August 16, 2019

Division of Dockets Management Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

CITIZEN PETITION

Novitum Pharma LLC
70 Lake Drive
East Windsor, NJ 08520
Phone Number: (845)652 0377

Novitium Pharma LLC a specialty pharmaceutical company focusing on developingand marketing of generic drugs, submits this citizen petition under 21 C.F.R. § 10.30 to request the Commissioner of Food and Drug Administration (FDA) to designate a Reference standard (RS) for Oxandrin (Oxandrolone) Tablets 2.5mg & 10mg (NDA 013718). The 2.5mg & 10mg are currently designated as RLD in the Orange book. The 10mg is currently designated as RS in the Orange book.

Currently the brand name manufacturer, Gemini Laboratories has discontinued the distribution of Oxandrin Tablets. RLD/RS for this product is not available on the market and therefore, Novitium Pharma LLC, requests that FDA promptly designate a RS to facilitate generic drug development.

I. Actions Requested

This petition requests the Commissioner of FDA to take the following actions:
FDA designate the generic product made by PAR Pharmaceutical Inc (A077827) as the RS of Oxandrin Tablets (NDA 013718) since PAR has the maximum share of sales in the market.

II. Statement of Grounds

A. Introduction

As per the orange book, Oxandrin (Oxandrolone) Tablets 2.5mg & 10mg (NDA 013718) was originally made by Gemini Laboratories LLC and was approved by FDA prior to Jan 1 1982. There are four generic manufacturers that have gained FDA approval to market this product: PAR Pharmaceutical Inc (A077827; current market leader), Upsher-Smith Laboratories LLC (A076761 & A078033), Roxane Laboratories Inc (A077249) and Sandoz Inc (A076897). Roxane Laboratories Inc (A077249) and Sandoz Inc (A076897) were discontinued later.

B. Factual Background

Novitium Pharma has licensed the Approved NDA 013718 from the NDA Holder, Gemini Laboratories LLC to manufacture and market the drug product recently. Being the regulatory agent for Oxandrin Tablets, we are aware that Oxandrin Tablets is neither manufactured nor marketed by its brand name manufacturer, Gemini Laboratories LLC and hence RLD/RS is not available in the market.

Subsequently, Novitium Pharma has contacted FDA to designate the generic product made by PAR Pharmaceutical Inc (A077827) as the RS of Oxandrin Tablets. FDA has assigned the docket no.: FDA-2018-P-3422 for this citizen petition.

However, on March 04, 2019, we received a communication from FDA stating that we will be notified once FDA reaches a decision on this. In continuation of this, we would like to provide additional information that we received a request from FDA on July 27, 2018 to submit a PLR/PLLR conversion labeling supplement to FDA.

Considering the fact this NDA was approved long before on 07/21/1964, we were left with only minimum information to update the label. Based on the FDA's request, we have updated the label with the available minimum information we have and submitted the revised label to FDA. Subsequently, FDA refused to file our response owing to the reason that we did not provide a complete response to all the FDA's comments. Now that there is no possibility for the availability of the RLD from the NDA holder to be in the market, Novitium Pharma is contacting FDA to designate the generic product made by PAR Pharmaceutical Inc (A077827) as the RS of Oxandrin Tablets.

We were advised by FDA that:

"You may petition the Agency through citizen petition procedure under 21 CFR 10.25(a) and 21 CFR 10.30. If the citizen petition is granted, a new listed drug will be designated as reference standard. We note that FDA has the authority to designate a reference standard."

We believe we shall apply FDA's guidance for Oxandrin Tablets 2.5mg & 10mg.

RS is needed for Oxandrin Tablets 2.5mg & 10mg to facilitate product development

The Drug Price Competition and Patent Term Restoration Act (Public Law 98- 417), informally known as the Hatch-Waxman Act, was passed in 1984 by United States Congress to encourage the development of generic products. Compared to brand name products, generic products have the same therapeutic effects on patients, but are generally sold at much lower price. The flourish of generic products greatly reduced the drug price and saved the public healthcare costs. A reference listed drug (RLD) (21 CFR 314.94 (a) (3) means the listed drug identified by FDA as the drug product upon which an applicant relies in seeking approval of its ANDA. The availability of RLD is critical for generic manufacturer to develop its generic product.

Gemini Laboratories LLC, the brand name manufacturer, has discontinued Oxandrin Tablets 2.5mg & 10mg (NDA 013718) and therefore, currently there is no RLD/RS available on the market for generic manufacturers to develop generic version for Oxandrin Tablets 2.5mg & 10mg. As suggested by FDA, Novitium Pharma, submits a citizen's petition requesting a RS for Oxandrin Tablets 2.5mg & 10mg (NDA 013718).

