

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

205122Orig1s000

Trade Name: Qudexy XR

Generic Name: Topiramate

Sponsor: Upsher-Smith Laboratories, Inc.

Approval Date: March 11, 2014

Indications: Initial Monotherapy in Patients Greater than or Equal to 10 Years of Age with Partial Onset (POS) or Primary Generalized Tonic-Clonic (PGTC) Seizures.

Adjunctive Therapy in Patients Greater than or Equal to 2 Years of Age with Partial Onset Seizures or Primary Generalized Tonic-Clonic Seizures, and Seizures Associated with Lennox-Gastaut Syndrome (LGS).

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APPROVAL LETTER



NDA 205122

NDA APPROVAL

Upsher-Smith Laboratories, Inc.
Attention: Mark Cierpial
Director, Regulatory Affairs
6701 Evenstad Drive
Maple Grove, MN 55369

Dear Mr. Cierpial:

Please refer to your New Drug Application (NDA) dated February 11, 2013, received February 11, 2013, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Qudexy XR (topiramate) extended-release capsules 25 mg, 50 mg, 100 mg, 150 mg, and 200 mg.

We acknowledge receipt of your amendments dated May 21, 2013, May 24, 2013, July 17, 2013, August 7, 2013, August 30, 2013, September 19, 2013, September 27, 2013, October 28, 2013, November 19, 2013, December 2, 2013, December 4, 2013, December 9, 2013, December 17, 2013, January 16, 2014, February 11, 2014, February 21, 2014, February 25, 2014, March 3, 2014, and March 6, 2014.

This new drug application provides for the use of Qudexy XR (topiramate) extended-release capsules for the following indications:

- Initial Monotherapy in patients ≥ 10 years of age with partial onset (POS) or primary generalized tonic-clonic (PGTC) seizures
- Adjunctive therapy in patients ≥ 2 years of age with partial onset seizures or primary generalized tonic-clonic seizures, and seizures associated with Lennox-Gastaut syndrome (LGS)

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

WAIVER OF HIGHLIGHTS SECTION

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the package insert, Medication Guide). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the carton and immediate container labels submitted on March 3, 2014, and March 6, 2014, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 205122.**” Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Appropriately Labeled

This product is appropriately labeled for use as:

1. Initial monotherapy in POS or PGTC seizures: 10 years to less than 17 years old
2. Adjunctive therapy in POS: 2 years to less than 17 years old
3. Adjunctive therapy in PGTC seizures or seizures associated with LGS: 2 years to less than 17 years old

Therefore, no additional studies are needed in these pediatric age groups for these indications.

Partially Waived

We are waiving the pediatric study requirement for the following indications and age groups because studies are impossible or highly impracticable (because of the small number of patients and the difficulty diagnosing such age groups):

1. Initial monotherapy in POS or PGTC seizures: birth to less than 2 years old
2. Adjunctive therapy in POS: birth to less than 1 month old
3. Adjunctive therapy in PGTC seizures and seizures associated with LGS: birth to less than 2 years old

Partially Deferred

We are deferring submission of your pediatric studies for the following indications and age groups because this product is ready for approval for use in adults and the pediatric studies have not been completed:

1. Initial monotherapy in POS and PGTC seizures: 2 years to less than 10 years old
2. Adjunctive therapy in POS: 1 month to less than 2 years old

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. These required studies are listed below.

- 2137-1 Develop an age-appropriate formulation of Qudexy XR (topiramate) extended-release capsules that can be used in children ages 1 month to less than 2 years old.

Final Report Submission: March 31, 2017

- 2137-2 A study to evaluate the pharmacokinetics (PK) and tolerability of the age-appropriate formulation of Qudexy XR (topiramate) extended-release capsules, developed in PMR 2137-1, as adjunctive therapy in children ages 1 month to less than 2 years with partial onset seizures (POS).

Final Protocol Submission: September 30, 2017

Study Completion: September 30, 2020

Final Report Submission: April 30, 2021

- 2137-3 An adequately controlled study to assess the efficacy and safety of the age-appropriate formulation of Qudexy XR (topiramate) extended-release capsules, developed in PMR 2137-1, as adjunctive therapy in children ages 1 month to less than 2 years with POS.

Final Protocol Submission: July 31, 2021

Study Completion: July 31, 2026

Final Report Submission: April 30, 2027

Submit the protocol(s) to your IND 69257, with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as a NDA or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>.

Information and Instructions for completing the form can be found at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, contact Taura Holmes, PharmD, Regulatory Project Manager, via email or telephone at Taura.Holmes@fda.hhs.gov or (301) 796-1932.

Sincerely,

{See appended electronic signature page}

Eric Bastings, MD
Deputy Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure:

Content of Labeling (Package Insert and Medication Guide)

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
03/11/2014