence Issues: (Compare bioequivalency values: Insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			X
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.			X
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.		X	

NOTES/QUESTIONS TO THE CHEMIST:

FOR THE RECORD:

- Review based on the labeling of Oxandrin® tablets (NDA 13-718) approved April 21, 2003.
- PATENT/ EXCLUSIVITIES**
See Page 1 and #11 of FTR.
- MANUFACTURING FACILITY**
Eon Labs, Inc.
4700 Eon Drive
Wilson, NC 27893
- SCORING:**
NDA - 2.5 mg scored, 10 mg unscored
ANDA - 2.5 mg bisected, 10 mg unscored
- STORAGE CONDITIONS:**
NDA - Store at Room Temperature (59-77°F)
ANDA - Store at 20-25° (68-77°F) excursions permitted to 15°-30°C (59-86°F) [see USP Controlled Room Temperature]
USP- Preserve in tight, light-resistant containers
- DISPENSING RECOMMENDATIONS:**
NDA - Dispense in a tight, light-resistant, child-resistant container.
ANDA - Dispense in a tight, light-resistant containers as defined in the USP, with a child-resistant closure, as required.
- INACTIVE INGREDIENTS:**
The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 82 of Volume A1.1.
- PACKAGING CONFIGURATIONS:**
NDA- 2.5 mg and 10 mg bottles of 100

ANDA- 2.5 mg and 10 mg bottles of 100 and 1000
- CONTAINER/CLOSURE SYSTEM:**
2.5 mg Bottles of 100 60 cc white, round, opaque HDPE, 38 mm white PP CRC, _____
innerseal/liner (_____) and white pulp liner, 16 gram cotton

2.5 mg Bottles of 1000 250 cc white opaque HDPE, 45 mm white PP screw caps, _____
innerseal/liner (_____) and white pulp liner, 16 gram cotton

10 mg Bottles of 100 100 cc white, round, opaque HDPE, 38 mm white PP CRC, _____
innerseal/liner (_____) and white pulp liner, 16 gram cotton

10 mg Bottles of 1000 950 cc white, round, opaque HDPE, 53 mm white PP screw caps, _____
innerseal/liner (_____) and white pulp liner, 16 gram cotton

(Vol. A1.3, p. 422)
- The tablet have been accurately described in the HOW SUPPLIED section as required by 21 CFR 206, et al. (Imprinting of Solid Oral Dosage Form Products for Human Use; Final Rule, effective 9/13/95).

2.5 mg white, modified oval, debossed "E 271" on one side and bisected on the reverse side

10 mg white, capsule-shaped, debossed "E 272" on one side and plain on the reverse side

11. The following Email was sent to Debbie Catterson from Martin Shimer:

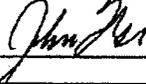
From: Shimer, Martin
Sent: Wednesday, May 04, 2005 12:51 PM
To: Catterson, Debra M
Cc: Park, Sarah Soojung
Subject: ANDA 76-897, Eon's Oxandrolone

Debbie,

Eon submitted a patent amendment on April 27, 2005 addressing the patents covering NDA 13-718 Oxandrin Tablets. Eon states that the '147, '799, '699 and '351 patents were late listed for Eon and therefore Eon declines to address these patents. They have provided a MOU statement to the '313 patent as this patent was timely filed. So this is just a heads up that they should be making some changes to their labeling to correspond to the MOU statement provided in the patent amendment.

Thanks,

Marty

Date of Review:	May 10, 2005		
Dates of Submission:	May 4, 2005		
Primary Reviewer:	Postelle Birch 	Date:	5/10/05
Team Leader:	John Grace 	Date:	5-11-05

cc: ANDA: 76-897
DUP/DIVISION FILE
HFD-613/PBirch /JGrace (no cc)
V:\FIRMSAMEON\LTRS&REV\76-897apsupercede.label.DOC
Review

**This Labeling Approval Summary supersedes the Labeling Approval Summary
dated July 11, 2005 and August 1, 2005.**

**APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

ANDA Number: 76-897

Dates of Submission: November 15, 2006, November 14, 2006 and November 6, 2006

Applicant's Name: Sandoz Inc.

Established Name: Oxandrolone Tablets, USP 2.5 mg and 10 mg

BASIS OF APPROVAL:

CONTAINER LABELS

2.5 mg Bottles of 100 and 1000 tablets
Satisfactory as of November 14, 2006 submission.

10 mg Bottles of 100 and 1000 tablets
Satisfactory as of November 14, 2006 submission.

PROFESSIONAL PACKAGE INSERT LABELING:

Satisfactory in FPL as of November 15, 2006 submission.

REFERENCE LISTED DRUG:

Was this approval based upon a petition? Yes, citizens petition

What is the RLD on the 356(h) form: Oxandrin® tablets

NDA Number: NDA 13-718

NDA Drug Name: Oxandrin® tablets

NDA Firm: BTG Pharmaceuticals

Date of Approval of NDA Insert and supplement #: June 20, 2005/S-023

Has this been verified by the MIS system for the NDA? Yes

Was this approval based upon an OGD labeling guidance? **OGD labeling template.**

Basis of Approval for the Container Labels: side-by-side

Basis of Approval for the Carton Labeling: side-by-side

Patent Data – NDA 13-718

No	Expiration	Use Code	Use	File	Labeling Impact
5872147	12/05/2017	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6090799	07/18/2017	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6576659	12/05/2017	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6670351	10/20/2012	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6828313	12/05/2017	U-585	To promote weight gain after weight loss in certain types of patients	MOU	Carve-out

Exclusivity Data - NDA 13-718

Code/sup	Expiration	Use Code	Description	Labeling Impact
M-42	6/20/2008		Addition of a geriatric use subsection to the precautions section of the package insert and geriatric dosing information	OGD labeling template

FOR THE RECORD:

1. Review based on the on a OGD labeling template created on November 3, 2006.
2. PATENT/ EXCLUSIVITIES
See above.
3. MANUFACTURING FACILITY
Sandoz, Inc., 4700 Sandoz Drive, Wilson, NC 27893
4. SCORING:
NDA - 2.5 mg scored, 10 mg unscored
ANDA - 2.5 mg bisected, 10 mg unscored
5. STORAGE CONDITIONS:
NDA - Store at Room Temperature (59 °-77 °F)
ANDA - Store at 20 °-25 ° (68 °-77 °F) [see USP Controlled Room Temperature]
USP- Preserve in tight, light-resistant containers
6. DISPENSING RECOMMENDATIONS:
NDA - Dispense in a tight, light-resistant, child-resistant container.
ANDA - Dispense in a tight, light-resistant containers as defined in the USP, with a child-resistant closure, as required.
7. INACTIVE INGREDIENTS:
The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 82 of Volume A1.1.
8. PACKAGING CONFIGURATIONS:
NDA- 2.5 mg and 10 mg bottles of 100
ANDA- 2.5 mg in bottles of 100 and 1000 and 10 mg bottles of 100 and 1000
9. CONTAINER/CLOSURE SYSTEM:
2.5 mg Bottles of 100 60 cc white, round, opaque HDPE, 38 mm white PP CRC, innerseal/liner () and white pulp liner, 16 gram cotton
2.5 mg Bottles of 1000 250 cc white opaque HDPE, 45 mm white PP screw caps, innerseal/liner () and white pulp liner, 16 gram cotton
10 mg Bottles of 100 100 cc white, round, opaque HDPE, 38 mm white PP CRC, innerseal/liner () and white pulp liner, 16 gram cotton
10 mg Bottles of 1000 950 cc white, round, opaque HDPE, 53 mm white PP screw caps, innerseal/liner () and white pulp liner, 16 gram cotton
(Vol. A1.3, p. 422)
10. The tablet have been accurately described in the HOW SUPPLIED section as required by 21 CFR 206,et al. (Imprinting of Solid Oral Dosage Form Products for Human Use; Final Rule, effective 9/13/95).
2.5 mg white, modified oval, debossed "E 271" on one side and bisected on the reverse side
10 mg white, capsule-shaped, debossed "E 272" on one side and plain on the reverse side

Date of Review: November 15, 2006

Dates of Submission: November 15, 2006, November 14, 2006 and November 6, 2006

Primary Reviewer: Postelle Birch-Smith

Team Leader: John Grace

cc: ANDA: 76-897
DUP/DIVISION FILE

2 PAGES WITHHELD IN FULL

[]

proof date	4/24/06	5/4/06
proof #	1	2
proof date		
proof #		

proof approval form

[]

NOTE: Proof colors do not represent exact PMS colors. Please check current PMS guide.

Cyan

Magenta

Yellow

Black

PMS 362 Grass

PMS 541 Blue

Wind direction #4

THIS WAY

9/16" Unvarnished Area

Lot No.:

Exp. Date:

USUAL DOSAGE: See accompanying literature for complete prescribing information.
Store at 20°-25°C (68°-77°F) [see USP Controlled Room Temperature].
Dispense contents in a light, light-resistant container as defined in the USP with a child-resistant closure, as required.
Rev. 04/06
L8518

NDC 0185-0271-01
Oxandrolone Tablets USP
2.5 mg
Rx only
100 Tablets

SANDOZ

Each tablet contains Oxandrolone USP 2.5 mg

KEEP TIGHTLY CLOSED.

KEEP THIS AND ALL MEDICATION OUT OF THE REACH OF CHILDREN.

Sandoz Inc.
Pittsford, NJ 08540

0185-0271-01

Customer: Sandoz: Oxandrolone 2.5 mg 100 tablets USP

P.O. No #: _____

Job number: SDZ177

Size: GB 1 1/8 x 4 1/4

Comments: L8518

ELECTRONICALLY SPELL CHECKED BY: PROOFREAD INTERNALLY BY: DATE:

Reviewed by:	Date
--------------	------

Submit Revised Proof:	Date
Proof Approved By:	Date

proof date	4/24/06	5/4/06	
proof #	1	2	
proof date			
proof #			

proof approval form

9/16" Unvarnished Area

NOTE: Proof colors do not represent exact PMS colors. Please check current PMS guide.

	Cyan
	Magenta
	Yellow
	Black
	PMS 362 Grass
	PMS 541 Blue

THIS WAY



Wind direction #4

NDC 0185-0271-10

Oxandrolone

Tablets USP

2.5 mg

Rx only

1000 Tablets

SANDOZ

USUAL DOSAGE: See accompanying literature for complete prescribing information.

Store at 20°-25°C (68°-77°F) (see USP Controlled Room Temperature).

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

Rev. 04/06
L8525

Each tablet contains:
Oxandrolone USP 2.5 mg

KEEP TIGHTLY CLOSED.

KEEP THIS AND ALL MEDICATION OUT OF THE REACH OF CHILDREN.

Sandoz Inc.
Princeton, NJ 08540



0185-0271-10 8

Customer: Sandoz: Oxandrolone 2.5 mg 1000 tablets

P.O. No #: _____

Job number: SDZ176

Size: B 2 x 6

Comments: L8525

ELECTRONICALLY SPELL CHECKED BY:	DATE:

Reviewed by:	Date

Submit Revised Proof:	Date
Proof Approved By:	Date

[

proof date	4/24/06	4/28/06	5/4/06
proof #	1	2	3
proof date			
proof #			

proof approval form

9/16" Unvarnished Area

NOTE: Proof colors do not represent exact PMS colors. Please check current PMS guide.

-  Cyan
-  Magenta
-  Yellow
-  Black
-  PMS 186 Red
-  PMS 541 Blue

THIS WAY 

Wind direction #4

NDC 0185-0272-01

Oxandrolone 

Tablets USP

10 mg 

Rx only

100 Tablets

SANDOZ 

USUAL DOSAGE: See accompanying literature for complete prescribing information.

Store at 20°-25°C (68°-77°F) (see USP Controlled Room Temperature).

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

Rev. 04/06
L8532

Each tablet contains:
Oxandrolone USP10 mg

KEEP TIGHTLY CLOSED.

KEEP THIS AND ALL MEDICATION OUT OF THE REACH OF CHILDREN.

Sandoz Inc.
Princeton, NJ 08540

0185-0272-013

Customer: Sandoz: Oxandrolone 10 mg 100 tablets

P.O. No #: _____

Job number: SDZ174

Size: A 2" x 5-1/4"

Comments: L8532

ELECTRONICALLY SPELL CHECKED BY:	PROOFREAD INTERNALLY BY:	DATE:

Reviewed by:	Date

Submit Revised Proof:	Date
Proof Approved By:	Date

proof date	4/24/06	5/4/06
proof #	1	2
proof date		
proof #		

proof approval form

orig.
unvarnished
Area

NOTE: Proof colors do not represent exact PMS colors. Please check current PMS guide.

	Cyan
	Magenta
	Yellow
	Black
	PMS 186 Red
	PMS 541 Blue



 Wind direction #4

NDC 0185-0272-10

Oxandrolone 
Tablets USP

10 mg

Rx only

1000 Tablets

SANDOZ

Each tablet contains:
Oxandrolone USP.....10 mg

KEEP TIGHTLY CLOSED.

KEEP THIS AND ALL
MEDICATION OUT OF
THE REACH OF
CHILDREN.

Sandoz Inc.
Princeton, NJ 08540

0185-0272-105

USUAL DOSAGE: See accompanying literature for complete prescribing information.

Store at 20°-25°C (68°-77°F) [see USP Controlled Room Temperature].

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

Rev. 04/06
L8539

Lot No.:
Exp. Date:

Customer: **Sandoz: Oxandrolone 10 mg x 1000 tablets**

P.O. No #: **SDZ173**

Job number: **SDZ173**

Size: **H 3" x 6"**

Comments: **L8539**

ELECTRONICALLY SPELL CHECKED BY:	PROOFREAD INTERNALLY BY:	DATE:

Reviewed by:	Date

Submit Revised Proof:	Date
Proof Approved By:	Date

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Postelle Birch
11/22/2006 02:29:05 PM
MEDICAL OFFICER

John Grace
11/22/2006 02:33:32 PM
MEDICAL OFFICER

This Labeling Approval Summary supersedes the Labeling Approval Summary dated November 15, 2006, November 14, 2006 and November 6, 2006.

**APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

ANDA Number: 76-897 Date of Submission: November 29, 2006

Applicant's Name: Sandoz Inc.

Established Name: Oxandrolone Tablets, USP 2.5 mg and 10 mg

BASIS OF APPROVAL:

CONTAINER LABELS

2.5 mg and 10 mg bottles of 100 and 1000 tablets
Satisfactory as of November 14, 2006 submission.

PROFESSIONAL PACKAGE INSERT LABELING:

Satisfactory in FPL as of November 29, 2006 submission.

REFERENCE LISTED DRUG:

Was this approval based upon a petition? Yes, citizens petition

What is the RLD on the 356(h) form: Oxandrin® tablets

NDA Number: NDA 13-718

NDA Drug Name: Oxandrin® tablets

NDA Firm: BTG Pharmaceuticals

Date of Approval of NDA Insert and supplement #: June 20, 2005/S-023

Has this been verified by the MIS system for the NDA? Yes

Was this approval based upon an OGD labeling guidance? **OGD labeling template.**

Basis of Approval for the Container Labels: side-by-side

Basis of Approval for the Carton Labeling: side-by-side

Patent Data – NDA 13-718

No	Expiration	Use Code	Use	File	Labeling Impact
5872147	12/05/2017	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6090799	07/18/2017	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6576659	12/05/2017	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6670351	10/20/2012	U-585	To promote weight gain after weight loss in certain types of patients	Firm declined to address due to late file	None See FTR
6828313	12/05/2017	U-585	To promote weight gain after weight loss in certain types of patients	MOU	Carve-out

Exclusivity Data - NDA 13-718

Code/sup	Expiration	Use Code	Description	Labeling Impact
M-42	6/20/2008		Addition of a geriatric use subsection to the precautions section of the package insert and geriatric dosing information	OGD labeling template

FOR THE RECORD:

1. This review was based on a revised OGD labeling template created on November 29, 2006. We note that the initial directions to applicants on the appropriate labeling for oxandrolone tablets contained inadvertent errors. We instructed applicants to make revisions to correct these errors and re-submit revised labeling. We have reviewed the revised labeling and have determined that the errors have been corrected.

2. PATENT/ EXCLUSIVITIES
See above table.
3. MANUFACTURING FACILITY
Sandoz, Inc., 4700 Sandoz Drive, Wilson, NC 27893
4. SCORING:
NDA - 2.5 mg scored, 10 mg unscored
ANDA - 2.5 mg bisected, 10 mg unscored
5. STORAGE CONDITIONS:
NDA - Store at Room Temperature (59 °-77 °F)
ANDA - Store at 20 °-25 ° (68 °-77 °F) [see USP Controlled Room Temperature]
USP- Preserve in tight, light-resistant containers
6. DISPENSING RECOMMENDATIONS:
NDA - Dispense in a tight, light-resistant, child-resistant container.
ANDA - Dispense in a tight, light-resistant containers as defined in the USP, with a child-resistant closure, as required.
7. INACTIVE INGREDIENTS:
The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 82 of Volume A1.1.
8. PACKAGING CONFIGURATIONS:
NDA- 2.5 mg and 10 mg bottles of 100
ANDA- 2.5 mg in bottles of 100 and 1000 and 10 mg bottles of 100 and 1000
9. CONTAINER/CLOSURE SYSTEM:
2.5 mg Bottles of 100 60 cc white, round, opaque HDPE, 38 mm white PP CRC, innerseal/liner () and white pulp liner, 16 gram cotton
2.5 mg Bottles of 1000 250 cc white opaque HDPE, 45 mm white PP screw caps, innerseal/liner () and white pulp liner, 16 gram cotton
10 mg Bottles of 100 100 cc white, round, opaque HDPE, 38 mm white PP CRC, innerseal/liner () and white pulp liner, 16 gram cotton
10 mg Bottles of 1000 950 cc white, round, opaque HDPE, 53 mm white PP screw caps, innerseal/liner () and white pulp liner, 16 gram cotton
(Vol. A1.3, p. 422)
10. The tablet have been accurately described in the HOW SUPPLIED section as required by 21 CFR 206,et al. (Imprinting of Solid Oral Dosage Form Products for Human Use; Final Rule, effective 9/13/95).
2.5 mg white, modified oval, debossed "E 271" on one side and bisected on the reverse side
10 mg white, capsule-shaped, debossed "E 272" on one side and plain on the reverse side

Date of Review: November 30, 2006

Date of Submission: November 29, 2006

Primary Reviewer: Postelle Birch-Smith

Team Leader: John Grace

cc: ANDA: 76-897
DUP/DIVISION FILE

[]

proof date	4/24/06	5/4/06	
proof #	1	2	
proof date			
proof #			

proof approval form

NOTE: Proof colors do not represent exact PMS colors. Please check current PMS guide.

	Cyan
	Magenta
	Yellow
	Black
	PMS 362 Grass
	PMS 541 Blue

.....

THIS WAY

Wind direction #4

9/16"
Unvarnished
Area

Lot No.:
Exp. Date:

USUAL DOSAGE: See accompanying literature for complete prescribing information.
Store at 20°-25°C (68°-77°F) (see USP Controlled Room Temperature).
Dispense contents in a light, light-resistant container as defined in USP when a child-resistant closure is required.
Rx only
100 Tablets
L8518

SANDOZ

NDC 0185-0271-01
**Oxandrolone
Tablets USP**
2.5 mg

Each tablet contains:
Oxandrolone USP 2.5 mg

KEEP TIGHTLY CLOSED.
KEEP THIS AND ALL MEDICATION OUT OF THE REACH OF CHILDREN.
Sandoz Inc.
Princeton, NJ 08540

0185-0271-01

Customer: **Sandoz: Oxandrolone 2.5 mg 100 tablets USP**

P.O. No #: _____

Job number: **SDZ177**

Size: **GB 1 1/8 x 4 1/4**

Comments: **L8518**

ELECTRONICALLY SPELL CHECKED BY:	PROOFREAD INTERNALLY BY:	DATE:

Reviewed by:	Date

Submit Revised Proof:	Date
Proof Approved By:	Date

proof date	4/24/06	5/4/06	
proof #	1	2	
proof date			
proof #			

proof approval form

9/16" Unvarnished Area

NOTE: Proof colors do not represent exact PMS colors. Please check current PMS guide.

Cyan


Magenta


Yellow


Black


PMS 362 Grass


PMS 541 Blue


THIS WAY


Wind direction #4

NDC 0185-0271-10

Oxandrolone
Tablets USP

2.5 mg

Rx only

1000 Tablets

SANDOZ

USUAL DOSAGE: See accompanying literature for complete prescribing information.

Store at 20°-25°C (68°-77°F) [see USP Controlled Room Temperature].

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

Rev. 04/06 L8525

Each tablet contains: Oxandrolone USP 2.5 mg

KEEP TIGHTLY CLOSED.

KEEP THIS AND ALL MEDICATION OUT OF THE REACH OF CHILDREN.

Sandoz Inc. Princeton, NJ 08540

0185-0271-108

Customer: **Sandoz: Oxandrolone 2.5 mg 1000 tablets**

P.O. No #: _____

Job number: **SDZ176**

Size: **B 2 x 6**

Comments: **L8525**

ELECTRONICALLY SPELL CHECKED BY:	PROOFREAD INTERNALLY BY:	DATE:

Reviewed by:	Date

Submit Revised Proof:	Date
Proof Approved By:	Date

proof date	4/24/06	4/28/06	5/4/06
proof #	1	2	3
proof date			
proof #			

proof approval form

9/16" Unvarnished Area

NOTE: Proof colors do not represent exact PMS colors. Please check current PMS guide.

	Cyan
	Magenta
	Yellow
	Black
	PMS 186 Red
	PMS 541 Blue

THIS WAY 

Wind direction #4

NDC 0185-0272-01

Oxandrolone 

Tablets USP

10 mg

Rx only

100 Tablets

SANDOZ

USUAL DOSAGE: See accompanying literature for complete prescribing information.

Store at 20°-26°C (68°-77°F) [see USP Controlled Room Temperature].

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

Rev. 04/06
L8532

Each tablet contains:
Oxandrolone USP10 mg

KEEP TIGHTLY CLOSED.

KEEP THIS AND ALL MEDICATION OUT OF THE REACH OF CHILDREN.

Sandoz Inc.
Princeton, NJ 08540

0185-0272-013

Lot No.:
Exp. Date:

Customer: Sandoz: Oxandrolone 10 mg 100 tablets

P.O. No #: _____

Job number: SDZ174

Size: A 2" x 5-1/4"

Comments: L8532

ELECTRONICALLY SPELL CHECKED BY:	PROOFREAD INTERNALLY BY:	DATE:

Reviewed by:	Date

Submit Revised Proof:	Date
Proof Approved By:	Date

proof date	4/24/06	5/4/06	
proof #	1	2	
proof date			
proof #			

proof approval form

9/16" unfinished Area

NOTE: Proof colors do not represent exact PMS colors. Please check current PMS guide.

	Cyan
	Magenta
	Yellow
	Black
	PMS 186 Red
	PMS 541 Blue

THIS WAY

Wind direction #4

NDC 0185-0272-10

Oxandrolone 

Tablets USP

10 mg 

Rx only

1000 Tablets

SANDOZ

Rev. 04/06
L8539

Each tablet contains:
Oxandrolone USP.....10 mg

KEEP TIGHTLY CLOSED.

KEEP THIS AND ALL MEDICATION OUT OF THE REACH OF CHILDREN.

Sandoz Inc.
Princeton, NJ 08540

USUAL DOSAGE: See accompanying literature for complete prescribing information.

Store at 20°-25°C (68°-77°F) [see USP Controlled Room Temperature].

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

Lot No.:
Exp. Date:

0185-0272-105

Customer: **Sandoz: Oxandrolone 10 mg x 1000 tablets**

P.O. No #: _____

Job number: **SDZ173**

Size: **H 3" x 6"**

Comments: **L8539**

ELECTRONICALLY SPELL CHECKED BY:	PROOFREAD INTERNALLY BY:	DATE:

Reviewed by:	Date

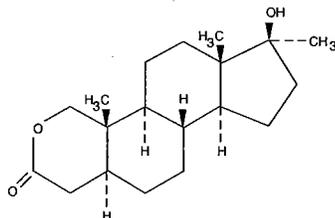
Submit Revised Proof:	Date
Proof Approved By:	Date

Oxandrolone Tablets USP

Rx only

DESCRIPTION

Oxandrolone oral tablets contain 2.5 mg or 10 mg of the anabolic steroid oxandrolone. Oxandrolone is 17β-hydroxy-17α-methyl-2-oxa-5α-androstan-3-one with the following structural formula:

Molecular Formula: C₁₉H₃₀O₃

Molecular Weight: 306.44

Inactive ingredients include: hypromellose, lactose monohydrate, pregelatinized starch, and magnesium stearate.

CLINICAL PHARMACOLOGY

Anabolic steroids are synthetic derivatives of testosterone. Certain clinical effects and adverse reactions demonstrate the androgenic properties of this class of drugs. Complete dissociation of anabolic and androgenic effects has not been achieved. The actions of anabolic steroids are therefore similar to those of male sex hormones with the possibility of causing serious disturbances of growth and sexual development if given to young children. Anabolic steroids suppress the gonadotropic functions of the pituitary and may exert a direct effect upon the testes.

During exogenous administration of anabolic androgens, endogenous testosterone release is inhibited through inhibition of pituitary luteinizing hormone (LH). At large doses, spermatogenesis may be suppressed through feedback inhibition of pituitary follicle-stimulating hormone (FSH).

Anabolic steroids have been reported to increase low-density lipoproteins and decrease high-density lipoproteins. These levels revert to normal on discontinuation of treatment.

INDICATIONS AND USAGE

Oxandrolone is indicated as adjunctive therapy to offset the protein catabolism associated with prolonged administration of corticosteroids, and for the relief of the bone pain frequently accompanying osteoporosis (see **DOSE AND ADMINISTRATION**).

DRUG ABUSE AND DEPENDENCE

Oxandrolone is classified as a controlled substance under the Anabolic Steroids Control Act of 1990 and has been assigned to Schedule III (non-narcotic).

CONTRAINDICATIONS

1. Known or suspected carcinoma of the prostate or the male breast.
2. Carcinoma of the breast in females with hypercalcemia (androgenic anabolic steroids may stimulate osteolytic bone resorption).
3. Pregnancy, because of possible masculinization of the fetus. Oxandrolone has been shown to cause embryotoxicity, fetotoxicity, infertility, and masculinization of female animal offspring when given in doses 9 times the human dose.
4. Nephrosis, the nephrotic phase of nephritis.
5. Hypercalcemia.

WARNINGS

PELIOSIS HEPATIS, A CONDITION IN WHICH LIVER AND SOMETIMES SPLENIC TISSUE IS REPLACED WITH BLOOD-FILLED CYSTS, HAS BEEN REPORTED IN PATIENTS RECEIVING ANDROGENIC ANABOLIC STEROID THERAPY. THESE CYSTS ARE SOMETIMES PRESENT WITH MINIMAL HEPATIC DYSFUNCTION, BUT AT OTHER TIMES THEY HAVE BEEN ASSOCIATED WITH LIVER FAILURE. THEY ARE OFTEN NOT RECOGNIZED UNTIL LIFE-THREATENING LIVER FAILURE OR INTRA-ABDOMINAL HEMORRHAGE DEVELOPS. WITHDRAWAL OF DRUG USUALLY RESULTS IN COMPLETE DISAPPEARANCE OF LESIONS.

LIVER CELL TUMORS ARE ALSO REPORTED. MOST OFTEN THESE TUMORS ARE BENIGN AND ANDROGEN-DEPENDENT, BUT FATAL MALIGNANT TUMORS HAVE BEEN REPORTED. WITHDRAWAL OF DRUG OFTEN RESULTS IN REGRESSION OR CESSATION OF PROGRESSION OF THE TUMOR. HOWEVER, HEPATIC TUMORS ASSOCIATED WITH ANDROGENS OR ANABOLIC STEROIDS ARE MUCH MORE VASCULAR THAN OTHER HEPATIC TUMORS AND MAY BE SILENT UNTIL LIFE-THREATENING INTRA-ABDOMINAL HEMORRHAGE DEVELOPS. BLOOD LIPID CHANGES THAT ARE KNOWN TO BE ASSOCIATED WITH INCREASED RISK OF ATHEROSCLEROSIS ARE SEEN IN PATIENTS TREATED WITH ANDROGENS OR ANABOLIC STEROIDS. THESE CHANGES INCLUDE DECREASED HIGH-DENSITY LIPOPROTEINS AND SOMETIMES INCREASED LOW-DENSITY LIPOPROTEINS. THE CHANGES MAY BE VERY MARKED AND COULD HAVE A SERIOUS IMPACT ON THE RISK OF ATHEROSCLEROSIS AND CORONARY ARTERY DISEASE.

Cholestatic hepatitis and jaundice may occur with 17-alpha-alkylated androgens at a relatively low dose. If cholestatic hepatitis with jaundice appears or if liver function tests become abnormal, oxandrolone should be discontinued and the etiology should be determined. Drug-induced jaundice is reversible when the medication is discontinued.

In patients with breast cancer, anabolic steroid therapy may cause hypercalcemia by stimulating osteolysis. Oxandrolone therapy should be discontinued if hypercalcemia occurs.

Edema with or without congestive heart failure may be a serious complication in patients with pre-existing cardiac, renal, or hepatic disease. Concomitant administration of adrenal cortical steroid or ACTH may increase the edema.

In children, androgen therapy may accelerate bone maturation without producing compensatory gain in linear growth. This adverse effect results in compromised adult height. The younger the child, the greater the risk of compromising final mature height. The effect on bone maturation should be monitored by assessing bone age of the left wrist and hand every 6 months (see **PRECAUTIONS, Laboratory Tests**).

Geriatric patients treated with androgenic anabolic steroids may be at an increased risk for the development of prostatic hypertrophy and prostatic carcinoma.

ANABOLIC STEROIDS HAVE NOT BEEN SHOWN TO ENHANCE ATHLETIC ABILITY.

PRECAUTIONS

Concurrent dosing of oxandrolone and warfarin may result in unexpectedly large increases in the International Normalized Ratio (INR) or prothrombin time (PT). When oxandrolone is prescribed to patients being treated with warfarin, doses of warfarin may need to be decreased significantly to maintain the desirable INR level and diminish the risk of potentially serious bleeding (See **PRECAUTIONS, Drug Interactions).**

General

Women should be observed for signs of virilization (deepening of the voice, hirsutism, acne, clitoromegaly). Discontinuation of drug therapy at the time of evidence of mild virilism is necessary to prevent irreversible virilization. Some virilizing changes in women are irreversible even after prompt discontinuance of therapy and are not prevented by concomitant use of estrogens. Menstrual irregularities may also occur.

Anabolic steroids may cause suppression of clotting factors II, V, VII, and X, and an increase in prothrombin time.

Information for Patients

The physician should instruct patients to report immediately any use of warfarin and any bleeding.

The physician should instruct patients to report any of the following side effects of androgens:

Males: Too frequent or persistent erections of the penis, appearance or aggravation of acne.

Females: Hoarseness, acne, changes in menstrual periods, or more facial hair.

All patients: Nausea, vomiting, changes in skin color, or ankle swelling.

Geriatric Use: Certain geriatric use information is protected by marketing exclusivity.

Laboratory Tests

Women with disseminated breast carcinoma should have frequent determination of urine and serum calcium levels during the course of therapy (see **WARNINGS**).

Because of the hepatotoxicity associated with the use of 17-alpha-alkylated androgens, liver function tests should be obtained periodically.



