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APPLICATION NUMBER:

214522Orig1s000

NON-CLINICAL REVIEW(S)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Memo
PHARMACOLOGY/TOXICOLOGY NDA/BLA REVIEW AND EVALUATION

Application number:	214522
Supporting document/s:	0000 and 0009
Applicant's letter date:	04/23/2020 and 10/27/2020
CDER stamp date:	04/23/2020 and 10/27/2020
Product:	Tadliq (tadalafil oral suspension)
Indication:	Pulmonary Arterial Hypertension
Applicant:	CMP Development LLC (CMP)
Clinical Review Division:	Division of Cardiology and Nephrology
Pharm/Tox Division:	Division of Pharmacology and Toxicology/ Office of Cardiology, Hematology, Endocrinology, Nephrology
Reviewer:	Xi Yang, PhD, DABT
Supervisor/Team Leader:	Jean Wu, MD, PhD
Clinical Division Director:	Norman Stockbridge, MD, PhD
Project Manager:	Christine (Tina) Sadr, MS

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1 Executive Summary

1.1 Introduction

Tadalafil is a phosphodiesterase 5 (PDE5) inhibitor indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability. Adcirca® (Tadalafil tablets) has been marketed since 2009 (NDA 022332).

The applicant's product is an oral suspension (Tadalafil 4 mg/mL Oral Suspension), which could be used as an alternative dosage for patients preferring ready-to-use liquid formulation, and the reference listed drug (RLD), Adcirca®, is available as tablets.

This NDA is submitted via 505(b)(2) pathway and relies on FDA's previous findings of Adcirca®, the RLD. The proposed indication is same as the RLD. No additional nonclinical studies have been submitted to the current application.

1.2 Brief Discussion of Nonclinical Findings

No additional nonclinical studies were submitted to the current application. The sponsor relied on FDA's previous findings of safety of the RLD (Adcirca®) for nonclinical evaluation.

There are no novel excipients in the drug product. All excipients used in the formulation are compendial except for peppermint flavor.

A few inconsistencies between tables of the peppermint flavor composition were identified during the review process and discussed with the CMC reviewer. An Information Request (IR) was initiated by the CMC team to clarify the discrepancies and confirm the individual components. In the response to the IR received on October 27, 2020, the applicant provided an updated table in the nonclinical overview. Among the (b) (4) components of the peppermint flavor, (b) (4) in the previously approved product, and the other (b) (4) components have Joint Expert Committee on Food Additives (JECFA) status, with most of them also have Generally Recognized as Safe (GRAS) status. In general, the agency accepts JECFA determinations because JECFA serves as an independent scientific expert committee which performs risk assessments and provides advice to FAO, WHO, and the member countries of both organizations, including the United States. Therefore, the amount of the excipients in the proposed formulation generates no concerns for the intended use.

There are no issues for impurities that require nonclinical safety evaluation.

1.3 Recommendations

1.3.1 Approvability

The application is approvable from a nonclinical perspective.

1.3.2 Additional Non-Clinical Recommendations

None

1.3.3 Labeling

In the sections relevant to nonclinical information, the sponsor proposed labeling is consistent with the current FDA-approved Adcirca® (NDA 022332) Prescribing Information (Revised: 09/2020) which is compliant with the Pregnancy and Lactation Labeling Rule (PLLR). This reviewer does not recommend any additional labeling changes.

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/

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