



**TRANSMITTED BY FACSIMILE**

Harriette Nadler, Ph.D.  
Sr. Director, Regulatory Affairs  
EUSA Pharma (USA), Inc.  
One Summit Square, Suite 201  
1717 Langhorne Newtown Road  
Langhorne, PA 19047

**RE: BLA 103608**  
ProstaScint<sup>®</sup> Kit (Capromab Pendetide)  
MA #91

Dear Dr. Nadler:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed a Key Fact Sheet (P-0488-10) (fact sheet) for ProstaScint<sup>®</sup> Kit (capromab pendetide) (ProstaScint) submitted by EUSA Pharma (USA) Inc. (EUSA) under cover of Form FDA-2253. The fact sheet is false or misleading because it presents efficacy claims for ProstaScint, but omits important risk information associated with the use of the drug, overstates the efficacy of the drug, and inadequately communicates the indication for the drug. Thus, the fact sheet misbrands the drug in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 352(a) and 321(n). Cf. 21 CFR 202.1(e)(5); (e)(6)(i).

**Background**

Below is the indication and summary of the most serious and most common risks associated with the use of ProstaScint.<sup>1</sup>

The INDICATIONS AND USAGE section of the FDA-approved product labeling (PI) states the following (in pertinent part):

Indium In 111 ProstaScint (Capromab Pendetide) is indicated as a diagnostic imaging agent in newly-diagnosed patients with biopsy-proven prostate cancer, thought to be clinically-localized after standard diagnostic evaluation (e.g. chest x-ray, bone scan, CT scan, or MRI), who are at high-risk for pelvic lymph node metastases. . . . It is not indicated in patients who are not at high risk.

Indium In 111 ProstaScint is also indicated as a diagnostic imaging agent in post-prostatectomy patients with a rising PSA [prostate-specific antigen] and a negative or equivocal standard metastatic evaluation in whom there is a high clinical suspicion of occult metastatic disease. The imaging performance of Indium In 111 ProstaScint

<sup>1</sup> This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece cited in this letter.

following radiation therapy has not been studied.

The information provided by Indium In 111 ProstaScint imaging should be considered in conjunction with other diagnostic information. Scans that are positive for metastatic disease should be confirmed histologically in patients who are otherwise candidates for surgery or radiation therapy unless medically contraindicated. Scans that are negative for metastatic disease should not be used in lieu of histological confirmation.

ProstaScint is not indicated as a screening tool for carcinoma of the prostate nor for readministration for the purpose of assessment of response to treatment.

ProstaScint is contraindicated in patients who are hypersensitive to it or any other product of murine origin or to Indium In 111 chloride. The WARNINGS section of the PI indicates that patient management should not be based on ProstaScint scan results without appropriate confirmatory studies since there was a high rate of false positive and false negative image interpretations observed in pivotal trials. Indium In 111 ProstaScint images should be interpreted only by physicians who have had specific training in ProstaScint image interpretation. Additional Warnings include allergic reactions, including anaphylaxis, which can occur in patients who receive murine antibodies. Furthermore, medications for the treatment of hypersensitivity reactions should be available during the administration of this agent. The WARNINGS section also states that ProstaScint may induce human anti-mouse antibodies which may interfere with some immunoassays, including those used to assay PSA (prostate-specific antigen) and digoxin.

Furthermore, according to the PRECAUTIONS section, care should be taken to minimize radiation exposure to the patients as well as medical personnel. Only physicians and other professionals appropriately qualified in the safe use of radionuclides should use ProstaScint. There may be Indium In 111 ProstaScint clearance and imaging localization observed in the bowel, blood pool, kidneys, and urinary bladder. The bladder should be catheterized and irrigated when obtaining all 72-120 hour planar and Single-Photon Emission Computed Tomography (SPECT) images. In addition, a cathartic should be administered the evening before imaging and a cleansing enema should be administered within an hour before each 72-120 hour imaging session.

The most commonly reported adverse reactions were increases in bilirubin, hypotension, and hypertension.

### **Omission of Risk Information**

Promotional materials are misleading if they fail to reveal material facts in light of the representations made by the materials or with respect to consequences that may result from the use of the drug as recommended or suggested by the materials. The fact sheet presents efficacy claims for ProstaScint, but omits all contraindications, important warnings and precautions, and the most commonly reported adverse reactions associated with the use of the ProstaScint (see Background). By omitting this important risk information, the fact sheet misleadingly suggests that ProstaScint is safer than has been demonstrated by substantial evidence or substantial clinical experience.

