CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

215064Orig1s000

OTHER ACTION LETTERS

NDA 215064

COMPLETE RESPONSE

Amryt Pharmaceuticals DAC
c/o Biologics Consulting Group, Inc
Attention: Norman Baylor, PhD
President & CEO
1555 King Street Suite 300
Alexandria, VA 22314

Dear Dr. Baylor:

Please refer to your new drug application (NDA) dated and received March 30, 2021, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Filsuvez (birch triterpenes) gel.

We acknowledge receipt of your major amendment dated September 27, 2021, which extended the goal date by three months.

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.

CLINICAL

(1) The submitted data do not provide substantial evidence of effectiveness for the use of Filsuvez (birch triterpenes) gel for the proposed indication of treatment of wounds associated with inherited epidermolysis bullosa (EB). Although the primary endpoint for Study BEB-13 was met (Filsuvez treatment resulted in an increased proportion of subjects with first complete closure of the EB target wound within 45 days relative to control gel), the pre-specified and exploratory secondary endpoints provide limited support for a substantial benefit with active treatment. The trajectory of treatment effects for Filsuvez and control gel appear similar from Day 0 to Day 90 for total body wound burden, body surface area percentage, itch, procedural pain and background pain, suggesting that there were no meaningful differences between treatment arms.

(2) Supportive studies BEB-10, BBW-11, BSG-12, and BSH-12 were open-label, intra-individual design studies. Due to their design and significant amounts of data unavailable for blinded assessment, these studies are not suitable for providing confirmatory evidence.

(3) There are inadequate data to support a mechanism of action for Filsuvez in EB. The short-term in vitro studies referenced in this application used cells cultured from healthy volunteers; there are no data on the drug's effect on the basement membrane defects in EB. While the product may have modest effects on non-EB partial thickness wounds, it is not possible to extrapolate the results of trials conducted in subjects with burn wounds and split-thickness donor wounds to patients with EB.

Thus, we have concluded that there are insufficient data in your application to support a determination that Filsuvez treatment reliably results in accelerated wound healing or reduced total wound burden. To address this concern, submit additional confirmatory evidence of effectiveness of your product for EB or specific subsets of the EB population.

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.

CARTON AND CONTAINER LABELING

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

PROPRIETARY NAME

Please refer to correspondence dated, June 9, 2021, which addresses the proposed proprietary name, Filsuvez. This name was found conditionally 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

[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

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.

If you have any questions, call Qianyiren Song, Regulatory Project Manager at 301-796-2581.

Sincerely,

{See appended electronic signature page}

Julie G. Beitz, MD
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/

JULIE G BEITZ
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