CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

217347Orig1s000

OTHER ACTION LETTERS

NDA 217347

COMPLETE RESPONSE

Botanix SB Inc.
Attention: Matthew Callahan
Board Director
3602 Horizon Drive, Suite 160
King of Prussia, PA 19406

Dear Matthew Callahan:

Please refer to your new drug application (NDA) dated and received September 23, 2022, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for sofpironium bromide.

We also acknowledge receipt of your amendment dated September 13, 2023, which was not reviewed for this action. You may incorporate applicable sections of the amendment by specific reference as part of your response to the deficiencies cited in this letter.

We have completed our review of this application, 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.

HUMAN FACTORS

Based on the evaluation of the human factors (HF) study results, the user interface does not support the safe and effective use of the proposed product.

The results of the HF validation study demonstrated several use errors/close calls/use difficulties with critical tasks that may result in harm to the patient or others, or compromised efficacy. Specifically, we note that there are risks associated with potential underdose, overdose and inadvertent exposure to others, with symptoms of local site reaction, transient mydriasis, blurred vision, dry mouth, and urinary hesitation. We acknowledge the additional mitigations implemented post-validation; however, our review indicates that additional risk mitigations are necessary.

Information needed to resolve this deficiency:

1. Review the HF study results and subjective feedback to identify potential areas of optimization.
2. Implement additional design modifications and user interface revisions identified in item #1 above, along with the following:

a. Label the applicator with the applicator's intended use/purpose because several users in the HF validation study indicated that they did not understand what the applicator was, or how to use it.

b. Revise the instructions for use (IFU) to address the subjective feedback that:

   i. The IFU has too much information

   ii. Certain information in the IFU lacks salience

   iii. The IFU was folded which may have contributed to missed steps

c. Place the statement "wash hands with soap and water immediately after use" on the principal display panel of the carton and container labeling to emphasize this important information, based on the residual risk and subjective feedback related to the task of washing hands.

3. Consider implementing a mitigation to address the foreseeable use issue of users of this product tilting the applicator to apply to the underarm(s) and spilling the gel, as observed in the HF validation study.

4. Conduct another HF validation study to demonstrate that the revised user interface supports the safe and effective use of the product.

PRESCRIBING INFORMATION

We reserve comment 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[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.

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.[3]

[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
[3] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

CARTON AND CONTAINER LABELING

We reserve comment on the proposed labeling until the application is otherwise adequate.

PROPRIETARY NAME

Please refer to correspondence dated, August 28, 2023 which addresses the proposed proprietary name, Sofdra. 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.

(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, call Craig Johnson, Regulatory Project Manager, at 301-796-3921.

Sincerely,

{See appended electronic signature page}

Nikolay P. Nikolov, MD
Acting Office Director
Office of Immunology and Inflammation
Office of New Drugs
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/

NIKOLAY P NIKOLOV
09/22/2023 04:31:37 PM