Rev. 12/06

ZANBOS

Oxandrolone

Tablets USP

Rx only

Periodic (every 6 months) x-ray examinations of bone age should be made during treatment of children to determine the rate of bone maturation and the effects of androgen therapy on the epiphyseal centers.

Androgenic anabolic steroids have been reported to increase low-density lipoproteins and decrease high-density lipoproteins. Therefore, caution is required when administering these agents to patients with a history of cardiovascular disease or who are at risk for cardiovascular disease. Serum determination of lipid levels should be performed periodically and therapy adjusted accordingly. Hemoglobin and hematocrit should be checked periodically for polycythemia in patients who are receiving high doses of anabolic steroids.

Drug Interactions

Anticoagulants: Anabolic steroids may increase sensitivity to oral anticoagulants. Dosage of the anticoagulant may have to be decreased in order to maintain desired prothrombin time. Patients receiving oral anticoagulant therapy require close monitoring, especially when anabolic steroids are started or stopped.

Warfarin: A multidose study of oxandrolone, given as 5 or 10 mg BID in 15 healthy subjects concurrently treated with warfarin, resulted in a mean increase in S-warfarin half-life from 26 to 48 hours and AUC from 4.55 to 12.08 ng•hr/mL; similar increases in R-warfarin half-life and AUC were also detected. Microscopic hematuria (9/15) and gingival bleeding (1/15) were also observed. A 5.5-fold decrease in the mean warfarin dose from 6.13 mg/day to 1.13 mg/day (approximately 80-85% reduction of warfarin dose), was necessary to maintain a target INR of 1.5. When oxandrolone therapy is initiated in a patient already receiving treatment with warfarin, the INR or prothrombin time (PT) should be monitored closely and the dose of warfarin adjusted as necessary until a stable target INR or PT has been achieved.

Furthermore, in patients receiving both drugs, careful monitoring of the INR or PT, and adjustment of the warfarin dosage if indicated are recommended when the oxandrolone dose is changed or discontinued. Patients should be closely monitored for signs and symptoms of occult bleeding.

Oral Hypoglycemic Agents: Oxandrolone may inhibit the metabolism of oral hypoglycemic agents.

Adrenal Steroids or ACTH: In patients with edema, concomitant administration with adrenal cortical steroids or ACTH may increase the edema.

Drug/Laboratory Test Interactions

Anabolic steroids may decrease levels of thyroxine-binding globulin, resulting in decreased total T_4 serum levels and increased resin uptake of T_3 and T_4 . Free thyroid hormone levels remain unchanged. In addition, a decrease in PBI and radioactive iodine uptake may occur.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal Data: Oxandrolone has not been tested in laboratory animals for carcinogenic or mutagenic effects. In 2-year chronic oral rat studies, a dose-related reduction of spermatogenesis and decreased organ weights (testes, prostate, seminal vesicles, ovaries, uterus, adrenals, and pituitary) were shown.

Human Data: Liver cell tumors have been reported in patients receiving long-term therapy with androgenic anabolic steroids in high doses (see **WARNINGS**).

Withdrawal of the drugs did not lead to regression of the tumors in all cases. Geriatric patients treated with androgenic anabolic steroids may be at an increased risk for the development of prostatic hypertrophy and prostatic carcinoma.

Pregnancy

Teratogenic effects—Pregnancy Category X (see **CONTRAINDICATIONS**).

Nursing Mothers

It is not known whether anabolic steroids are excreted in human milk. Because of the potential of serious adverse reactions in nursing infants from oxandrolone, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Anabolic agents may accelerate epiphyseal maturation more rapidly than linear growth in children and the effect may continue for 6 months after the drug has been stopped. Therefore, therapy should be monitored by x-ray studies at 6-month intervals in order to avoid the risk of compromising adult height. Androgenic anabolic steroid therapy should be used very cautiously in children and only by specialists who are aware of the effects on bone maturation (see **WARNINGS**).

ADVERSE REACTIONS

Patients with moderate to severe COPD or COPD patients who are unresponsive to bronchodilators should be monitored closely for COPD exacerbation and fluid retention.

The following adverse reactions have been associated with use of anabolic steroids:

Hepatic

Cholestatic jaundice with, rarely, hepatic necrosis and death. Hepatocellular neoplasms and peliosis hepatis with long-term therapy (see **WARNINGS**). Reversible changes in liver function tests also occur including increased bromsulfophthalein (BSP) retention, changes in alkaline phosphatase and increases in serum bilirubin, aspartate aminotransferase (AST, SGOT) and alanine aminotransferase (ALT, SGPT).

In Males

Prepubertal: Phallic enlargement and increased frequency or persistence of erections.

Postpubertal: Inhibition of testicular function, testicular atrophy and oligospermia, impotence, chronic priapism, epididymitis, and bladder irritability.

In Females

Clitoral enlargement, menstrual irregularities.

CNS

Habituation, excitation, insomnia, depression, and changes in libido.

Hematologic

Bleeding in patients on concomitant anticoagulant therapy.

Breast

Gynecomastia.

Larynx

Deepening of the voice in females.

Hair

Hirsutism and male pattern baldness in females.

Skin

Acne (especially in females and prepubertal males).

Skeletal

Premature closure of epiphyses in children (see **PRECAUTIONS, Pediatric Use**).

Fluid and Electrolytes

Edema, retention of serum electrolytes (sodium chloride, potassium, phosphate, calcium).

Metabolic/Endocrine

Decreased glucose tolerance (see **PRECAUTIONS, Laboratory Tests**), increased creatinine excretion, increased serum levels of creatinine phosphokinase (CPK). Masculinization of the fetus. Inhibition of gonadotropin secretion.

OVERDOSAGE

No symptoms or signs associated with overdosage have been reported. It is possible that sodium and water retention may occur.

The oral LD_{50} of oxandrolone in mice and dogs is greater than 5,000 mg/kg. No specific antidote is known, but gastric lavage may be used.

DOSAGE AND ADMINISTRATION

Therapy with anabolic steroids is adjunctive to and not a replacement for conventional therapy. The duration of therapy with oxandrolone will depend on the response of the patient and the possible appearance of adverse reactions. Therapy should be intermittent.

Adults

The response of individuals to anabolic steroids varies. The daily adult dosage is 2.5 mg to 20 mg given in 2 to 4 divided doses. The desired response may be achieved with as little as 2.5 mg or as much as 20 mg daily. A course of therapy of 2 to 4 weeks is usually adequate. This may be repeated intermittently as indicated.

Children

For children the total daily dosage of oxandrolone is ≤ 0.1 mg per kilogram body weight or ≤ 0.045 mg per pound of body weight. This may be repeated intermittently as indicated.

HOW SUPPLIED

Oxandrolone Tablets USP are supplied as follows:

2.5 mg Tablets: white, modified oval-shaped, debossed "E 271" on one side and bisected on the reverse side.

Bottles of 100
Bottles of 1000

10 mg Tablets: white, capsule-shaped, debossed "E 272" on one side and plain on the reverse side.

Bottles of 100
Bottles of 1000

Store at 20° - 25°C (68° - 77°F) [see USP Controlled Room Temperature].

Sandoz Inc.
Princeton, NJ 08540

Rev. 12/06
MF0271REV12/06
OS8072

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Postelle Birch
11/30/2006 05:29:51 PM
MEDICAL OFFICER

John Grace
12/1/2006 10:08:12 AM
MEDICAL OFFICER

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-897

CHEMISTRY REVIEW(S)



ANDA #76-897

**Oxandrolone Tablets USP,
2.5 mg and 10 mg**

Eon Labs, Inc.

**Robert Iser
Office of Generic Drugs
Division of Chemistry III
Team 4**



Table of Contents

Table of Contents	2
Chemistry Review Data Sheet.....	3
The Executive Summary.....	7
I. Recommendations	7
A. Recommendation and Conclusion on Approvability	7
B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable.....	7
II. Summary of Chemistry Assessments	7
A. Description of the Drug Product(s) and Drug Substance(s)	7
B. Description of How the Drug Product is Intended to be Used.....	7
C. Basis for Approvability or Not-Approval Recommendation	8
III. Administrative.....	8
A. Reviewer's Signature.....	8
B. Endorsement Block.....	8
C. CC Block.....	8
Chemistry Assessment.....	9



Chemistry Review Data Sheet

Chemistry Review Data Sheet

- 1. ANDA #: 76-897
- 2. REVIEW #: 1
- 3. REVIEW DATE: 2-20-2004
- 4. REVIEWER: Robert Iser
- 5. PREVIOUS DOCUMENTS:

<u>Previous Documents</u>	<u>Document Date</u>
Original	11-Nov-2003

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Original	11-Nov-2003
New Amendment	11-Dec-2003

7. NAME & ADDRESS OF APPLICANT:

Name:	Eon Labs, Inc.
Address:	4700 Eon Drive Wilson, NC 27893
Representative:	Steven W. Brown
Telephone:	(252) —

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name:	N/A
b) Non-Proprietary Name (USAN):	Oxandrolone Tablets, USP

9. LEGAL BASIS FOR SUBMISSION:

Reference Listed Drug:	Oxandrin ® Tablets, NDA# 13-718 (Based on 10 mg strength)
RLD Company:	BTG Pharmaceuticals
Patent Certification:	No listed patents, page 7
Exclusivity:	None, page 7

Chemistry Review Data Sheet

10. PHARMACOLOGICAL CATEGORY: Androgen/Anabolic Steroid

11. DOSAGE FORM: Tablets

12. STRENGTH/POTENCY: 2.5 mg and 10 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: Rx OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product – Form Completed

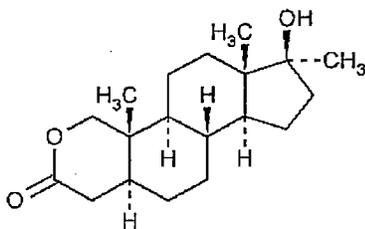
Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA,
MOLECULAR WEIGHT:

Oxandrolone

$C_{19}H_{30}O_3$

17 β -Hydroxy-17-methyl-2-oxa-5 α -androstan-3-one [53-39-4].





CHEMISTRY REVIEW



Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
1	1	[]	Oxandrolone	1	Inadequate	19-Feb-2004	Reviewed by R. Iser
1	1	[]	1	4	N/A		
1	1	[]	1	4	N/A		
1	1	[]	1	4	N/A		
1	1	[]	1	4	N/A		
1	1	[]	1	4	N/A		
1	1	[]	1	4	N/A		
1	1	[]	1	4	N/A		
1	1	[]	1	4	N/A		
1	1	[]	1	4	N/A		
1	1	[]	1	4	N/A		
1	1	[]	1	4	N/A		
1	1	[]	1	4	N/A		
1	1	[]	1	4	N/A		

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")



Chemistry Review Data Sheet

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Pending		
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Pending		
EA	Satisfactory	2/19/2004	Robert Iser
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt.

Yes No If no, explain reason(s) below:



The Chemistry Review for ANDA 76-897

The Executive Summary

Product: Oxandrolone Tablets USP, 2.5 mg and 10mg
Firm: Eon Labs, Inc.

I. Recommendations

- A. **Recommendation and Conclusion on Approvability**
NOT Approvable. MINOR will be issued. (Review #1)
- B. **Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable N/A**

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug Product:

The proposed drug product, Oxandrolone Tablets USP, 2.5 mg and 10 mg, is a non-sterile product.

The inactive ingredients for Oxandrolone Tablets USP are: Pregelatinized Starch NF, Hypromellose USP, Lactose Monohydrate NF, Magnesium Stearate NF, and ~~_____~~

Drug Substance:

The applicant's specifications for Oxandrolone USP are based on the USP monograph and drug substance manufacturer specifications.

Batch Sizes:

The size of proposed commercial scale 2.5mg and 10mg batches are _____, and _____ tablets, respectively. The size of the exhibit batches for both strengths were _____, _____ tablets.

B. Description of How the Drug Product is Intended to be Used

The drug product will be marketed as a prescription anabolic steroid, with proposed tablet strengths of 2.5 and 10 mg, packaging in 100 and 1000 count bottles.

The proposed expiration dating for the product is 24 months; based on three month accelerated data and the recommended storage conditions are the USP Long term stability conditions.



Executive Summary Section

C. Basis for Approvability or Not-Approval Recommendation

The recommendation of Not-Approvability is based on a significant number of deficiencies. This CMC review has identified deficiencies related to Components and Composition, Synthesis, Raw Material Controls, Container Closure System, Laboratory Controls, and Stability. All deficiencies are included in # 36.

The status of the bio data review and labeling review are still pending.

Based on the deficiencies described in #36, the drug product cannot be classified as safe and effective in this (first) review cycle. The firm will be informed regarding the classification of these deficiencies as a minor amendment.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

HFD-620/R.Iser-Review Chemist/2-20-04; revised 2-24-04
HFD-623/D.Gill-Team Leader/
HFD-617/S.Park-Project Manger/

V:FIRMSAMEON\LTRS&REV\76897.RV1.doc

C. CC Block

Cc:

ANDA 76-897
Division File
Duplicate Jacket
Field Copy

25 PAGES WITHHELD IN FULL



ANDA #76-897

**Oxandrolone Tablets USP,
2.5 mg and 10 mg**

Eon Labs, Inc.

**Robert Iser
Office of Generic Drugs
Division of Chemistry III
Team 4**



Table of Contents

Table of Contents	2
Chemistry Review Data Sheet	3
The Executive Summary	7
I. Recommendations.....	7
A. Recommendation and Conclusion on Approvability.....	7
B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable.....	7
II. Summary of Chemistry Assessments.....	7
A. Description of the Drug Product(s) and Drug Substance(s).....	7
B. Description of How the Drug Product is Intended to be Used.....	7
C. Basis for Approvability or Not-Approval Recommendation.....	7
III. Administrative.....	8
A. Reviewer's Signature.....	8
B. Endorsement Block.....	8
C. CC Block.....	8
Chemistry Assessment	9



Chemistry Review Data Sheet

Chemistry Review Data Sheet

- 1. ANDA #: 76-897
- 2. REVIEW #: 2
- 3. REVIEW DATE: 4-26-2004
- 4. REVIEWER: Robert Iser

5. PREVIOUS DOCUMENTS:

<u>Previous Documents</u>	<u>Document Date</u>
Original	11-Nov-2003
New Amendment	11-Dec-2003

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Minor Amendment	26-Mar-2004

7. NAME & ADDRESS OF APPLICANT:

Name:	Eon Labs, Inc.
Address:	4700 Eon Drive Wilson, NC 27893
Representative:	Steven W. Brown
Telephone:	(252) 234-2224

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: N/A
- b) Non-Proprietary Name (USAN): Oxandrolone Tablets, USP

9. LEGAL BASIS FOR SUBMISSION:

Reference Listed Drug:	Oxandrin ® Tablets, NDA# 13-718 (Based on 10 mg strength)
RLD Company:	BTG Pharmaceuticals
Patent Certification:	No listed patents, page 7
Exclusivity:	None, page 7

10. PHARMACOLOGICAL CATEGORY:

Androgen/Anabolic Steroid
Tablets

11. DOSAGE FORM:

12. STRENGTH/POTENCY:

2.5 mg and 10 mg

13. ROUTE OF ADMINISTRATION:

Oral

14. Rx/OTC DISPENSED:

X Rx OTC

Chemistry Review Data Sheet

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

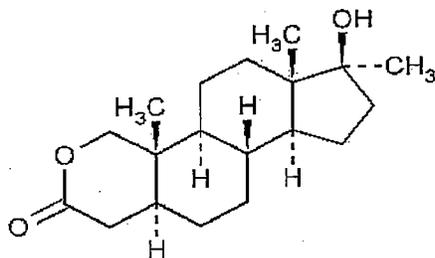
SPOTS product – Form Completed
 Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Oxandrolone

$C_{19}H_{30}O_3$

17 β -Hydroxy-17-methyl-2-oxa-5 α -androstan-3-one [53-39-4].





Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
1	1	[redacted]	Oxandrolone	1	Adequate	23-Apr-2004	Reviewed by R. Iser
1	1	[redacted]	[redacted]	4	N/A		
1	1	[redacted]	[redacted]	4	N/A		
1	1	[redacted]	[redacted]	4	N/A		
1	1	[redacted]	[redacted]	4	N/A		
1	1	[redacted]	[redacted]	4	N/A		
1	1	[redacted]	[redacted]	4	N/A		
1	1	[redacted]	[redacted]	4	N/A		
1	1	[redacted]	[redacted]	4	N/A		
1	1	[redacted]	[redacted]	4	N/A		
1	1	[redacted]	[redacted]	4	N/A		
1	1	[redacted]	[redacted]	4	N/A		
1	1	[redacted]	[redacted]	4	N/A		
1	1	[redacted]	[redacted]	4	N/A		
1	1	[redacted]	[redacted]	4	N/A		

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A



CHEMISTRY REVIEW



Chemistry Review Data Sheet

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Pending		
Methods Validation	N/A		
Labeling	Deficient	4/26/2004	Postelle Birch
Bioequivalence	Pending		
EA	Satisfactory	2/19/2004	Robert Iser
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt.

Yes No If no, explain reason(s) below:



Executive Summary Section

The Chemistry Review for ANDA 76-897

The Executive Summary

Product: Oxandrolone Tablets USP, 2.5 mg and 10mg
Firm: Eon Labs, Inc.

I. Recommendations

- A. Recommendation and Conclusion on Approvability**
NOT Approvable. MINOR will be issued. (Review #2)
- B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable N/A**

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug Product:

The proposed drug product, Oxandrolone Tablets USP, 2.5 mg and 10 mg, is a non-sterile product.

The inactive ingredients for Oxandrolone Tablets USP are: Pregelatinized Starch NF, Hypromellose USP, Lactose Monohydrate NF, Magnesium Stearate NF, and _____

Drug Substance:

The applicant's specifications for Oxandrolone USP are based on the USP monograph and drug substance manufacturer specifications.

Batch Sizes:

The size of proposed commercial scale 2.5mg and 10mg batches are _____, and _____ tablets, respectively. The size of the exhibit batches for both strengths were _____ tablets.

B. Description of How the Drug Product is intended to be used

The drug product will be marketed as a prescription anabolic steroid, with proposed tablet strengths of 2.5 and 10 mg, packaging in 100 and 1000 count bottles.

The proposed expiration dating for the product is 24 months; based on three month accelerated data and the recommended storage conditions are the USP Long term stability conditions.

C. Basis for Approvability or Not-Approval Recommendation

The recommendation of Not-Approvability is based on a significant number of deficiencies. This CMC review has identified deficiencies related to Raw Material Controls, Laboratory Controls,



Executive Summary Section

Containers, and Stability. All deficiencies are included. The status of the bio data review is still pending; and the labeling review is not satisfactory.

Based on the deficiencies, the drug product cannot be classified as safe and effective in this (second) review cycle. The firm will be informed regarding the classification of these deficiencies as a minor amendment.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

 5/19/04

HFD-620/R.Iser-Review Chemist/4-26-2004; revised 4-30-2004/
HFD-623/D.Gill-Team Leader/
HFD-617/S.Park-Project Manger/

V:FIRMSAMEONLTRS&REV\76897.RV2.doc

C. CC Block

Cc:

ANDA 76-897
Division File
Duplicate Jacket
Field Copy

18 PAGES WITHHELD IN FULL



ANDA #76-897

**Oxandrolone Tablets USP,
2.5 mg and 10 mg**

Eon Labs, Inc.

**Robert Iser
Office of Generic Drugs
Division of Chemistry III
Team 4**



Table of Contents

Table of Contents	2
Chemistry Review Data Sheet.....	3
The Executive Summary.....	7
I. Recommendations.....	7
A. Recommendation and Conclusion on Approvability	7
B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable	7
II. Summary of Chemistry Assessments	7
A. Description of the Drug Product(s) and Drug Substance(s)	7
B. Description of How the Drug Product is Intended to be Used.....	7
C. Basis for Approvability or Not-Approval Recommendation	8
III. Administrative.....	8
A. Reviewer's Signature	8
B. Endorsement Block	8
C. CC Block.....	8
Chemistry Assessment	9



Chemistry Review Data Sheet

Chemistry Review Data Sheet

- 1. ANDA #: 76-897
- 2. REVIEW #: 3
- 3. REVIEW DATE: 11-24-2004
- 4. REVIEWER: Robert Iser

5. PREVIOUS DOCUMENTS:

<u>Previous Documents</u>	<u>Document Date</u>
Original	11-Nov-2003
Amendment	11-Dec-2003
Minor Amendment	26-Mar-2004

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Minor Amendment	20-August-2004

7. NAME & ADDRESS OF APPLICANT:

Name:	Eon Labs, Inc.
Address:	4700 Eon Drive Wilson, NC 27893
Representative:	Sadie Ciganek
Telephone:	

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: N/A
- b) Non-Proprietary Name (USAN): Oxandrolone Tablets, USP

9. LEGAL BASIS FOR SUBMISSION:

Reference Listed Drug:	Oxandrin ® Tablets, NDA# 13-718 (Based on 10 mg strength)
RLD Company:	BTG Pharmaceuticals
Patent Certification:	No listed patents, page 7
Exclusivity:	None, page 7

10. PHARMACOLOGICAL CATEGORY:

Androgen/Anabolic Steroid

11. DOSAGE FORM:

Tablets

12. STRENGTH/POTENCY:

2.5 mg and 10 mg

13. ROUTE OF ADMINISTRATION:

Oral

14. Rx/OTC DISPENSED:

X Rx ___ OTC



CHEMISTRY REVIEW



Chemistry Review Data Sheet

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product – Form Completed

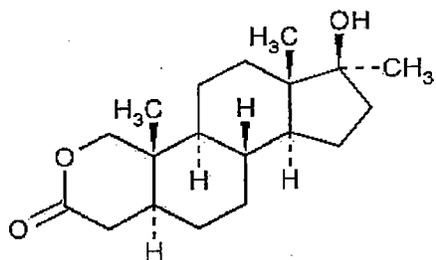
Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Oxandrolone

$C_{19}H_{30}O_3$

17 β -Hydroxy-17-methyl-2-oxa-5 α -androstan-3-one [53-39-4].





CHEMISTRY REVIEW



Chemistry Review Data Sheet

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Pending		
Methods Validation	N/A		
Labeling	Satisfactory	9/21/2004	Postelle Birch
Bioequivalence	Satisfactory	11/16/2004	S. Shrivistava
EA	Satisfactory	2/19/2004	Robert Iser
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt.
 Yes No If no, explain reason(s) below:



Executive Summary Section

The Chemistry Review for ANDA 76-897**The Executive Summary**

Product: Oxandrolone Tablets USP, 2.5 mg and 10mg
Firm: Eon Labs, Inc.

I. Recommendations

- A. Recommendation and Conclusion on Approvability**
NOT Approvable. Minor amendment will be issued. (Review #3)
- B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable N/A**

II. Summary of Chemistry Assessments**A. Description of the Drug Product(s) and Drug Substance(s)****Drug Product:**

The proposed drug product, Oxandrolone Tablets USP, 2.5 mg and 10 mg, is a non-sterile product.

The inactive ingredients for Oxandrolone Tablets USP are: Pregelatinized Starch NF, Hypromellose USP, Lactose Monohydrate NF, Magnesium Stearate NF, and _____

Drug Substance:

The applicant's specifications for Oxandrolone USP are based on the USP monograph and drug substance manufacturer specifications.

Batch Sizes:

The size of proposed commercial scale 2.5mg and 10mg batches are _____, and _____ tablets, respectively. The size of the exhibit batches for both strengths were _____ tablets.

B. Description of How the Drug Product is intended to be used

The drug product will be marketed as a prescription anabolic steroid, with proposed tablet strengths of 2.5 and 10 mg, packaging in 100 and 1000 count bottles.

The proposed expiration dating for the product is 24 months; based on three month accelerated data and the recommended storage conditions are:

Store at 20° - 25 °C (68° - 77 °F), excursions permitted to 15° - 30 °C (59° - 86 °F), [see USP Controlled Room Temperature]. No storage conditions are currently found in the RLD packing insert; however, it is noted on the bottle label as: Store at Room Temperature (59° - 77° F)



Executive Summary Section

C. Basis for Approvability or Not-Approval Recommendation

The recommendation of Not-Approvability is based on a significant number of deficiencies. This CMC review has identified deficiencies related to Raw Material Controls, Laboratory Controls, and Stability. All deficiencies are included. The status of the bio data review is satisfactory; and the labeling review is satisfactory. The site inspections are pending.

Based on the deficiencies, the drug product cannot be classified as safe and effective in this (third) review cycle. The firm will be informed regarding the classification of these deficiencies as a minor amendment.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

HFD-630/R.Iser, M.S.-Review Chemist/11-24-04; revised 12-6-04/  12/13/04
HFD-630/D.Gill, Ph.D.-Team Leader/
HFD-617/S.Park, Pharm.D.-Project Manger/

V:FIRMSAMEON\LTRS&REV\76897.RV3.doc

C. CC Block

Cc:

ANDA 76-897
Division File
Duplicate Jacket
Field Copy

20 PAGES WITHHELD IN FULL



ANDA #76-897

**Oxandrolone Tablets USP,
2.5 mg and 10 mg**

Sandoz Inc.

**Robert Iser
Office of Generic Drugs
Division of Chemistry III
Team 4**

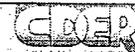
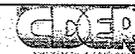
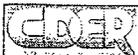


Table of Contents

Table of Contents.....	2
Chemistry Review Data Sheet	3
The Executive Summary	7
I. Recommendations.....	7
A. Recommendation and Conclusion on Approvability.....	7
B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable	7
II. Summary of Chemistry Assessments.....	7
A. Description of the Drug Product(s) and Drug Substance(s).....	7
B. Description of How the Drug Product is Intended to be Used	7
C. Basis for Approvability or Not-Approval Recommendation	8
III. Administrative	8
A. Reviewer's Signature	8
B. Endorsement Block	8
C. CC Block.....	8
Chemistry Assessment.....	9



Chemistry Review Data Sheet

Chemistry Review Data Sheet

- 1. ANDA #: 76-897
- 2. REVIEW #: Addendum to Review 4
- 3. REVIEW DATE: 2-25-2005; revised 3-9-05; revised 4-6-05
- 4. REVIEWER: Robert Iser

5. PREVIOUS DOCUMENTS:

<u>Previous Documents</u>	<u>Document Date</u>
Original	11-Nov-2003
Amendment	11-Dec-2003
Minor Amendment	26-Mar-2004
Minor Amendment	20-August-2004

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Minor Amendment	11-Feb-2005
Telephone Amendment	31-Mar-2005

7. NAME & ADDRESS OF APPLICANT:

Name: Sandoz Inc.
 Address: 4700 Eon Drive
 Wilson, NC 27893
 Representative: Steven Brown
 Telephone: _____
 Fax:

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: N/A
- b) Non-Proprietary Name (USAN): Oxandrolone Tablets, USP

9. LEGAL BASIS FOR SUBMISSION:

Reference Listed Drug: Oxandrin ® Tablets, NDA# 13-718
 (Based on 10 mg strength)
 RLD Company: Savient Pharmaceuticals
 Patent Certification: No listed patents, review #1
 Exclusivity: None, review #1

10. PHARMACOLOGICAL CATEGORY:

Androgen/Anabolic Steroid

Chemistry Review Data Sheet

11. DOSAGE FORM: Tablets
12. STRENGTH/POTENCY: 2.5 mg and 10 mg (maximum 50 mg daily)
13. ROUTE OF ADMINISTRATION: Oral
14. Rx/OTC DISPENSED: Rx OTC
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

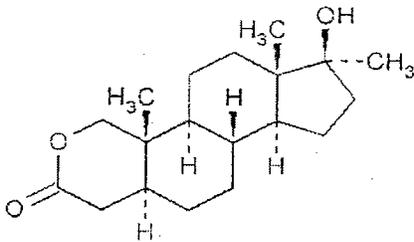
SPOTS product – Form Completed
 Not a SPOTS product

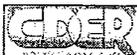
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA,
MOLECULAR WEIGHT:

Oxandrolone

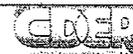
$C_{19}H_{30}O_3$

17 β -Hydroxy-17-methyl-2-oxa-5 α -androstan-3-one [53-39-4].





CHEMISTRY REVIEW



Chemistry Review Data Sheet

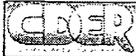
18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Satisfactory	4/25/2005	J. D'Ambrogio
Methods Validation	N/A		
Labeling	Satisfactory	11/22/2005	Postelle Birch
Bioequivalence	Satisfactory	11/16/2004	S. Shrivistava
EA	Satisfactory	2/19/2004	Robert Iser
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt.

Yes No If no, explain reason(s) below:



The Chemistry Review for ANDA 76-897

The Executive Summary

Product: Oxandrolone Tablets USP, 2.5 mg and 10mg
Firm: Eon Labs, Inc.

I. Recommendations

- A. Recommendation and Conclusion on Approvability
Approvable.
- B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug Product:

The proposed drug product, Oxandrolone Tablets USP, 2.5 mg and 10 mg, is a non-sterile product.

The inactive ingredients for Oxandrolone Tablets USP are: Pregelatinized Starch NF, Hypromellose USP, Lactose Monohydrate NF, Magnesium Stearate NF, and _____

Drug Substance:

The applicant's specifications for Oxandrolone USP are based on the USP monograph and drug substance manufacturer specifications.

Batch Sizes:

The size of proposed commercial scale 2.5mg and 10mg batches are _____, and _____ tablets, respectively. The size of the exhibit batches for both strengths were _____ tablets.

B. Description of How the Drug Product is intended to be used

The drug product will be marketed as a prescription anabolic steroid, with proposed tablet strengths of 2.5 and 10 mg, packaging in 100 and 1000 count bottles.

The proposed expiration dating for the product is 24 months; based on three month accelerated data and the recommended storage conditions are:

Store at 20° - 25 °C (68° - 77 °F), excursions permitted to 15° - 30 °C (59° - 86 °F), [see USP Controlled Room Temperature]. No storage conditions are currently found in the RLD packing insert; however, it is noted on the bottle label as: Store at Room Temperature (59° - 77° F)



Executive Summary Section

C. Basis for Approvability or Not-Approval Recommendation

CMC is approvable. The status of the bio data review is satisfactory; the labeling review is satisfactory; and the site inspections are satisfactory.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

HFD-630/R.Iser, M.S.-Review Chemist/2-25-05; revised 3-9-05; revised 4-6-05/
HFD-630/D.Gill, Ph.D.-Team Leader/
HFD-617/S.Park, Pharm.D.-Project Manger/

V:FIRMSAMAEON\LTRS&REV\76897.RV3.doc

C. CC Block

Cc:

ANDA 76-897
Division File
Duplicate Jacket
Field Copy

17 PAGES WITHHELD IN FULL



CHEMISTRY REVIEW



Chemistry Assessment Section

cc: ANDA 76-897
ANANDA DUP
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-630 / R. Iser- Review Chemist *R. Iser 11/27/06*
HFD-630 / D. Gill - Team Leader *D. Gill 11-28-06*
HFD-617 / S. Park - Project Manager *S. Park Matheny 11/28/06*

F/T by: EW

V:\FIRMSAM\EON\LTRS&REV\76897. Addendum to Review 4

CMC APPROVABLE

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-897

BIOEQUIVALENCE REVIEW(S)

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	76-897
Drug Product Name	Oxandrolone Tablets, USP
Strength	2.5 mg, 10 mg
Applicant Name	Eon Labs
Address	Wilson, NC
Submission Date(s)	November 11, 2003
Amendment Date(s)	
Reviewer	S. P Shrivastava, Ph.D.
First Generic	Yes
File Location	V:\firmsam\EON\ltrs&rev\76897N1103

I. Executive Summary

This application references Oxandrin® (oxandrolone) tablet (2.5 and 10 mg) and the Orange Book lists 10 mg as the RLD. The firm has submitted one fasting BE study on 10 mg tablets, and requested waivers of in vivo testing for the 2.5 mg strength.

