

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-488

PHARMACOLOGY REVIEW(S)



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

MEMO: PHARMACOLOGY/TOXICOLOGY EVALUATION

NDA NUMBER: 22-488
SERIAL NUMBER: 000
DATE RECEIVED BY CENTER: March 4, 2009
PRODUCT: LYRICA® (pregabalin) oral solution
INTENDED CLINICAL POPULATION: Patients with neuropathic pain, post-herpetic neuralgia, and fibromyalgia
SPONSOR: Pfizer Inc.
DOCUMENTS REVIEWED: Electronic Submission
REVIEW DIVISION: Division of Anesthesia, Analgesia, and Rheumatology Drug Products (HFD-170)
PHARM/TOX REVIEWER: Kathleen Young, Ph.D.
PHARM/TOX SUPERVISOR: Adam Wasserman, Ph.D.
DIVISION DIRECTOR: Bob Rappaport, M.D.
PROJECT MANAGER: Diana Walker

Date of review submission to Division File System (DFS): November 6, 2009

MEMO

Background: This submission is for LYRICA® (pregabalin) Oral Solution, CV for the treatment of adults with neuropathic pain associated with diabetic peripheral neuropathy (DPN), post herpetic neuralgia (PHN), and fibromyalgia at recommended doses of up to a maximum of 600 mg daily (30 ml at 20 mg/ml), administered in 2 or 3 divided doses per day. LYRICA® (pregabalin) is approved and marketed (NDA 21-446, December 30, 2004) in hard capsule form (25-300 mg) for the same indications and maximum dosing levels as here proposed as well as being approved under other NDAs (N21-724 for Adjunctive therapy for adult patients with partial onset seizures). (b) (4)

The drug product consists of pregabalin (20 mg/ml), methylparaben (methyl parahydroxybenzoate), propylparaben (propyl parahydroxybenzoate), monobasic sodium phosphate anhydrous, dibasic sodium phosphate anhydrous, sucralose, artificial strawberry #11545, and purified water vehicle. The excipients are NF, USP and/or Ph.Eur., except for Artificial Strawberry Flavor # 11545. The Artificial Strawberry Flavor #11545 is an excipient in another, approved drug product and has GRAS status for inclusion as a flavoring agent in foods (see DMF (b) (4) Authority to Reference granted).

Nonclinical support for marketing approval of the proposed drug product is by reference to the approved NDA 21-446 for the capsule form, under which pregabalin pharmacology and toxicology were fully characterized according to the Guidance for Industry on Non-Clinical Safety Studies for the Conduct of Human Clinical Trials for Pharmaceuticals; ICH-M3(R2) and Agency recommendations. No new non-clinical pharmacology or toxicology information was requested nor submitted for the proposed oral solution product. The proposed indication includes no changes from that for the approved pregabalin capsule product with regard to maximum recommended daily drug substance dose, treatment duration, and patient population. There are no novel excipients in the proposed oral solution formulation. The impurities and degradation products in the to-be-marketed drug product have been identified and measured below threshold level for qualification, and have undergone thorough review by the Chemistry, Manufacturing and Control review team.

Conclusions:

The nonclinical pharmacology and toxicology information that is cross-referenced to the original NDA submission (NDA 21-446) for the pregabalin capsule formulation is adequate and acceptable to support marketing approval of NDA 22-488 for the proposed liquid form.

Recommendations:

LYRICA® (pregabalin) Oral solution 20 mg/ml is approvable from a pharmacology and toxicology point of view.

There are no unresolved toxicology issues at this time, and no recommendations for Phase 4 (Post-Marketing) nonclinical pharmacology and toxicology studies. Changes to the proposed drug product labeling, if any, will be addressed under separate labeling review.

APPENDIX/ATTACHMENTS: NONE

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22488	ORIG-1	PFIZER CHEMICAL CORP	LYRICA (PREGABALIN)

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/s/

KATHLEEN A YOUNG
11/06/2009

ADAM M WASSERMAN
11/06/2009

I concur. The application may be approved from the nonclinical standpoint.