

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**216482Orig1s000**

**OTHER ACTION LETTERS**



NDA 216482

**COMPLETE RESPONSE**

Liqmeds Worldwide Limited  
c/o MA Pharmaceutical Consulting, Inc.  
384 Silver Sage Lane  
St. Augustine, FL 32095

Attention: Shehla Uraizee, PhD, RPh  
President, MA Pharmaceutical Consulting, Inc.

Dear Dr. Uraizee:

Please refer to your new drug application (NDA) dated and received March 8, 2022, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for (b) (4) (mycophenolate mofetil oral suspension).

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reason for this action below and, where possible, our recommendations to address this issue.

**RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS**

As described in our correspondences dated June 22 and October 17, 2022, in accordance with section 505-1 of the FDCA, we have determined that a risk evaluation and mitigation strategy (REMS) is necessary for mycophenolate mofetil to ensure that the benefits of the drug outweigh the risks of first trimester pregnancy loss and congenital malformations.

Your application cannot be approved without a REMS; therefore, you must include your proposed REMS to address this deficiency. Our communications dated June 22 and October 17, 2022, provide information about the elements your proposed REMS must include.

For administrative purposes, designate all submissions related to the proposed REMS "PROPOSED REMS for NDA 216482-AMENDMENT."

To facilitate review of your submission, we request that you submit your proposed REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms or website screenshots, are only in PDF format, they may be submitted as such, but Word format is preferred.

## **SUBMISSION OF REMS DOCUMENT IN SPL FORMAT**

In addition to submitting the proposed REMS as described above, submit the REMS document in Structured Product Labeling (SPL) format as described in the Guidance for Industry, *Providing Regulatory Submission in Electronic Format – Content of the Risk Evaluation and Mitigation Strategies Document Using Structured Product Labeling*.

For more information on submitting REMS in SPL format, please email [FDAREMSwebsite@fda.hhs.gov](mailto:FDAREMSwebsite@fda.hhs.gov).

## **PRESCRIBING INFORMATION**

We reserve any additional comments on the proposed labeling until the application is otherwise adequate. We encourage you to review the labeling review resources on the Prescription Drug Labeling Resources<sup>1</sup> and Pregnancy and Lactation Labeling Final Rule<sup>2</sup> websites, including regulations and related guidance documents and the Selected Requirements for Prescribing Information (SRPI) – a checklist of important format items from labeling regulations and guidances.

If you revise labeling, use the SRPI checklist to ensure that the Prescribing Information conforms with format items in regulations and guidances. Your response must include updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at FDA.gov.<sup>3</sup>

## **PROPRIETARY NAME**

Refer to the correspondence dated November 17, 2022, which addresses the proposed proprietary name, (b) (4). This name was found acceptable pending approval of the application in the current review cycle. Please resubmit the proposed proprietary name when you respond to the application deficiencies.

## **SAFETY UPDATE**

When you respond to the above deficiency(ies), include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all nonclinical and clinical studies/trials of the drug under consideration regardless of indication, dosage form, or dose level.

(1) Describe in detail any significant changes or findings in the safety profile.

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<sup>1</sup> <https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources>

<sup>2</sup> <https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-drugs-final-rule>

<sup>3</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

- (2) When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:
- Present new safety data from the studies/clinical trials for the proposed indication using the same format as in the original submission.
  - Present tabulations of the new safety data combined with the original application data.
  - Include tables that compare frequencies of adverse events in the original application with the retabulated frequencies described in the bullet above.
  - For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.
- (3) Present a retabulation of the reasons for premature trial discontinuation by incorporating the drop-outs from the newly completed trials. Describe any new trends or patterns identified.
- (4) Provide case report forms and narrative summaries for each subject who died during a clinical trial or who did not complete a trial because of an adverse event. In addition, provide narrative summaries for serious adverse events.
- (5) Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original application data.
- (6) Provide updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).
- (7) Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.
- (8) Provide English translations of current approved foreign labeling not previously submitted.

## **OTHER**

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application.

A resubmission must fully address all the deficiencies listed in this letter and should be clearly marked with "**RESUBMISSION**" in large font, bolded type at the beginning of the

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Silver Spring, MD 20993  
[www.fda.gov](http://www.fda.gov)

cover letter of the submission. The cover letter should clearly state that you consider this resubmission a complete response to the deficiencies outlined in this letter. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the draft Guidance for Industry, *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*.

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, call Saharat Patanavanich, Regulatory Project Manager, at (240) 402-0139.

Sincerely,

*{See appended electronic signature page}*

Ozlem Belen, MD, MPH  
Deputy Director  
Division of Rheumatology and Transplant Medicine  
Office of Immunology and Inflammation  
Office of New Drugs  
Center for Drug Evaluation and Research

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**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.**  
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/s/  
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OZLEM A BELEN  
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