NDA 217225/S-001

COMPLETE RESPONSE

Astellas Pharma US, Inc
Attention: Carol Soo
Senior Director, Global Regulatory Affairs
2375 Waterview Drive
Northbrook, IL 60062

Dear Carol Soo:

Please refer to your supplemental new drug application (sNDA) dated and received January 19, 2024, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for IZERVAY (avacincaptad pegol intravitreal solution).

This "Prior Approval" supplement with clinical data to your application proposes a new, expanded dosing regimen (beyond 12 months) for the approved indication of treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

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.

In the study results from ISEE2008 (GATHER2), the geographic atrophy (GA) growth rate for the every month (EM) arm is numerically higher than the every other month (EOM) arm. However, per the pre-specified testing procedure, formal statistical inferential conclusion could only be made for the comparison of EM versus Sham. Thus, your proposal to extend the dosing interval was not supported by the submitted data and was not replicated in a second adequate and well controlled study.

Data from adequate and well-controlled studies which demonstrate the efficacy of Izervay (avacincaptad pegol ophthalmic solution) 20 mg/mL solution with an extended dosing regimen should be submitted to support your proposed labeling revisions.

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

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

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.

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 supplemental application data.
- Include tables that compare frequencies of adverse events in the supplemental 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.

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

(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 supplemental 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*.

If you have any questions, contact Michael Puglisi, Senior, Regulatory Project Manager via email at michael.puglisi@fda.hhs.gov or call 301-796-0791.

Sincerely,

{See appended electronic signature page}

William M. Boyd, MD
Deputy Director
Division of Ophthalmology
Office of Specialty Medicine
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/

WILLIAM M BOYD
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