CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

214952Orig1s000

OTHER ACTION LETTERS

NDA 214952

COMPLETE RESPONSE

CMP Development LLC
Attention: Ellen Chrismon
Regulatory Affairs Manager
P.O. Box 147
8026 US Highway 264A
Farmville, NC 27828

Dear Ms. Chrismon:

Please refer to your new drug application (NDA) dated October 2, 2020, received October 2, 2020, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for sildenafil oral suspension, 10 mg/ml.

We acknowledge receipt of your amendment dated October 29, 2021, which constituted a complete response to our August 5, 2021, action letter.

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 reasons for this action below and, where possible, our recommendations to address these issues.

FACILITY INSPECTIONS

(1) During a recent inspection of the (b) (4) (FEI (b) (4)) manufacturing facility for this application, our field investigator conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved. Please list communications submitted to, or held with, the Agency to facilitate resolution of the observed objectionable conditions, or deficiencies, noted at the facility.

PRESCRIBING INFORMATION

(2) We reserve comment on the proposed labeling until the application is otherwise adequate. When you resubmit your application, please reference the draft labeling you submitted on June 30, 2021. We encourage you to review the labeling review resources on the Prescription Drug Labeling Resources[1] and

[1] https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources

Pregnancy and Lactation Labeling Final Rule[2] 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.

PROPRIETARY NAME

(3) Please refer to correspondence dated, January 30, 2022, which addresses the proposed proprietary name, Liqrev. 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 deficiencies, 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.

(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.

[2] https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-drugs-final-rule

(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 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, contact Christine (Tina) Sadr, Regulatory Health Project Manager, at 240-402-6554.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, MD, PhD
Director
Division of Cardiology and Nephrology
Office of Cardiology, Hematology, Endocrinology, and Nephrology
Center for Drug Evaluation and Research

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.

/s/

NORMAN L STOCKBRIDGE
04/28/2022 12:11:15 PM

NDA 214952

COMPLETE RESPONSE

CMP Development LLC
Attention: Ellen Barkley
Regulatory Affairs Manager
P.O. Box 147
8026 US Highway 264A
Farmville, NC 27828

Dear Ms. Barkley:

Please refer to your new drug application (NDA) dated October 2, 2020, received October 5, 2020, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for LIQREV (sildenafil) oral suspension, 10 mg/ml.

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 reasons for this action below and, where possible, our recommendations to address these issues.

PRODUCT QUALITY

(1) Facility Inspections:

a. During a review of records requested under section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act, the FDA communicated issues with the (b) (4), FEI (b) (4) manufacturing facility named in your application. Satisfactory resolution of the remaining issues is required before this application may be approved. The FDA will communicate the outstanding issues to the facility no later than 10 business days from issuing this Complete Response letter. Please contact (b) (4), FEI (b) (4) manufacturing facility for additional information.

An inspection of the (b) (4), FEI (b) (4) facility is required before the application can be approved. FDA must ensure that the facility is able to conduct the listed manufacturing operations in compliance with CGMP. Because of restrictions on travel, we are unable to conduct an inspection of the (b) (4) (b) (4) facility prior to (b) (4) We will continue to monitor the public health situation as well as travel restrictions. We are actively working to

define an approach for scheduling outstanding inspections once safe travel may resume and based on public health need and other factors.

For more information, please see the FDA guidances related to COVID 19. These guidances can be found at https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-related-guidancedocuments-industry-fda-staff-and-other-stakeholders.

During a recent inspection of the [redacted] (b) (4) FEI [redacted] (b) (4) manufacturing facility for this application, our field investigator conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved. Please list communications submitted to or held with the Agency to facilitate resolution of the observed objectionable conditions, or deficiencies, noted at the facility.

b. During a recent inspection of the [redacted] (b) (4) FEI [redacted] (b) (4) testing facility for this application, our field investigator conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved. Please list communications submitted to or held with the Agency to facilitate resolution of the observed objectionable conditions, or deficiencies, noted at the facility.

PRESCRIBING INFORMATION

(2) We reserve further comment on the proposed labeling until the application is otherwise adequate. When you resubmit your application, please reference the draft labeling you submitted on June 30, 2021. We encourage you to review the labeling review resources on the Prescription Drug Labeling Resources[1] and Pregnancy and Lactation Labeling Final Rule[2] 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.

[1] https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources
[2] https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-drugs-final-rule

PROPRIETARY NAME

(3) Please refer to correspondence dated, March 22, 2021 which addresses the proposed proprietary name, LIQREV. 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 deficiencies, 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.

(2) When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:

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(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 patient 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.

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(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.

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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, contact Christine (Tina) Sadr, Regulatory Health Project Manager, at 240-402-6554.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, MD, PhD
Director
Division of Cardiology and Nephrology
Office of Cardiology, Hematology, Endocrinology, and Nephrology
Center for Drug Evaluation and Research

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.

/s/

NORMAN L STOCKBRIDGE
08/05/2021 10:02:15 AM