The fasting study is a single-dose two-way crossover study using 23 male and female normal healthy volunteers given a dose of 10 mg. The results (point estimate, 90% CI) of the fasting BE study are: LAUC_t of 102, 94.57-110.75%; LAUC_i of 103, 94.41-112.30%; and LC_{max} of 102, 95.18-108.80%.

The study is incomplete due to partial stability and dissolution data. The long-term stability data of oxandrolone in plasma is provided for 36 days. Long-term stability data for 48 days is requested. The waiver of BE study for 2.5 mg strength is denied. Application is incomplete.

II. Table of Contents

I.	Executive Summary.....	1
II.	Table of Contents.....	1
III.	Submission Summary.....	2
	A. Drug Product Information.....	2
	B. PK/PD Information.....	2
	C. Contents of Submission.....	3
	D. Pre-Study Bioanalytical Method Validation.....	3
	E. In Vivo Studies.....	4
	1. Single-dose Fasting Bioequivalence Study.....	4
	F. Formulation.....	5
	G. In Vitro Dissolution.....	5
	H. Waiver Request(s).....	5
	I. Deficiency Comments.....	6
	J. Recommendations.....	6
IV.	Appendix.....	8
	A. Individual Study Reviews.....	8
	1. Single-dose Fasting Bioequivalence Study.....	8
	a) Study Design.....	8

b)	Clinical Results	9
c)	Bioanalytical Results	10
d)	Pharmacokinetic Results	11
B.	Formulation Data	15
C.	Dissolution Data	15
D.	Consult Reviews	16
E.	SAS Output	16

III. Submission Summary

A. Drug Product Information

Test Product	Oxandrolone Tablets, USP
Reference Product	Oxandrin® Tablets, 10 mg
RLD Manufacturer	Savient Pharms (Previously BTG Pharmaceuticals)
NDA No.	13-718
RLD Approval Date	November 5, 01
Indication	Oxandrolone is indicated as adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections, or severe trauma

B. PK/PD Information

Bioavailability (Oral)	97%
Food Effect	Not indicated
T_{max}	1 Hour
Metabolism	Partially metabolized in liver
Excretion	30% Excreted as parent drug. Other free metabolites in urine are also excreted.
Half-life (terminal)	9.4 hrs.
Relevant OGD or DBE History	<p>ANDA: 76-761 (Upsher-Smith, 4/19/04, In queue)</p> <p>CD: 99-111 ———, 02-464 – For BE, requested fasting study and to measure parent drug in the plasma</p> <p>02-235 ———, 02-327 ———, 02-354 ———</p> <p>Dissolution in 500 mL of 30% isopropyl alcohol using Paddle at 100 rpm, and sampling at 15, 30, 45, 60, 75 and 90 minutes.</p> <p>Protocol: 00-041 ——— 2.5 mg – accepted single-dose fasting study and requested dissolution as above.</p>
Agency Guidance	None
Drug Specific Issues (if any)	None

C. Contents of Submission

Study Types	Yes/No?	How many?
Single-dose fasting	Y	1
Single-dose fed	N	
Steady-state	N	
In vitro dissolution	Y	
Waiver requests	Y	1
BCS Waivers	N	
Vasoconstrictor Studies	N	
Clinical Endpoints	N	
Failed Studies	N	
Amendments	N	

D. Pre-Study Bioanalytical Method Validation

	Parent
Analyte name	Oxandrolone
Internal Standard	Propranolol.HCl
Method description	LC/MS/MS
QC range	2.4 to 240 ng/mL
Standard curve range	1 to 300 ng/mL
Limit of quantitation	1 ng/mL
Average recovery of Drug (%)	80.6
Average Recovery of Int. Std (%)	85.6
QC Intraday precision range (%)	1.1 to 11.7
QC Intraday accuracy range (%)	92.1 to 111
QC Interday precision range (%)	1.9 to 4.7
QC Interday accuracy range (%)	95 to 102
Bench-top stability at Rm Temp (hrs)	24
Stock stability (days) at 4 °C	32
Processed stability at Rm Temp (hrs)	52
Processed stability at 4 °C (hrs)	74
Freeze-thaw stability (cycles)	6
Long-term storage stability at -20 °C (days)	36
Dilution integrity	Y
Specificity	Y
SOPs submitted	Y
Bioanalytical method is acceptable	N (Due to inadequate data for long-term storage stability)
20% Validation Chromatograms included (Y/N)	Y
Random or Serial Selection of Chrom	Serial

E. In Vivo Studies

1. Single-dose Fasting Bioequivalence Study

Study Summary, Fasting Bioequivalence Study	
Study No.	10380605
Study Design	Two-way crossover
No. of subjects enrolled	24
No. of subjects completing	23
No. of subjects analyzed	23
Subjects (Healthy or Patients?)	Healthy
Sex(es) included (how many?)	Male Female
Test product	A=Eon Pharm's oxandrolone tablet, USP
Reference product	B=BTG Pharmaceutical's Oxandrin® tablet, USP
Strength tested	10 mg
Dose	1 x 10 mg

Summary of Statistical Analysis, Fasting Bioequivalence Study		
Parameter	Point Estimate	90% Confidence Interval
AUC _{0-t}	1.02	94.57-110.75
AUC _∞	1.03	94.41-112.30
C _{max}	1.02	95.18-108.80

Reanalysis of Study Samples, Fasting Bioequivalence Study Additional information in Appendix, Table 6								
Reason why assay was repeated	Number of samples reanalyzed				Number of recalculated values used after reanalysis			
	Actual number		% of total assays		Actual number		% of total assays	
	T	R	T	R	T	R	T	R
Unacceptable chromatography	0	1	0	0.11	0	1	0.0	0.11
Low internal Standard	2	2	0.23	0.23	2	2	0.23	0.23
High internal standard	0	1	0.0	0.11	0	1	0.0	0.11
Peak in pre-dose sample	1	0	0.11		1	0	0.11	0.0
Total (n=874)	3	4	0.34	0.45	3	4	0.34	0.45

The use of recalculated plasma concentration data did not change the study outcome.

F. Formulation

Location in appendix Section IV.B, Page 15
 Are inactive ingredients within IIG limits? Y
 If no, list ingredients outside of limits N/A
 If a tablet, is the product scored? Y
 If yes, which strengths are scored? 2.5 mg
 Is scoring of RLD the same as test? Y
 Is the formulation acceptable? Y
 If not acceptable, why? N/A

G. In Vitro Dissolution

Source of Method (USP, FDA or Firm) In-house
 Medium 1% Tween 80®
 Volume (mL) 500 mL
 USP Apparatus type II (Paddle)
 Rotation (rpm) 100 rpm
 Firm's proposed specifications NLT — in 180 minutes
 FDA-recommended method and specifications Medium – 500 mL of 30% Isopropyl alcohol Apparatus II (Paddle) at 100 rpm
 F2 metric calculated? Y
 If no, reason why F2 not calculated N/A
 Is method acceptable? No
 If not then why? Need dissolution data based on the FDA method.

F2 metric, lower strengths compared to highest strength			
Low strength	Highest strength	F2 metric for test	F2 metric for RLD
2.5 mg	10 mg	68.78	80.70

F2 metric, test compared to reference	
Strength	F2 metric
2.5 mg	76.45
10 mg	64.21

H. Waiver Request(s)

Strengths for which waivers are requested 2.5 mg
 Regulation cited Based on BE study on 10 mg strength, in vitro dissolution data and formulation proportionality.
 Proportional to strength tested in vivo? Yes
 Is dissolution acceptable? No
 Waivers granted? No
 If not then why? Due to deficiencies

I. Deficiency Comments

1. The firm has provided the long-term stability data for 36 days. Stability data for 48 days at -20 °C is requested.
2. The firm should provide comparative dissolution data using the following method:

Medium: 500 mL 30% Isopropyl alcohol
Apparatus: II (Paddle) at 100 rpm.
Sampling times: 15, 30, 45, 60, 75 and 90 minutes or until — of the labeled drug is dissolved.

J. Recommendations

1. The bioequivalence study conducted by Eon Labs under fasting conditions on its oxandrolone tablet, USP, 10 mg, Lot # RDW00278 comparing it to Oxandrin® tablet, 10 mg, Lot #2F3013, manufactured by Savient Pharmaceuticals, is incomplete due to deficiency #1 cited above.
2. The dissolution testing conducted by the firm on its oxandrolone tablets, 2.5 mg and 10 mg, Lot #s RDW00277 and RDW00278, comparing them to Oxandrin® tablets, 2.5 mg and 10 mg, Lot #s C201546 and 2F3013, manufactured by Savient Pharmaceuticals, is incomplete due to deficiency #2 cited above.
3. The formulation for the 2.5 mg strength tablets is proportionally similar to the 10 mg strength of the test product, which underwent bioequivalence testing. However, in the absence of acceptable bioequivalence study and dissolution data, the waiver of *in vivo* bioequivalence study requirements for the 2.5 mg tablet of the test product is not granted at this time.
4. From the bioequivalence point of view, the firm has not met the requirements of *in vivo* and *in vitro* bioequivalence study, and the application is incomplete.

The firm should be informed of the deficiencies and recommendations.

S. P. Shrivastava

S. P. Shrivastava, Ph.D.
Reviewer, Branch II

Gur Jai Pal Singh 7-28-04

Gur Jai Pal Singh, Ph.D.
Team Leader, Branch II

Barbara M. David 7/29/04

Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence
Office of Generic Drugs

for

IV. Appendix

A. Individual Study Reviews

1. Single-dose Fasting Bioequivalence Study

a) Study Design

Study Information	
Study Number	10380605
Study Title	A relative bioavailability study of oxandrolone, 10 mg tablets, under fasting conditions
Clinical Site	3
Principal Investigator	
Study/Dosing Dates	7/12/03-7/14/03 and 7/21/03 – 7/23/03
Analytical Site	
Analytical Director	
Analysis Dates	8/15/03 – 8/29/03
Storage Period (no. of days from the first day of sample collection to the last day of sample analysis)	48

Treatment ID	Test	Reference
Test or Reference	A	B
Product Name	Oxandrolone tablets	Oxandrin® tablets
Manufacturer	Eon Pharma, LLC	BTG Pharmaceuticals
Batch/Lot No.	RDW00278	2F3013
Manufacture Date	6/2003	----
Expiration Date	----	6/2004
Strength	10 mg	10 mg
Dosage Form	Tablet	Tablet
Batch Size	— tablets	----
Production Batch Size	—, tablets	----
Potency (%)	97.7	95.4
Content Uniformity (mean, %CV)	97.3 (95.2-100.4)	94.2 (92.3-95.1)
Formulation	See Appendix Section B	
Dose Administered	1 x 10 mg	1 x 10 mg
Route of Administration	Oral	

No. of Sequences	2
No. of Periods	2
No. of Treatments	2
No. of Groups	1
Washout Period	1 week
Randomization Scheme	AB: 3, 4, 5, 10, 12, 13, 15, 16, 19, 21, 23, 24
Blood Sampling Times	BA: 1, 2, 6, 7, 8, 9, 11, 14, 17, 18, 20, 22
Blood Volume Collected/Sample	Pre-study (0), and at 0.5, 1, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 8, 12, 16, 24, 30, 36, 48, 60 hrs. post-dose
Blood Sample Processing/Storage	Plasma separated and stored at -20 °C
IRB Approval	Y
Informed Consent	Y
Subjects Demographics	See Table 1
Length of Fasting	10 hrs
Length of Confinement	46 hrs
Safety Monitoring	Blood pressure and heart rate monitored at pre-dose, and at 3 hrs. post-dose, prior to leaving the clinic (~36 hrs. post dose), and at 60 hrs. return visit.

Comments on Study Design:

b) Clinical Results

Table 1 Demographics of Study Subjects

Age, yrs.		Weight, lbs.		Age Groups		Gender		Race	
				Range	%	Sex	%	Category	%
				<18	0.0			Caucasian	4.2
Mean	35	Mean	187	18-40	62.5	Male	83.3	Afr. Amer.	50.0
SD	12.1	SD	37.0	41-64	33.3	Female	16.7	Hispanic	29.2
Range	19-66	Range	111-281	65-75	4.2			Asian	8.3
				>75	0.0			Others	8.3

Table 2 Dropout Information

Subject #	Reason	Period	Replaced?
24	Adverse reactions including emesis, fever, headache, soar throat, fatigue ear pressure	II	No

Table 3 Study Adverse Events

Adverse Event Description	# in Test Group	# in Ref. Group
Elevated SGOT	0	1
Emesis	1	0
Total:	1	1

Table 4 Protocol Deviations

Type	Subject #s (Test)	Subject #s (Ref.)
Blood sampling (-1 to +11 minutes)	4	7

Comments on Dropouts/Adverse Events/Protocol Deviations:

The adverse events and protocol deviations did not compromise the outcome of the study.

c) Bioanalytical Results

Table 5 Assay Quality Control – Within Study

QC Conc. (ng/mL)	Parent								
	2.4	24	240						
Inter day Precision (%CV)	8.7	8.7	10.6						
Inter day Accuracy (%)	95.0	105	97.5						
Cal. Standards Conc. (ng/mL)	1	2	4	10	20	40	100	250	300
Inter day Precision (%CV)	2.4	4.6	3.8	6.6	4.5	2.4	2.9	3.3	5.3
Inter day Accuracy (%)	99.6	99.5	100	103	103	110	92.4	97.2	97.0
Linearity Range (range of R values)	0.9965-0.9987								

Comments on Study Assay Quality Control:

Any interfering peaks in chromatograms?	N
Were 20% of chromatograms included?	Y
Were chromatograms serially or randomly selected?	Serially

Comments on Chromatograms: Raw data are acceptable.

Table 6 SOP's dealing with analytical repeats of study samples

SOP No.	Date of SOP	SOP Title
L200.108	6/20/01	Sample Analysis

Table 7 Additional Comments on Repeat Assays

Were all SOPs followed?	Y
Did recalculation of plasma concentrations change the study outcome?	N
Does the reviewer agree with the outcome of the repeat assays?	Y
If no, reason for disagreement	N/A

Summary/Conclusions, Study Assays: The methods validation is incomplete due to lack of adequate long-term stability data.

d) Pharmacokinetic Results

Table 8 Arithmetic Mean Pharmacokinetic Parameters

Mean plasma concentrations are presented in Table 11 and Figure 1

PARAMETER	MEAN1	CV1	MEAN2	CV2	RMEAN12
AUCI	2514.61	24.81	2473.26	29.36	1.02
AUCI	2446.04	23.42	2419.39	28.22	1.01
C _{MAX}	198.70	20.93	197.91	26.72	1.00
KE	0.08	32.14	0.10	33.68	0.79
LAUCI	2445.01	0.01	2377.45	0.01	1.03
LAUCI	2385.08	0.01	2332.32	0.01	1.02
LC _{MAX}	194.39	0.11	190.68	0.15	1.02
T _{1/2}	10.23	38.43	8.31	51.00	1.23
T _{MAX}	3.78	26.68	4.43	19.02	0.85

Table 9 Geometric Means and 90% Confidence Intervals

	LSM1	LSM2	RLSM12	LOWCI12	UPPCI12
PARAMETER					
AUCI	2514.32	2470.45	1.02	92.87	110.68
AUCT	2445.16	2417.36	1.01	93.32	108.98
C _{MAX}	198.65	198.25	1.00	93.68	106.72
LAUCI	2445.29	2374.84	1.03	94.41	112.30
LAUCT	2384.89	2330.29	1.02	94.57	110.75
LC _{MAX}	194.41	191.04	1.02	95.18	108.80

Table 10 Additional Study Information

Root mean square error, AUC _{0-t}	0.155519
Root mean square error, AUC _∞	0.17077
Root mean square error, C _{max}	0.13166
K _{el} and AUC _∞ determined for how many subjects?	23
Do you agree or disagree with firm's decision?	Agree
Indicate the number of subjects with the following:	----
-measurable drug concentrations at 0 hr	0
-first measurable drug concentration as C _{max}	0
Were the subjects dosed as more than one group?	No

Comments on Pharmacokinetic and Statistical Analysis:

The reviewer analyzed data and PK parameters are presented in Figure 1 and Tables 8-11 AND Fig. 1.

- The pharmacokinetic parameters and 90% confidence intervals for 23 subjects calculated by the reviewer agree with firm's calculations.
- LAUCT and LAUCi showed no statistically significant treatment or sequence effect.

Conclusion: The study is incomplete due to inadequate methods validation.

Summary and Conclusions, Single-Dose Fasting Bioequivalence Study: The fasting study is incomplete due to indicated deficiencies.

Table 11 Mean Plasma Concentrations, Single-Dose Fasting Bioequivalence Study

(ng/mL)

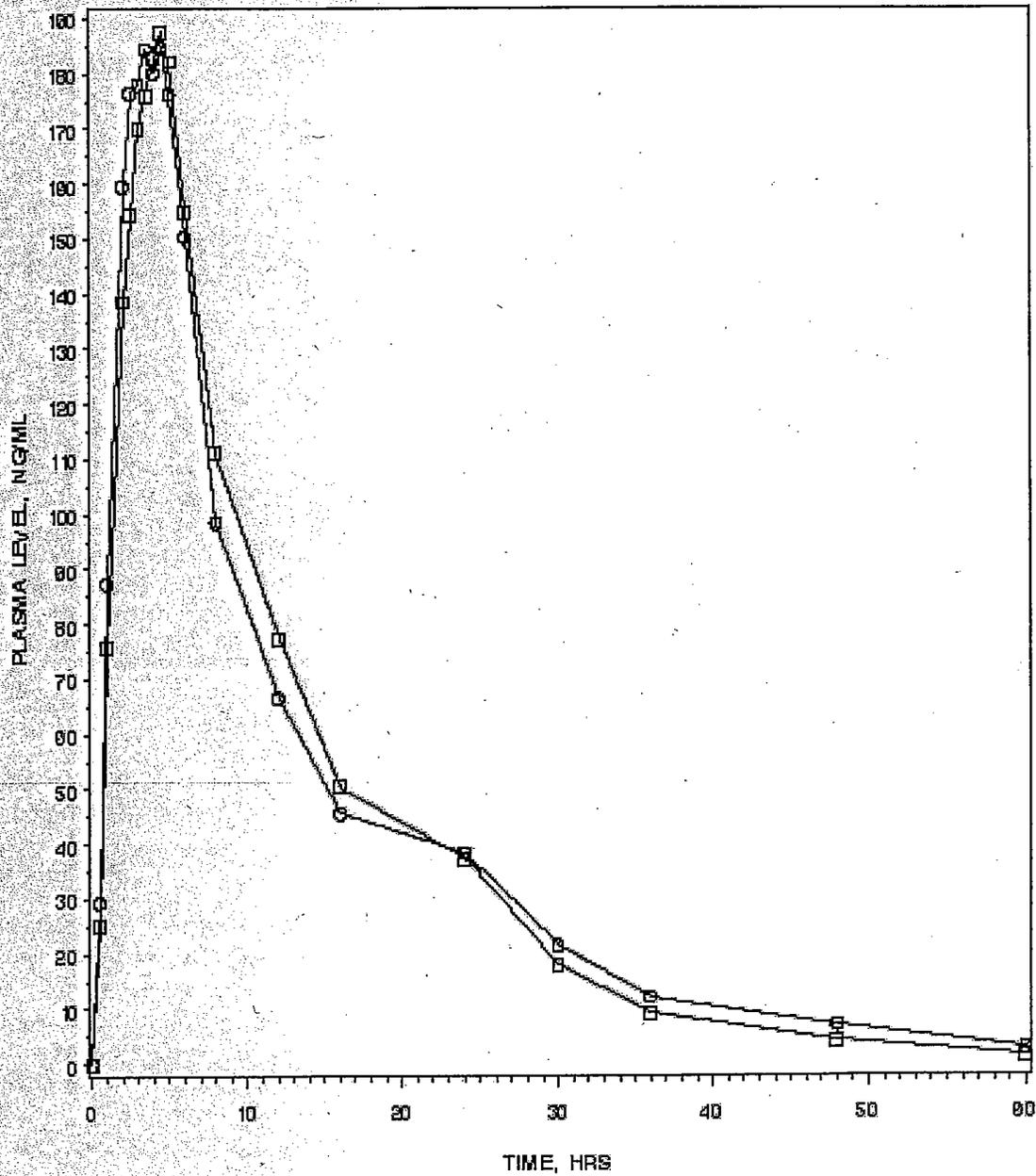
	MEAN1	CV1	MEAN2	CV2	RMEAN12
TIME HR					
0	0.00		0.00		
0.5	29.52	50.65	25.44	57.14	1.16
1	87.43	32.33	75.67	44.47	1.16
2	159.58	24.41	138.59	37.58	1.15
2.5	176.50	22.77	154.33	33.55	1.14
3	178.00	20.64	170.02	32.36	1.05
3.5	184.43	21.88	176.18	29.95	1.05
4	180.17	22.93	182.80	29.02	0.99
4.5	184.96	22.60	187.60	27.98	0.99
5	176.39	22.86	182.31	27.21	0.97
6	150.48	22.11	155.08	28.02	0.97
8	98.52	26.92	111.11	31.74	0.89
12	66.51	31.14	77.13	29.44	0.86
16	45.58	38.79	50.35	38.96	0.91
24	38.31	40.13	37.26	48.65	1.03
30	21.48	40.59	17.94	52.94	1.20
36	12.13	45.40	9.11	61.98	1.33
48	7.05	87.40	4.22	172.73	1.67
60	2.70	140.05	1.34	262.97	2.02

Mean1=test, Mean2=Ref; Unit=ng/mL

Figure 1 Mean Plasma Concentrations, Single-Dose Fasting Bioequivalence Study

PLASMA OXANDOLONE LEVELS: ALL SUBJECTS(N=23)

OXANDOLONE TABLETS, 10 MG, ANDA #70-887
UNDER FASTING CONDITIONS
DOSE= 1 X (10 MG)



TRT 000 1 888 2

1=TEST(EON) 2=REF(BTG PHARMACEUT)

B. Formulation Data

Table 12 Composition of 2.5 and 10 mg Strengths

Ingredients	2.5 mg		10 mg	
	mg/tablet	%w/w	mg/tablet	%w/w
Oxandrolone, USP	2.5		10.0	
Pregelatinized Starch, NF				
Hypromellose, USP				
Lactose Monohydrate, NF				
Magnesium Stearate, NF				
Total Core Wt.				

C. Dissolution Data

Table 13 Dissolution of 2.5 mg Strength

Sampling Time, min	Test Product, Strength - 2.5 mg Lot No. RDW00277			Reference Product, Strength - 2.5 mg Lot No. C201546		
	Mean	%CV	Range	Mean	%CV	Range
30	35.5	11.6		34.8	6.3	
60	59.0	8.2		55.3	8.4	
120	78.0	2.8		79.6	5.7	
150	81.1	2.6		84.9	5.5	
180	83.7	2.1		85.8	5.8	
240	86.8	3.2		90.1	4.8	
F2	T vs. R		76.45			

Table 14 Dissolution of 10 mg Strength

Sampling Time, min	Test Product, Strength - 10 mg Lot No. RDW00278			Reference Product, Strength - 10 mg Lot No. 2F3013		
	Mean	%CV	Range	Mean	%CV	Range
30	29.5	5.3		30.9	5.2	
60	52.3	4.3		55.7	2.7	
120	75.3	2.6		79.7	4.1	
150	78.7	1.6		84.2	3.0	
180	81.2	2.4		88.9	1.8	
240	86.3	2.0		92.1	1.4	
F2	T vs. R					
F2	T vs. T	2.5 vs 10 mg				
F2	R vs. R	2.5 vs 10 mg				

D. Consult Reviews

E. SAS Output

Fasting Study Data (N=23)	 76897FS.TXT
Fasting Study SAS Program (N=23)	 76897fs.txt
Fasting Study SAS Output (N=23)	 76897FS.OUT.txt

BIOEQUIVALENCE DEFICIENCIES

ANDA: 76-897

APPLICANT: Eon Labs., Inc.

DRUG PRODUCT:

Oxandrolone Tablet, USP, 10 mg, 2.5 mg

The Division of Bioequivalence has completed its review of your submission(s) acknowledged on the cover sheet. The following deficiencies have been identified:

1. You have provided the long-term stability data for — days. Stability data for — days at — is requested because the samples were stored for that long.
2. Please provide comparative dissolution data using the following method:

Medium:	500 mL of 30% Isopropyl alcohol
Apparatus:	II (Paddle) at 100 rpm.
Sampling times:	15, 30, 45, 60, 75 and 90 minutes or until — of the labeled drug is dissolved.

Sincerely yours,

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

CC: ANDA 76-897
ANDA DUPLICATE
DIVISION FILE
HFD-651/ Bio Drug File
HFD-650/ SShrivastava

X:\NEW\FIRMSAM\EON\trs&rev\76897N1103
Printed in final on 07/20/04

Endorsements: (Final with Dates)

HFD-655/SShrivastava

SS
7/29/04

HFD-655/ GJPSingh

Copy 7-29-04

HFD-650/ D. Conner

BRD 7/29/04

Ad

BIOEQUIVALENCY - INCOMPLETE

submission date: 11/18/03

1. **FASTING STUDY (STF)**

Strengths: 10 mg

Clinical:

Outcome: IC

Analytical:

2. **DISSOLUTION DATA (DIS)**

All Strengths

Outcome: IC

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	76-897
Drug Product Name	Oxandrolone tablets, USP
Strength	2.5 and 10 mg
Applicant Name	Eon Labs, Inc.
Address	Laurelton, NY
Submission Date(s)	
Amendment Date(s)	August 25, 2004
Reviewer	S. P. Shrivastava
First Generic	Yes
File Location	V:\firmsam\Eon\ltrs&rev\76897a0804.doc

I. Executive Summary

On November 11, 2003, the firm submitted a BE study. The study had inadequate stability and dissolution data (Review, SShrivastava, Appendix, Section B, Attachment-1).

In this submission, the firm has responded to the deficiencies and submitted adequate stability data, and additional dissolution results as requested.

The dissolution data for 2.5 and 10 mg strengths are acceptable. However, acceptance of dissolution testing method and specification is requested. The waiver of BE study for the 2.5 mg strength is pending acceptance of dissolution testing method by the firm. The application is incomplete.

II. Table of Contents

I. Executive Summary.....	1
II. Table of Contents.....	1
III. Submission Summary.....	2
A. Drug Product Information.....	2
B. Contents of Submission.....	2
C. PK/PD Information.....	2
D. Deficiency, Firm's Response and Reviewer's Comments.....	2
E. Recommendations.....	3
IV. Appendix.....	5
A. Dissolution Data.....	5
B. Additional Attachments.....	8

III. Submission Summary

A. Drug Product Information and PK/PD Information (Original Review, SShrivastava Section B, Attachment-1).

Relevant OGD History: For ANDA 76-761 (Upsher-Smith) 2.5 mg strength, the DBE accepted the firm's dissolution testing method consisting of 500 mL of 0.75% SDS in 0.1 N HCl at 37 °C and Apparatus II at 75 rpm. For further historical background, see the original Review, SShrivastava, Section B, Attachment-1.

B. Contents of Submission

Study Types	Yes/No?	How many?
Single-dose fasting	N	
Single-dose fed	N	
Steady-state	N	
In vitro dissolution	Y	
Waiver requests	Y	1
BCS Waivers	N	
Vasoconstrictor Studies	N	
Clinical Endpoints	N	
Failed Studies	N	
Amendments	Y	

C. Deficiency, Firm's Response and Reviewer's Comments

DEFICIENCY #1. *You have provided the long-term stability data for 36 days. Stability data for 48 days at -20 °C is requested because the samples were stored for that long.*

Firm's Response: The firm has demonstrated that the long-term stability (at -20 °C) of oxandrolone in human plasma at 2.4, 24 and 240 ng/mL concentrations is at least 378 days.

Reviewer's Comment: The firm's response is acceptable.

DEFICIENCY #2. *Please provide comparative dissolution data using the following method:*

Medium: 500 mL of 30% Isopropyl alcohol
Apparatus: II (Paddle) at 100 rpm.
Sampling times: 15, 30, 45, 60, 75 and 90 minutes or until ~~100~~% of the labeled drug is dissolved.

Firm's Response: The firm has provided dissolution of 2.5 and 10 mg strengths (T and R) in 30% isopropyl alcohol (IPA), and of 10 mg strength (T and R) in 0.5% sodium lauryl sulfate

(SLS), 1% SLS and 2% Tween-80® media using the above method. Data are summarized in Appendix, Tables 3-7.

The firm has previously submitted dissolution in 1% Tween-80® in water, and has requested for FDA's approval of the method and specification (Appendix, Tables 1 and 2, also see Review, SShrivastava, 7/29/04, Section B, Attachment-1).

Reviewer's Comment

1. The F2 similarity factor for isopropyl alcohol, 0.5% SLS and 1% SLS are \llcorner , indicating that dissolution profiles of test and reference products are not similar.
2. The F2 similarity factor for 1% and 2% Tween-80® are — indicating that dissolution profiles of test and reference products are similar. The firm's request for approval of 1% Tween-80® media for the dissolution is acceptable. However, firm's proposal to set the specification of NLT — in 180 minutes is not acceptable. Therefore, the reviewer in consultation with the DBE Dissolution Expert set the specification as recommended below (Appendix, Section B, Attachment-2). Based on the submitted data, then firm should be able to meet the recommended specification at Stage 1.

Conclusion: The firm's proposed dissolution method using 500 mL 1% Tween-80® in water, and USP Apparatus II (Paddle) at 100 rpm, is acceptable, the proposed specification is not acceptable.

D. Recommendations

1. The bioequivalence study conducted by Eon Labs under fasting conditions on its oxandrolone tablet, USP, 10 mg, Lot # RDW00278 comparing it to Oxandrin® tablet, 10 mg, Lot #2F3013, manufactured by Savient Pharmaceuticals, is acceptable.
2. The dissolution testing conducted by the firm on its oxandrolone tablets, 2.5 mg and 10 mg, Lot #s RDW00277 and RDW00278, comparing them to Oxandrin® tablets, 2.5 mg and 10 mg, Lot #s C201546 and 2F3013, manufactured by Savient Pharmaceuticals, is acceptable.

The dissolution testing should be conducted in 500 mL of 1% Tween-80® in water using USP Apparatus II (Paddle) at 100 rpm. The test product should meet the following dissolution specification:

Not less than — (Q) of the labeled amount of the drug in the dosage form is dissolved in 120 minutes.

3. The formulation for the 2.5 mg strength tablets is proportionally similar to the 10 mg strength of the test product, which underwent bioequivalence testing. The waiver of in vivo bioequivalence study requirements for the 2.5 mg strength tablets is pending acceptance of the dissolution specification by the firm.

The firm should be informed of the deficiency and recommendations.

S. P. Shrivastava

10/19/04

Surendra P. Shrivastava, Ph.D.
Reviewer, Branch II

Date

Gur Jai Pal Singh

10-19-04

Gur Jai Pal Singh, Ph.D.
Team Leader, Branch II

Date

Barbara M. Conner

10/20/04

In

Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence
Office of Generic Drugs

Date

IV. Appendix

A. Dissolution Data

Data in Tables 1 and 2 are copied from the review of the original application, and are provided for comparison with other dissolution methods.