## **Overstatement of Efficacy**

Promotional materials are misleading if they represent or suggest that a drug is more effective than has been demonstrated by substantial evidence or substantial clinical experience. The fact sheet includes the following claims:

4. Fused ProstaScint Scans: Confidence in Prostate Cancer Staging
  - a. Higher confidence in patient selection for definitive and salvage treatment options
  - b. Scans positive outside pelvis indicate poor prognosis
    - i. Central Abdominal Uptake (CAU) of ProstaScint indicated poor prognosis
    - ii. Central abdominal signal (CAU uptake vs. non-CAU): 10-fold increased prostate cancer death

The claims presented above suggest that ProstaScint is effective for confidently determining specific treatment options (i.e., definitive and salvage) or as a prognostic indicator for prostate cancer patients, when this has not been demonstrated by substantial evidence or substantial clinical experience. The imaging performance of ProstaScint was evaluated in two phase three trials which compared the accuracy of interpreted ProstaScint images to the results of surgical staging and histopathologic analysis. The overall accuracy of the interpreted ProstaScint images was 63% in patients with a high clinical suspicion for occult recurrent or residual prostate cancer and 68% in patients with clinically-localized prostate cancer who were at high risk for metastases. Furthermore, the PI specifically warns that patient management should not be based on ProstaScint scan results without appropriate confirmatory studies since there was a high rate of false positive and false negative image interpretations in the pivotal trials. Moreover, the PI indicates that the information provided by ProstaScint imaging should be considered in conjunction with other diagnostic information.

## **Inadequate Communication of Indication**

The fact sheet fails to adequately communicate ProstaScint's full approved indication. We acknowledge that the fact sheet does include the following information pertaining to the drug's indication:

1. ProstaScint<sup>®</sup> (Capromab Pendetide) is a diagnostic imaging agent approved in:
  - a. Newly-diagnosed patients with biopsy-proven prostate cancer, thought to be clinically localized after standard diagnostic evaluation, who are at high risk for pelvic lymph node metastases
  - b. In post-prostatectomy patients with a rising PSA and a negative or equivocal standard metastatic evaluation, in whom there is a high clinical suspicion of occult metastatic disease

However, the fact sheet fails to include the following information from the INDICATIONS AND USAGE section of the PI:

The imaging performance of Indium In 111 ProstaScint following radiation therapy has not been studied.

The information provided by Indium In 111 ProstaScint imaging should be considered in conjunction with other diagnostic information. Scans that are positive for metastatic disease should be confirmed histologically in patients who are otherwise candidates for surgery or radiation therapy unless medically contraindicated. Scans that are negative for metastatic disease should not be used in lieu of histological confirmation.

ProstaScint is not indicated as a screening tool for carcinoma of the prostate nor for readministration for the purpose of assessment of response to treatment.

By omitting this important information, the fact sheet fails to communicate the full approved indication for ProstaScint, including important limitations of use.

### **Conclusion and Requested Action**

For the reasons discussed above, the fact sheets misbranded ProstaScint in violation of the FD&C Act, 21 U.S.C. 352(a) and 321(n). Cf. 21 CFR 202.1(e)(5); (e)(6)(i).

OPDP requests that EUSA immediately cease the dissemination of violative promotional materials for ProstaScint such as those described above. Please submit a written response to this letter on or before December 28, 2011, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for ProstaScint that contain violations such as those described above, and explaining your plan for discontinuing use of such violative materials.

Please direct your response to the undersigned by facsimile at (301) 847-8444, or at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, Division of Professional Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266**. Please note that the Division of Drug Marketing, Advertising, and Communications (DDMAC) has been reorganized and elevated to the Office of Prescription Drug Promotion (OPDP). OPDP consists of the Immediate Office, the Division of Professional Promotion (DPP) and the Division of Direct-to-Consumer Promotion (DDTCP). To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP. In addition, OPDP recently migrated to a different tracking system. Therefore, OPDP letters will now refer to MA numbers instead of MACMIS numbers. Please refer to the MA # in addition to the NDA number in all future correspondence relating to this particular matter. OPDP reminds you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for ProstaScint comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

James S. Dvorsky, PharmD  
Regulatory Review Officer  
Division of Professional Promotion  
Office of Prescription Drug Promotion

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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JAMES S DVORSKY  
12/13/2011