Summary Review

Date	November 4, 2021
From	Valerie Amspacher, PharmD Tiffany R Farchione, MD
Subject	Summary Review
NDA/BLA # Supp #	210526
PDUFA Goal Date	November 4, 2021
Proprietary / Established (USAN) names	DYANAVEL XR (amphetamine) extended-release tablets
Dosage forms / strength	5 mg, 10 mg, 15 mg, and 20 mg amphetamine base
Proposed Indication(s)	Treatment of Attention Deficit Hyperactivity Disorder (ADHD)
Recommended:	*Approval*

1. Introduction to Review

This NDA resubmission seeks approval for DYANAVEL XR (amphetamine) extended-release tablets equivalent to 5 mg, 10 mg, 15 mg, and 20 mg amphetamine base. It is a 505(b)(2) application which relies upon the Agency's findings of safety and effectiveness for NDA 208147 (DYANAVEL XR Suspension). The listed drug (LD) was approved 19 Oct 2015 for the same indication of Treatment of Attention Deficit Hyperactivity Disorder (ADHD).

Submission assessed	Date received	Disciplines affected
Supporting document 28; eCTD 0027	22 Jul 20	Drug product, drug substance, process/facilities, biopharmaceutics

2. Background/Regulatory History/Previous Actions/Foreign Regulatory Actions/Status

This is the third review cycle for this application. A second complete response letter dated 21 Jan 2021 was sent to the Applicant. This review will focus only on new information submitted to resolve the deficiencies stated in the letter.

3. CMC

3.1. General product quality considerations

Drug substance, drug product, process and biopharmaceutics reviews all recommended approval in the last review cycle and the recommendation remains approval for this review cycle.

3.1.1. Facilities review/inspection

The facilities review recommends approval. The follow-up inspection was conducted on 05/03/2021-06/08/2021 and the status of the drug product manufacturing site, Tris Pharma, Inc., FEI: 3004712471, has been updated to voluntary action indicated (VAI). The subject facility is adequate for the proposed responsibilities of the application based on the acceptable inspection outcome and profile.

3.2. Other notable issues *(resolved or outstanding)*

N/A

4. Labeling

This application is based on bioequivalence to the LD. As such, the product label is aligned with the LD label except where there are product-specific differences. Given that the new formulation, DYANAVEL XR (amphetamine) extended-release tablets, has a similar safety profile, shares similar indications, and has a similar health care practitioner audience as the LD, it was decided to have a single FPI covering both the extended-release suspension and the extended-release tablets. Some of the revisions include:

- Dosage and Administration (Section 2) was reorganized to include a new Section 2.3 "Administration Information" that includes administration information for both labeled products.

- Warnings and Precautions (Section 5) and Drug Abuse and Dependence (Section 9) were revised to include recent class language, where appropriate.

- Clinical Pharmacology – Pharmacokinetics (Section 12.3) was revised to include data for the extended-release tablet formulation.

- Description (Section 11) was revised to align with USP<7> (which requires the identification of active ingredients) and the misbranding provisions of the FD&C Act, (e)(1)(A) 50 by adding the established name and quantity and the proportion of each active ingredient. In addition, a statement noting that the dosage strengths are expressed in terms of amphetamine base was added to the Description section and Dosage Forms and Strengths (Section 3) in accordance with the FDA salt policy.

- Medication Guide was revised to include new product specific information. The Division of Medical Policy Programs (DMPP) reviewed the MG and the Office of Prescription Drug Promotion (OPDP) reviewed both the PI and the MG. There were no changes to the Instructions for Use (IFU) document under this NDA.

5. Conclusions and Recommendations

All outstanding deficiencies have now been resolved. This application will be approved.

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/s/

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