1. METHOD-1: 500 mL 1% Apparatus II (Paddle) at 100 rpm

Table 1. Dissolution of 2.5 mg Strength (n=12, previously submitted data)

Sampling Time, min	Test Product, Strength - 2.5 mg Lot No. RDW00277			Reference Product, Strength - 2.5 mg Lot No. C201546		
	Mean	%CV	Range	Mean	%CV	Range
30	35.5	11.6		34.8	6.3	
60	59.0	8.2		55.3	8.4	
120	78.0	2.8		79.6	5.7	
150	81.1	2.6		84.9	5.5	
180	83.7	2.1		85.8	5.8	
240	86.8	3.2		90.1	4.8	
F2	T vs. R		76.45			

Table 2. Dissolution of 10 mg Strength (n=12, previously submitted data)

Sampling Time, min	Test Product, Strength - 10 mg Lot No. RDW00278			Reference Product, Strength - 10 mg Lot No. 2F3013		
	Mean	%CV	Range	Mean	%CV	Range
30	29.5	5.3		30.9	5.2	
60	52.3	4.3		55.7	2.7	
120	75.3	2.6		79.7	4.1	
150	78.7	1.6		84.2	3.0	
180	81.2	2.4		88.9	1.8	
240	86.3	2.0		92.1	1.4	
F2	T vs. R		64.21			
F2	T vs. T	2.5 vs. 10 mg	68.78			
F2	R vs. R	2.5 vs. 10 mg	80.70			

2. **METHOD-2:** 500 mL 2% ———— ↻, Apparatus II (Paddle) at 100 rpm.

Table 3. Dissolution of 10 mg Strength (n=6)

Sampling Time, min	Test Product, Strength - 10 mg Lot No. RDW00278			Reference Product, Strength - 10 mg Lot No. 2F3013		
	Mean	%CV	Range	Mean	%CV	Range
15	13.7	3.8	↖ ↗	15.4	4.2	↖ ↗
30	25.6	4.0		31.4	3.5	
45	38.8	3.0		51.0	7.1	
60	49.2	2.8		60.5	1.6	
75	60.1	4.6		68.8	1.4	
90	64.0	1.7		74.2	1.4	
120	74.0	1.5		83.2	1.3	
180	81.8	2.0		88.0	1.1	
240	85.7	1.1		89.5	1.3	
F2	T vs. R	53.71		↖ ↗		

3. **METHOD-3:** 500 mL Isopropyl alcohol (IPA), Apparatus II (Paddle) at 100 rpm,

Table 4. Dissolution of 2.5 mg Strength (n=12)

Sampling Time, min	Test Product, Strength - 2.5 mg Lot No. RDW00277			Reference Product, Strength - 2.5 mg Lot No. C201546		
	Mean	%CV	Range	Mean	%CV	Range
15	13.8	23.2	↖ ↗	44.8	10.0	↖ ↗
30	30.5	18.0		72.2	6.9	
45	46.4	12.0		84.1	5.2	
60	61.0	13.1		91.1	4.7	
75	74.6	12.6		95.8	4.3	
90	87.2	12.2		99.1	2.6	
120	96.7	8.4		98.7	2.8	
180	101.6	3.2		100.9	3.1	
240	103.2	2.6		97.9	3.9	
F2	T vs. R	30.04		↖ ↗		

3. **METHOD-3 (cont'd):** 500 mL Isopropyl alcohol (IPA), Apparatus II (Paddle) at 100 rpm,

Table 5. Dissolution of 10 mg Strength (n=12)

Sampling Time, min	Test Product, Strength - 10 mg Lot No. RDW00278			Reference Product, Strength - 10 mg Lot No. 2F3013		
	Mean	%CV	Range	Mean	%CV	Range
15	8.6	23.3	L J	21.8	21.5	L J
30	16.8	21.8		42.9	8.4	
45	27.9	19.1		60.4	7.3	
60	38.0	9.7		73.1	8.1	
75	48.1	10.8		80.0	6.5	
90	56.7	7.0		83.4	6.6	
120	71.8	5.6		86.3	7.5	
180	91.9	1.9		90.9	4.4	
240	94.2	2.5		91.9	3.1	
F2	T vs. R			31.17		
F2	T vs. T	2.5 vs. 10 mg	35.18			
F2	R vs. R	2.5 vs. 10 mg	36.68			

4. **METHOD-4:** 500 mL 0.5% Sodium Lauryl Sulfate, Apparatus II (Paddle) at 100 rpm.

Table 6. Dissolution of 10 mg Strength (n=6)

Sampling Time, min	Test Product, Strength - 10 mg Lot No. RDW00278			Reference Product, Strength - 10 mg Lot No. 2F3013		
	Mean	%CV	Range	Mean	%CV	Range
15	13.4	5.8	L J	36.1	4.4	L J
30	26.6	6.1		66.1	4.2	
45	39.1	5.8		86.0	2.3	
60	50.6	5.9		91.9	2.0	
75	64.0	5.9		92.2	3.2	
90	74.8	5.2		93.4	1.0	
120	90.2	4.3		93.1	1.3	
180	96.2	1.1		93.6	1.2	
240	97.1	1.0		93.5	0.9	
F2	T vs. R	27.48				

5. **METHOD-5:** 500 mL 1% Sodium Lauryl Sulfate, Apparatus II (Paddle) at 100 rpm.

Table 7. Dissolution of 10 mg Strength (n=6)

Sampling Time, min	Test Product, Strength - 10 mg Lot No. RDW00278			Reference Product, Strength - 10 mg Lot No. 2F3013		
	Mean	%CV	Range	Mean	%CV	Range
15	17.0	32.8	7	49.4	4.0	7
30	26.2	23.7		80.3	2.2	
45	42.1	6.3		93.0	1.0	
60	53.8	5.8		95.9	0.8	
75	66.1	5.2		96.2	0.3	
90	78.0	4.3		95.9	0.4	
120	93.7	2.8		96.4	0.9	
180	91.5	1.1		103.3	1.5	
240	97.8	1.6		95.4	0.7	
F2	T vs. R	24.16				

B. Additional Attachments

Attachment-1



76897n1103.doc

Attachment-2

-----Original Message-----

From: Tran, Nhan L
Sent: Wednesday, October 06, 2004 9:48 AM
To: Shrivastava, Surendra P
Subject: Eon's Oxandrolone Tablet Dissolution

If I had a choice between the method proposed by the firm (1% Tween 80) and our recommended method (isopropyl alcohol)

If we accept the firm method, I think the following spec is appropriate: NLT (Q) in 120 minutes. They should be able to meet S1 level for all strengths with no problems.

I hope this will help you in making decision.

Thanks,

CC: ANDA 76-897
ANDA DUPLICATE
DIVISION FILE
HFD-651/ Bio Drug File
HFD-650/ SShrivastava

v:\FIRMSAM\EON\ltrs&rev\76897a0804
Printed in final on 10/5/04

Endorsements: (Final with Dates)

HFD-655/SShrivastava

SB
10/19/04

HFD-655/GJPSingh

Cross 10-19-04

HFD-650/ D. Conner

BWD 10/20/04

BIOEQUIVALENCE - INCOMPLETE

1. STUDY AMENDMENT (STA)

Submission date: 8/25/04

Strengths: 2.5 and 10 mg

Outcome: IC

WinBio Comments: Application is Incomplete.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-897

ADMINISTRATIVE DOCUMENTS

RECORD OF TELEPHONE CONVERSATION

<p>Reference is made to the firm's faxes dated June 4, and June 10, 2004 requesting clarification of deficiencies 4, 7, and 14 of the Minor Deficiency Letter dated May 24, 2004.</p>	<p>DATE: June 10, 2004</p>
<p><u>Deficiency 7:</u> The firm stated that disintegration is not a meaningful test, and that the RLD product that they tested did not meet the USP specification for disintegration. The firm also stated that they have already petitioned the USP to accept their dissolution method. The firm asked if the disintegration test is necessary if the dissolution test is acceptable by the Division of Bioequivalence. The firm also asked if they can claim in the labeling that the drug product is not USP.</p>	<p>ANDA NUMBER 76-897</p>
<p>The Agency stated that the disintegration test is a legal requirement. If the firm chooses to not meet the USP disintegration specification, the firm can chose to wait until the USP accepts and publishes the firm's recommendation. Regarding the Labeling, the firm may consult with the Labeling Branch regarding the inclusion of a statement in the Labeling that the drug product does not meet the USP requirement. Dr. Shrivastava communicated a Bioequivalency comment to the firm. He stated that the firm did not follow the FDA dissolution method. He asked the firm to develop a dissolution method and provide a comparison data and rationale for the best method.</p>	<p>TELECON INITIATED BY FIRM</p>
<p><u>Deficiency 3:</u> The firm stated that they will be correcting the mistake.</p>	<p>PRODUCT NAME: Oxandrolone Tablets USP, 2.5 mg and 10 mg</p>
<p><u>Deficiency 4:</u> The firm stated that the USP does not have a specification for melting point, but only states that the melting point should be 225°C. The melting point is stated as 235°-238°C in the Merck Index. The firm stated there is a big difference in these two references. The firm stated that the melting point differences in their submission are due to the decomposition which occurs during the melting range, which then changes the melting point. Therefore, they cannot obtain an accurate melting point. The firm stated that they can set a range, but the range cannot be as narrow as the Agency would like. The firm asked what the purpose of the melting point test is and asked if any alternative and better test would be acceptable. The firm proposed the _____ test. The firm stated that the _____ test will be in the reduced testing of the vendor validation program. The firm stated that they will test the first batch _____ will be conducted on _____ The Agency and the firm agreed that the firm will submit a justification of the decomposition, wide melting point range, and an alternate test method.</p>	<p>FIRM NAME: Eon Labs, Inc.</p>
<p><u>Deficiency 14:</u> The firm asked for clarification of this deficiency. The Agency stated that we needed to see stressed conditions to access the degradation and to make sure that there is sufficient degradation. The firm stated that they have an SOP for forced degradation studies with specified conditions. The firm stated that they will increase the sensitivity to see the impurity peaks.</p>	<p>FIRM REPRESENTATIVES Sadie Ciganek Siya Moghaddam Nitin Sheth</p>
<p>The firm's response will be submitted in their next Minor Amendment.</p>	<p>TELEPHONE NUMBER: _____</p>
	<p>FDA REPRESENTATIVES Dave Gill Bob Iser Surendra Shrivastava Sarah Park</p>
	<p>SIGNATURES: Dave Gill <i>DGill</i> Bob Iser Surendra Shrivastava Sarah Park <i>S. Park 6/14/04</i> <i>[Signature]</i> 6/14/04</p>

CC: ANDA 76-897
Division File

RECORD OF TELEPHONE CONVERSATION

Reference is made to the minor amendment dated February 11, 2005. The following deficiencies/comments were communicated to the firm.

1. The drug substance data provided does not justify the proposed specification for ~~_____~~. Please reduce the drug substance specification for ~~_____~~ to NMT ~~_____%~~. Also, please provide the revised specifications.

The firm agreed to provide the requested information.

2. The Drug Master File (~~_____~~) is currently inadequate. The DMF holder, ~~_____~~, has been notified. Please do not respond to this letter until the DMF holder has notified you that they have responded to the deficiencies.

The firm stated that they have received notification from the DMF holder in reference to the deficiencies.

3. There is concern that the proposed sample preparation change to the drug substance ~~_____~~ method, { ~~_____~~ }

~~_____~~
~~_____~~
 Please comment.

The firm agreed to not ~~_____~~. The firm stated that they will submit a revised specifications and method of the raw material. They also made a commitment that if ~~_____~~ appear as a result, proper investigation will be conducted and the Agency will be notified.

4. If the known impurities specified for the release and stability analysis of the drug product are process impurities, the specifications should not be higher than drug substance specifications. Please reduce your known impurity specifications to match your drug substance specifications. As an alternative, the process impurities can be removed from the drug product release and stability specifications if the following information is provided:

DATE

March 29, 2005

ANDA NUMBER

76-897

IND NUMBER

TELECON

INITIATED BY: FDA

PRODUCT NAME

Oxandrolone Tablet USP,
2.5 mg and 10 mg

FIRM NAME

Eon Labs, Inc.

FIRM'S REPRESENTATIVES:

Sadie Ciganek
 Siya Moghaddam
 Steve Brown
 Jeff Bauer

TELEPHONE NUMBER

~~_____~~

- a. A statement from the supplier that _____ are process impurities.
- b. Accumulated data to show that the _____ impurities do not increase over time in all stability samples and conditions.
- c. Drug product release and stability specifications revising all references to Impurities or Related Compounds to Degradation Products.
- d. Revised specifications for Individual Unknown specification to Largest Unknown Degradation Product at NMT _____.
- e. Revised specifications for the Total Impurities specification to Total Degradation products, and a revised and justified Total Degradation Product specification based on your observed data and/or analysis of the RLD at or close to expiry.
- f. Addition of a reference to the release and stability specifications that process impurities are not included in the reported total.

The firm agreed to remove the _____ from the drug product release and stability specifications and to provide the requested information. The firm stated that they will revise the impurity specifications of the Total Unknown Degradation Products to NMT _____ and the Total Degradation Products to NMT _____.

5. An LOQ of NMT _____ is not suitable for the release and stability analysis of the drug product as the limit of NMT _____, for _____ is not acceptable. Please optimize the current method to reduce the LOQ or develop another method for analysis of _____ with a suitable LOQ.

The Agency and the firm agreed that once the _____ is removed from the drug product release and stability specifications, the current LOQ will not be an issue.

**FDA
REPRESENTATIVES:**

Dave Gill
Bob Iser
Lisa Kim

CC: ANDA 76-897

Division File

V:\FIRMSAME\ON\LTRS&REV\76897tc032905.doc

RECORD OF TELEPHONE CONVERSATION

<p>The firm was asked to provide a revised copy for DS specification in conformance with USP 29 –Supplement 2, and an acknowledgement that the USP methods are the official methods.</p> <p>The firm acknowledged they will comply with the requests and send a commitment and copy of assay specifications that match the USP via miscellaneous correspondence tomorrow.</p>	<p>ANDA NUMBER 76-897</p>
	<p>DATE: 11/15/06</p>
	<p>TELECON</p>
	<p>INITIATED BY: Agency</p>
	<p>PRODUCT NAME Oxandrolone</p>
	<p>FIRM NAME Sandoz Inc.</p>
	<p>ANDA REPRESENTATIVES: Diedrich Bartel</p>
	<p>TELEPHONE NUMBER _____</p>
	<p>FDA REPRESENTATIVES: Dave Gill DSG:ll Leigh Ann Matheny <i>L Matheny</i></p>

CC: ANDA 76-897
Division File

V:\FIRMS\NZ\SANDOZ\TELECONS\76897_TC_111506.doc

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-897

CORRESPONDENCE

November 11, 2003

*505(j)(2)(A)
Noted
7 January 2004*

Mr. Gary J. Buehler, Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

**RE: Original ANDA
Oxandrolone Tablets USP, 2.5 mg and 10 mg**

Dear Mr. Buehler:

Pursuant to section 505(j) of the Federal Food, Drug and Cosmetic Act, and in accordance with the provisions of the regulations 21 CFR§314.94, enclosed is an original Abbreviated New Drug Application for Oxandrolone Tablets USP, 2.5 mg and 10 mg. This application consists of the following volumes:

- Volume 1 Basis of submission, patent and exclusivity certifications, Section 505(j)(2)(A) information, labeling, signed disclosure statement, dissolution profiles, certificates of analysis, and components and composition statements.
- Volume 2 Raw material control data, facility description; contract testing labs, manufacturing and packaging records including Executed Batch and Packaging records, and in-process information.
- Volume 3 Container/closure information, finished product controls, methods validation, stability data, debarment certification and environmental impact statement.
- Volume 4 & 5 Bioequivalence study summary and test results. (Also included is a diskette containing the raw data).

A full table of contents precedes each appropriately paginated volume.

We have also enclosed three (3) copies of the analytical methods validation package in separate volumes.

Mr. G. J. Buehler

November 11, 2003

Page 1 of 2 RECEIVED

NOV 13 2003

OGD/ODER

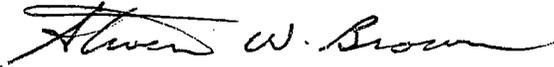
In addition to the archival and review copies, we certify that we have submitted a certified true copy of the chemistry, manufacturing and controls data to the District Field Office, Atlanta, Georgia. Subsequent amendments or supplements containing chemistry, manufacturing and controls data will also be submitted to the District Field Office.

During your review, if there are any comments or questions concerning this application, you may contact us by telephone at (252) _____ or via facsimile at (252) _____

Please advise us if you require any additional information.

Sincerely,

Eon Labs, Inc.

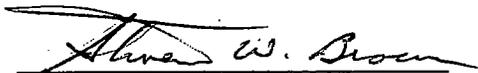


Steven W. Brown, R.Ph.
Director, Regulatory Affairs

Section III PATENT CERTIFICATION/EXCLUSIVITY

No Relevant Patents

In the opinion and to the best knowledge of Eon Labs, Inc., there are no patents that claim the listed drug referred to in this application or that claim a use of the listed drug. A copy of page ADA60 from the 23rd edition of the FDA publication Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") is enclosed on the second page following this page.

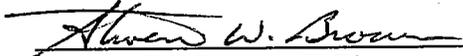


Steven W. Brown, R.Ph.
Director, Regulatory Affairs
Eon Labs, Inc.

07 November 2003
Date

Exclusivity Statement

Eon Labs, Inc., certifies that there is no effective period of marketing exclusivity associated with NDA 13-718 (Oxandrin[®] Tablets, BTG Pharmaceuticals). A copy of page ADA60 from the 23rd edition of the FDA publication Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") is enclosed on the following page.



Steven W. Brown, R.Ph.
Director, Regulatory Affairs
Eon Labs, Inc.

67 November 2003

Date

PRESCRIPTION AND OTC DRUG PRODUCT
PATENT AND EXCLUSIVITY DATA

APPL/PROD NUMBER	INGREDIENT NAME; TRADE NAME	PATENT NUMBER	PATENT EXPIRES	USE CODE	EXCLUS CODE	EXCLUS EXPIRES
020007 003	ONDANSETRON HYDROCHLORIDE; ZOFRAN PRESERVATIVE FREE	5578628	FEB 16, 2005	U-44		
020781 001	ONDANSETRON; ZOFRAN ODT	5955488	NOV 14, 2015			
		6063802	NOV 14, 2015			
		5578628	FEB 16, 2005	U-330		
		4695578	JAN 25, 2006	U-330		
		4753789	JUN 24, 2006	U-330		
020781 002	ONDANSETRON; ZOFRAN ODT	5955488	NOV 14, 2015			
		6063802	NOV 14, 2015			
		5578628	FEB 16, 2005	U-330		
		4695578	JAN 25, 2006	U-330		
		4753789	JUN 24, 2006	U-330		
020766 001	ORLISTAT; XENICAL	4598089	JUN 18, 2009		NCE	APR 23, 2004
021087 001	OSELTAMIVIR PHOSPHATE; TAMIFLU	6004996	JAN 06, 2018		NCE	OCT 27, 2004
		5763483	DEC 27, 2016		I-317	NOV 17, 2003
		5866601	FEB 02, 2016			
		5952375	FEB 02, 2016			
021246 001	OSELTAMIVIR PHOSPHATE; TAMIFLU	5763483	DEC 27, 2016	U-376	I-317	NOV 17, 2003
		5866601	FEB 02, 2016		NDF	DEC 14, 2003
		5952375	FEB 02, 2016		NCE	OCT 27, 2004
021492 001	OXALIPLATIN; ELOXATIN	5420319	APR 07, 2013		NCE	AUG 09, 2007
		5338874	APR 07, 2013			
		5290961	JAN 12, 2013			
021492 002	OXALIPLATIN; ELOXATIN	5420319	APR 07, 2013		NCE	AUG 09, 2007
		5338874	APR 07, 2013			
		5290961	JAN 12, 2013			
020776 001	OXAPROZIN POTASSIUM; DAYPRO ALTA	4620974	NOV 04, 2003		NE	OCT 17, 2005
015539 002	OXAZEPAM; SERAX	4620974	NOV 04, 2003			
015539 004	OXAZEPAM; SERAX	4620974	NOV 04, 2003			
015539 006	OXAZEPAM; SERAX	4620974	NOV 04, 2003			
021014 001	OXCARBAZEPINE; TRILEPTAL	4783337	SEP 16, 2003		NCE	JAN 14, 2005
021014 002	OXCARBAZEPINE; TRILEPTAL	5674895	MAY 22, 2015		NCE	JAN 14, 2005
021014 003	OXCARBAZEPINE; TRILEPTAL	5082668	SEP 16, 2003		NCE	JAN 14, 2005
021285 001	OXCARBAZEPINE; TRILEPTAL	5840754	MAY 22, 2015		NCE	JAN 14, 2005
020897 001	OXYBUTYNIN CHLORIDE; DITROPAN XL	4612008	SEP 16, 2003		NCE	JAN 14, 2005
		4519801	JUL 12, 2002			
		5912268	MAY 22, 2015	U-378		
		6124355	MAY 22, 2015	U-393		
		6262115	MAY 22, 2015			
		4783337	MAR 16, 2004			
		4519801	JAN 12, 2003			
		4612008	MAR 16, 2004			
		5082668	MAR 16, 2004			
		5674895	MAR 16, 2004			
		5840754	MAR 16, 2004			
		5912268	NOV 22, 2015			
		6124355	NOV 22, 2015			
		6262115	NOV 22, 2015			
		4783337	MAR 16, 2004			
		4519801	JAN 12, 2003			
		4612008	MAR 16, 2004			
		5082668	MAR 16, 2004			
		5674895	MAR 16, 2004			
		5840754	MAR 16, 2004			
		5912268	NOV 22, 2015			
		6124355	NOV 22, 2015			
		6262115	NOV 22, 2015			
		4783337	MAR 16, 2004			
		4519801	JAN 12, 2003			
		4612008	MAR 16, 2004			
		5082668	MAR 16, 2004			
		5674895	MAR 16, 2004			
		5840754	MAR 16, 2004			
		5912268	NOV 22, 2015			
		6124355	NOV 22, 2015			
		6262115	NOV 22, 2015			
		4783337	MAR 16, 2004			
		4519801	JAN 12, 2003			
		4612008	MAR 16, 2004			
		5082668	MAR 16, 2004			
		5674895	MAR 16, 2004			
		5840754	MAR 16, 2004			
		5912268	NOV 22, 2015			
		6124355	NOV 22, 2015			
		6262115	NOV 22, 2015			
		4783337	MAR 16, 2004			
		4519801	JAN 12, 2003			
		4612008	MAR 16, 2004			
		5082668	MAR 16, 2004			
		5674895	MAR 16, 2004			
		5840754	MAR 16, 2004			
		5912268	NOV 22, 2015			
		6124355	NOV 22, 2015			
		6262115	NOV 22, 2015			
		4783337	MAR 16, 2004			
		4519801	JAN 12, 2003			
		4612008	MAR 16, 2004			
		5082668	MAR 16, 2004			
		5674895	MAR 16, 2004			
		5840754	MAR 16, 2004			
		5912268	NOV 22, 2015			
		6124355	NOV 22, 2015			
		6262115	NOV 22, 2015			

NAI
Camphire
30-Dec-03

December 11, 2003

NEW CORRESP

NC

Mr. Gary J. Buehler, Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

AMENDMENT

Re: **ANDA 76-897**
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Mr. Buehler:

Reference is made to our Abbreviated New Drug Application dated November 11, 2003, submitted pursuant to section 505(j) of the Federal Food, Drug and Cosmetic Act, for Oxandrolone Tablets USP, 2.5 mg and 10 mg; ANDA 76-897.

Responsive to the telephone request of December 10, 2003, from Dr Arianne Camphire, enclosed are the four cGMP Certifications for the Analytical Testing Laboratories referenced in Section 10 of our ANDA for Oxandrolone Tablets USP, 2.5 mg and 10 mg.

A certified true copy of this amendment has been submitted to the District Field Office, Atlanta, Georgia.

Please advise us at (252) _____ if you require any additional information.

Sincerely,

Eon Labs, Inc.



Steven W. Brown, R.Ph.
Director, Regulatory Affairs

RECEIVED
DEC 12 2003
OGD/CDER

Mr. G. J. Buehler

December 11, 2003

Page 1 of 1

ANDA 76-897

Eon Labs, Inc.
Attention: Steven W. Brown
4700 Eon Drive
Wilson, NC 27893
|||||||

JAN 13 2004

Dear Sir:

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

Reference is made to the telephone conversations dated December 10, 2003 and December 11, 2003 and your correspondences dated December 11, 2003.

NAME OF DRUG: Oxandrolone Tablets USP, 2.5 mg and 10 mg

DATE OF APPLICATION: November 11, 2003

DATE (RECEIVED) ACCEPTABLE FOR FILING: November 13, 2003

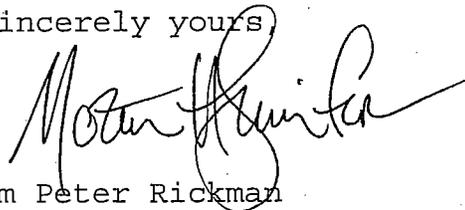
We will correspond with you further after we have had the opportunity to review the application.

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

Should you have questions concerning this application, contact:

Sarah Kim
Project Manager
(301) 827-5848

Sincerely yours,

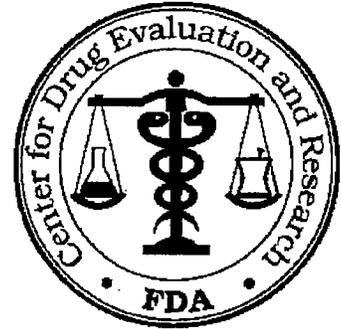


Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

MINOR AMENDMENT

ANDA 76-897

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)



MAR - 1 2004

TO: APPLICANT: Eon Labs, Inc.

TEL: _____

ATTN: Steven W. Brown

FAX: _____

FROM: Sarah Park

PROJECT MANAGER: 301-827-5725

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated November 11, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Oxandrolone Tablets USP, 2.5 mg and 10 mg.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (5 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

Chemistry comments provided. Bioequivalency and Labeling comments will be provided under separate covers.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

588

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 76-897

APPLICANT: Eon Labs, Inc.

MAR - 1 2004

DRUG PRODUCT: Oxandrolone Tablets USP, 2.5 mg and 10 mg

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. On pages 81 and 85 of the components and composition section, it is noted that the commercial batch size for the 10 mg tablet is _____ tablets; however, on page 199 and in the batch record the commercial batch size is listed as _____ tablets. Also, the amount per batch of each component on page 85 is based on a _____ tablet batch. Please clarify and make the appropriate revisions.
2. The Drug Master File _____ listed for the supplier is currently inadequate. The DMF holder, _____ has been notified. Please do not respond to this letter until the DMF holder has notified you that they have responded to the deficiencies.
3. Your specification for Identification testing of drug substance lot # WD00324 should be revised from conforms to conforms to a reference standard. Please submit your revised certificate of analysis for lot # WD00324.
4. Please establish drug substance specifications for specified, unspecified, and total impurities based on a specific method, such as HPLC, and justify the proposed acceptance criteria.
5. The drug substance specifications for Residual solvents are high. Please revise the residual solvent specifications for the drug substance based on your observed results.
6. A specification for melting point should be added for the Oxandrolone drug substance. Please add a specification for melting point for Oxandrolone drug substance and provide a revised certificate of analysis.

7. Particle size results are not included for the drug substance lot that was used in the submission batches. Please provide representative particle size results for a lot of drug substance. The specification of NLT — through a — needs to be revised to cover the entire particle size range and should provide for — particle size distribution ranges. The revised specification should be based on the drug substance used for the bio-batch.
8. Your test method, page 607, states that a USP Reference standard, Certified In-House standard or the equivalent is to be used for Oxandrolone analysis, and for the related compounds, a manufacturer's reference standard, certified in-house standard, or equivalent is to be used. It is not stated if a USP or a certified in-house standard was used for the analysis of the submission batches of Oxandrolone USP tablets, or if a manufacturer's reference standard or certified in-house standard was used for the related compounds testing. Please provide a statement of what standards were used for the analysis of the submission batches. Also, please provide the results and procedure for qualification of certified in-house Oxandrolone and related compounds standards.
9. The certificate of analysis for Magnesium Stearate lot # WS01221 used in the submission batches is not included. Please provide a certificate of analysis for Magnesium Stearate lot # WS01221.
10. The provided manufacturer's results for USP <661> and <671> container testing have dates ranging from 1995-2000. Please provide current results for USP <661> and <671> container testing.
11. It is stated on page 411, that the proposed in-process specifications for blend uniformity is — %; however, on page 604, the specification is listed as — . Please explain which blend uniformity specification is correct.

12. Samples were taken, for both strengths, during the tablet compression representative of processing extremes; and additional samples were taken at the start, middle, and end for the 10 mg bio-batch (#RDW00278). Results are not included. Please provide the results for testing at the processing extremes; and at the start, middle and end of batch RDW00278.
13. All USP tests must be included in the specification for the drug product. Please revise the drug product specification to include disintegration.
14. The drug product release and stability specifications for impurities are high. Please revise and justify the drug product release and stability specifications for impurities based on your observed results, and provide a revised certificate of analysis for the 2.5 mg and 10 mg drug product.
15. The drug product loss on drying specification should be based on the results of the bio-batch. Please provide LOD results for the bio-batch # RDW00278.
16. A reference to the chemical names for impurities should be included in the specifications for the drug product release and stability. Please revise your specifications to include a reference to chemical names for all known impurities.
17. No information is given for the comparability of the Oxandrolone USP monograph method for assay (GC) and your in-house HPLC method for assay. Please provide method comparability data for your in-house method versus the USP monograph method for assay.
18. No acceptance criteria are included in the method validation reports for any of the validation tests. Please revise your method validation reports to include a reference to the acceptance criteria for each test and a statement of whether or not the test passes the listed acceptance criteria.
19. There is no forced degradation or stress testing information included in the method validation report. Please provide forced degradation or stress testing results for the drug product method validation.

20. The stability assay specification proposed for both tablet strengths conforms to the USP specification (92.0-108.0%); however, the current stability reports reference an assay limit of _____ %. Please revise your stability reports to include an assay specification conforming to the USP specifications.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. The labeling and bioequivalence portions of your application are pending. Deficiencies, if any, will be conveyed to you under separate covers.
2. A satisfactory cGMP compliance evaluation for the firms referenced in the ANDA is required for approval. We have requested an evaluation from the Division of Manufacturing and Product Quality.
3. The assay and disintegration specifications for the bio-batch do not conform to the USP specifications. Also, a specification of "TBD" is not acceptable for impurities of the bio-batch. A regulatory specification should be established for impurities testing of the bio-batch. Please correct these specifications.
4. Please be advised that the use of in-house analytical methods for testing the drug product does not relieve you from meeting the compendial standards. In the event of a dispute, the official USP method will prevail.

5. The dissolution specification for your drug product will be established by the Division of Bioequivalence. The dissolution data for release and stability will be evaluated based on the criteria set by the Division of Bioequivalence.

Sincerely yours,

DS Gill

for Vilayat A. Sayeed, Ph.D.
Director
Division of Chemistry III
Office of Generic Drugs
Center for Drug Evaluation and Research

MINOR AMENDMENT

ANDA 76-897

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)



MAY 21 2004

TO: APPLICANT: Eon Labs, Inc.

TEL: 252-234-2224

ATTN: Steven W. Brown

FAX: 252-234-2323

FROM: Sarah Park

PROJECT MANAGER: 301-827-5725

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated November 11, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Oxandrolone Tablets USP, 2.5 mg and 10 mg.