Conclusion

For the foregoing reasons, FDA should immediately designate a RS for Oxandrin Tablets 2.5mg & 10mg (NDA 013718). The prompt action shall facilitate the generic product development which is beneficial to the reduction of drug price and subsequently, to the reduction of overall public healthcare costs.

C. Environmental Impact

The actions requested in this petition will have no significant effect on the human environment.

D. Economic Impact

Petitioner will, upon request by the Commissioner, submit economic impact information, in accordance with 21 C.F.R. § 10.30(b).

E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioners which are unfavorable to the petition.

Respectfully submitted,

Muthusamy Shanmugam
Digitally signed by Muthusamy Shanmugam
Date: 2019.08.16 16:51:27 -04'00'

Muthusamy Shanmugam
President, Novitium Pharma LLC
70 Lake Drive,
East Windsor, NJ 08520
Phone #: +1 (845) 652 0377

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Mkt.Status	Active Ingredient	Proprietary Name	Appl No	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
RX	OXANDROLONE	OXANDRIN	N013718	TABLET	ORAL	2.5MG	AB	RLD		GEMINI LABORATORIES LLC
RX	OXANDROLONE	OXANDRIN	N013718	TABLET	ORAL	10MG	AB	RLD	RS	GEMINI LABORATORIES LLC
RX	OXANDROLONE	OXANDROLONE	A077827	TABLET	ORAL	2.5MG	AB			PAR PHARMACEUTICAL INC
RX	OXANDROLONE	OXANDROLONE	A076761	TABLET	ORAL	2.5MG	AB			UPSHER-SMITH LABORATORIES LLC
RX	OXANDROLONE	OXANDROLONE	A077827	TABLET	ORAL	10MG	AB			PAR PHARMACEUTICAL INC
RX	OXANDROLONE	OXANDROLONE	A078033	TABLET	ORAL	10MG	AB			UPSHER-SMITH LABORATORIES LLC
DISCN	OXANDROLONE	OXANDROLONE	A077249	TABLET	ORAL	2.5MG				ROXANE LABORATORIES INC
DISCN	OXANDROLONE	OXANDROLONE	A076897	TABLET	ORAL	2.5MG				SANDOZ INC
DISCN	OXANDROLONE	OXANDROLONE	A077249	TABLET	ORAL	10MG				ROXANE LABORATORIES INC
DISCN	OXANDROLONE	OXANDROLONE	A076897	TABLET	ORAL	10MG				SANDOZ INC

GEMINI
LABORATORIES

Gemini Laboratories, LLC
1200 US Highway 22 East, Suite 3
Bridgewater, NJ 08807

O: 908.450-7550
info@gemini-labs.com
www.gemini-labs.com

To
The Commissioner
U.S. Food and Drug Administration
Central Document Room
5901-B Ammendale Rd.
Beltsville, MD 20705-1266

February 21, 2017

Reference: Regulatory Agent Appointment Letter for the NDA #013718, OXANDRIN® (oxandrolone) Tablets, USP 2.5 mg and 10 mg.

Dear Sir/Madam,

Gemini Laboratories, LLC hereby declares that we have appointed:

Muthusamy Shanmugam
Founder and President
Novitium Pharma LLC
70 Lake Drive, East Windsor
New Jersey, USA 08520
Telephone No: +1-845-652-0377
Fax No: +1-609-469-5921

as our regulatory agent for the NDA #013718, OXANDRIN® (oxandrolone) Tablets, USP 2.5 mg and 10 mg. FDA may send Novitium Pharma LLC any communications pertaining to the product mentioned above.

Novitium Pharma LLC is authorized to sign and submit the below documents in addition to all subsequent changes and supplements for this NDA#013718:

- Cover letter
- FDA Form 356h
- Debarment Certification
- cGMP Certification
- Reprocessing Statement
- Stability Commitment

Sincerely,

Michael Turnamian
Vice President of Commercial Operations
Gemini Laboratories, LLC

U.S. FOOD & DRUG ADMINISTRATION

Muthusamy Shanmugam
President
Novitium Pharma LLC
70 Lake Drive
East Windsor, NJ 08520

Re: Docket No. FDA-2018-P-3422

MAR 0 4 2019

Dear Mr. Shanmugam:

I am writing to inform you that the Food and Drug Administration (FDA or the Agency) has not yet resolved the issues raised in your citizen petition received on September 6, 2018. Your petition requests that the Agency designate the generic product made by PAR Pharmaceutical Inc. (A077827) as the reference standard of Oxandrin Tablets (NDA 013718).

