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APPLICATION NUMBER:

202207Orig1s000

OFFICE DIRECTOR MEMO

MEMORANDUM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
CDER/OND/ODE-IV

Date: 03/11/2013
From: Shaw T. Chen, M.D., Ph.D., Deputy Director, ODE-IV
To: File, NDA-202207
Subject: Approval of NDA 202207, Lymphoseek (technetium Tc 99m tilmanocept)

This is the ODE memo to concur with the approval of this NDA, as recommended by the Division of Medical Imaging Products (DMIP). Lymphoseek is a new diagnostic radiopharmaceutical to map the lymphatic system. It is indicated for use with a hand-held gamma counter to assist in the localization of lymph nodes draining a primary tumor site in patients with breast cancer or melanoma.

This is a second cycle review for this NDA, which was submitted originally on August 10, 2011. The first cycle review was completed on September 10, 2012 with resolution of all issues except for facility inspections. The application was resubmitted on October 30, 2012. During this second cycle, the facility inspection was completed successfully and the NDA is now ready for approval.

As noted in the Division Director's memo by Dr. Rieves, reviews by all scientific disciplines, including clinical/statistical/clinical pharmacology/nonclinical toxicology, were completed during the first cycle. Other than the facility inspection, no other approvability issues or needs of postmarketing requirements/commitments were identified. In his final Office Director Decisional Memo for Regulatory Action of September 7, 2012, Dr. Charles Ganley also summarized the review findings and concurred with the conclusion that the facility inspection is the only regulatory issues un-resolved at the first cycle, as stated in the Complete Response to the original submission.

All supporting data, including results of clinical studies, are referred to the respective primary/secondary reviews, and summarized again in Dr. Rieves's division director's memo for the second cycle. Since no major update or change to Dr. Ganley's ODE memo is necessitated by the resubmission, his summary will not be reiterated in this memo.

New Information in the 2nd Cycle Review

1. Facility inspection

As noted in the 2nd cycle CMC review, and documented in the FDA Establishment Evaluation System's (EES) Summary Report of February 13, 2013, the applicant's facility is now considered acceptable. The only reason for non-approval at the first cycle is thus resolved.

2. Safety Updates

The applicant has submitted 4 safety updates on the ongoing NEO3-06 trial at 120-day increments after submission of the original NDA (525-551 patients in each updates, from December 8, 2011 through November 28, 2012). The safety updates have been reviewed by Dr. Branda Ye of DMIP, her conclusion of no significant change in the overall safety profile of Lymphoseek is concurred.

3. Citizen Petition

A citizen petition (FDA-2011-P-0450, dated June 2, 2011) was submitted by MSMB Capital Management LLC, a hedge fund investment firm which short sells Navidea (the NDA applicant) stocks, requesting that the application not be approved because they did not provide a sufficient database to obtain a sentinel node claim. The sponsor in this application was not seeking a sentinel node indication, so it is not relevant to the current application. The petition also requested that specific comparative agents and confirming pathological findings be required in the imaging studies for approval of Lymphoseek, which was rejected after a thorough review by the DMIP team. This petition will be denied on March 13, before the NDA is approved.

Conclusions

This NDA is ready for approval, after the Citizen Petition mentioned above is formally denied.

cc:
ORIG: NDA- 202207
Director, ODE-IV
Director, DMIP

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/s/

SHAW T CHEN
03/11/2013