Reference is also made to your amendment dated March 26, 2004.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (4 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

Chemistry comments provided.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

SAP

MAY 21 2004

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 76-897

APPLICANT: Eon Labs, Inc.

DRUG PRODUCT: Oxandrolone Tablets USP, 2.5 mg and 10 mg

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. Drug substance specifications were established for specified, unspecified, and total impurities but no justification of the specifications was included. Please provide a justification for your drug substance impurities specifications.
2. There is no limit of quantitation reported for the known impurity _____, in the drug substance test method; and the chemical names for the known impurities are not referenced in the drug substance specifications. Please revise your drug substance test method to include the LOQ for _____, and provide a reference to the chemical names in the drug substance specifications.
3. The results for melting point are included on page 27 of the amendment dated 26-Mar-2004. The results are _____ °C (beginning of melting) to _____ °C (melting point). The results fall outside of your specifications. Please explain the failing results for the drug substance melting point.
4. The melting point acceptance criteria that you have set for the drug substance are too wide. The range should be tighter for melting point, and the results should convey a range of melting that is typically within $\pm 2^\circ$. Please revise your melting point (range) acceptance criteria to tighten the range; and report your results as a melting range on the drug substance certificate of analysis. Also, please provide the revised certificate of analysis and specifications for the drug substance.
5. Please provide information pertaining to the Oxandrolone reference standard used in the qualification of your in-house reference standard, including lot number, comparative certificates of analysis and comparative spectra.

6. Please provide statements from DMF holders for your containers verifying that there have been no significant changes in the supplied components since the last USP <661> and <671> testing was performed.
7. Your proposed drug product release and stability limit of NMT _____ minutes for disintegration is not acceptable as it does not meet the USP monograph for this drug product. Your drug product release and stability specifications for disintegration should be revised to meet the current USP monograph. You may need to reevaluate the formulation or process for your drug product.
8. The drug product specifications were lowered for known and total impurities but no justification of the specifications was included. Also, related compounds are being reported that are below your method LOQ for impurities (Stated LOQ is _____% for known and _____% for unknown impurities). Please provide a justification for your drug product release and stability impurity specifications. Also, please explain the reporting of impurities that are below your method LOQ.
9. The Loss on drying acceptance criteria is given as NMT _____% in your response letter. The LOD acceptance criteria remains NMT _____% in the drug product release and stability specification provided. Please revise your drug product release and stability specifications to a LOD of NMT _____%, and please provide the revised documents.
10. Your response to deficiency #16 is unsatisfactory. Please revise your specifications for the release and stability of your drug product to include a reference to the chemical names for the known impurities that can be potentially observed; and please provide the revised specifications for drug product release and stability.
11. Please provide a comparison of the data for drug product assay analysis tested with the USP monograph (GC) method and your in-house _____ method. Please also include the acceptance criteria that you used to show comparability or superiority of your in-house method.

12. Acceptance criteria were not included for the drug substance residual solvents method validation report (ARMR 334). Please revise the drug substance residual solvents method validation report (ARMR 334) to include acceptance criteria.
13. There is no method validation report provided for the drug substance related substances method (O23). Please provide a method validation report for the drug substance related substances method.
14. Please provide information pertaining to the conditions used for the forced degradation studies including the following: the concentrations of the acid, base and oxidizing solutions; the light intensity utilized; the temperatures for the heat studies; and the time each sample was held in each stress condition. Also, forced degradation studies should be completed at conditions that exhibit reasonable percentages (about), of degradation. Please explain if increasing levels of the stress conditions (i.e. higher acid concentration, higher temperature, etc.) were tried until a reasonable amount of degradation was observed

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. If your comparability data shows that your in-house drug product assay method is superior to the current USP monograph method, we recommend that you petition the USP to include your method in the Oxandrolone Tablets, USP monograph.

2. Please provide all current stability results for your drug product.

Sincerely yours,

DSGill

f Vilayat A. Sayeed, Ph.D.
Director
Division of Chemistry III
Office of Generic Drugs
Center for Drug Evaluation and Research



Eon Labs

The Pharmacy Drug Company

March 26, 2004

Mr. Gary J. Buehler, Director,
Office of Generic Drugs, HFD-600
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

ORIG AMENDMENT

N/A

RE: ANDA 76-897 - MINOR AMENDMENT
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Mr. Buehler:

In accordance with 21 CFR 314.96, this submission constitutes an amendment to our ANDA for Oxandrolone Tablets USP, 2.5 mg and 10 mg (ANDA 76-897). It is being submitted in response to the letter from Dr. Vilayat A. Sayeed of the Division of Chemistry III, OGD, dated March 2, 2004. Each of the deficiencies cited in that correspondence are individually reiterated on the enclosed pages (in **bold type**) followed by our response and any supporting documents.

We certify that a true copy of the technical sections of this amendment to our ANDA for Oxandrolone Tablets USP, 2.5 mg and 10 mg has been submitted to the FDA, Atlanta District Office, 60 Eighth St. NE, Atlanta, GA 30309.

If there are any questions concerning this amendment, please contact either Mr. Steven W. Brown, R.Ph., Director, Regulatory Affairs, by telephone at (252) 234-2224, or Mr. Dietrich Bartel, B.S., Assistant Director, Regulatory Affairs, by telephone at (252) _____

Sincerely,

Eon Labs, Inc.

Steven W. Brown, R.Ph.
Director, Regulatory Affairs

RECEIVED

MAR 29 2004

OGD/CDER

SWB/jpt

Mr. G. J. Buehler

March 26, 2004

Page 1 of 1

A. Deficiencies:

1. On pages 81 and 85 of the components and composition section, it is noted that the commercial batch size for the 10 mg tablet is tablets; however, on page 199 and in the batch record the commercial batch size is listed as tablets. Also, the amount per batch of each component on page 85 is based on a tablet batch. Please clarify and make the appropriate revisions.

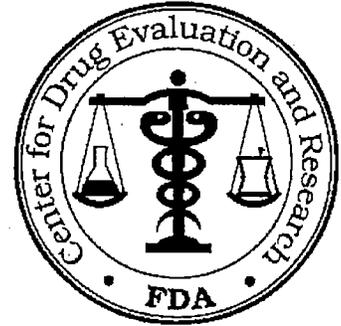
We thank you for pointing out this error. Pages 81 and 85 were revised to reflect the correct commercial batch size of tablets. The information on page 199 is correct and is based on data from the batch record on page 223. We also noticed an error on page 189, listed under the batch size column. The 10 mg strength reflects an incorrect batch size of tablets. However, the correct batch size should be tablets. The corrected pages immediately follow.

BIOEQUIVALENCY AMENDMENT

AUG 03 2004

ANDA 76-897

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)



APPLICANT: Eon Labs, Inc.

TEL: _____

ATTN: Steven W. Brown

FAX: _____

FROM: Aaron Sigler *AS*

PROJECT MANAGER: 301-827-5847

Dear Sir:

This facsimile is in reference to the bioequivalency data submitted on November 11, 2003, pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Oxandrolone Tablets USP, 2.5 mg and 10 mg.

Reference is also made to your amendment dated .

The Division of Bioequivalence has completed its review of the submission(s) referenced above and has identified deficiencies which are presented on the attached page. This facsimile is to be regarded as an official FDA communication and unless requested, a hard-copy will not be mailed.

You should submit a response to these deficiencies in accord with 21 CFR 314.96. Your amendment should respond to all the deficiencies listed. **Facsimiles or partial replies will not be considered for review**, nor will the review clock be reactivated until all deficiencies have been addressed. Your cover letter should clearly indicate that the response is a "Bioequivalency Amendment" and clearly identify any new studies (i.e., fasting, fed, multiple dose, dissolution data, waiver or dissolution waiver) that might be included for each strength. We also request that you include a copy of this communication with your response. Please submit a copy of your amendment in both an archival (blue) and a review (orange) jacket. Please direct any questions concerning this communication to the project manager identified above.

SPECIAL INSTRUCTIONS:

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

BIOEQUIVALENCE DEFICIENCIES

ANDA: 76-897

APPLICANT: Eon Labs., Inc.

DRUG PRODUCT: Oxandrolone Tablet, USP, 10 mg, 2.5 mg

The Division of Bioequivalence has completed its review of your submission(s) acknowledged on the cover sheet. The following deficiencies have been identified:

1. You have provided the long-term stability data for days. Stability data for days at °C is requested because the samples were stored for that long.
2. Please provide comparative dissolution data using the following method:

Medium: 500 mL of 30% Isopropyl alcohol
Apparatus: II (Paddle) at 100 rpm.
Sampling times: 15, 30, 45, 60, 75 and 90 minutes or until of the labeled drug is dissolved.

Sincerely yours,

sa

Barbara M. Davis

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



August 19, 2004

Mr. Gary J. Buehler, Director,
OGD, CDER, FDA HFD-600
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

ORIG AMENDMENT
N/AF

FINAL PRINTED LABELING AMENDMENT

Re: **ANDA 76-897**
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Mr. Buehler:

Reference is made to our Abbreviated New Drug Application dated November 11, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, and the provisions of the regulations 21 CFR §314.94, for Oxandrolone Tablets USP, 2.5 mg and 10 mg; ANDA 76-897.

Reference is also made to the facsimile correspondence dated April 27, 2004, from Ms. Postelle Birch, that identified specific deficiencies in the labels and labeling for the drug product.

In accordance with 21 CFR 314.96, we are submitting this amendment to our ANDA to provide responses to the cited labeling deficiencies. Each of the deficiencies is reiterated below (in **bold type**), followed by our response.

Please note:

The Final Printed Labeling in this submission is being provided **electronically** in Adobe Acrobat (*.pdf) format on the enclosed diskette in accordance with current agency requirements. In addition, the package insert labeling content, side-by-side comparison, and annotated changes are provided in both pdf, as well as MS Word (*.doc), formats.

RECEIVED

AUG 23 2004

OGD/CDER

FINAL PRINTED LABELING AMENDMENT

Labeling Deficiencies:**1. GENERAL COMMENT**

Revise the "Manufactured by:" address on all labeling to read:

**Eon Labs, Inc.
Wilson, NC 27893**

Eon Labs, Inc. labels all of its drug products in accordance with 21 CFR §201.1. Various subsections of 21 CFR 201.1 [e.g., (c)(4), (f), (g), and (j)], permit a firm to declare the company's corporate offices as the "Manufactured by:" address on drug product labeling (container and insert). For example:

- 201.1(c)(4) "For purposes of this paragraph, person, when it identifies a corporation, includes a parent, subsidiary, or affiliate company where the related companies are under common ownership and control."
- 201.1(j) "If a person manufacturers, packs, or distributes a drug or drug product at a place other than the person's principal place of business, the label may state the principal place of business in lieu of the actual place where such drug or drug product was manufactured or packed or is to be distributed, unless such statement would be misleading."

2. CONTAINER LABELS

See **GENERAL COMMENT**

Please refer to our response to deficiency 1, above.

3. INSERT

- a. Revise the chemical name of oxandrolone in the **DESCRIPTION** section to read:

17 β -hydroxy-17 α -methyl-2-oxa-5 α -androstan-3-one

- b. Using bold print, insert the following information as the first paragraph of the **PRECAUTIONS** section:

FINAL PRINTED LABELING AMENDMENT

Concurrent dosing of oxandrolone and warfarin may result in unexpectedly large increases in the INR or prothrombin time (PT). When oxandrolone is prescribed to patients being treated with warfarin, doses of warfarin may need to be decreased significantly to maintain the desirable INR level and diminish the risk of potentially serious bleeding. (See PRECAUTIONS: Drug Interactions).

- c. Insert the following information as the first paragraph of the "Information for patients" subsection of the PRECAUTIONS section:

The physician should instruct patients to report immediately any use of warfarin and any bleeding.

- d. Insert the following information as the second subsection of the PRECAUTIONS: Drug Interactions section:

Warfarin: A multidose study of oxandrolone, given as 5 or 10 mg BID in 15 healthy subjects concurrently treated with warfarin, resulted in a mean increase in S-warfarin half-life from 26 to 48 hours and similar increases in R-warfarin half-life and AUC were also detected. A 5.5-fold decrease in the mean warfarin dose from 6.13 mg/day to 1.13 mg/day (approximately 80-85% reduction of warfarin dose), was necessary to maintain a target INR of 1.5. INR or prothrombin time (PT) should be monitored closely for up to 4 weeks or until a stable INR or PT has been achieved. Monitoring of INR is recommended when the oxandrolone dose is changed or when oxandrolone is discontinued during concomitant therapy. Patients should be closely monitored for signs and symptoms of occult bleeding.

Please revise your labels and labeling, as instructed above, and submit 4 draft copies for a tentative approval or 12 final printed copies for a full approval of this application. If draft labeling is provided, please be advised that you will be required to submit 12 final printed copies of all labels and labeling at least 60 days prior to full approval of this application. In addition, you should be aware that color and other factors (print size, prominence, etc.) in final printed labeling could be found unacceptable and that further changes might be requested prior to approval.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -

FINAL PRINTED LABELING AMENDMENT

<http://www.fda.gov/cder/cdernew/listserv.html>

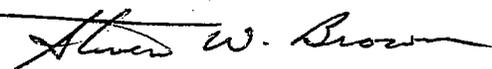
To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

The container labels and package insert labeling have been revised to include the requested changes. We have provided Final Printed container and package insert labeling, electronically in pdf format, on the enclosed diskette. In addition, a side-by-side comparison of our proposed Final Printed labeling with our last submission with all differences annotated and explained is provided. To facilitate your review, we have included MS Word versions of the content of the Final Printed package insert labeling, the side-by-side comparison, and the table of annotated differences.

If there are any questions concerning this labeling amendment, please contact either Mr. Steven W. Brown, R.Ph., Director, Regulatory Affairs, by telephone at _____, _____, or Mr. Dietrich Bartel, B.S., Assistant Director, Regulatory Affairs, by telephone at _____.

Sincerely,

Eon Labs, Inc.



Steven W. Brown, R.Ph.
Director, Regulatory Affairs

August 20, 2004

Vilayat A. Sayeed, Ph.D.
Director, HFD-630
Division of Chemistry III
Office of Generic Drugs
Center for Drug Evaluation and Research
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT
N/AM

- MINOR AMENDMENT -

**Re: Oxandrolone Tablets USP, 2.5 mg and 10 mg
ANDA 76-897**

Dear Dr. Sayeed:

Reference is made to your correspondence dated May 21, 2004 regarding our Abbreviated New Drug Application for Oxandrolone Tablets USP, 2.5 mg and 10 mg, **ANDA 76-897**. In accordance with the requirements outlined in 21 CFR 314.96, enclosed herein are our responses to the deficiencies noted in your letter.

COMMENT 1

Drug substance specifications were established for specified, unspecified, and total impurities but no justification of the specifications was included. Please provide a justification for your drug substance impurities specifications.

Response:

Eon Labs' specifications for related compounds - specified, unspecified, and total - for oxandrolone active pharmaceutical ingredient (API) were based on the established specifications of the ~~_____~~. The specifications are in accordance with the ICH guidance: Q3A-Qualification of Impurities in New Drug Substances and are listed in ~~_____~~ corresponding DMF ~~_____~~. The specifications are as follows:

_____	NMT _____
Total	NMT _____

Eon Labs, adopted the same specifications since they conform to the ICH standards and are supported by data in ~~_____~~ DMF.

RECEIVED

AUG 23 2004

OGD/CDER

COMMENT 2

There is no limit of quantitation reported for the known impurity ' _____' in the drug substance test methods; and the chemical names for the known impurities are not referenced in the drug substance specifications. Please revise your drug substance test method to include the LOQ for ' _____', and provide a reference to the chemical names in the drug substance specifications.

Response:

Upon method verification of the GC method for the determination of related compounds (manufacturer's method), it was realized that the _____ and oxandrolone peaks were not resolved. Eon Labs developed and validated an independent ' _____' method specifically for the _____ impurity. This method has an LOQ of _____%. The API monograph for oxandrolone, **O23-The Testing of Oxandrolone Raw Material**, has been amended to include the _____ procedure for testing of ' _____'. The revised monograph and corresponding validation report for the ' _____' method, **ARMR 416**, are provided, **ATTACHMENT 1**.

O23-The Testing of Oxandrolone Raw Material, has also been amended to list the chemical names of the known impurities with corresponding abbreviated nomenclature. A revised **Raw Material Specification and Analysis Report** form reflecting the abbreviated names of the known impurities is included in **ATTACHMENT 1**.

In addition to the changes noted above, **O23-The Testing of Oxandrolone Raw Material** was further changed to replace the titration assay method to HPLC to be in conformance with that used for the finished product. Accordingly, a method validation report for the quantitative determination of oxandrolone API by HPLC, **ARMR 415**, is provided, **ATTACHMENT 2**.

COMMENT 3

The results for melting point are included on page 27 of the amendment dated 26-Mar-2004. The results are _____ (beginning of melting) to _____ c (melting point). The results fail outside of your specifications. Please explain the failing results for the drug substance melting point.

Response:

The melting point test results submitted in our March 26, 2004 **MINOR AMENDMENT** were inadvertently taken from a research and development laboratory notebook generated at the initial stages of melting point method development. The data from the notebook was intended for information only in the preliminary assessment of the raw material. Therefore, the test results submitted in our amendment were not official and did not represent valid QC release data.

The melting point has now been repeated in accordance with the test criteria and procedure described in USP 27 <741> general chapter. The results meet our originally proposed specification, but exhibit a broad melting range, **ATTACHMENT 3**. A more detailed discussion regarding the melting point of oxandrolone is discussed in the following response to comment 4.

COMMENT 4

The melting point acceptance criteria that you have set for the drug substance are too wide. The range should be tighter for melting point, and the results should convey a range of melting that is typically within ± 2 . Please revise your melting point (range) acceptance criteria to tighten the range; and report your results as a melting range on the drug substance certificate of analysis. Also, please provide the revised certificate of analysis and specifications for the drug substance.

Response:

The melting point specification was discussed in the T-conference held on June 10th, 2004 between representatives from Eon Labs (Ms. Sadie Ciganek, Dr. Siya Moghaddam, and Dr. Nitin Sheth) and FDA (Dr. Dave Gill, Ms. Sarah Park, Dr. Surendra Shrivatava and Dr. Robert Iser). During that discussion, OGD indicated that the main reason for adding a melting point specification was for identification purposes and to characterize the crystalline structure of the API.

The melting point/range for oxandrolone currently published in scientific references is unclear. According to "The Merck Index", the melting point is specified as 235-238°C compared to the USP 27 which specifies "about 225°C". Even the raw material manufacturer ~~_____~~ differs from both with a very broad melting range specification of ~~_____~~. Laboratory studies performed by Eon Labs indicate that the drug substance does not have a sharp melting point and that the range observed from the start of the melt to the end is indeed very broad. Furthermore, experience shows inconsistent results from sample to sample even when tested from the same lot of API. The reason for this is unknown, but based on our studies and data from the raw material manufacturer ~~_____~~ THERMAL DECOMPOSITION of the API could be occurring upon melting.

Because of the inconsistent melting point observed for the API, we believe that a melting point specification for identification and/or crystalline structure may not be the most appropriate test method for oxandrolone. As an alternative, Eon Labs is proposing to use ~~_____~~ for identification and crystalline structure. This test is far more reliable and will serve the same purpose as the melting point. The ~~_____~~ method was developed for Eon Labs by ~~_____~~, a FDA approved contract laboratory. A study report from ~~_____~~ Laboratory Report #165648.1, which includes supporting data for the ~~_____~~ method is provided, ATTACHMENT 4.

The Raw Material Specification and Analysis Report form has been amended to replace the melting point specification with ~~_____~~ (see ATTACHMENT 1).

COMMENT 5

Please provide information pertaining to the Oxandrolone reference standard used in the qualification of your in-house reference standard, including lot number, comparative certificates of analysis and comparative spectra.

the USP disintegration specification for disintegration. The data was clearly outside the USP criteria for disintegration with results ranging from 7-10 minutes for the 10 mg dosage strength. The failing data was used in support of our petition to the USP to remove the disintegration specification from the Monograph for oxandrolone.

Pursuant to the June 10th conference call, further discussions were held with OGD regarding the same issue. During those discussions, it was agreed that Eon Labs would test and submit data from additional brand lots of Oxandrin® (Savient) to provide further evidence that commercially available product does not meet USP for disintegration. A total of 8 Oxandrin® lots (5 x 2.5 mg and 3 x 10 mg) were purchased from the open market and evaluated. Results showed that 2 out of 3 lots (10 mg) and 1 out of 5 lots (2.5 mg) did not meet the USP disintegration criteria with results ranging from up to 30 minutes. This data is tabulated and presented in the **Research Report No. 08, ATTACHMENT 9.**

Upon visual observation during the disintegration testing, it was concluded that both the Eon Labs' drug product and the Oxandrin® are "erosion" not "disintegrating" tablets. Pictures were taken during disintegration to further prove this point and are included in the **Research Report No. 08** mentioned above. The disintegration study provides strong evidence that the disintegration testing for this product is not appropriate and should be removed from the USP.

As discussed in our T-conference on June 10th, 2004 and agreed by all parties, dissolution testing is a far more valuable *in vitro* tool for measuring the release rate of solid oral dosage forms. Dissolution testing on each batch ensures that the tablet is performing in accordance with expectations and provides the assurance needed that the drug is being released in the formulation. Dissolution data for the drug product have been submitted to the Division of Bioequivalence (DOB) in a separate amendment as requested in a letter received from DOB on August 3, 2004.

Based on what we believe to be concrete evidence that the USP disintegration test for oxandrolone is inappropriate, Eon Labs is seeking approval of its ANDA while its petition is pending at the USP; or, we request that OGD to take immediate action to resolve this issue with the USP in order to clear the way for generic approvals. In lieu of the above, we are requesting that OGD take immediate action to initiate a field investigation of all Oxandrin® lots in the market place to determine if they meet the USP disintegration requirement.

COMMENT 8

The drug product specifications were lowered for known and total impurities but no justification of the specifications was included. Also, related compounds are being reported that are below your method LOQ for impurities (stated LOQ is 0.1% for known and 0.5% for unknown impurities). Please provide a justification for your drug product release and stability impurity specifications. Also, please explain the reporting of impurities that are below your method LOQ.

Response:

The specifications for the known and total related compounds in the finished product were lowered in our March 26, 2004 **MINOR AMENDMENT** to be consistent with the specifications of the raw material. Also, the reduction of impurity levels was based on data from the CRT stability study (12 month) which showed no significant increase of impurities during the time intervals tested. Because of this, Eon Labs was confident that it could lower its specifications for known and total related compounds to NMT 0.1% and 0.5%, respectively.

With regards to impurity data being reported below the LOQ, it is common practice at Eon Lab's to report an actual test result during product development testing even if that result is below the LOQ. This is done so that any trends in degradation can be more readily observed by the Analytical Research & Development Department (AR&D) during the early stages of development to correct or trouble shoot problems. Please be assured that for commercial batch manufacturing, the QC laboratory **DOES NOT** report values below the LOQ limit; they specify either "LT" or "conforms" on the official QC testing record.

COMMENT 9

The Loss on drying acceptance criteria is given as NMT _____ in your response letter. The LOD acceptance criterion remains NMT _____ % in the drug product release and stability specifications provided. Please revise your drug product release and stability specifications to a LOD of NMT _____, and please provide the revised documents.

Response:

We confirm that the LOD limit was reduced in our March 26, 2004 **MINOR AMENDMENT** to NMT _____ however, the master records were inadvertently not changed at that time. We have now amended the following master documents to reflect the revised LOD limit **ATTACHMENT 10**.

- a). **Product Monograph, O005QC**
- b). **Quality Control Finished Tablet Specification & Report Form**
- c). **Post Approval Stability Commitment**

COMMENT 10

Your response in deficiency #16 is unsatisfactory. Please revise your specifications for the release and stability of your drug product to include a reference to the chemical names for the known impurities that can be potentially observed; and please provide the revised specifications for drug product release and stability.

Response:

The **Product Monograph, O005QC, Quality Control Finished Tablet Specification & Report Form, and Post Approval Stability Commitments** have been amended to include the chemical names of the two known impurities in the finished product: _____ Only the abbreviated nomenclature is used on the specification sheets and stability protocols for simplification purposes (see **ATTACHMENT 9**). _____ was not included as a known impurity in the finished product since it is a process related impurity that is monitored in the raw material.

COMMENT 11

Please provide a comparison of the data for drug product assay analysis tested with the USP monograph (GC) methods and your in-house _____ method. Please also include the acceptance criteria that you used to show comparability or superiority of your in-house methods.

Response:

A cross over study was performed on the 9 month CRT stability samples comparing the USP GC method (packed column) with Eon Labs in-house method. Due to the problem with GC injections, it was necessary to use an internal standard for the analysis. The peaks for oxandrolone and the internal standard in the GC method were very broad. The RSD for the bracketing for the GC method was reported at _____ compared to Eon Labs _____ method of _____. Also, duplicate injections for the second assay in the USP's method differed by more than _____% from each other.

Based on this data we believe that Eon's method is more accurate and reproducible than USP's method. A side-by-side comparison of the two methods is provided for your review, ATTACHMENT 11.

COMMENT 12

Acceptance criteria were not included for the drug substance residual solvents methods validation report (ARMR 334). Please revise the drug substance residual solvents method validation report (ARMR 334) to include acceptance criteria.

Response:

The revised method validation report, ARMR 334, for residual solvents in the drug product has been amended to include acceptance criteria, ATTACHMENT 12.

COMMENT 13

There is no method validation report provided for the drug substance related substances method (C2#). Please provide a method validation report for the drug substance related substances method.

Response:

The test method used by Eon Labs for determining related compounds in the drug substance (excluding _____) was provided and validated by the API manufacturer, _____. Eon Labs has performed an "abbreviated" validation of the vendor's method which includes, linearity, LOD/LOQ, ruggedness, and recovery to ensure that the vendors method performs satisfactorily in Eon Labs QC laboratory. The "abbreviated" related compound method validation package is provided, ATTACHMENT 13.

COMMENT 14

Please provide information pertaining to the conditions used for the forced degradation studies including the following: the concentrations of the acid, base and oxidizing solutions; the light intensity utilized; the temperatures for the heat studies; and the time each sample was held in each stress condition. Also, forced degradation studies should be completed at conditions that exhibit reasonable percentages (about _____ of degradation. Please explain if increasing levels of the stress conditions (i.e. higher acid concentration, higher temperature, etc.) were tried until a reasonable amount of degradation was observed.

Response:

Eon Labs typically performs forced degradation studies for all its ANDA products exposing the raw material and finished product to acid, base, peroxide, light and extreme temperatures. According to our internal SOP, which describes the criteria for conducting forced degradation studies, recovery of the active should be between [redacted]. The information from these studies, which includes the test conditions for acid/base/peroxide concentrations, intensity of light, temperatures and exposure time are summarized in corresponding methods validation reports known as **Analytical Research Method Validation Reports (ARMRs)**.

The method validation report for oxandrolone assay, **ARMR 344**, was submitted in the original application. Although forced degradation studies were done at that time, the data was not included in **ARMR 344**. The reason for this omission was that oxandrolone does not absorb light making it difficult to detect any degradation peaks for the drug product. A [redacted] (connected to the [redacted]) was also tried during the studies to better monitor degradation peaks, but the results also did not show many peaks. It was concluded that the forced degradation studies did not provide significant information for the [redacted] method and the data was not included in the assay validation report.

The forced degradation studies were repeated in response to your comment. Sample preparation was done using a higher concentration to intensify any signals with increased levels of stress conditions (higher temperature and longer exposure) to exaggerate degradation peaks for better detection. With higher concentrations and greater stress conditions, we were able to see additional peaks and achieve a reasonable level of degradation. A forced degradation study report, **Research Report No. 07**, which summarizes this data and provides the study conditions for acid, base, temperatures, and exposure time are provided, **ATTACHMENT 14**.

In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

COMMENT 1

If your comparability data shows that your in-house drug product assay method is superior to the current USP monograph method, we recommend that you petition the USP to include your methods in the Oxandrolone Tablets, USP monograph.

Response:

We acknowledge your comment and have already petitioned the USP to adopt our assay method as an alternate USP monograph article.

COMMENT 2

Please provide all current stability results for your drug product.

Response:

Submitted herein is the most current CRT stability data ([redacted]) for Oxandrolone Tablets, USP, 2.5 mg, and 10 mg, **ATTACHMENT 15**.

We hope our responses satisfactorily address your comments. If you require further information to complete your review, do not hesitate to let me know. I can be reached at (

Very truly yours,

Eon Labs, Inc.

Sadie M. Ciganek

Sadie M. Ciganek

Vice President Regulatory Affairs

August 25, 2004

Dale P. Conner, Ph.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT
N/AB

- BIOEQUIVALENCY AMENDMENT -

**Re: Oxandrolone Tablets USP, 2.5 mg and 10 mg
ANDA 76-897**

Dear Dr. Conner:

Reference is made to your correspondence dated August 03, 2004 regarding our Abbreviated New Drug Application for Oxandrolone Tablets USP, 2.5 mg and 10 mg, ANDA 76-897. In accordance with the requirements set forth in 21 CFR 314.96, enclosed herein are our responses to the deficiencies noted in your letter.

COMMENT:

The Division of Bioequivalence has completed its review of your submission(s) acknowledged on the cover sheet. The following deficiencies have been identified:

- 1. You have provided the long-term stability data for 36 days. Stability data for 48 days at -20°C is requested because the samples were stored for that long.**

Response:

The stability of Oxandrolone in plasma with EDTA during frozen storage conditions has been documented over the course of 378 days (**ATTACHMENT A**). Control concentrations of 240 ng/mL, 24.0 ng/mL, and 2.40 ng/mL are stable when stored at -20°C ± -10°C for this period of time.

COMMENT:

- 2. Please provide comparative dissolution data using the following method:**

Medium:	500 mL of 30% Isopropyl alcohol.
Apparatus:	II (Paddle) at 100 rpm.
Sampling times:	15, 30, 45, 60, 75 and 90 minutes or until <u> </u>% of the labeled drug is dissolved.

RECEIVED

AUG 26 2004

OGD/CDER

Response:

Eon has performed the comparative dissolution studies as requested using 30% IPA as a dissolution medium. The results are shown in Tables 1 and 2 and summarized in Figure 1 in a DISSOLUTION PROFILE REPORT (**ATTACHMENT B**). The results show that the dissolution

rate of Oxandrolone from Eon's Oxandrolone Tablets is slower than that of the reference listed drug. However, both products have been shown to be bioequivalent *in vivo*.

Eon also performed additional dissolution studies (for information only) using various dissolution methods. The studies were carried out with 0.5% and 1.0% SLS, and 2 % tween 80. Information relating to other dissolution methods were requested during a T-conference on June 10th, 2004 by Dr. Surendra Shrivatava, Division of Bioequivalence. The study report which includes data from the different dissolution methods and the study conditions is provided in ATTACHMENT C.

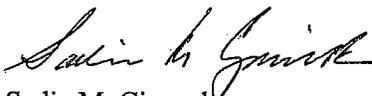
Originally,, Eon Labs developed a dissolution method using 1% tween 80 in water. This method was filed in the original ANDA and has already been reviewed. The results show that the dissolution profiles for Oxandrolone (Oxandrin®) using 1% tween 80 in water were comparable for each dose strength. Thus, it can be concluded that this dissolution test is suitable for both the brand and generic Oxandrolone Tablets. We are proposing to maintain this method for QC release of our product for the following reason:

According to the FDA Guidance for Industry: *Dissolution testing of immediate release solid oral dosage forms, August, 1997, in vitro* specifications should be established based on a dissolution profile that based on acceptable bioequivalence study. In addition, the Guidance states, "If the dissolution of the generic drug product is substantially different compared to that of the reference listed drug and the *in vivo* data remain acceptable, a different dissolution specification for the generic product may be set." Dissolution test conditions generally recommend the use of apparatus 1 and 2 with varying agitation. If needed, the addition of a surfactant may be used. The use of a hydroalcoholic medium has been generally discouraged by FDA.