FDA has been unable to reach a decision on your petition because it raises complex issues requiring extensive review and analysis by Agency officials. This interim response is provided in accordance with FDA regulations on citizen petitions (21 CFR 10.30(e)(2)). We will respond to your petition as soon as we have reached a decision on your request.

Sincerely,

Carol J. Bennett
Acting Director
Office of Regulatory Policy
Center for Drug Evaluation and Research

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 013718

PRIOR APPROVAL SUPPLEMENT REQUEST

Gemini Laboratories, LLC
C/O Muthusamy Shanmugam
Founder and President
Novitium Pharma LLC
70 Lake Drive, East Windsor
New Jersey, USA 08520

Dear Mr. Shanmugam:

Please refer to your New Drug Application (NDA) for Oxandrin (oxandrolone) tablets. Please also refer to the supplemental NDA (sNDA), NDA 013718/S-029, dated October 13, 2010, that proposed Physician Labeling Rule (PLR) format and the correspondence dated July 18, 2014, that withdrew this PLR conversion labeling supplement. Finally, please refer to your correspondence dated February 6, 2018, that stated your intention to re-market Oxandrin.

We also refer to the requirements on content and format of labeling for human prescription drug and biological products, and the implementation plan for complying with those requirements, published in the *Federal Register* in January 2006 (see *Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products*, 71 FR 3922, January 24, 2006, and see 21 CFR 201.56(b and c). According to the implementation plan, the Oxandrin labeling must be in PLR format. The Oxandrin labeling must also comply with the content and format of the Pregnancy and Lactation Labeling Rule (PLLR) given that an efficacy supplement was approved on June 20, 2005.

Therefore, submit a PLR/PLLR conversion labeling supplement within **four** months of the date of this letter.

Before submitting your supplement, consider reviewing the labeling review resources on the PLR Requirements of Prescribing Information website (http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm) including:

- Physician Labeling Rule on the content and format of the prescribing information,
- Regulations and related guidance documents,
- Selected Requirements for Prescribing Information (SRPI) − a checklist of 41 important format items from labeling regulations and guidances.
- Labeling presentations including "Converting Labeling for Older Drugs from the Old Format to the PLR Format"

(https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/UCM584741.pdf), and
- Other labeling resources

Also consider reviewing the labeling resources on the Pregnancy and Lactation Labeling (Drugs) Final Rule website (https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Labeling/ucm093307.htm) including:

- PLLR rule and draft guidance
- PLLR labeling presentations

Submit draft labeling for your prescribing information (PI) as a prior approval supplement to this application, addressing all of the PLR and PLLR requirements. To facilitate review of your submission, we recommend that you clearly mark on the cover letter "**Labeling/PLR and PLLR Conversion**" and that you provide a highlighted or marked-up copy that shows all your proposed changes, as well as a clean Word version and a clean version in PDF format. The marked-up copy should also include annotations that support all your proposed changes, including annual reportable changes. Please also provide a clean version of the last approved labeling in the "old" format. Your supplement must include updated content of labeling in structured product labeling (SPL) format, according to 21 CFR 314.50(l)(1)(i) (see http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm).

Your PI must contain a summary of the essential scientific information needed for the safe and effective use of your product and must be informative and accurate and neither promotional in tone nor false or misleading. You must update your PI when new information becomes available that causes the labeling to become inaccurate, false, or misleading [see 21 CFR 201.56(a)].

For your reference, the following comments were provided to a previous owner of your NDA during our review of NDA 013718/S-029. Please ensure that your supplement addresses the comments below.

Indications and Usage

1. In the first sentence, "Oxandrin is indicated as adjunctive therapy to promote…" Specify to what therapy Oxandrin is adjunctive to.

2. As per 21CFR 201.57(c) (2) Oxandrin should treat a "recognized disease or condition", or a "manifestation of a recognized disease of condition", or "provide relief of symptoms associated with a recognized disease or condition." The language in the current Indications and Usage Section does not comply with the above mentioned regulations. Please provide alternative language and indicate what data presented to the Agency to date support this language (for instance, what data support the indication of offsetting the protein catabolism associated with prolonged administration of

corticosteroids or the indication of providing relief of the bone pain associated with osteoporosis).

Dosage and Administration

3. After you provide new language for the labeled indication, clarify the dosing for each indication (different, the same, what is the basis for the dose).

4. Define "intermittent therapy" and the duration between the therapies.

5. Specify the maximum duration of therapy for each indication.

6. Is the length of each course of therapy the same for each population? In the "Adults" subsection, the label states that a course of therapy of 2 to 4 weeks is usually adequate. Does this also apply to children and geriatric patients as well?

