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RESEARCH**

APPLICATION NUMBER:

208223Orig1s000

SUMMARY REVIEW

Summary Review for Regulatory Action

Date	(electronic stamp)
From	Eric Bastings, MD
Subject	Division Director Summary Review
NDA/BLA #	208223
Supplement #	
Applicant Name	Dr. Reddy's Lab
Date of Submission	March 30, 2015
PDUFA Goal Date	January 30, 2016
Proprietary Name / Established (USAN) Name	Zembrace SymTouch (Sumatriptan Injection)
Dosage Forms / Strength	3 mg/0.5 mL subcutaneous injection
Proposed Indication(s)	Acute treatment of migraine with or without aura in adults
Action	Approval

Material Reviewed/Consulted	Names of discipline reviewers
OND Action Package, including:	
Medical Officer Review	Ramesh Raman, MD
Pharmacology Toxicology Review	Charles Thompson, Ph.D.
CMC Review/OBP Review	Sherita Mclamore Hines, Ph.D.
CMC Microbiology Review	David Bateman, Ph.D.
Clinical Pharmacology Review	Om Anand, Ph.D.
OPDP	Dhara Shah, PharmD
OSI	Xiaohan Cai, Ph.D. and Hasan A. Irier, Ph.D.
CDTL Review	Heather Fitter, M.D.
OSE/DMEPA	Justine Harris
CDRH	Sapana Patel

OND=Office of New Drugs

OSE= Office of Surveillance and Epidemiology

DMEPA=Division of Medication Error Prevention and Analysis

OSI=Office of Scientific Investigations

CDTL=Cross-Discipline Team Leader

1. Introduction and Background

The 505(b)(2) application under review is for a new sumatriptan autoinjector to be indicated for the acute treatment of migraine headache with or without aura. The reference product, Imitrex injection, is currently marketed under NDA 20,080 as a 4-mg and a 6-mg prefilled syringe to be used with an autoinjector, and as a 6-mg vial for injection of doses of 1 to 6 mg. The new product developed by the applicant is a pre-filled autoinjector designed to deliver 3 mg of sumatriptan, which is a dose that cannot currently be administered through an autoinjector, but is both safe and effective.

The applicant submitted clinical pharmacology studies to support the bioequivalence of their product to a 3 mg dose of Imitrex injection, and relies on the findings of safety and efficacy of that dose in NDA 20,080. The applicant also submitted the results of a usability study in patients during a migraine attack.

2. CMC/Device

I concur with the conclusions reached by the chemistry reviewer regarding the acceptability of the manufacturing of the drug product and drug substance. Manufacturing site inspections were acceptable. Stability testing supports an expiry of 12 months. There are no other outstanding issues.

I concur with the conclusions reached by the device reviewer regarding the acceptability of the prefilled autoinjector. Manufacturing site inspections were acceptable.

3. Nonclinical Pharmacology/Toxicology

No new nonclinical information was submitted as part of this 505(b)(2) application.

4. Clinical Pharmacology/Biopharmaceutics

I concur with the conclusions reached by the clinical pharmacology/biopharmaceutics reviewer that there are no outstanding clinical pharmacology/ biopharmaceutics issues that preclude approval.

The applicant submitted the results of three clinical pharmacology studies conducted to support a pharmacokinetic bridge between the new product and Imitrex injection. A first PK study (DFP-11/CD/001) failed to meet bioequivalence criteria. A second study (DFP-11/CD/002) was conducted with better controls, and established bioequivalence between the new product and a corresponding dose of Imitrex. The applicant conducted a third study (DFP-11/CD/003), which established dose-normalized bioequivalence of their new product versus Imitrex STATdose system at 4 mg/0.5 mL and 6 mg/0.5 mL.

Dr. Xiaohan Cai and Dr. Hasan Irier conducted an audit of study DFP-11/CD/002 (pivotal bioequivalence trial) and concluded that the data from the audited study are reliable.

5. Clinical Microbiology

Not applicable.

6. Clinical/Statistical-Efficacy

This 505(b)(2) application relies on the finding of efficacy of sumatriptan doses of 1 mg to 6 mg injected subcutaneously made in NDA 20,080.

7. Safety

This 505(b)(2) application relies on the finding of safety of subcutaneous doses of sumatriptan up to 6 mg made in NDA 20,080.

There were no new safety findings in the PK studies conducted by the applicant.

8. Advisory Committee Meeting

An advisory committee meeting was not required for this application.

9. Pediatrics

PREA was not triggered by this application.

10. Other Relevant Regulatory Issues

A human factors validation study evaluated migraine patients in three groups of 15 patients each: patients trained to the use of injection but with no injection experience (trained naïve), patients untrained naïve and patients who had used injections before but were untrained to this particular device (untrained experienced). All patients were assessed following one unaided injection into either the thigh or upper arm. All patients were successful in administering a full dose injection, unaided, without patterns of failures or use errors. Some participants were unable to confirm if the injection was complete; the applicant addressed this issue by changing

the IFU, which she found acceptable. The FDA review concludes that the usability of the product is acceptable.

The proposed proprietary name was found acceptable by DMEPA.

There are no other unresolved relevant regulatory issues.

11. Labeling

All labeling issues were resolved.

12. Decision/Action/Risk Benefit Assessment

For this 505(b)(2) application, the applicant has established an adequate bridge to the Imitrex Injection NDA 20,080. The applicant has also provided adequate information to support the use of the new prefilled autoinjector. Even though the sumatriptan dose administered by this new product (3 mg) is lower than the maximum recommended dose allowed for Imitrex Injection (6 mg), it is a clearly effective dose that may address the needs of some migraine patients. Patients will also have the option to repeat dosing, up to the maximum cumulative daily dose of 12 mg currently allowed for Imitrex Injection. Therefore, I will issue an approval letter for this application.

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

/s/

ERIC P BASTINGS
01/28/2016