Therefore, Eon Labs feels that the dissolution method using 1% tween 80 in water is the preferred method for Oxandrolone Tablets. For this reason, we have requested USP to consider and approve our dissolution method for inclusion into the monograph for Oxandrolone Tablets, USP.

We hope our responses satisfactorily address your comments. If you require further information to complete your review, do not hesitate to let me know. I can be reached at _____

Very truly yours,
Eon Labs, Inc.



Sadie M. Ciganek
Vice President Regulatory Affairs

September 2, 2004

ORIG AMENDMENT

Mr. Gary J. Buehler, Director,
OGD, CDER, FDA HFD-600
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

NIAF

FINAL PRINTED LABELING AMENDMENT

Re: **ANDA 76-897**
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Mr. Buehler:

Reference is made to our Abbreviated New Drug Application dated November 11, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, and the provisions of the regulations 21 CFR §314.94, for Oxandrolone Tablets USP, 2.5 mg and 10 mg; ANDA 76-897.

Reference is also made to the facsimile correspondence dated April 27, 2004, from Ms. Postelle Birch, that identified specific deficiencies in the labels and labeling for the drug product.

In accordance with 21 CFR 314.96, we are submitting this amendment to our ANDA to provide responses to the cited labeling deficiencies. Each of the deficiencies is reiterated below (in **bold type**), followed by our response.

Please note:

The Final Printed Labeling in this submission is being provided electronically in Adobe Acrobat (*.pdf) format on the enclosed diskette in accordance with current agency requirements. In addition, the package insert labeling content, side-by-side comparison, and annotated changes are provided in both pdf, as well as MS Word (.doc), formats.

RECEIVED

SEP 03 2004

OGD/CDER

FINAL PRINTED LABELING AMENDMENT

Labeling Deficiencies:**1. GENERAL COMMENT**

Revise the "Manufactured by:" address on all labeling to read:

**Eon Labs, Inc.
Wilson, NC 27893**

Eon Labs, Inc. labels all of its drug products in accordance with 21 CFR §201.1. Various subsections of 21 CFR 201.1 [e.g., (c)(4), (f), (g), and (j)], permit a firm to declare the company's corporate offices as the "Manufactured by:" address on drug product labeling (container and insert). For example:

- 201.1(c)(4) "For purposes of this paragraph, person, when it identifies a corporation, includes a parent, subsidiary, or affiliate company where the related companies are under common ownership and control."
- 201.1(j) "If a person manufacturers, packs, or distributes a drug or drug product at a place other than the person's principal place of business, the label may state the principal place of business in lieu of the actual place where such drug or drug product was manufactured or packed or is to be distributed, unless such statement would be misleading."

2. CONTAINER LABELS

See **GENERAL COMMENT**

Please refer to our response to deficiency 1, above.

3. INSERT

- a. Revise the chemical name of oxandrolone in the **DESCRIPTION** section to read:

17 β -hydroxy-17 α -methyl-2-oxa-5 α -androstan-3-one

- b. Using bold print, insert the following information as the first paragraph of the **PRECAUTIONS** section:

FINAL PRINTED LABELING AMENDMENT

Concurrent dosing of oxandrolone and warfarin may result in unexpectedly large increases in the INR or prothrombin time (PT). When oxandrolone is prescribed to patients being treated with warfarin, doses of warfarin may need to be decreased significantly to maintain the desirable INR level and diminish the risk of potentially serious bleeding. (See PRECAUTIONS: Drug Interactions).

- c. Insert the following information as the first paragraph of the "Information for patients" subsection of the PRECAUTIONS section:

The physician should instruct patients to report immediately any use of warfarin and any bleeding.

- d. Insert the following information as the second subsection of the PRECAUTIONS: Drug Interactions section:

Warfarin: A multidose study of oxandrolone, given as 5 or 10 mg BID in 15 healthy subjects concurrently treated with warfarin, resulted in a mean increase in S-warfarin half-life from 26 to 48 hours and similar increases in R-warfarin half-life and AUC were also detected. A 5.5-fold decrease in the mean warfarin dose from 6.13 mg/day to 1.13 mg/day (approximately 80-85% reduction of warfarin dose), was necessary to maintain a target INR of 1.5. INR or prothrombin time (PT) should be monitored closely for up to 4 weeks or until a stable INR or PT has been achieved. Monitoring of INR is recommended when the oxandrolone dose is changed or when oxandrolone is discontinued during concomitant therapy. Patients should be closely monitored for signs and symptoms of occult bleeding.

Please revise your labels and labeling, as instructed above, and submit 4 draft copies for a tentative approval or 12 final printed copies for a full approval of this application. If draft labeling is provided, please be advised that you will be required to submit 12 final printed copies of all labels and labeling at least 60 days prior to full approval of this application. In addition, you should be aware that color and other factors (print size, prominence, etc.) in final printed labeling could be found unacceptable and that further changes might be requested prior to approval.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -

FINAL PRINTED LABELING AMENDMENT

<http://www.fda.gov/cder/cdernew/listserv.html>

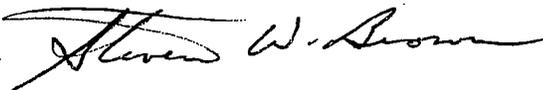
To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

The container labels and package insert labeling have been revised to include the requested changes. We have provided Final Printed container and package insert labeling, electronically in pdf format, on the enclosed diskette. In addition, a side-by-side comparison of our proposed Final Printed labeling with our last submission with all differences annotated and explained is provided. To facilitate your review, we have included MS Word versions of the content of the Final Printed package insert labeling, the side-by-side comparison, and the table of annotated differences.

If there are any questions concerning this labeling amendment, please contact either Mr. Steven W. Brown, R.Ph., Director, Regulatory Affairs, by telephone at () , or Mr. Dietrich Bartel, B.S., Assistant Director, Regulatory Affairs, by telephone at () .

Sincerely,

Eon Labs, Inc.



Steven W. Brown, R.Ph.
Director, Regulatory Affairs

BIOEQUIVALENCY AMENDMENT

ANDA 76-897

OCT 21 2004

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)



APPLICANT: Eon Labs, Inc.

TEL: _____

ATTN: Steven W. Brown

FAX: _____

FROM: Aaron Sigler *AS*

PROJECT MANAGER: 301-827-5847

Dear Sir:

This facsimile is in reference to the bioequivalency data submitted on August 25, 2004, pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Oxandrolone Tablets USP, 2.5 mg and 10 mg.

The Division of Bioequivalence has completed its review of the submission(s) referenced above and has identified deficiencies which are presented on the attached page. This facsimile is to be regarded as an official FDA communication and unless requested, a hard-copy will not be mailed.

You should submit a response to these deficiencies in accord with 21 CFR 314.96. Your amendment should respond to all the deficiencies listed. **Facsimiles or partial replies will not be considered for review**, nor will the review clock be reactivated until all deficiencies have been addressed. Your cover letter should clearly indicate that the response is a "Bioequivalency Amendment" and clearly identify any new studies (i.e., fasting, fed, multiple dose, dissolution data, waiver or dissolution waiver) that might be included for each strength. We also request that you include a copy of this communication with your response. Please submit a copy of your amendment in both an archival (blue) and a review (orange) jacket. Please direct any questions concerning this communication to the project manager identified above.

SPECIAL INSTRUCTIONS:

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

BIOEQUIVALENCE DEFICIENCIES

ANDA: 76-897

APPLICANT: Eon Labs, Inc.

DRUG PRODUCT:

Oxandrolone Tablet, USP
2.5 mg and 10 mg

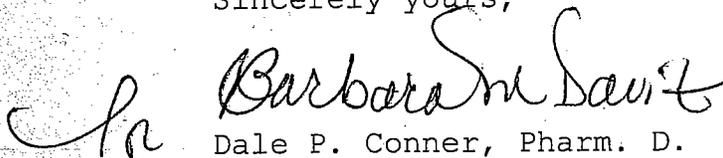
The Division of Bioequivalence has completed its review of your submission(s) acknowledged on the cover sheet. The following deficiency has been identified:

Please acknowledge your acceptance of the following dissolution method and specification.

The dissolution testing should be conducted in 500 mL of 1% Tween-80® using USP Apparatus II (Paddle) at 100 rpm. The test product should meet the following dissolution specification:

Not less than $\frac{1}{2}$ (Q) of the labeled amount of the drug in the dosage form is dissolved in 120 minutes.

Sincerely yours,



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

November 4, 2004

Mr. Gary J. Buehler, Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

ORIG AMENDMENT

N/AB

BIOEQUIVALENCY AMENDMENT

Re: **ANDA 76-897**
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Mr. Buehler:

Reference is made to our Abbreviated New Drug Application dated November 11, 2003, submitted pursuant to section 505(j) of the Federal Food, Drug and Cosmetic Act, for Oxandrolone Tablets USP, 2.5 mg and 10 mg; ANDA 76-897.

In addition, we refer to the facsimile transmission from the Division of Bioequivalence dated October 21, 2004, identifying a dissolution deficiency in the application (copy enclosed).

In response to the deficiency, we acknowledge and accept the following dissolution method and specification for Oxandrolone Tablets USP, 2.5 mg and 10 mg:

The dissolution testing will be conducted in 500 mL of 1% Tween-80[®] using USP apparatus II (paddle) at 100 rpm. The test product must meet the following dissolution specification:

Not less than $\frac{1}{2}$ (Q) of the labeled amount of the drug in the dosage form is dissolved in 120 minutes

RECEIVED

NOV 05 2004

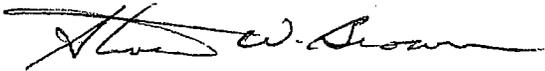
OGD / CDFR

We certify that a true copy of this Bioequivalency Amendment to our Abbreviated New Drug Application for Oxandrolone Tablets USP, 2.5 mg and 10 mg, has been sent to the Food and Drug Administration, Atlanta District Office, 60 Eighth Street NE, Atlanta, Georgia 30309.

Please advise us at _____ if you require any additional information.

Sincerely,

Eon Labs, Inc.



Steven W. Brown, R.Ph.
Director, Regulatory Affairs

MINOR AMENDMENT

ANDA 76-897

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

DEC 13 2004



TO: APPLICANT: Eon Labs, Inc.

TEL: _____

ATTN: Sadie M. Ciganek

FAX: _____

FROM: Sarah Park

PROJECT MANAGER: 301-827-5725

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated November 11, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Oxandrolone Tablets USP, 2.5 mg and 10 mg.

Reference is also made to your amendment dated August 20, 2004.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (5 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

Chemistry comments provided.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT: Minor

ANDA: 76-897

APPLICANT: Eon Labs, Inc.

DRUG PRODUCT: Oxandrolone Tablets USP, 2.5 mg and 10 mg

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. Regarding your drug substance and drug product specifications:
 - a. For your drug substance and drug product, please classify the known specified impurities as process impurities or degradation products, including the route of formation for any classified as degradation products.
 - b. For the drug substance and drug product (release and stability), please justify or qualify the proposed impurity or degradant limits based on your provided classification.
 - c. Please revise your drug substance specification for unknown impurities from NMT _____ to NMT _____.
 - d. Please clarify if the result for the _____ impurity is included in the drug substance total impurities calculation.
 - e. The location of the full chemical names for _____ and _____ in the drug substance specifications is unclear. Please clarify the location of the full chemical names in the drug substance specification.
 - f. The specification of "conforms" is not acceptable for the drug substance _____ test. Please propose suitable specifications for the drug substance _____ test. Also, please provide an explanation for the extra sample peak observed at ~ _____° in the provided _____ report.
 - g. Please label your in-house drug substance assay method as an alternate to the current USP monograph assay

test. Please also label your drug product assay test as an alternative to the USP monograph test, and provide the revised specifications.

2. Regarding your current LOQ for known and unknown drug product related compounds; please state whether the current LOQs for the method (_____, for known and _____ for unknown) can be improved. If lowering of the LOQ values is not possible, please justify the current limits.
3. Your method validation report for the determination of the _____ impurity by GC does not include a reference to the acceptance criteria used. Please provide the acceptance criteria set prior to the method validation testing.
4. In the method validation report for the determination of the _____ impurity by GC levels of recovery, the recovery results are reported ranging from _____, for the impurity. Please explain the low recovery results observed.
5. Please comment on the following observation: based on the results of the repeated forced degradation study, are changes to current sample concentrations in the method warranted to ensure observation of all potential degradation products?
6. Regarding the current stability data provided in attachment #15, please make the following revisions to your stability data sheets and provide the revised sheets.
 - a. A revision of the Loss on Drying specification to NMT _____
 - b. The reporting of numerical results for disintegration
 - c. Reporting of the individual known related compounds, with reference to the full chemical name, separately, as in the release specifications
7. Due to the light sensitivity of the drug substance, please provide photostability data for the drug product in the proposed commercial packaging configurations.

8. Please provide stability data using the dissolution acceptance criteria recommended by the Division of Bioequivalence.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comment in your response:

1. The decision regarding approval of your drug product release and stability specifications for disintegration, including the proposed acceptance criteria of NMT — minutes, is currently pending.

Sincerely yours,

DSG:ae

f Vilayat A. Sayeed, Ph.D.
Director
Division of Chemistry III
Office of Generic Drugs
Center for Drug Evaluation and Research

February 11, 2005

Vilayat A. Sayeed, Ph.D., Director
Division of Chemistry III
OGD, CDER, FDA, HFD-630
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

ORIG AMENDMENT

N/am

MINOR AMENDMENT

RE: ANDA 76-897
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Dr. Sayeed:

References is made to our Abbreviated New Drug Application dated November 11, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Oxandrolone Tablets USP, 2.5 mg and 10 mg; ANDA 76-897.

In addition, reference is made to the facsimile correspondence dated December 13, 2004, informing us that our application was deficient and, therefore, Not Approvable. That correspondence stated that we were to take an action described under 21 CFR §314.120, to either amend or withdraw the application, and that any amendment would be considered to represent a **MINOR AMENDMENT**.

Further reference is made to the teleconference of January 5th, 2005, during which many of the deficiencies outlined below were discussed in detail between the OGD project team (Dr. Gill, Dr Iser, and Ms. Park) and Eon Labs (Ms. Ciganek, Mr. Brown, Dr. Moghaddam, and Dr. Sheth).

Therefore, pursuant to 21 CFR §314.96, we are submitting this **MINOR AMENDMENT** to respond to the deficiencies cited in your letter, and as addressed per our agreement in the teleconference. Each deficiency is reiterated below **(in bold type)**, followed by our response.

RECEIVED

FEB 15 2005

V. A. Sayeed, Ph.D.

OGD / CDER

Page 1 of 6

A. Deficiencies:

1. Regarding your drug substance and drug product specifications

- a. For your drug substance and drug product, please classify the known specified impurities as process impurities or degradation products, including the route of formation for any classified as degradation products.

We have confirmed with our API manufacturer, [redacted] and through available scientific literature that the [redacted] known related compounds identified in our oxandrolone specifications are process related impurities. Information regarding these impurities was provided in [redacted] oxandrolone DMF # [redacted]. With regard to the route of formation of the degradants, there are no identified degradation impurities for oxandrolone; therefore, information relating to the route of formation is not applicable.

- b. For the drug substance and drug product (release and stability), please justify or qualify the proposed impurity or degradant limits based on your provided classification.

This comment was discussed in great detail during our teleconference on January 5th, 2005. Eon Labs was informed that the FDA is now applying the ICH criteria for qualification of impurities to generic drugs. All impurities above the ICH threshold of 0.10% must be qualified. If qualification was not possible, then the impurity limits must be reduced to a level where qualification was no longer necessary.

The impurities are well known and characterized. We performed comparison testing of the brand product versus our [redacted] for the impurities; however, the impurities did not appear in the brand at the levels proposed for our product.

Based on this testing and discussions with the API manufacturer, we have tightened the impurity specifications for [redacted] and [redacted] to [redacted]%. Accordingly, a revised **Raw Material Specification and Analysis Report** form and the analytical test method, "The testing of Oxandrolone raw material" (Method #O23), reflecting the reduced impurity specification are provided, **ATTACHMENT 1**.

- c. Please revise your drug substance specification for unknown impurities from NMT [redacted] to NMT [redacted].

We have revised the [redacted] unknown impurities specification to NMT [redacted]. **ATTACHMENT 1**.

- d. Please clarify if the result for the _____ impurity is included in the drug substance total impurities calculation.

We confirm that the result for the _____ impurity is included in the total impurities calculation.

- e. The location of the full chemical names for _____ and _____ in the drug substance specifications is unclear. Please clarify the location of the full chemical names in the drug substance specification.

We inadvertently neglected to add the full chemical names of the impurities to the analytical test method. _____ We have now revised the method to include this information (refer to test method pages 10 & 13 of 18), **ATTACHMENT 1**.

- f. The specification of "conforms" is not acceptable for the _____ test. Please propose suitable specifications for the _____ test. Also, please provide an explanation for the extra sample peak observed at _____° in the provided _____ report.

We have revised our acceptance criteria for the _____ test as shown on the **Raw Material Specification and Analysis Report** form and the analytical test method, "The testing of Oxandrolone raw material" (see **ATTACHMENT 1**), to:

"The _____ pattern of Oxandrolone standard and sample, is concordant and shows the characteristic diffraction signals at the specified 2θ values.

An explanation for the extra sample peak observed at _____° in the _____ report is enclosed, **ATTACHMENT 2**.

- g. Please label your in-house drug substance assay method as an alternate to the current USP monograph assay test. Please also label your drug product assay test as an alternative to the USP monograph test, and provide the revised specifications.

We have revised our in-house API assay method in the analytical test method, "The testing of Oxandrolone raw material" (Method #O23); and the finished product monograph, "Oxandrolone Tablets, 2.5 mg and 10 mg" (O005QC), to include appropriate language that the assay methods are alternatives to the current USP tests. Please see pages 2 of 18, and 5 of 21, in **ATTACHMENT 1** and **ATTACHMENT 3**, respectively.

2. Regarding your current LOQ for known and unknown drug product related compounds; please state whether the current LOQs for the method (____ for known and ____ for unknown) can be improved. If lowering of the LOQ values is not possible, please justify the current limits.

Eon, in consultation with _____, has reduced the specifications for the known related compounds, _____ and _____, to _____ each.

The LOQ level of _____, for _____, for _____, and _____ for unknown related compounds are justified, based on the current specifications of _____ for _____ and _____, and _____, for any unknown related compound. As discussed during the teleconference, oxandrolone has limited solubility in the diluent (the LOQ is based on the maximum concentration possible for oxandrolone), and there are significant amounts of excipients present in the dosage form (e.g., for the 2.5 mg tablet, there are _____ mg of excipients in _____ mL of the diluent). Therefore, it is not possible to reduce the LOQ value from what is currently indicated.

As we discussed in the teleconference, the known related compounds are process related impurities and are monitored in the raw material. Since the solubility of oxandrolone is greater without significant amounts of excipients present, the LOQ for _____ in the raw material method is _____%, the LOQ for _____ in the GC method is _____ and any other related compound is _____.

Because Oxandrolone is a poorly soluble drug, the LOQ of _____ for the unknown related compounds is based on the maximum possible concentration of oxandrolone in the presence of the excipients. Therefore, it is not possible to reduce the LOQ level.

3. Your method validation report for the determination of the _____ impurity by GC does not include a reference to the acceptance criteria used. Please provide the acceptance criteria set prior to the method validation testing.

The acceptance criteria set for related compound verification recovery using the GC method is _____. These specifications were set prior to this method verification for the determination of _____, by GC in the drug substance, ATTACHMENT 4.

4. In the method validation report for the determination of the _____ impurity by GC levels of recovery, the recovery results are reported ranging from _____ for the impurity. Please explain the low recovery results observed.

The results for the related compound recovery of _____ by the GC method ranged from _____ to _____. These results fall within the acceptance criteria of _____ to _____ for the recovery of the related compounds, **ATTACHMENT 4**.

5. **Please comment on the following observation: based on the results of the repeated forced degradation study, are changes to current sample concentrations in the method warranted to ensure observation of all potential degradation products?**

As per the assay, the sample concentration for the repeated forced degradation studies was _____ $\mu\text{g/mL}$; however, no significant degradation peaks were observed. In order to improve the sensitivity of the repeated forced degradation studies, it was decided to increase the sample concentration from _____ $\mu\text{g/mL}$ to _____ $\mu\text{g/mL}$, and to change the _____ sensitivity to the maximum, _____. With these modifications, more degradation peaks were observed.

As per the related compound determination method, the sample concentration is _____ $\mu\text{g/mL}$ (double the concentration used for the repeated forced degradation studies) with the _____ sensitivity set at the maximum, _____. We believe this concentration of the related compounds sample is sufficient to detect and quantify the related compounds.

6. **Regarding the current stability data provided in attachment #15, please make the following revisions to your stability data sheets and provide the revised sheets.**

- a. **A revision of the Loss on Drying specification to NMT '_____'**

Previously, we had revised the stability reports to reflect an LOD specification of NMT _____, but neglected to include them. They are now enclosed, along with revised **Post Approval Stability Commitments, ATTACHMENT 6**.

- b. **The reporting of numerical results for disintegration**

According to the USP method, there are no numeric values to report for disintegration. The numeric values submitted in our earlier response to the disintegration issue were for information only, and not for official release.

- c. **Reporting of the individual known related compounds, with reference to the full chemical name, separately, as in the release specifications**

We were not able to effectuate the requested change on the enclosed stability data sheets; because the most recent test station was mid-December 2004, at about the same time your comments issued. However, we will revise the stability reports at the next test station in June 2005.

7. Due to the light sensitivity of the drug substance, please provide photostability data for the drug product in the proposed commercial packaging configurations.

There is no evidence that oxandrolone is light sensitive, and we are unaware of any photostability issues with this drug, both in solid form and in solution. Our forced degradation studies / ~~_____~~ , do not show any degradation peaks.

Likewise, there is no evidence of degradation from our CRT stability studies where the drug product is stored in the proposed commercial container-closure system (white HDPE bottles, ~~_____~~ , and CR or Screw cap closure (which is the same packaging configuration used for the brand product).

8. Please provide stability data using the dissolution acceptance criteria recommended by the Division of Bioequivalence.

Dissolution testing was conducted on the three-month accelerated stability samples of both strengths of the drug product in both packaging configurations (100 and 1,000 count containers). The report is enclosed, **ATTACHMENT 5**.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comment in your response:

1. The decision regarding approval of your drug product release and stability specifications for disintegration, including the proposed acceptance criteria of NMT ~~_____~~ minutes, is currently pending.

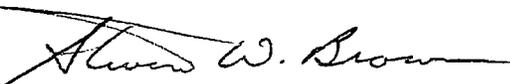
We acknowledge that a decision is pending on the approval of our drug product release and stability disintegration specification, and the proposed acceptance criteria of NMT ~~_____~~ minutes; and that discussions are currently on-going regarding the disintegration requirement for our product.

We certify that a true copy of the technical sections of this amendment to our ANDA for Oxandrolone Tablets USP, 2.5 mg and 10 mg has been submitted to the FDA Atlanta District Office, 60 Eighth St. NE, Atlanta, GA 30309.

Please advise us by telephone at (~~_____~~) , between 9:00 a.m. and 5:00 p.m., if you require any additional information.

Sincerely,

Eon Labs, Inc.



Steven W. Brown, R.Ph.
Director, Regulatory Affairs

2005-03-17 09:40
03/17/2005 08:47 FAX

Eon Labs V
EON LABS ADMINISTRATION → REG AFF LAUREL
1944-003

MAR. 16. 2005 5:24PM

FDA OGD CHEM3

NO. 499

P. 1

ANDA 76-897

MAR 17 AM 9 03



OFFICE OF GENERIC DRUGS

Food and Drug Administration
HFD-600, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Fax: 301-594-0180

FAX TRANSMISSION COVER SHEET

DATE: March 16, 2005

TO: APPLICANT: Eon Labs, Inc.

TEL: _____

ATTN: Sadie Ciganek

FAX: _____

FROM: Sarah Park

PROJECT MANAGER: 301-827-5724

TOTAL NUMBER OF PAGES : 2
(EXCLUDING COVER SHEET)

Special Instructions:

This is in reference to the telephone conference scheduled for Tuesday, March 29, 2005 at 2:00 PM EST.
Please see attached a list of topics that will be discussed during the telephone conference.

Prior to the telephone conference, please provide a list of representatives (name and title) who will be participating in the telephone conference. The list can be faxed to my attention at 301-827-9274.

Thank you,

Sarah Park

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

RECEIVED
MAR 17 2005

2005-03-17 09:09

03/17/2005 08:48 FAX

Eon labs

V

P. 3/3

EON LABS ADMINISTRATION • REG AFF LAUREL

0003/003

MAR. 16. 2005 5:24PM

FDA OGD CHEM3

NO. 499

P. 3

- e. Revised specifications for the Total Impurities specification to Total Degradation products, and a revised and justified Total Degradation Product specification based on your observed data and/or analysis of the RLD at or close to expiry.
 - f. Addition of a reference to the release and stability specifications that process impurities are not included in the reported total.
5. An LOQ of NMT is not suitable for the release and stability analysis of the drug product as the limit of NMT for is not acceptable. Please optimize the current method to reduce the LOQ or develop another method for analysis of with a suitable LOQ.

March 31, 2005

ORIG AMENDMENT

N/A/M

Vilayat A. Sayeed, Ph.D., Director
Division of Chemistry III
OGD, CDER, FDA, HFD-630
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

TELEPHONE AMENDMENT

RE: ANDA 76-897
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Dr. Sayeed:

Reference is made to our Abbreviated New Drug Application dated November 11, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Oxandrolone Tablets USP, 2.5 mg and 10 mg; ANDA 76-897.

In addition, reference is made to the facsimile correspondence of deficiencies dated March 16, 2005 (copy enclosed), informing us of topics to be discussed during the teleconference of March 29, 2005. The teleconference participants for the Office of Generic Drugs were Ms. Lisa Kim, Dr. Robert Iser, and Dr. David Gill; while, the participants for Eon Labs were Ms. Sadie M. Ciganek, Dr. Siya Moghaddam, Dr. Jeffery Bauer, and Mr. Steven W. Brown.

Pursuant to 21 CFR §314.96, we are submitting this **TELEPHONE AMENDMENT** to respond to the deficiencies cited in the facsimile of March 16, 2005, and as addressed per our agreement in the teleconference of March 29, 2005. Each of the deficiencies is reiterated below (**in bold type**), followed by our response.

- 1. The drug substance data provided does not justify the proposed specification for _____ . Please reduce the drug substance specification for _____ to NMT _____. Also, please provide the revised specifications.**

We have lowered the _____ specification acceptance criteria for _____ to NMT _____. The revised **Raw Material Specification and Analysis Report** form for Oxandrolone USP (EDP# F978) is enclosed (**Attachment 1**).

RECEIVED

APR 04 2005

OGD/CDER

TELEPHONE AMENDMENT

**ANDA 76-897
Oxandrolone Tablets USP, 2.5 mg and 10 mg**

- b. Accumulated data to show that the ~~_____~~ impurities do not increase over time in all stability samples and conditions.**

The available stability data, although somewhat limited (refer to the amendment dated February 11, 2005), indicate that the ~~_____~~ process impurities, ~~_____~~ and ~~_____~~ do not increase over time from the levels seen in the API.

- c. Drug product release and stability specifications revising all references to Impurities or Related Compounds to Degradation Products.**

We have revised the drug product release and stability specifications so that they now reference Degradation Compounds instead of Impurities or Related Compounds (**Attachments 5 & 6**).

- d. Revised specifications for Individual Unknown specification to Largest Unknown Degradation Product at NMT ~~_____~~.**

The drug product release and stability specifications now refer to an Individual Unknown Degradation Compound at NMT ~~_____~~, instead of an Individual Unknown Impurity or Related Compound (**Attachments 5 & 6**).

- e. Revised specifications for the Total Impurities specification to Total Degradation products, and a revised and justified Total Degradation Product specification based on your observed data and/or analysis of the RLD at or close to expiry.**

The drug product release and stability specifications were revised to refer to Total Degradation Compounds with an acceptance criteria of NMT ~~_____~~, as agreed during the March 29, 2005 teleconference (**Attachment 5 & 6**).

- f. Addition of a reference to the release and stability specifications that process impurities are not included in the reported total.**

We have revised the finished product monograph, which is used during drug product release and stability testing, to include a note that the acceptance criteria for Total Degradation Compounds (NMT ~~_____~~, does not include the process impurities, ~~_____~~ or ~~_____~~, (refer to page 14 of the Monograph # **O005QC** in **Attachment 7**).

TELEPHONE AMENDMENT

ANDA 76-897

Oxandrolone Tablets USP, 2.5 mg and 10 mg

5. An LOQ of NMT _____ is not suitable for the release and stability analysis of the drug product as the limit of NMT _____ for _____, is not acceptable. Please optimize the current method to reduce the LOQ or develop another method for analysis of _____ with suitable LOQ.

Based on our responses to the comments contained in item 4 (a – f), the fact that we have eliminated _____ from the drug product release and stability specifications, and as agreed during the March 29, 2005 teleconference; we believe that this comment is no longer an issue and has been rendered moot.

We are hopeful that these responses will allow the agency to make the determination that our ANDA for Oxandrolone Tablets USP, 2.5 mg and 10 mg may be approved.

We certify that a true copy of the technical sections of this Telephone Amendment to our ANDA for Oxandrolone Tablets USP, 2.5 mg and 10 mg has been submitted to the FDA Atlanta District Office, 60 Eighth St. NE, Atlanta, GA 30309.

Please advise us if you require any additional information.

Sincerely,

Eon Labs, Inc.



Steven W. Brown, R.Ph.
Director, Regulatory Affairs

PA:
State 147, 1351,
659 & 799 are
late listed.
MOU to 313.
Dunham
5/4/05

MXP

April 26, 2005

Gary J. Buehler, Director
OGD, CDER, FDA, HFD-600
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

PATENT AMENDMENT

RE: **ANDA 76-897**
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Mr. Buehler:

Reference is made to our Abbreviated New Drug Application dated November 11, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Oxandrolone Tablets USP, 2.5 mg and 10 mg; ANDA 76-897.

Additionally, reference is made to the April 22, 2005, telephone request from Mr. Martin Shimer for an amendment to address the patents that are in effect for the Reference Listed Drug (RLD), Oxandrin[®] Tablets (Savient).

