CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202107Orig1s000

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202107

NDA APPROVAL

Corcept Therapeutics
Attention: Luana Staiger
Regulatory Affairs
149 Commonwealth Drive
Menlo Park, CA 94025

Dear Ms. Staiger:

Please refer to your New Drug Application (NDA) dated April 15, 2011, received April 18, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Korlym (mifepristone) tablets, 300 mg.

We acknowledge receipt of your amendments dated April 19, 22, and 25, June 9 and 30, July 11, 12, 13 (2), 20, and 27, August 4 (2) and 12, September 21 (2), October 4, 17, and 19, November 10, 18, and 21, and December 7 and 14, 2011, January 19 and 23, and February 6, 9, and 15, 2012. We also acknowledge receipt of your e-mails dated February 17, 2012, which includes the agreed-upon labeling.

This new drug application provides for the use of Korlym (mifepristone) for the control of hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery.

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.

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 and Medication Guide).

Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CONTAINER LABELS

We acknowledge your February 12, 2012, submission containing final printed container labels.

Submit final printed container labels that are identical to the enclosed container labels 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 titled "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 202107**." Approval of this submission by FDA is not required before the labeling is used.

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

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess a known serious risk of endometrial hyperplasia and retinopathy associated with long-term exposure to Korlym (mifepristone) therapy, and to assess a signal of a serious risk of major adverse cardiovascular events due to reductions in HDL-cholesterol associated with the use of Korlym (mifepristone).

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

1875-1 A drug utilization study to better characterize the reporting rates of adverse events associated with the long-term use of Korlym (mifepristone). These data will provide a denominator for the adverse events of special interest (endometrial hyperplasia and/or vaginal bleeding, retinopathy, and major adverse cardiovascular events) reported through enhanced pharmacovigilance and associated with long-term exposure to Korlym (mifepristone) therapy.

The timetable you submitted on February 12, 2012, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	06/2012
Interim Report Submissions:	08/2012
	02/2013
	02/2014
	02/2015
	02/2016
Final Report Submission:	02/2017

Finally, increased exposure to mifepristone is associated with serious risks for severe hypokalemia and adrenal insufficiency. Mifepristone is a CYP3A4 substrate and it is anticipated that co-administration with strong CYP3A4 inhibitors may be necessary. We have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to characterize the effect of co-administration of strong CYP3A4 inhibitors on increasing mifepristone drug levels and to assess the potential for the known serious risks of severe hypokalemia and adrenal insufficiency.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

1875-2 A drug-drug interaction clinical trial to determine a quantitative estimate of the change in exposure of mifepristone following co-administration of ketoconazole (a strong CYP3A4 inhibitor).

The timetable you submitted on February 12, 2012, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	08/2012
Trial Completion:	05/2013
Final Report Submission:	08/2013

Submit the protocols to your IND 076480, with a cross-reference letter to this NDA. Submit all final reports to your NDA.

Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **"Required Postmarketing Protocol Under 505(o)", "Required Postmarketing Final Report Under 505(o)", "Required Postmarketing Correspondence Under 505(o)"**.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

We acknowledge receipt of your submission dated April 15, 2011, of a proposed risk evaluation and mitigation strategy (REMS). We have determined that, at this time, a REMS is not necessary for Korlym (mifepristone) to ensure that its benefits outweigh its risks. We will notify you if we become aware of new safety information and make a determination that a REMS is necessary.

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. For instruction on completing the Form FDA 2253, see page 2 of the Form.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.