7. Specify the age ranges for each of the 3 subgroups listed in this section (adults, children, geriatrics).

Dosage Forms and Strengths

8. If you intend to retain the labeling statement indicating that the Oxandrin tablets are scored, you must provide evidence that Oxandrin meets the guidelines and criteria for a scored tablet. Provide evidence that the tablets are "functionally" scored. Refer to draft Guidance for Industry - Tablet Scoring: Nomenclature, Labeling, and Data Evaluation, found at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269921.pdf%22.

Contraindications

9. Explain why "carcinoma of breast with hypercalcemia" and "hypercalcemia" are discussed separately. For females with carcinoma of the breast, is Oxandrin contraindicated only if patients have hypercalcemia? If you believe that hypercalcemia alone should be a contraindication, provide information to support this contraindication.

10. We are proposing that Oxandrin should be contraindicated in all patients with breast cancer (males and females) regardless of hypercalcemia due to the possible stimulation of estrogen-responsive tumors. Do you concur? If not, please explain why not.

11. Explain what is the basis for the nephrosis contraindications?

Warnings and Precautions

12. Is there any recommended monitoring for surveillance of peliosis hepatis?

13. Provide an explanation as to why the subset of COPD patients who are unresponsive to bronchodilators are at increased risk for disease exacerbation during Oxandrin use. What data support this statement?

Adverse Reactions

14. Are any of the listed adverse reactions listed in Section 6 from postmarketing reports, or do they all originate in the registration clinical studies?

Drug Interactions

15. For each drug interaction listed, propose practical instructions for preventing or decreasing the likelihood of the interaction.

Overdosage

16. How do you relate the information provided in the label to humans, particularly the following statement: "the oral LD50 of oxandrolone in mice and dogs is greater than 5,000 mg/kg"?

Clinical Pharmacology

17. The label states that in a single dose pharmacokinetic study of 10 mg Oxandin in young male volunteers, the mean elimination half-life was 10.4 hours. Please verify this number and confirm if this is correct. Also provide the study number from which this information is derived.

If you have any questions, call Peter Franks, Regulatory Project Manager, at (240) 402-4197.

Sincerely,

{See appended electronic signature page}

William Chong, M.D.
Director (Acting)
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

WILLIAM H CHONG
07/27/2018

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 013718/S-031

REFUSAL TO FILE

Gemini Laboratories, LLC
C/O Muthusamy Shanmugam
Founder and President
Novitium Pharma LLC
70 Lake Drive, East Windsor
New Jersey, USA 08520

Dear Mr. Shanmugam:

Please refer to your supplemental New Drug Application (NDA) dated November 27, 2018, received November 27, 2018, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Oxandrin (oxandrolone) tablets.

After a preliminary review, we find your application is not sufficiently complete to permit a substantive review. Therefore, we are refusing to file this application under 21 CFR 314.101(d) for the following reasons:

The submitted PLR/PLLR labeling does not contain a summary of the essential scientific information needed for the safe and effective use of your product as described in 21 CFR 201.56(a).

In our Prior Approval Supplement Request letter, dated July 27, 2018, we requested that your PLR/PLLR labeling supplement include responses to specific questions that we included in the letter regarding the Prescribing Information. The labeling supplement received did not include responses to all our requests.

As per 21 CFR 201.57(c)(2), Oxandrin should be indicated to treat a "recognized disease or condition", or a "manifestation of a recognized disease of condition," or "provide relief of symptoms associated with a recognized disease or condition."

The language in the current Indications and Usage section does not comply with the above-mentioned regulations. Provide alternative language and indicate what data presented to the Agency to date support this language (for instance, what data support the indication of offsetting the protein catabolism associated with prolonged administration of corticosteroids or the indication of providing relief of the bone pain associated with osteoporosis).

Please note that this filing review represents a preliminary review of the application and is not indicative of deficiencies that would be identified if we performed a complete review.

Within 30 days of the date of this letter, you may request in writing a Type A meeting about our refusal to file the application. A meeting package should be submitted with this Type A meeting request. To file this application over FDA's protest, you must avail yourself of this meeting.

If, after the meeting, you still do not agree with our conclusions, you may request that the application be filed over protest. In that case, the filing date will be 60 days after the date you requested the meeting. The application will be considered a new original application for user fee purposes, and you must remit the appropriate fee. If you choose to file over protest, FDA will generally not review any amendments to the application and will generally not issue information requests during the review cycle. Resubmission goals will not apply to any resubmission of this application.

If you have any questions, call Peter Franks, Regulatory Project Manager, at (240) 402-4197.

Sincerely yours,

{See appended electronic signature page}

William Chong, M.D.
Deputy Director (Acting)
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

WILLIAM H CHONG
01/22/2019 10:39:20 AM