Pursuant to 21 CFR §314.96, we are submitting this **PATENT AMENDMENT** to address the five patents on the RLD that are listed in the agency's electronic publication, "Approved Drug Products with Therapeutic Equivalence Evaluations" (the Electronic Orange Book [EOB]). The following patents appear in the EOB:

Patent Number	Patent Expires	Patent Code
5,872,147	December 05, 2017	U585
6,670,351	October 20, 2012	U585
6,576,659	December 05, 2017	U585
6,090,799	July 18, 2017	U585
6,828,313	December 05, 2017	U585

The first four patents (5,872,147, 6,670,351, 6,576,659, and 6,090,799) were listed late by the NDA holder, Savient, and; therefore, according to 21 CFR§314.94(a)(12)(vi), we are not required to submit an amended patent certification if the holder of the approved application for the listed drug does not submit the required information on the patent within 30 days of issuance of the patent. However, we have provided a certification for U.S. Patent Number 6,828,313

RECEIVED

APR 27 2005

OGD / CDER

PATENT AMENDMENT

ANDA 76-897

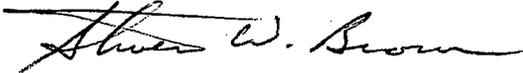
Oxandrolone Tablets USP, 2.5 mg and 10 mg

We certify that a true copy of the technical sections of this Patent Amendment to our ANDA for Oxandrolone Tablets USP, 2.5 mg and 10 mg, has been submitted to the FDA Atlanta District Office, 60 Eighth St. NE, Atlanta, GA 30309.

Please advise us if you require any additional information.

Sincerely,

Eon Labs, Inc.



Steven W. Brown, R.Ph.
Director, Regulatory Affairs

April 26, 2005

Ms. Mary H. Woleske
District Director
Atlanta District Office
Food and Drug Administration
60 Eighth Street, NE
Atlanta, GA 30309

PATENT AMENDMENT

Re: ANDA 76-897
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Ms. Woleske:

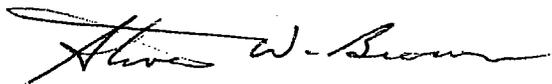
Enclosed is the Field Copy of our Patent Amendment to our ANDA for Oxandrolone Tablets USP, 2.5 mg and 10 mg. It contains all amended chemistry, manufacturing, and controls information for the manufacture of the drug product.

We certify that this is a true copy of the technical sections contained in the archival and review copies of the Patent Amendment to our ANDA for Oxandrolone Tablets USP, 2.5 mg and 10 mg, submitted to the Office of Generic Drugs.

Please advise us if you require any additional information.

Sincerely,

Eon Labs, Inc.



Steven W. Brown, R.Ph.
Director, Regulatory Affairs

**APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,
OR AN ANTIBIOTIC DRUG FOR HUMAN USE**

(Title 21, Code of Federal Regulations, 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT Eon Labs, Inc.	DATE OF SUBMISSION April 26, 2005
TELEPHONE NO. (Include Area Code) (252) 234-2222	FACSIMILE (FAX) Number (Include Area Code) (252) 234-2323
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 4700 Eon Drive Wilson, NC 27893 CFN 1062246	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued)	76-897	
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Oxandrolone Tablets	PROPRIETARY NAME (trade name) IF ANY	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) 17β-hydroxy-17α-methyl-2-oxa-5α-androstan-3-one	CODE NAME (If any)	
DOSAGE FORM: Tablet	STRENGTHS: 2.5 mg and 10 mg	ROUTE OF ADMINISTRATION: Oral

(PROPOSED) INDICATION(S) FOR USE:
Indicated as adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections, or severe trauma, and for the relief of bone pain accompanying osteoporosis.

APPLICATION INFORMATION

APPLICATION TYPE (check one) <input type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50) <input checked="" type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR Part 601)
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input type="checkbox"/> 505 (b)(1) <input type="checkbox"/> 505 (b)(2)
IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug Oxandrin® Holder of Approved Application Savient Pharmaceuticals
TYPE OF SUBMISSION (check one) <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO A PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> PRIOR APPROVAL (PA)
REASON FOR SUBMISSION Patent Amendment
PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)
NUMBER OF VOLUMES SUBMITTED One THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g., Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

See attached.

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

RECEIVED

APR 26 7 2005

OGD / CDER

Section 505(j)(2)(A)(viii) Statement

The applicant, Eon Labs, Inc., acknowledges **U.S. Patent No. 6,828,313** associated with NDA 13-718 for Oxandrin[®] Tablets (Savient Pharmaceuticals) shown in the 25th Edition of the FDA electronic publication entitled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Electronic Orange Book" [EOB]). This patent will expire on December 5, 2017.

The applicant certifies under Section 505 (j)(2)(A)(viii) of the Federal Food, Drug, and Cosmetics Act that this patent is a method of use patent, claiming methods to promote weight gain after weight loss in certain type of patients (U585 in the EOB), and that this patent does not claim any of the indications for which the applicant is seeking approval.

Steven W. Brown, R.Ph.
Director, Regulatory Affairs
Eon Labs, Inc.

Date

May 4, 2005

ORIG AMENDMENT
N/AF

Mr. Gary J. Buehler, Director,
OGD, CDER, FDA HFD-600
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

FINAL PRINTED LABELING AMENDMENT

Re: ANDA 76-897
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Mr. Buehler:

Reference is made to our Abbreviated New Drug Application dated November 11, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, and the provisions of the regulations 21 CFR §314.94, for Oxandrolone Tablets USP, 2.5 mg and 10 mg; ANDA 76-897.

In addition, reference is made to the April 22, 2005, telephone request from Mr. Martin Shimer for an amendment to address the patents that are listed in the "Electronic Orange Book" (EOB) for the Reference Listed Drug (RLD), Oxandrin[®] Tablets (Savient).

Finally, we refer to the PATENT AMENDMENT dated April 26, 2005, in which we provided a certification under Section 505(j)(2)(A)(viii) of the Federal Food, Drug, and Cosmetics Act that U.S. Patent No. 6,828,313 is a method of use patent, claiming a method to promote weight gain after weight loss in certain types of patients (U585 in the EOB), and that this patent does not claim any of the indications for which we are seeking approval.

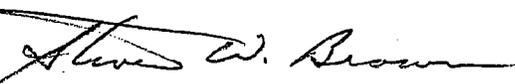
In accordance with 21 CFR 314.96, we are submitting this amendment to our ANDA to provide final printed labeling that "carves-out" the language protected by the patent.

The Final Printed Labeling and annotated side-by-side comparison are being provided electronically in Adobe Acrobat (*.pdf) format on the enclosed diskette in accordance with current agency requirements.

Please advise us if you require any additional information.

Sincerely,

Eon Labs, Inc.



Steven W. Brown, R.Ph.
Director, Regulatory Affairs

RECEIVED

MAY 05 2005

OGD / CDER

July 11, 2005

Mr. Gary J. Buehler, Director
Office of Generic Drugs
CDER, FDA, HFD-600
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

N/AF

LABELING AMENDMENT

RE: ANDA 76-897
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Mr. Buehler:

Reference is made to our Abbreviated New Drug Application dated November 11, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, and the provisions of the regulations 21 CFR§314.94, for Oxandrolone Tablets USP, 2.5 mg and 10 mg; ANDA 76-897.

Reference is also made to a telephone conversation of July 11, 2005 between Mr. Dietrich Bartel and Ms. Postelle Birch, that identified specific deficiencies in the labeling for the drug product. Changes identified are outlined in the annotations of the Package Insert Revisions.

The final printed labeling, side by side comparison and table of annotations is provided electronically on the enclosed diskette in pdf format in accordance with the new guidance to industry regarding electronic submission. In addition, product insert text is also provided in Word format.

Since this amendment contains only labeling, we are not filing this amendment to the FDA Atlanta District Office.

If there are any questions concerning this amendment, please contact me by telephone at (252) between 8:00 a.m. and 5:00 p.m., or by facsimile at (252,

Sincerely,

Eon Labs, Inc.



Dietrich Bartel, B.S.
Assistant Director, Regulatory Affairs

RECEIVED

JUL 13 2005

OGD/CDER

August 1, 2005

ORIG AMENDMENT

M/AF

Mr. Gary J. Buehler, Director
Office of Generic Drugs
CDER, FDA, HFD-600
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

LABELING AMENDMENT

RE: ANDA 76-897
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Mr. Buehler:

Reference is made to our Abbreviated New Drug Application dated November 11, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, and the provisions of the regulations 21 CFR§314.94, for Oxandrolone Tablets USP, 2.5 mg and 10 mg; ANDA 76-897.

We also make reference to the telephone communication from Ms. Postelle Birch, Division of Labeling and Program Support, OGD to Eon Labs, Inc. on July 28, 2005.

Reference is made to the following labeling changes being submitted for your review.

A. Indications and Usage

Paragraph one was edited to read: "Oxandrolone is indicated to offset the protein catabolism associated with prolonged administration of corticosteroids, and for the relief of the bone pain frequently accompanying osteoporosis (see **DOSAGE AND ADMINISTRATION**)."

B. Information for Patients

The "**Geriatric Use**:" section _____

C. Dosage and Administration

The "**Geriatric Use**" section _____

The final printed labeling, side by side comparison and table of annotations is provided electronically on the enclosed diskette in pdf format in accordance with the new guidance to industry regarding electronic submission. In addition, product insert text is also provided in Word format.

RECEIVED

AUG 03 2005

OGD / CDER

Since this amendment contains only labeling, we are not filing this amendment to the FDA Atlanta District Office.

If there are any questions concerning this amendment, please contact me by telephone at (252) _____ between 8:00 a.m. and 5:00 p.m., or by facsimile at (252) _____

Sincerely,

Eon Labs, Inc.

A handwritten signature in cursive script that reads "Dietrich Bartel".

Dietrich Bartel, B.S.
Director, Regulatory Affairs



Mass
Change for
Aug. 05
Dove

August 26, 2005

Ms. Carrie Lemley
Food and Drug Administration
Metro Park North II
7500 Standish Place
Rockville, MD 20855-2773

- GENERAL CORRESPONDENCE -

Re: CHANGE IN OWNERSHIP OF EON LABS, INC.

Dear Ms. Lemley:

Please be advised that Eon Labs, Inc. (Eon Labs) was recently acquired by Sandoz Inc. (Sandoz) in a corporate merger that closed on July 21st, 2005. Effective immediately, Eon will adopt the Sandoz name on all official correspondence to the agency and will begin operating under the Sandoz business structure.

In accordance with 21 CFR 314.72 (a), we are notifying you of the **CHANGE IN OWNERSHIP** of the corporation and are advising you that all rights, title and interest with regards to all of Eon Lab's ANDAs, approved and pending, will be transferred to Sandoz. The corporate headquarters for the new Sandoz will be 506 Carnegie Center, Suite 400, Princeton, NJ. 08540.

This is the next phase in the history of Eon Labs. We are looking forward to the coming challenges and intend to provide the agency with the same responsive interaction that was shared in the past. If you require additional information regarding the merger, feel free to call. I can be reached at (

Sincerely,
Sadie M. Ciganek

A handwritten signature in cursive script that reads "Sadie M. Ciganek".

Vice President Regulatory Affairs
Sandoz Inc.

Sandoz Inc.
227-15 N. Conduit Avenue, Laurelton, NY 11413 Phone: (718) 276-8600 Fax: (718) 276-8635



November 29, 2006

Mr. Gary J. Buehler, Director
Office of Generic Drugs
CDER, FDA, HFD-600
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

LABELING AMENDMENT - FPL

**RE: ANDA 76-897
Oxandrolone Tablets USP, 2.5 mg and 10 mg**

Dear Mr. Buehler:

Reference is made to our Abbreviated New Drug Application dated November 11, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, and the provisions of the regulations 21 CFR§314.94, for Oxandrolone Tablets USP, 2.5 mg and 10 mg; ANDA 76-897.

We also make reference to the telephone fax from Mr. Peter Rickman, OGD to Sandoz Inc. on November 29, 2006. We are submitting for review the final printed labeling for the Oxandrolone Tablets USP insert in pdf format. In addition, a side by side comparison and table of annotations is provided electronically on the enclosed CD in pdf format in accordance with the new guidance to industry regarding electronic submission.

Since this amendment contains only labeling, we are not filing this amendment to the FDA Atlanta District Office.

If there are any questions concerning this amendment, please contact Dietrich Bartel, B.S., Director, Regulatory Affairs by telephone at () between 8:00 a.m. and 5:00 p.m., or by facsimile at ()

Sincerely,

Sandoz Inc.

Deborah Goff, B.S., R.A.C.
Regulatory Affairs Associate II

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION		Form Approved: OMB No. 0910-0338 Expiration Date: September 30, 2008 See OMB Statement on page 2.	
APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE		FOR FDA USE ONLY	
<i>(Title 21, Code of Federal Regulations, 314 & 601)</i>		APPLICATION NUMBER	
APPLICANT INFORMATION			
NAME OF APPLICANT Sandoz Inc.		DATE OF SUBMISSION November 29, 2006	
TELEPHONE NO. (Include Area Code) (252) 234-2222		FACSIMILE (FAX) Number (Include Area Code) (252) 234-2323	
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 4700 Sandoz Drive Wilson, NC 27893 CFN 1062246		AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE	
PRODUCT DESCRIPTION			
NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued)			76-897
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Oxandrolone Tablets USP		PROPRIETARY NAME (trade name) IF ANY	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) 17β-hydroxy-17-methyl-2-oxa-5α-androstan-3-one			CODE NAME (If any)
DOSAGE FORM: Tablet	STRENGTHS: 2.5 mg and 10 mg	ROUTE OF ADMINISTRATION: Oral	
(PROPOSED) INDICATION(S) FOR USE: Indicated as adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections, or severe trauma, and for the relief of bone pain accompanying osteoporosis.			
APPLICATION DESCRIPTION			
APPLICATION TYPE <i>(check one)</i> <input type="checkbox"/> NEW DRUG APPLICATION (CDA, 21 CFR 314.50) <input checked="" type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)			
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input type="checkbox"/> 505 (b)(1) <input type="checkbox"/> 505 (b)(2)			
IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug Oxandrin[®] Holder of Approved Application Savient Pharmaceuticals			
TYPE OF SUBMISSION <i>(check one)</i> <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO A PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER			
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____			
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> PRIOR APPROVAL (PA)			
REASON FOR SUBMISSION Labeling Amendment – Final Printed Labeling			
PROPOSED MARKETING STATUS <i>(check one)</i> <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)			
NUMBER OF VOLUMES SUBMITTED One	THIS APPLICATION IS <input type="checkbox"/> PAPER <input checked="" type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC		
ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.) Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g., Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.			
See attached.			
Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)			
N/A			

This application contains the following items: (Check all that apply)

<input type="checkbox"/>	1. Index
<input checked="" type="checkbox"/>	2. Labeling (check one) <input type="checkbox"/> Draft Labeling <input checked="" type="checkbox"/> Final Printed Labeling
<input type="checkbox"/>	3. Summary (21 CFR 314.50(e))
<input type="checkbox"/>	4. Chemistry section
<input type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
<input type="checkbox"/>	B. Samples (21 CFR 314.50(e)(1); 21 CFR 601.2(a)) (Submit only upon FDA's request)
<input type="checkbox"/>	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
<input type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
<input type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
<input type="checkbox"/>	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
<input type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
<input type="checkbox"/>	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
<input type="checkbox"/>	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
<input type="checkbox"/>	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
<input type="checkbox"/>	12. Case report forms (e.g., 21 CFR 314.50(f)(2); 21 CFR 601.2)
<input type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (e))
<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C.355(b)(2) or (j)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input type="checkbox"/>	16. Debarment certification (FD&C Act 306(k)(1))
<input type="checkbox"/>	17. Field copy certification (21 CFR 314.50(l)(3))
<input type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input type="checkbox"/>	20. OTHER (Specify)

CERTIFICATION

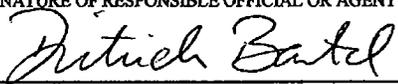
I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT 	TYPED NAME AND TITLE Dietrich Bartel, B. S. Director, Regulatory Affairs	DATE <i>29 Nov. 2006</i>
---	--	-----------------------------

ADDRESS (Street, City, State, and ZIP Code) 4700 Sandoz Drive, Wilson, NC 27893	TELEPHONE NUMBER Direct: _____
--	--

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
1401 Rockville Pike
Rockville, MD 20852-1448

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

ANDA 76-897
Oxandrolone Tablets USP, 2.5 mg and 10 mg

ESTABLISHMENT INFORMATION

Approved Site:

CFN 1062246

Sandoz Inc.
4700 Sandoz Drive
Wilson, NC 27893

Contact: Dietrich Bartel, B.S., Director, Regulatory Affairs

Telephone: _____

Facsimile: _____

Operations Performed: (1) manufacture and process drug products, and in-process materials; (2) package drug products; (3) label drug products; (4) test raw material components, drug product containers, closures, packaging materials, in-process materials, finished drug products, and stability; (5) warehousing and shipping.

The site is ready for inspection. The last inspection was February 15 to 17, 2006.

NOV 29 PM 12:53

Telephone Fax

ANDA 76-897
OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place
Rockville, MD 20855-2773
301-827-0507



TO: Sandoz, Inc.

TEL:

ATTN: Dietrich Bartel

FAX:

FROM: Wm Peter Rickman

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Oxandrolone Tablets, USP
Pages (including cover): 2

SPECIAL INSTRUCTIONS:

Labeling Comments

Per conversation, please see attached label with mark-ups.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

2 PAGES WITHHELD IN FULL

ANDA 76-897
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Oxandrolone Tablets USP, 2.5 mg and 10 mg
Insert (OS8072) – Final Printed Labeling

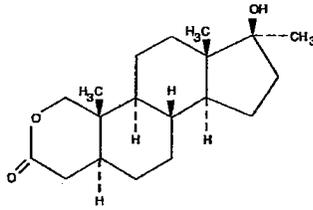
Oxandrolone Tablets USP

R_x only



DESCRIPTION

Oxandrolone oral tablets contain 2.5 mg or 10 mg of the anabolic steroid oxandrolone. Oxandrolone is 17β-hydroxy-17α-methyl-2-oxa-5α-androstan-3-one with the following structural formula:



Molecular Formula: C₁₉H₃₀O₃ Molecular Weight: 306.44

Inactive ingredients include: hypromellose, lactose monohydrate, pregelatinized starch, and magnesium stearate.

CLINICAL PHARMACOLOGY

Anabolic steroids are synthetic derivatives of testosterone. Certain clinical effects and adverse reactions demonstrate the androgenic properties of this class of drugs. Complete dissociation of anabolic and androgenic effects has not been achieved. The actions of anabolic steroids are therefore similar to those of male sex hormones with the possibility of causing serious disturbances of growth and sexual development if given to young children. Anabolic steroids suppress the gonadotropic functions of the pituitary and may exert a direct effect upon the testes.

During exogenous administration of anabolic androgens, endogenous testosterone release is inhibited through inhibition of pituitary luteinizing hormone (LH). At large doses, spermatogenesis may be suppressed through feedback inhibition of pituitary follicle-stimulating hormone (FSH).

Anabolic steroids have been reported to increase low-density lipoproteins and decrease high-density lipoproteins. These levels revert to normal on discontinuation of treatment.

INDICATIONS AND USAGE

Oxandrolone is indicated as adjunctive therapy to offset the protein catabolism associated with prolonged administration of corticosteroids, and for the relief of the bone pain frequently accompanying osteoporosis (see **DOSE AND ADMINISTRATION**).

DRUG ABUSE AND DEPENDENCE

Oxandrolone is classified as a controlled substance under the Anabolic Steroids Control Act of 1990 and has been assigned to Schedule III (non-narcotic).

CONTRAINDICATIONS

1. Known or suspected carcinoma of the prostate or the male breast.
2. Carcinoma of the breast in females with hypercalcemia (androgenic anabolic steroids may stimulate osteolytic bone resorption).
3. Pregnancy, because of possible masculinization of the fetus. Oxandrolone has been shown to cause embryotoxicity, fetotoxicity, infertility, and masculinization of female animal offspring when given in doses 9 times the human dose.
4. Nephrosis, the nephrotic phase of nephritis.
5. Hypercalcemia.

WARNINGS

PELJOSIS HEPATIS, A CONDITION IN WHICH LIVER AND SOMETIMES SPLENIC TISSUE IS REPLACED WITH BLOOD-FILLED CYSTS, HAS BEEN REPORTED IN PATIENTS RECEIVING ANDROGENIC ANABOLIC STEROID THERAPY. THESE CYSTS ARE SOMETIMES PRESENT WITH MINIMAL HEPATIC DYSFUNCTION, BUT AT OTHER TIMES THEY HAVE BEEN ASSOCIATED WITH LIVER FAILURE. THEY ARE OFTEN NOT RECOGNIZED UNTIL LIFE-THREATENING LIVER FAILURE OR INTRA-ABDOMINAL HEMORRHAGE DEVELOPS. WITHDRAWAL OF DRUG USUALLY RESULTS IN COMPLETE DISAPPEARANCE OF LESIONS.

LIVER CELL TUMORS ARE ALSO REPORTED. MOST OFTEN THESE TUMORS ARE BENIGN AND ANDROGEN-DEPENDENT, BUT FATAL MALIGNANT TUMORS HAVE BEEN REPORTED. WITHDRAWAL OF DRUG OFTEN RESULTS IN REGRESSION OR CESSATION OF PROGRESSION OF THE TUMOR. HOWEVER, HEPATIC TUMORS ASSOCIATED WITH ANDROGENS OR ANABOLIC STEROIDS ARE MUCH MORE VASCULAR THAN OTHER HEPATIC TUMORS AND MAY BE SILENT UNTIL LIFE-THREATENING INTRA-ABDOMINAL HEMORRHAGE DEVELOPS. BLOOD LIPID CHANGES THAT ARE KNOWN TO BE ASSOCIATED WITH INCREASED RISK OF ATHEROSCLEROSIS ARE SEEN IN PATIENTS TREATED WITH ANDROGENS OR ANABOLIC STEROIDS. THESE CHANGES INCLUDE DECREASED HIGH-DENSITY LIPOPROTEINS AND SOMETIMES INCREASED LOW-DENSITY LIPOPROTEINS. THE CHANGES MAY BE VERY MARKED AND COULD HAVE A SERIOUS IMPACT ON THE RISK OF ATHEROSCLEROSIS AND CORONARY ARTERY DISEASE.

Cholestatic hepatitis and jaundice may occur with 17-alpha-alkylated androgens at a relatively low dose. If cholestatic hepatitis with jaundice appears or if liver function tests become abnormal, oxandrolone should be discontinued and the etiology should be determined. Drug-induced jaundice is reversible when the medication is discontinued.

In patients with breast cancer, anabolic steroid therapy may cause hypercalcemia by stimulating osteolysis. Oxandrolone therapy should be discontinued if hypercalcemia occurs.

Edema with or without congestive heart failure may be a serious complication in patients with pre-existing cardiac, renal, or hepatic disease. Concomitant administration of adrenal cortical steroid or ACTH may increase the edema.

In children, androgen therapy may accelerate bone maturation without producing compensatory gain in linear growth. This adverse effect results in compromised adult height. The younger the child, the greater the risk of compromising final mature height. The effect on bone maturation should be monitored by assessing bone age of the left wrist and hand every 6 months (see **PRECAUTIONS, Laboratory Tests**).

Geriatric patients treated with androgenic anabolic steroids may be at an increased risk for the development of prostatic hypertrophy and prostatic carcinoma.

ANABOLIC STEROIDS HAVE NOT BEEN SHOWN TO ENHANCE ATHLETIC ABILITY.

PRECAUTIONS

Concurrent dosing of oxandrolone and warfarin may result in unexpectedly large increases in the International Normalized Ratio (INR) or prothrombin time (PT). When oxandrolone is prescribed to patients being treated with warfarin, doses of warfarin may need to be decreased significantly to maintain the desirable INR level and diminish the risk of potentially serious bleeding (See **PRECAUTIONS, Drug Interactions**).

General

Women should be observed for signs of virilization (deepening of the voice, hirsutism, acne, clitoromegaly). Discontinuation of drug therapy at the time of evidence of mild virilism is necessary to prevent irreversible virilization. Some virilizing changes in women are irreversible even after prompt discontinuance of therapy and are not prevented by concomitant use of estrogens. Menstrual irregularities may also occur.

Anabolic steroids may cause suppression of clotting factors II, V, VII, and X, and an increase in prothrombin time.

Information for Patients

The physician should instruct patients to report immediately any use of warfarin and any bleeding.

The physician should instruct patients to report any of the following side effects of androgens:

Males: Too frequent or persistent erections of the penis, appearance or aggravation of acne.

Females: Hoarseness, acne, changes in menstrual periods, or more facial hair.

All patients: Nausea, vomiting, changes in skin color, or ankle swelling.

Geriatric Use: Certain geriatric use information is protected by marketing exclusivity.

Laboratory Tests

Women with disseminated breast carcinoma should have frequent determination of urine and serum calcium levels during the course of therapy (see **WARNINGS**). Because of the hepatotoxicity associated with the use of 17-alpha-alkylated androgens, liver function tests should be obtained periodically.



0271
 Oxandrolone Tablets USP
 Rev. 12/06
 EON

Periodic (every 6 months) x-ray examinations of bone age should be made during treatment of children to determine the rate of bone maturation and the effects of androgen therapy on the epiphyseal centers.

Androgenic anabolic steroids have been reported to increase low-density lipoproteins and decrease high-density lipoproteins. Therefore, caution is required when administering these agents to patients with a history of cardiovascular disease or who are at risk for cardiovascular disease. Serum determination of lipid levels should be performed periodically and therapy adjusted accordingly. Hemoglobin and hematocrit should be checked periodically for polycythemia in patients who are receiving high doses of anabolic steroids.

Drug Interactions

Anticoagulants: Anabolic steroids may increase sensitivity to oral anticoagulants. Dosage of the anticoagulant may have to be decreased in order to maintain desired prothrombin time. Patients receiving oral anticoagulant therapy require close monitoring, especially when anabolic steroids are started or stopped.

Warfarin: A multidose study of oxandrolone, given as 5 or 10 mg BID in 15 healthy subjects concurrently treated with warfarin, resulted in a mean increase in S-warfarin half-life from 26 to 48 hours and AUC from 4.55 to 12.08 ng•hr/mL; similar increases in R-warfarin half-life and AUC were also detected. Microscopic hematuria (9/15) and gingival bleeding (1/15) were also observed. A 5.5-fold decrease in the mean warfarin dose from 6.13 mg/day to 1.13 mg/day (approximately 80-85% reduction of warfarin dose), was necessary to maintain a target INR of 1.5. When oxandrolone therapy is initiated in a patient already receiving treatment with warfarin, the INR or prothrombin time (PT) should be monitored closely and the dose of warfarin adjusted as necessary until a stable target INR or PT has been achieved.

Furthermore, in patients receiving both drugs, careful monitoring of the INR or PT, and adjustment of the warfarin dosage if indicated are recommended when the oxandrolone dose is changed or discontinued. Patients should be closely monitored for signs and symptoms of occult bleeding.

Oral Hypoglycemic Agents: Oxandrolone may inhibit the metabolism of oral hypoglycemic agents.

Adrenal Steroids or ACTH: In patients with edema, concomitant administration with adrenal cortical steroids or ACTH may increase the edema.

Drug/Laboratory Test Interactions

Anabolic steroids may decrease levels of thyroxine-binding globulin, resulting in decreased total T₄ serum levels and increased resin uptake of T₃ and T₄. Free thyroid hormone levels remain unchanged. In addition, a decrease in PBI and radioactive iodine uptake may occur.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal Data: Oxandrolone has not been tested in laboratory animals for carcinogenic or mutagenic effects. In 2-year chronic oral rat studies, a dose-related reduction of spermatogenesis and decreased organ weights (testes, prostate, seminal vesicles, ovaries, uterus, adrenals, and pituitary) were shown.

Human Data: Liver cell tumors have been reported in patients receiving long-term therapy with androgenic anabolic steroids in high doses (see **WARNINGS**). Withdrawal of the drugs did not lead to regression of the tumors in all cases.

Geriatric patients treated with androgenic anabolic steroids may be at an increased risk for the development of prostatic hypertrophy and prostatic carcinoma.

Pregnancy

Teratogenic effects: Pregnancy Category X (see **CONTRAINDICATIONS**).

Nursing Mothers

It is not known whether anabolic steroids are excreted in human milk. Because of the potential of serious adverse reactions in nursing infants from oxandrolone, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Anabolic agents may accelerate epiphyseal maturation more rapidly than linear growth in children and the effect may continue for 6 months after the drug has been stopped. Therefore, therapy should be monitored by x-ray studies at 6-month intervals in order to avoid the risk of compromising adult height. Androgenic anabolic steroid therapy should be used very cautiously in children and only by specialists who are aware of the effects on bone maturation (see **WARNINGS**).

ADVERSE REACTIONS

Patients with moderate to severe COPD or COPD patients who are unresponsive to bronchodilators should be monitored closely for COPD exacerbation and fluid retention.

The following adverse reactions have been associated with use of anabolic steroids:

Hepatic

Cholestatic jaundice with, rarely, hepatic necrosis and death. Hepatocellular neoplasms and peliosis hepatis with long-term therapy (see **WARNINGS**). Reversible changes in liver function tests also occur including increased brom-sulphthalein (BSP) retention, changes in alkaline phosphatase and increases in serum bilirubin, aspartate aminotransferase (AST, SGOT) and alanine aminotransferase (ALT, SGPT).

In Males

Prepubertal: Phallic enlargement and increased frequency or persistence of erections.

Postpubertal: Inhibition of testicular function, testicular atrophy and oligospermia, impotence, chronic priapism, epididymitis, and bladder irritability.

In Females

Clitoral enlargement, menstrual irregularities.

CNS

Habituation, excitation, insomnia, depression, and changes in libido.

Hematologic

Bleeding in patients on concomitant anticoagulant therapy.

Breast

Gynecomastia.

Larynx

Deepening of the voice in females.

Hair

Hirsutism and male pattern baldness in females.

Skin

Acne (especially in females and prepubertal males).

Skeletal

Premature closure of epiphyses in children (see **PRECAUTIONS, Pediatric Use**).

Fluid and Electrolytes

Edema, retention of serum electrolytes (sodium chloride, potassium, phosphate, calcium).

Metabolic/Endocrine

Decreased glucose tolerance (see **PRECAUTIONS, Laboratory Tests**), increased creatinine excretion, increased serum levels of creatinine phosphokinase (CPK). Masculinization of the fetus. Inhibition of gonadotropin secretion.

OVERDOSAGE

No symptoms or signs associated with overdosage have been reported. It is possible that sodium and water retention may occur.

The oral LD₅₀ of oxandrolone in mice and dogs is greater than 5,000 mg/kg. No specific antidote is known, but gastric lavage may be used.

DOSAGE AND ADMINISTRATION

Therapy with anabolic steroids is adjunctive to and not a replacement for conventional therapy. The duration of therapy with oxandrolone will depend on the response of the patient and the possible appearance of adverse reactions. Therapy should be intermittent.

Adults

The response of individuals to anabolic steroids varies. The daily adult dosage is 2.5 mg to 20 mg given in 2 to 4 divided doses. The desired response may be achieved with as little as 2.5 mg or as much as 20 mg daily. A course of therapy of 2 to 4 weeks is usually adequate. This may be repeated intermittently as indicated.

Children

For children the total daily dosage of oxandrolone is ≤ 0.1 mg per kilogram body weight or ≤ 0.045 mg per pound of body weight. This may be repeated intermittently as indicated.

HOW SUPPLIED

Oxandrolone Tablets USP are supplied as follows:

2.5 mg Tablets: white, modified oval-shaped, debossed "E 271" on one side and bisected on the reverse side.

Bottles of 100

Bottles of 1000

10 mg Tablets: white, capsule-shaped, debossed "E 272" on one side and plain on the reverse side.

Bottles of 100

Bottles of 1000

Store at 20° - 25°C (68° - 77°F) [see USP Controlled Room Temperature].

