

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

210526Orig1s000

OTHER ACTION LETTERS



NDA 210526

COMPLETE RESPONSE

Emory Partners, LLC
Attention: Norma J. Cappetti
Regulatory Agent
2031 Route 130
Monmouth Junction, NJ 08852

Dear Ms. Cappetti:

Please refer to your new drug application (NDA) dated and received September 25, 2017, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Dyanavel XR (amphetamine) extended-release tablets 5 mg, 10 mg, 15 mg, and 20 mg.

We acknowledge receipt of your amendment dated July 22, 2020, which constituted a complete response to our July 25, 2018, action letter.

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

FACILITY INSPECTIONS

During a recent inspection of the Tris Pharma, Inc. (FEI: 3004712471) manufacturing facility for this application, our field investigator conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved.

PRESCRIBING INFORMATION

We reserve comment on the proposed labeling until the application is otherwise adequate. We encourage you to review the labeling review resources on the PLR Requirements for Prescribing Information¹ and Pregnancy and Lactation Labeling Final Rule² websites, including regulations and related guidance documents and the Selected

¹ <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm>

² <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Labeling/ucm093307.htm>

Requirements for Prescribing Information (SRPI) – a checklist of important format items from labeling regulations and guidances.

MEDICATION GUIDE

Add the following bolded statement or appropriate alternative to the carton and container labels per 21 CFR 208.24(d): "**ATTENTION PHARMACIST: Each patient is required to receive the accompanying Medication Guide.**"

PROPRIETARY NAME

Please refer to correspondence dated October 20, 2020, which addresses the proposed proprietary name, Dyanavel XR. This name was found acceptable pending approval of the application in the current review cycle. Please resubmit the proposed proprietary name when you respond to the application deficiencies.

SAFETY UPDATE

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all nonclinical and clinical studies/trials of the drug under consideration regardless of indication, dosage form, or dose level.

- (1) Describe in detail any significant changes or findings in the safety profile.
- (2) When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:
 - Present new safety data from the studies/clinical trials for the proposed indication using the same format as in the original submission.
 - Present tabulations of the new safety data combined with the original application data.
 - Include tables that compare frequencies of adverse events in the original application with the retabulated frequencies described in the bullet above.
 - For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.
- (3) Present a retabulation of the reasons for premature trial discontinuation by incorporating the drop-outs from the newly completed trials. Describe any new trends or patterns identified.

- (4) Provide case report forms and narrative summaries for each patient who died during a clinical trial or who did not complete a trial because of an adverse event. In addition, provide narrative summaries for serious adverse events.
- (5) Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original application data.
- (6) Provide updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).
- (7) Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.
- (8) Provide English translations of current approved foreign labeling not previously submitted.

OTHER

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application.

A resubmission must fully address all the deficiencies listed in this letter and should be clearly marked with "**RESUBMISSION**" in large font, bolded type at the beginning of the cover letter of the submission. The cover letter should clearly state that you consider this resubmission a complete response to the deficiencies outlined in this letter. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*.

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, contact CAPT Kofi Ansah, PharmD, RAC, Senior Regulatory Project Manager, at (301) 796-4158 or Kofi.Ansah@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Tiffany R. Farchione, MD
Director
Division of Psychiatry
Office of Neuroscience
Office of New Drugs
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/

TIFFANY R FARCHIONE
01/21/2021 10:43:55 PM



NDA 210526

COMPLETE RESPONSE

Tris Pharma, Inc.
Attention: Norma J. Cappetti
Vice President, Regulatory Affairs
2033 Route 130, Suite D
Monmouth Junction, NJ 08852

Dear Ms. Cappetti:

Please refer to your New Drug Application (NDA) dated and received September 25, 2017, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Dyanavel XR (amphetamine) extended-release tablets 5 mg, 10 mg, 15 mg, and 20 mg.

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

FACILITY INSPECTIONS

1. During a recent inspection of the Tris Pharma, Inc. (FEI: 3004712471) manufacturing facility for this application, our field investigator conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved.

REGULATORY

2. Your 505(b)(2) application relies upon the Agency's finding of safety and effectiveness for NDA 011522 for Adderall Tablets for which you submitted Paragraph IV certification with respect to U.S. Patent Number 6,384,020 ('020 patent), listed in FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations" (the Orange Book) as described in 21 CFR 314.54(a)(1)(vi). However, you have not provided documentation of receipt by each person identified in 21 CFR 314.52(a) of the required notice of Paragraph IV certification for the '020 patent. Acceptable forms of documentation are described in 21 CFR 314.52(e). You are also reminded that you must notify FDA within 14 days of the filing of any legal action filed within 45 days of receipt of the notice of Paragraph IV certification by any recipient, if applicable (see 21 CFR 314.107(f)(2)).

PRESCRIBING INFORMATION

3. We reserve comment on the proposed labeling until the application is otherwise adequate. We encourage you to review the labeling review resources on the [PLR Requirements for Prescribing Information](#) and [Pregnancy and Lactation Labeling Final Rule](#) websites, including regulations and related guidance documents and the Selected Requirements for Prescribing Information (SRPI) – a checklist of important format items from labeling regulations and guidances.

If you revise labeling, use the SRPI checklist to ensure that the prescribing information conforms with format items in regulations and guidances. Your response must include updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

CARTON AND CONTAINER LABELING

4. Submit draft carton and container labeling revised as follows:

We note the size of the established name has been increased on the revised container labels submitted on July 12, 2018. However, the established name is now too prominent relative to the proprietary name. Decrease the size of the established name so that it is ½ the size of the proprietary name. Consider increasing the size of the proprietary name while decreasing the size of the established name.

MEDICATION GUIDE

5. Add the following bolded statement or appropriate alternative to the carton and container labels per 21 CFR 208.24(d): **"ATTENTION PHARMACIST: Each patient is required to receive the enclosed Medication Guide."**

PROPRIETARY NAME

6. Please refer to correspondence dated April 16, 2018, which addresses the proposed proprietary name, Dyanavel XR. This name was found acceptable pending approval of the application in the current review cycle. Please resubmit the proposed proprietary name when you respond to the application deficiencies.

OTHER

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application.

A resubmission must fully address all the deficiencies listed in this letter and should be clearly marked with "**RESUBMISSION**" in large font, bolded type at the beginning of the cover letter of the submission. The cover letter should clearly state that you consider this resubmission a complete response to the deficiencies outlined in this letter. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the draft FDA Guidance for Industry, "Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products," December 2017 at <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM590547>.

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, contact CAPT Kofi Ansah, PharmD, RAC, Senior Regulatory Project Manager, at (301)796-4158 or email: Kofi.Ansah@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Mitchell Mathis, MD
Director
Division of Psychiatry Products
Office of Drug Evaluation I
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/

MITCHELL V Mathis
07/25/2018