Sandoz Inc.
Princeton, NJ 08540

Rev. 12/06
MF0271REV12/06
OS8072

ANDA 76-897
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Oxandrolone Tablets USP, 2.5 mg and 10 mg
Insert (OS8072) – Redline Comparison

Document comparison done by DeltaView on Wednesday, November 29, 2006
3:00:57 PM

Document 1	file://G:/BusUnits/Regulatory Affairs/USWY/DeptData/Products/Oxandrolone/Labeling/In Process/OS8072 Rev 12-06/OS8072 Rev 11-06A Content.doc
Document 2	file://G:/BusUnits/Regulatory Affairs/USWY/DeptData/Products/Oxandrolone/Labeling/In Process/OS8072 Rev 12-06/OS8072 Rev 12-06 Content.doc
Rendering set	Standard

<u>Insertion</u>
<u>Deletion</u>
<u>Moved from</u>
<u>Moved to</u>

8 PAGES WITHHELD IN FULL

ANDA 76-897
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Oxandrolone Tablets USP, 2.5 mg and 10 mg
Insert (OS8072) – MS Word Version

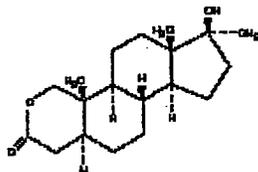
Oxandrolone Tablets USP



Rx only

DESCRIPTION

Oxandrolone oral tablets contain 2.5 mg or 10 mg of the anabolic steroid oxandrolone. Oxandrolone is 17 β -hydroxy-17 α -methyl-2-oxa-5 α -androstan-3-one with the following structural formula:



Molecular Formula: C₁₉H₃₀O₃

Molecular Weight: 306.44

Inactive ingredients include: hypromellose, lactose monohydrate, pregelatinized starch, and magnesium stearate.

CLINICAL PHARMACOLOGY

Anabolic steroids are synthetic derivatives of testosterone. Certain clinical effects and adverse reactions demonstrate the androgenic properties of this class of drugs. Complete dissociation of anabolic and androgenic effects has not been achieved. The actions of anabolic steroids are therefore similar to those of male sex hormones with the possibility of causing serious disturbances of growth and sexual development if given to young children. Anabolic steroids suppress the gonadotropic functions of the pituitary and may exert a direct effect upon the testes.

During exogenous administration of anabolic androgens, endogenous testosterone release is inhibited through inhibition of pituitary luteinizing hormone (LH). At large doses, spermatogenesis may be suppressed through feedback inhibition of pituitary follicle-stimulating hormone (FSH).

Anabolic steroids have been reported to increase low-density lipoproteins and decrease high-density lipoproteins. These levels revert to normal on discontinuation of treatment.

INDICATIONS AND USAGE

Oxandrolone is indicated as adjunctive therapy to offset the protein catabolism associated with prolonged administration of corticosteroids, and for the relief of the bone pain frequently accompanying osteoporosis (see **DOSAGE AND ADMINISTRATION**).

DRUG ABUSE AND DEPENDENCE

Oxandrolone is classified as a controlled substance under the Anabolic Steroids Control Act of 1990 and has been assigned to Schedule III (non-narcotic).

CONTRAINDICATIONS

1. Known or suspected carcinoma of the prostate or the male breast.
2. Carcinoma of the breast in females with hypercalcemia (androgenic anabolic steroids may stimulate osteolytic bone resorption).
3. Pregnancy, because of possible masculinization of the fetus. Oxandrolone has been shown to cause embryotoxicity, fetotoxicity, infertility, and masculinization of female animal offspring when given in doses 9 times the human dose.
4. Nephrosis, the nephrotic phase of nephritis.
5. Hypercalcemia.

WARNINGS

PELIOSIS HEPATIS, A CONDITION IN WHICH LIVER AND SOMETIMES SPLENIC TISSUE IS REPLACED WITH BLOOD-FILLED CYSTS, HAS BEEN REPORTED IN PATIENTS RECEIVING ANDROGENIC ANABOLIC STEROID THERAPY. THESE CYSTS ARE SOMETIMES PRESENT WITH MINIMAL HEPATIC DYSFUNCTION, BUT AT OTHER TIMES THEY HAVE BEEN ASSOCIATED WITH LIVER FAILURE. THEY ARE OFTEN NOT RECOGNIZED UNTIL LIFE-THREATENING LIVER FAILURE OR INTRA-ABDOMINAL HEMORRHAGE DEVELOPS. WITHDRAWAL OF DRUG USUALLY RESULTS IN COMPLETE DISAPPEARANCE OF LESIONS.

LIVER CELL TUMORS ARE ALSO REPORTED. MOST OFTEN THESE TUMORS ARE BENIGN AND ANDROGEN-DEPENDENT, BUT FATAL MALIGNANT TUMORS HAVE BEEN REPORTED. WITHDRAWAL OF DRUG OFTEN RESULTS IN REGRESSION OR CESSATION OF PROGRESSION OF THE TUMOR. HOWEVER, HEPATIC TUMORS ASSOCIATED WITH ANDROGENS OR ANABOLIC STEROIDS ARE MUCH MORE VASCULAR THAN OTHER HEPATIC TUMORS AND MAY BE SILENT UNTIL LIFE-THREATENING INTRA-ABDOMINAL HEMORRHAGE DEVELOPS. BLOOD LIPID CHANGES THAT ARE KNOWN TO BE ASSOCIATED WITH INCREASED RISK OF ATHEROSCLEROSIS ARE SEEN IN PATIENTS TREATED WITH ANDROGENS OR ANABOLIC STEROIDS. THESE CHANGES INCLUDE DECREASED HIGH-DENSITY LIPOPROTEINS AND SOMETIMES INCREASED LOW-DENSITY LIPOPROTEINS. THE CHANGES MAY BE VERY MARKED AND COULD HAVE A SERIOUS IMPACT ON THE RISK OF ATHEROSCLEROSIS AND CORONARY ARTERY DISEASE.

Cholestatic hepatitis and jaundice may occur with 17-alpha-alkylated androgens at a relatively low dose. If cholestatic hepatitis with jaundice appears or if liver function tests become abnormal, oxandrolone should be discontinued and the etiology should be determined. Drug-induced jaundice is reversible when the medication is discontinued.

In patients with breast cancer, anabolic steroid therapy may cause hypercalcemia by stimulating osteolysis. Oxandrolone therapy should be discontinued if hypercalcemia occurs.

Edema with or without congestive heart failure may be a serious complication in patients with pre-existing cardiac, renal, or hepatic disease. Concomitant administration of adrenal cortical steroid or ACTH may increase the edema.

In children, androgen therapy may accelerate bone maturation without producing compensatory gain in linear growth. This adverse effect results in compromised adult height. The younger the child, the greater the risk of compromising final mature height. The effect on bone maturation should be monitored by assessing bone age of the left wrist and hand every 6 months (see **PRECAUTIONS, Laboratory Tests**).

Geriatric patients treated with androgenic anabolic steroids may be at an increased risk for the development of prostatic hypertrophy and prostatic carcinoma.

ANABOLIC STEROIDS HAVE NOT BEEN SHOWN TO ENHANCE ATHLETIC ABILITY.

PRECAUTIONS

Concurrent dosing of oxandrolone and warfarin may result in unexpectedly large increases in the International Normalized Ratio (INR) or prothrombin time (PT). When oxandrolone is prescribed to patients being treated with warfarin, doses of warfarin may need to be decreased significantly to maintain the desirable INR level and diminish the risk of potentially serious bleeding (See PRECAUTIONS, Drug Interactions).

General

Women should be observed for signs of virilization (deepening of the voice, hirsutism, acne, clitoromegaly). Discontinuation of drug therapy at the time of evidence of mild virilism is necessary to prevent irreversible virilization. Some virilizing changes in women are irreversible even after prompt discontinuance of therapy and are not prevented by concomitant use of estrogens. Menstrual irregularities may also occur.

Anabolic steroids may cause suppression of clotting factors II, V, VII, and X, and an increase in prothrombin time.

Information for Patients

The physician should instruct patients to report immediately any use of warfarin and any bleeding.

The physician should instruct patients to report any of the following side effects of androgens:

Males: Too frequent or persistent erections of the penis, appearance or aggravation of acne.

Females: Hoarseness, acne, changes in menstrual periods, or more facial hair.

All patients: Nausea, vomiting, changes in skin color, or ankle swelling.

Geriatric Use:

Certain geriatric use information is protected by marketing exclusivity.

Laboratory Tests

Women with disseminated breast carcinoma should have frequent determination of urine and serum calcium levels during the course of therapy (see **WARNINGS**).

Because of the hepatotoxicity associated with the use of 17-alpha-alkylated androgens, liver function tests should be obtained periodically.

Periodic (every 6 months) x-ray examinations of bone age should be made during treatment of children to determine the rate of bone maturation and the effects of androgen therapy on the epiphyseal centers.

Androgenic anabolic steroids have been reported to increase low-density lipoproteins and decrease high-density lipoproteins. Therefore, caution is required when administering these agents to patients with a history of cardiovascular disease or who are at risk for cardiovascular disease. Serum determination of lipid levels should be performed periodically and therapy adjusted accordingly.

Hemoglobin and hematocrit should be checked periodically for polycythemia in patients who are receiving high doses of anabolic steroids.

Drug Interactions

Anticoagulants: Anabolic steroids may increase sensitivity to oral anticoagulants. Dosage of the anticoagulant may have to be decreased in order to maintain desired prothrombin time. Patients receiving oral anticoagulant therapy require close monitoring, especially when anabolic steroids are started or stopped.

Warfarin: A multidose study of oxandrolone, given as 5 or 10 mg BID in 15 healthy subjects concurrently treated with warfarin, resulted in a mean increase in S-warfarin half-life from 26 to 48 hours and AUC from 4.55 to 12.08 ng•hr/mL; similar increases in R-warfarin half-life and AUC were also detected. Microscopic

hematuria (9/15) and gingival bleeding (1/15) were also observed. A 5.5-fold decrease in the mean warfarin dose from 6.13 mg/day to 1.13 mg/day (approximately 80-85% reduction of warfarin dose), was necessary to maintain a target INR of 1.5. When oxandrolone therapy is initiated in a patient already receiving treatment with warfarin, the INR or prothrombin time (PT) should be monitored closely and the dose of warfarin adjusted as necessary until a stable target INR or PT has been achieved.

Furthermore, in patients receiving both drugs, careful monitoring of the INR or PT, and adjustment of the warfarin dosage if indicated are recommended when the oxandrolone dose is changed or discontinued. Patients should be closely monitored for signs and symptoms of occult bleeding.

Oral Hypoglycemic Agents: Oxandrolone may inhibit the metabolism of oral hypoglycemic agents.

Adrenal Steroids or ACTH: In patients with edema, concomitant administration with adrenal cortical steroids or ACTH may increase the edema.

Drug/Laboratory Test Interactions

Anabolic steroids may decrease levels of thyroxine-binding globulin, resulting in decreased total T4 serum levels and increased resin uptake of T3 and T4. Free thyroid hormone levels remain unchanged. In addition, a decrease in PBI and radioactive iodine uptake may occur.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal Data: Oxandrolone has not been tested in laboratory animals for carcinogenic or mutagenic effects. In 2-year chronic oral rat studies, a dose-related reduction of spermatogenesis and decreased organ weights (testes, prostate, seminal vesicles, ovaries, uterus, adrenals, and pituitary) were shown.

Human Data: Liver cell tumors have been reported in patients receiving long-term therapy with androgenic anabolic steroids in high doses (see **WARNINGS**). Withdrawal of the drugs did not lead to regression of the tumors in all cases. Geriatric patients treated with androgenic anabolic steroids may be at an increased risk for the development of prostatic hypertrophy and prostatic carcinoma.

Pregnancy

Teratogenic effects-Pregnancy Category X (see **CONTRAINDICATIONS**).

Nursing Mothers

It is not known whether anabolic steroids are excreted in human milk. Because of the potential of serious adverse reactions in nursing infants from oxandrolone, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Anabolic agents may accelerate epiphyseal maturation more rapidly than linear growth in children and the effect may continue for 6 months after the drug has been stopped. Therefore, therapy should be monitored by x-ray studies at 6-month intervals in order to avoid the risk of compromising adult height. Androgenic anabolic steroid therapy should be used very cautiously in children and only by specialists who are aware of the effects on bone maturation (see **WARNINGS**).

ADVERSE REACTIONS

Patients with moderate to severe COPD or COPD patients who are unresponsive to bronchodilators should be monitored closely for COPD exacerbation and fluid retention.

The following adverse reactions have been associated with use of anabolic steroids:

Hepatic

Cholestatic jaundice with, rarely, hepatic necrosis and death. Hepatocellular neoplasms and peliosis hepatis with long-term therapy (see **WARNINGS**).

Reversible changes in liver function tests also occur including increased bromsulfophthalein (BSP) retention, changes in alkaline phosphatase and increases in serum bilirubin, aspartate aminotransferase (AST, SGOT) and alanine aminotransferase (ALT, SGPT).

In Males

Prepubertal: Phallic enlargement and increased frequency or persistence of erections.

Postpubertal: Inhibition of testicular function, testicular atrophy and oligospermia, impotence, chronic priapism, epididymitis, and bladder irritability.

In Females

Clitoral enlargement, menstrual irregularities.

CNS

Habituation, excitation, insomnia, depression, and changes in libido.

Hematologic

Bleeding in patients on concomitant anticoagulant therapy.

Breast

Gynecomastia.

Larynx

Deepening of the voice in females.

Hair

Hirsutism and male pattern baldness in females.

Skin

Acne (especially in females and prepubertal males).

Skeletal

Premature closure of epiphyses in children (see **PRECAUTIONS, Pediatric Use**).

Fluid and Electrolytes

Edema, retention of serum electrolytes (sodium chloride, potassium, phosphate, calcium).

Metabolic/Endocrine

Decreased glucose tolerance (see **PRECAUTIONS, Laboratory Tests**), increased creatinine excretion, increased serum levels of creatinine phosphokinase (CPK). Masculinization of the fetus. Inhibition of gonadotropin secretion.

OVERDOSAGE

No symptoms or signs associated with overdosage have been reported. It is possible that sodium and water retention may occur.

The oral LD50 of oxandrolone in mice and dogs is greater than 5,000 mg/kg. No specific antidote is known, but gastric lavage may be used.

DOSAGE AND ADMINISTRATION

Therapy with anabolic steroids is adjunctive to and not a replacement for conventional therapy. The duration of therapy with oxandrolone will depend on the response of the patient and the possible appearance of adverse reactions. Therapy should be intermittent.

Adults

The response of individuals to anabolic steroids varies. The daily adult dosage is 2.5 mg to 20 mg given in 2 to 4 divided doses. The desired response may be achieved with as little as 2.5 mg or as much as 20 mg daily. A course of therapy of 2 to 4 weeks is usually adequate. This may be repeated intermittently as indicated.

Children

For children the total daily dosage of oxandrolone is ≤ 0.1 mg per kilogram body weight or ≤ 0.045 mg per pound of body weight. This may be repeated intermittently as indicated.

HOW SUPPLIED

Oxandrolone Tablets USP are supplied as follows:

2.5 mg Tablets: white, modified oval-shaped, debossed " E 271" on one side and bisected on the reverse side.

Bottles of 100

Bottles of 1000

10 mg Tablets: white, capsule-shaped, debossed " E 272" on one side and plain on the reverse side.

Bottles of 100

Bottles of 1000

Store at 20°-25°C (68°-77°F) [see USP Controlled Room Temperature].

Sandoz Inc.
Princeton, NJ 08540

Rev. 12/06
MF0271REV12/06
OS8072

FACSIMILE TRANSMITTAL SHEETDATE: June 10, 2004TIME: 2:00 pmTO: Ms. Sarah Parks

COMPANY:

FROM: Sadie M. Ciganek

MY FAX NUMBER: 1-718-276-8635

Re: **Oxandralone Tablets**
ANDA 76-897

Dear Sarah;

In anticipation of our scheduled conference call today at 2:00 PM, I would like to include two other topics for discussion in addition to the disintegration vs. dissolution issue previously sent to you in our June 4th fax. We hope that the team leader and someone from the Division of Bioequivalence will be present in the meeting.

The two additional items for discussion are Comment #4 (melting point) and #14 (forced degradation studies) from your May 24, 2004 deficiency letter.

I look forward to having a meeting and hope that our issues can be resolved.

Best Regards,

Sadie M. Ciganek
Vice President Regulatory Affairs

FACSIMILE TRANSMITTAL SHEET

DATE: June 4, 2004

TIME: 10:30 am

TO: Ms. Sarah Parks

COMPANY:

FROM: Sadie M. Ciganek

MY FAX NUMBER: 1-718-276-8635

Oxandrolone Tablets, USP, 2.5 mg and 10 mg
ANDA 76-897

Dear Sarah:

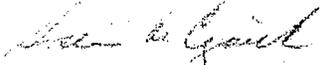
With regard to our recent phone conversation of June 4th, 2004, we are requesting a T-conference with your department to discuss the following issue:

Reference: FDA deficiency letter dated May 21, 2004. Comment #7

We need to discuss comment #7 for disintegration. We are proposing to _____

_____ since it is more appropriate for this product.

Best Regards,



Sadie M. Ciganek
Vice President Regulatory Affairs

ORIG AMENDMENT

July 21, 2005

N/S

Gary J. Buehler, RPh.
Director, HFD-600
Office of Generic Drugs
Center for Drug Evaluation & Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

**- GENERAL CORRESPONDENCE -
CHANGE IN OWNERSHIP OF EON LABS, INC.**

**Re: Oxandrolone Tablets, USP, 2.5 mg and 10 mg
ANDA 76-897**

Dear Mr. Buehler:

Eon Labs, Inc. (Eon Labs), the holder and owner of the above-referenced ANDA, was recently acquired by Sandoz Inc. (Sandoz), 506 Carnegie Center, Suite 400, Princeton, NJ, 08540 in a corporate merger that closed on July 20th, 2005. Effective immediately, Eon will adopt the Sandoz name on all official correspondence to the agency and will begin operating under the Sandoz business structure.

In accordance with **21 CFR 314.72 (a)**, we are notifying you of the **CHANGE IN OWNERSHIP** of the corporation and are advising you that all rights, title and interest with regards to our approved and pending applications will be transferred to Sandoz. The corporate headquarters for the new Sandoz will remain at the 506 Carnegie Center, Princeton, NJ address provided above.

In the new Sandoz organization, Regulatory Affairs will be coordinated from four separate locations. Each location will have a fully functional Regulatory Affairs Department headed by a Director (or equivalent) that will have responsibilities for filing ANDAs, annual reports, supplements, FPL labeling, deficiency letter responses, etc. Because of this organizational structure, there will be multiple points of interface between the new Sandoz and the agency. All four sites will report into the corporate Vice President Regulatory Affairs, Ms. Sadie M. Ciganek.

The Regulatory Affairs contact person for each site is provided below. This information will help facilitate future communication between the agency and the new Sandoz:

1) Sandoz (New York)
227-15 North Conduit Avenue,
Laurelton NY 11413

Ms. Enna Krivitsky
Ph: (718) —
Fax: (718): —

RECEIVED

AUG 01 2005

OGD / ODER

2). Sandoz (North Carolina)
4700 Eon Labs Drive
Wilson, NC 27893

Mr. Dietrich Bartel
Ph: ()
Fax:

3). Sandoz (Colorado)
2555 W Midway Blvd
Broomfield, CO 80020

Ms. Beth Brannon
Ph:
fax:

4). Sandoz (New Jersey)
2400 Route 130 North
Dayton, NJ 08810

Ms. Carmelle Lucas
Ph:
Fax:

This is the next phase in the history of Eon Labs. We are looking forward to the coming challenges and intend to provide the agency with the same responsive interaction that was shared in the past. If you require additional information regarding the merger, feel free to call. I can be reached at ()

Sincerely,
Sadie M. Ciganek

Sadie M. Ciganek for
Vice President Regulatory Affairs
Sandoz Inc.



November 6, 2006

Mr. Gary J. Buehler, Director
Office of Generic Drugs
CDER, FDA, HFD-600
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

ORIG AMENDMENT

WJAF

LABELING AMENDMENT – FINAL PRINTED LABELING

RE: **ANDA 76-897**
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Mr. Buehler:

Reference is made to our Abbreviated New Drug Application for Oxandrolone Tablets USP, 2.5 mg and 10 mg, ANDA 76-897; submitted on November 11, 2003.

Reference is also made to the FDA email dated November 3, 2006 from Ms. Postelle D. Birch-Smith, Labeling Reviewer, Office of Generic Drugs, Center for Drug Evaluation and Research. As requested, the package insert for Oxandrolone Tablets USP, 2.5 mg and 10 mg has been revised in accordance with the labeling template provided in the above referenced email.

There were no text changes required for the bottle labels previously submitted by Sandoz Inc. on September 2, 2004.

As required by the electronic labeling rule published December 11, 2003 (68 FR 69009), and the *Guidance for Industry: Providing Regulatory Submission in Electronic Format*, the Final Printed Labeling (FPL) and annotated changes are being submitted in Adobe Acrobat (*.pdf) format on the enclosed CD. In addition, the labeling content is provided in MS Word (.doc) format.

Since this amendment contains only labeling, we are not filing this labeling amendment with the FDA Atlanta District Office.

If there are any questions concerning this labeling amendment, please contact Dietrich Bartel, B.S., Director, Regulatory Affairs, by telephone at (252) _____ or by facsimile at (252) _____

Sincerely,

Sandoz Inc.

Deborah Goff
Deborah Goff, B.S., R.A.C.
Regulatory Affairs Associate II

RECEIVED
NOV 08 2006
OGD / CDER



SANDOZ

November 14, 2006

ORIGINAL

Mr. Gary J. Buehler, Director
Office of Generic Drugs
CDER, FDA, HFD-600
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

ORIG AMENDMENT

N/AF

LABELING AMENDMENT

RE: ANDA 76-897
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Mr. Buehler:

Reference is made to our Abbreviated New Drug Application dated November 11, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, and the provisions of the regulations 21 CFR§314.94, for Oxandrolone Tablets USP, 2.5 mg and 10 mg; ANDA 76-897.

We also make reference to the telephone communication from Ms. Postelle Birch, Division of Labeling and Program Support, OGD to Sandoz Inc. on November 14, 2006. Per her request, we are submitting for review the final printed labeling for Oxandrolone Tablets USP container labels in pdf format. In addition, a side by side comparison and table of annotations is provided electronically on the enclosed CD in pdf format in accordance with the new guidance to industry regarding electronic submission.

Since this amendment contains only labeling, we are not filing this amendment to the FDA Atlanta District Office.

If there are any questions concerning this amendment, please contact Dietrich Bartel, B.S., Director, Regulatory Affairs by telephone at (_____) between 8:00 a.m. and 5:00 p.m., or by facsimile at (_____)

Sincerely,

Sandoz Inc.

Deborah Goff

Deborah Goff, B.S., R.A.C.
Regulatory Affairs Associate II

RECEIVED
NOV 15 2006
OGD / CDER



ORIGINAL

November 15, 2006

Mr. Gary J. Buehler, Director
Office of Generic Drugs
CDER, FDA, HFD-600
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

ORIG AMENDMENT
N/A

LABELING AMENDMENT - FPL

RE: **ANDA 76-897**
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Mr. Buehler:

Reference is made to our Abbreviated New Drug Application dated November 11, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, and the provisions of the regulations 21 CFR§314.94, for Oxandrolone Tablets USP, 2.5 mg and 10 mg; ANDA 76-897.

We also make reference to the telephone communication from Mr. Peter Rickman, OGD to Sandoz Inc. on November 15, 2006. We are submitting for review the final printed labeling for the Oxandrolone Tablets USP insert in pdf format. In addition, a side by side comparison and table of annotations is provided electronically on the enclosed CD in pdf format in accordance with the new guidance to industry regarding electronic submission.

Since this amendment contains only labeling, we are not filing this amendment to the FDA Atlanta District Office.

If there are any questions concerning this amendment, please contact Dietrich Bartel, B.S., Director, Regulatory Affairs by telephone at _____, between 8:00 a.m. and 5:00 p.m., or by facsimile at _____.

Sincerely,

Sandoz Inc.

Deborah Goff, B.S., R.A.C.
Regulatory Affairs Associate II

RECEIVED
NOV 16 2006
OGD / CDER

Sandoz Inc.

4700 Sandoz Drive

Wilson, NC 27893



4700 Sandoz Drive
Wilson, N.C. 27893
Phone: (252) 234-2222
Fax: (252) 234-2323

Fax

To: Ms. Leigh Ann Matheny	From: Dietrich Bartel
Fax: 301-827-9274	Pages: 10
Phone: 301-827-5727	Date: 16 November 2006
Re: ANDA 76-897	CC:

Urgent For Review Please Comment Please Reply Please Recycle

Ms. Matheny,

As agreed, attached is a courtesy desk copy of the ANDA Correspondence being sent in hard copy (archive and review) to the OGD document room today by overnight courier.

Sincerely,

Dietrich Bartel

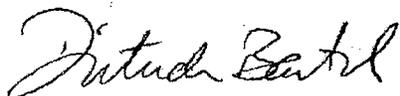
Sandoz Inc.

We certify that an exact duplicate copy of this submission has been filed to the FDA Atlanta District Office.

If there are any questions concerning this amendment, please contact Dietrich Bartel, Director, Regulatory Affairs by telephone at (_____) _____ between 8:00 a.m. and 5:00 p.m., or by facsimile at (_____) _____.

Sincerely,

Sandoz Inc.



Dietrich Bartel,
Director, Regulatory Affairs,
Sandoz Inc.



November 16, 2006

Ms. Mary H. Woleske
District Director
Atlanta District Office
Food and Drug Administration
60 Eighth Street, NE
Atlanta, GA 30309

Re: ANDA 76-897 – ANDA Correspondence
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Dear Ms. Woleske:

Enclosed is the field copy of the ANDA Correspondence to Sandoz' Abbreviated New Drug Application for Oxandrolone Tablets, USP 2.5 mg and 10 mg.

We certify that this is a true copy of the information contained in the archival and review copies of the Correspondence to our ANDA for Oxandrolone Tablets USP, 2.5 mg and 10 mg, submitted to the Office of Generic Drugs on this same date.

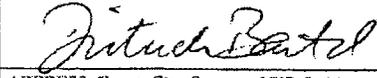
If there are any questions concerning this amendment, please contact Dietrich Bartel, Director, Regulatory Affairs, by telephone at (_____)

Sincerely,

Sandoz Inc.

Dietrich Bartel
Director, Regulatory Affairs

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE <i>(Title 21, Code of Federal Regulations, 314 & 601)</i>		Form Approved: OMB No. 0910-0338 Expiration Date: September 30, 2008 See OMB Statement on page 2.
		FOR FDA USE ONLY
		APPLICATION NUMBER
APPLICANT INFORMATION		
NAME OF APPLICANT Sandoz Inc.		DATE OF SUBMISSION November 16, 2006
TELEPHONE NO. (Include Area Code) (252) 234-2222		FACSIMILE (FAX) Number (Include Area Code) (252) 234-2323
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 4700 Sandoz Drive Wilson, NC 27893 CFN 1062246		AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE
PRODUCT DESCRIPTION		
NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (if previously issued)		76-897
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Oxandrolone Tablets USP		PROPRIETARY NAME (trade name) IF ANY
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (if any) 17β-hydroxy-17-methyl-2-oxa-5α-androstan-3-one		CODE NAME (if any)
DOSAGE FORM: Tablet	STRENGTHS: 2.5 mg and 10 mg	ROUTE OF ADMINISTRATION: Oral
(PROPOSED) INDICATION(S) FOR USE: Indicated as adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections, or severe trauma, and for the relief of bone pain accompanying osteoporosis.		
APPLICATION DESCRIPTION		
APPLICATION TYPE (check one) <input type="checkbox"/> NEW DRUG APPLICATION (CDA, 21 CFR 314.50) <input checked="" type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)		
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input type="checkbox"/> 505 (b)(1) <input type="checkbox"/> 505 (b)(2)		
IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug Oxandrin[®] Holder of Approved Application Savient Pharmaceuticals		
TYPE OF SUBMISSION (check one) <input type="checkbox"/> ORIGINAL APPLICATION <input type="checkbox"/> AMENDMENT TO A PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input checked="" type="checkbox"/> OTHER		
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____		
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> PRIOR APPROVAL (PA)		
REASON FOR SUBMISSION ANDA Correspondence		
PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)		
NUMBER OF VOLUMES SUBMITTED One	THIS APPLICATION IS <input type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC	
ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.) Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMP number, and manufacturing steps and/or type of testing (e.g., Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.		
See attached.		
Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)		
N/A		

This application contains the following items: <i>(Check all that apply)</i>		
<input type="checkbox"/>	1. Index	
<input checked="" type="checkbox"/>	2. Labeling <i>(check one)</i> <input type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling	
<input type="checkbox"/>	3. Summary (21 CFR 314.50(c))	
<input checked="" type="checkbox"/>	4. Chemistry section	
<input type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)	
<input type="checkbox"/>	B. Samples (21 CFR 314.50(e)(1); 21 CFR 601.2(a)) (Submit only upon FDA's request)	
<input type="checkbox"/>	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)	
<input type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)	
<input type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)	
<input type="checkbox"/>	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))	
<input type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)	
<input type="checkbox"/>	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)	
<input type="checkbox"/>	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)	
<input type="checkbox"/>	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)	
<input type="checkbox"/>	12. Case report forms (e.g., 21 CFR 314.50(f)(2); 21 CFR 601.2)	
<input type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))	
<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C.355(b)(2) or (j)(2)(A))	
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)	
<input type="checkbox"/>	16. Debarment certification (FD&C Act 306(k)(1))	
<input checked="" type="checkbox"/>	17. Field copy certification (21 CFR 314.50(l)(3))	
<input type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)	
<input type="checkbox"/>	19. Financial information (21 CFR Part 54)	
<input type="checkbox"/>	20. OTHER <i>(Specify)</i>	
CERTIFICATION		
<p>I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:</p> <ol style="list-style-type: none"> 1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820. 2. Biological establishment standards in 21 CFR Part 600. 3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660 and/or 809. 4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202. 5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12. 6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81. 7. Local, state and Federal environmental impact laws. <p>If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.</p> <p>The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.</p> <p>Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.</p>		
SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
	Dietrich Bartel, B. S. Director, Regulatory Affairs	16 Nov. 2006
ADDRESS <i>(Street, City, State, and ZIP Code)</i>	TELEPHONE NUMBER	
4700 Sandoz Drive, Wilson, NC 27893	Direct: _____	
<p>Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p>		
Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research Central Document Room 5901-B Amundson Road Beltsville, MD 20705-1266	Department of Health and Human Services Food and Drug Administration Center for Biologics Evaluation and Research 1401 Rockville Pike Rockville, MD 20852-1448	An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

ANDA 76-897
Oxandrolone Tablets USP, 2.5 mg and 10 mg

ESTABLISHMENT INFORMATION

Approved Site:

CFN 1062246

Sandoz Inc.
4700 Sandoz Drive
Wilson, NC 27893

Contact: Dietrich Bartel, B.S., Director, Regulatory Affairs

Telephone: (_____)

Facsimile: _____

Operations Performed: (1) manufacture and process drug products, and in-process materials; (2) package drug products; (3) label drug products; (4) test raw material components, drug product containers, closures, packaging materials, in-process materials, finished drug products, and stability; (5) warehousing and shipping.

The site is ready for inspection. The last inspection was February 15 to 17, 2006.

ANDA 76-897
Oxandrolone Tablets USP, 2.5 mg and 10 mg

Drug Substance Specification

2 PAGES WITHHELD IN FULL